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Faculdade de Ciências Farmacêuticas
Universidade de São Paulo

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Lectures

L01	Science and Technology Policies in health care	Reinaldo F. N. Guimarães - Brazil
L02	Quality assurance	Claudia Coral - Brazil
L03	Animal health in Brazil. How can pharmacists act?:	Mitika K. Hagiwara - Brazil
L04	Drug surveillance: diagnosis and perspectives	Nair Ramos de Souza - Brazil
L05	Structural changes and consequences in emulsions for topical applications	Stig E. Friberg - USA
L06	Planning of new candidates for chemical industries of pharmaceutical interest with symbiotic profile	Eliezer J. Barreiro - Brazil
L07	Home pharmacy	Sotero Serrate Mengue - Brazil
L08	Impact of stereoselectivity on the kinetic disposition and metabolism of drugs	Vera Lanchote - Brazil
L09	Molecular characteristics of Hepatitis C virus (HCV) core protein	David Peabody - USA
L10	Drug Development: Strategies for developing countries	Gino Del Ponte - Brazil
L11	Pharmaceutical assistance and the role of the official pharmaceutical laboratories	Tuyoshi Ninomya - Brazil
L12	The pharmacist in the context of pharmaceutical care in hospital	Marcelo Gastaldi - Brazil
L13	Adriamycin-induced mitochondrial cardiomyopathy	Kendall Wallace - USA
L14	Natural products as a resource for anticancer drugs	Manoel Odorico Moraes - Brazil
L15	Mitochondrial oxidative stress and atherogenesis: a possible connection	Aníbal Eugênio Vercesi - Brazil
L16	Disclosing the meanings embedded in pharmaceutical care practice	Djenane Ramalho de Oliveira - Brazil
L17	Cutaneous permeation of cosmetic ingredients in safety and efficacy studies	Jean Paul Marty - France

Symposia

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S6	Technological and biological aspects of drug delivery systems		
	S6.1	Design of micro and nanoparticles delivery systems	Osvaldo de Freitas - Brazil
	S6.2	Micro- and nanoparticulate drug delivery systems: a view on a process and product engineering	Maria Inês Ré - Brazil
	S6.3	Micro- and nanostructured delivery systems and biological applications	José Maciel Rodrigues Júnior - Brazil
S7	Strategies for medication safety		
	S7.1	A system-based approach to medication error reduction	Michael R. Cohen - USA
	S7.2	Education of medical students to reduce prescribing errors	Ajith Kumar Sankarankutty - Brazil
	S7.3	Studies on medication errors in Brazilian hospitals	Silvia Helena de Bortoli Cassiani - Brazil
	S7.4	Data analyses of CPOE system for detection of potential adverse drug event	Daniel Fábio Kawano - Brazil
S8	Apoptosis		
	S8.1	Mechanisms of cell death: cancer and the apoptotic machinery	João G. P. Amarante-Mendes - Brazil
	S8.2	Pharmacological interference with the apoptosis machinery	Fabíola Attié de Castro - Brazil
	S8.3	Cancer immunotherapy: On the TRAIL of a cure?	Thomas S. Griffith - USA
S9	Probiotics		
	S9.1	Probiotics: current state and prospects	Susana Marta Isay Saad - Brazil
	S9.2	Probiotics: studies from animal models and clinical trials	Jacques Robert Nicoli - Brazil
	S9.3	Probiotics: application in clinical practice	Carlos Daniel Magnoni - Brazil
S10	Pathogeny and therapy of autoimmune illnesses mediated by immunocomplexes		
	S10.1	Pathogenesis of diseases caused by immunocomplexes: role of neutrophils	Yara Maria Lucisano Valim – Brazil
	S10.2	Experimental model for illnesses triggered by immunocomplexes	Cleni Mara Marzocchi Machado - Brazil
	S10.3	Therapy of auto immune illnesses	Eduardo Antônio Donadi - Brazil
S11	Challenges of pharmaceutical care and clinical pharmacy		
	S11.1	Pharmaceutical care: advances and national policy	Norberto Rech - Brazil
	S11.2	Challenges and perspectives of clinical pharmacy	Julieta Ueta - Brazil
	S11.3	Challenges to pharmaceutical care and clinical pharmacy	Divaldo P. de Lyra Júnior - Brazil
	S11.4	Pratices in clinical pharmacy: an academic model	Dílson Braz da Silva Jr - Brazil
S12	Immune response modulation		
	S12.1	The role of gangliosides in modulating the function of IgE receptors	Constance Oliver - Brazil
	S12.2	New insights into signaling via IgE receptors	David Holowka - USA
	S12.3	Functional glycomics - role of glycoconjugates in immunity and development	Richard Dale Cummings - USA

Round Table

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Courses

C1	Chronic lymphoproliferative illnesses	
C1.1	General aspects of the lymphoproliferative illnesses and their classification	Maria de L. L. F. Chauffaille - Brazil
C1.2	Laboratorial diagnosis of chronic lymphoproliferative illnesses	Sérgio Luís Ramos Martins - Brazil
C2	An introduction to chemiluminescent determinations in the microplate	Paul Held - USA
C3	Pharmaceutical care: knowledge in communication and therapeutics	Julieta Ueta - Brazil Divaldo P. de Lyra Júnior - Brazil Dílson Braz da Silva Jr - Brazil
C4	Drug surveillance in Brazil	Nair Ramos de Souza - Brasil
C5	Use of LC-MS^n in pharmaceutical sciences	Norberto Peporine Lopes - Brazil
C6	Technological innovations in cosmetic research and development	Idalina M. N. S. Santos - Brazil Patrícia M. B. G. M. Campos - Brazil Jean Paul Marty - France

Abstracts

Some abstracts were classified in different areas, in accordance with commitee decision.
The correctness of the English language used in the abstract is the single responsability of the authors.
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Áreas / Areas

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Cosmetologia / *Cosmetology* (CO)
Farmacoepidemiologia/Farmacovigilância / *Pharmacoepidemiology / Drug Surveillance* (EV)
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Química e Biologia de Fármacos / *Chemistry and Biology of Drugs* (QB)
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Síntese de Fármacos / *Drug Synthesis* (SF)
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Toxicologia / *Toxicology* (TO)

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Lectures

L01 - SCIENCE AND TECHNOLOGY POLICIES IN HEALTH CARE

REINALDO FELIPE NERY GUIMARÃES

FIOCRUZ, Rio de Janeiro, RJ, Brasil

In many of the developing countries, Science and Technology Policies are still organized in a science-pushed fashion, that is, predominantly based on the organization of the supply-side. On the grounds of health research, that kind of organization can be undermining the efforts towards the setting of research priorities based in the demand side, which, in this case, are the needs of the public health policies. So, to bring closer health research priorities and health policy priorities, it is necessary to strengthen research activities based on demand.
In recent years, the Brazilian Ministry of Health has had a peripheral position with respect to health research organization and support in Brazil. However, since 2003, important political efforts have been made in order to guarantee to the Ministry of Health a more central role in coordinating the health research activities. To achieve this goal, political, institutional and financial measures were taken.
Among the member states of the Pan American Health Organization, in only two countries the national health authorities are the main organizers and supporters of health research. In these same two countries there are health research support agencies under those national health authorities. They are the United States and Canada. For the majority of Latin American countries, the main authorities respecting national research policy, including health research, are the Research Councils, normally apart from the Ministries of Health.

L02 - QUALITY ASSURANCE

CLAUDIA CORAL

Galena - Campinas, SP, Brasil

Quality assurance: definition, implementation, control and responsibilities.

L03 - PROBLEMATIC OF ANIMAL HEALTH IN BRAZIL: HOW PHARMACISTS ACT?

MITIKA K. HAGIWARA

Faculdade de Medicina Veterinária e Zootecnia da USP, São Paulo, SP, Brasil

L04 - DRUG SURVEILLANCE: DIAGNOSIS AND PERSPECTIVES

NAIR RAMOS DE SOUZA

Unidade de Farmacovigilância da ANVISA, Brasília, DF, Brasil

The new concept adopted by the World Health Organization in 2002, defines as the relative science to the detection, evaluation, understanding and prevention of the adverse effects, or any problems related to medicinal products. The creation of the Brazilian Health Surveillance Agency – ANVISA, in 1999, provided the initial steps to the consolidation of the National System of Pharmacovigilance**,** after establishing the National Center of Monitoring of Medicines, headquartered at ANVISA's Unit of Pharmacovigilance and was included as the 62nd member of the International Drug Monitoring Programme, co-ordinated by the Upssala Monitoring Centre – Sweden, as a collaborator to the World Health Organization. One of the difficulties to be faced was the lack of tradition among health professionals and service directors in notifying the occurrence of drug adverse effects. One of the strategies used to motivate this notification practice was the creation of a wide chain of hospitals called Sentinel Hospitals.Thus, the actions of Pharmacovigilance, besides dealing with the adverse effect, must promote actions to assure the rational use of medicine. In this perspective, Pharmacovigilance actions in Brazil are expected not only to be associated with monitoring of ADR but also to ensure the rational use of drugs.

L05 - STRUCTURAL CHANGES AND CONSEQUENCES IN EMULSIONS FOR TOPICAL APPLICATIONS

STIG E. FRIBERG

Chemistry Department - University of Virginia, Charlottesville, VA, Estados Unidos

Many attempts have been made to relate the action on the skin by emulsion formulations to the structure of the original formulation, but the success of these attempts has been limited. The lecture will introduce one possible reason for this lack of success, namely the drastic changes in emulsion structure during evaporation of water and volatile compounds. The lecture will demonstrate such changes; even for the simplest of emulsions. It will subsequently show such changes to give rise a most decisive difference in the behavior of two b acids during evaporation of otherwise identical emulsions.

L06 - PLANNING OF NEW CANDIDATES FOR CHEMICAL INDUSTRIES OF PHARMACEUTICAL INTEREST WITH SYMBIOTIC PROFILE

ELIEZER J. BARREIRO

LASSBIO - Faculdade de Farmácia, UFRJ, Rio de Janeiro, RJ, Brasil

Several rational approaches are known by medicinal chemist to drug design and in this lecture I will present a short account of ongoing research effort, performed at LASSBio-UFRJ, about the symbiotic approach to discover new anti-inflammatory lead-candidates. This approach was first employed by Baldwin, in 1979, in the search of vasodilator/β-adrenoceptor antagonist derivatives.[1] For instance, this strategy of rational design, consist in the incorporation of two mutually complementary activities into one chemical entity by selecting the appropriate pharmacophoric units of each one bioactive prototype. It will be describe the design, synthesis and anti-inflammatory profile of new symbiotic lead-compound candidates, structurally planned as anti-TNFað and phosphodiesterase (PDEi) inhibitor agent. In addition, it will be also presented the results about the effort performed in structural lead-optimization.
This work was supported by the following Brazilian grants: CNPq (470883/2004-9; 500185/2003-4), Pronex-FAPERJ (E-26/171162/2003) and FAPERJ (E-26/152172-2002).

[1] Baldwin, J. J., Lumma, W.C., Lundell, G. F., Ponticello, G. S., Raab, A. W., Engelhardt, E. L., Hirschmann, R., Sweet, C. S., Scriabine, A. *J. Med. Chem.* 1979, *22*, 1284.

L07 - HOME PHARMACY

SOTERO SERRATE MENGUE

UFRGS, Porto Alegre, RS, Brasil

A cross-sectional study was carried out to analyze how and where drug preparations are stored in households and to evaluate the kind of drugs stored, current usage and storage conditions. The data were collected by a questionnaire filled in during home visits. Of the 101 households visited, 98 had at least one drug in store, mean of 20, and the range 1-89 drugs. Storage places more frequently used were kitchen (43%), bedroom (28%) and bathroom (14%). Most drugs were for oral (67%) and topical (22%) administration. The most commonly encountered drugs were analgesic (18%), anti-inflammatory (6,5%) and antibacterial drugs (4,7%). The expiry date could be found in 83% of the products, and in 16% of these cases the drugs were beyond the expiry dates. In conclusion, there is a clear need of intervention of health professionals in favor of rational drug utilization and education concerning the proper storage of drug in households.

L08 - IMPACT OF STEREOSELECTIVITY ON THE KINETIC DISPOSITION AND METABOLISM OF DRUGS

VERA LÚCIA LANCHOTE

DACTB - Faculdade de Ciências Farmacêuticas de Ribeirão Preto/USP, Ribeirão Preto, SP, Brasil

Chirality is a fundamental characteristic of nature and has fascinated scientists since the middle of the 19th century. Stereoselectivity in pharmacokinetics and pharmacodynamics represents an important mechanism involved in the variability of the therapeutic response to chiral drugs. The influence of type-2 diabetes mellitus (DM) on the enantioselective pharmacokinetic and dynamic parameters of nisoldipine was investigated in hypertensive patients, showing that DM alters the kinetic disposition of both enantiomers, presumably due to a lower activity of CYP3A4, although it does not modify the clinical effect brought about by the reduction in blood pressure. The influence of chronic renal failure (CRF) on the stereoselective metabolism of metoprolol was investigated in hypertensive patients. CRF does not change the stereoselective kinetic disposition of metoprolol but modifies its stereoselective metabolism inducing some of the CYP enzymes involved in the formation of the metoprolol acidic metabolite. The association of ranitidine or cimetidine in the enantioselective metabolism of albendazole was investigated in patients with the active form of intraparenchymatous neurocysticercosis. The data suggest the involvement of CYP1A2 in the sulfonation of albendazole sulfoxide. Ranitidine did not alter the enantioselective metabolism of albendazole but cimetidine inhibited the sulfonation of (+)-albendazole sulfoxide in an enantioselective manner. There are data suggesting that diseases and drug interactions determine stereoselective differences in the rate of drug oxidation by cytochrome P-450.

L09 - MOLECULAR CHARACTERISTICS OF HEPATITIS C VIRUS (HCV) CORE PROTEIN

DAVID PEABODY

Department of Molecular Genetics and Microbiology, University of New Mexico School of Medicine, Albuquerque, NM, USA

RNA viruses frequently solve the problem of genome encapsidation and control of gene expression through interactions of viral proteins with specific targets in viral RNA. For example, the coat proteins of the RNA bacteriophages recognize a hairpin in the viral genome to repress translation of the viral replicase and to initiate encapsidation of the genome. We have studied the interactions of the coat proteins of several such viruses with their target RNAs as part of an effort to understand the molecular basis of RNA-protein recognition. The coat protein of bacteriophage MS2 represents one of the best-understood RNA-protein interactions yet studied, and thus provides an opportunity to describe in detail some of the basic principles of RNA-protein recognition. Study of other related phages shows that each of their coat proteins recognizes its own RNA on the surface of a large, structurally conserved ß-sheet. The differences in RNA-binding specificities that result from differences in the amino acids present on the ß-sheet surface show how this single structural framework can be adapted to the binding of diverse RNAs. A detailed understanding of RNA-protein recognition by viral proteins may eventually provide a basis for producing drugs that inhibit virus assembly by at the level of genome encapsidation. Recently we have extended our studies of viral RNA-protein interactions to the core protein of Hepatitis C Virus. Following our work on RNA bacteriophages, it was natural to suppose that specific encapsidation of HCV RNA is also the result of interaction between core protein and a recognition site in the viral genome. We find, however, that core protein binds RNA nonspecifically with high affinity, raising questions about how specific encapsidation is accomplished. RNA binding seems to involve interactions with three distinct regions of core protein, each rich in basic amino acids. These regions seems to act more or less independently in a protein that apparently lacks a definite tertiary structure, and probably belongs to the recently described class of proteins called intrinsically disordered or natively unfolded. Furthermore, core protein has been shown to possess RNA chaperone activity. Since non-specific RNA binding activity and structural disorder are frequently encountered features of RNA chaperones, it is likely that these two properties are related mechanistically to core protein's RNA chaperone activity.

L10 - DRUG DEVELOPMENT: STRATEGIES FOR DEVELOPING COUNTRIES

GINO DEL PONTE

DCF, Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

Drug development is a high risk business witch results in only 1 out of 5,000 screened compounds meeting the safety and efficacy profile to be approved as a medicine for human use. Currently, the total process of R&D of a new medicine takes from 11-15 years and it costs more than 800 million USD on average. Accordingly, is it possible in a country like ours, of late industrialization and no appropriate technological bases in the fine chemistry area, to acquire some degree of independence in the drug and medicinal field? In attempt to answer this question , different R&D models based on new molecules, biodiversity, me too, similarity and synthetic generics will be compared focusing on the context of the technological development of the industries.

L11 - PHARMACEUTICAL ASSISTANCE AND THE ROLE OF THE OFFICIAL PHARMACEUTICAL LABORATORIES

TUYOSHI NINOMYA

FURP Fundação do Remédio Popular, Guarulhos, SP, Brasil

1.Discuss the Brazilian health care model – SUS, focusing on its principles, and situate pharmaceutical care in this model.
2.Discuss the Brazilian Medication Policy as defined by the Ministry of Health, which guides SUS pharmaceutical care.
3.Discuss access to medication by people who depend on different SUS programs, ranging from basic care to medication for highly complex diseases.
4.Insert the role of official pharmaceutical labs in this process with a view to easier access to medication and more rational use, and discuss these labs' important role in R&D in the Brazilian pharmaceutical sector, especially to make available medication for diseases that are characterized as neglected.
5.Discuss the role of pharmaceutical professionals in pharmaceutical care, as an essential part of the multiprofessional team that characterizes this care.
6.Finally, present the FURP, including its mission and objectives, as an important instrument to consolidate SUS pharmaceutical care.

L12 - THE PHARMACIST IN THE CONTEXT OF PHARMACEUTICAL CARE IN HOSPITAL.

MARCELO GASTALDI

HOSP-PHARMA - Manipulação e Suprimentos Ltda., São Paulo, SP, Brasil

Pharmaceutical professional used to restrict themselves to internal activities in the hospital pharmacy, manipulating products and watching over the storage and registration of psychoactive substances.
Nowadays, pharmaceutical professionals' activities stand out by their efforts to decrease problems and optimize medication usage in activities close to the patient and the technical hospital team. Their participation has been noted not only by transformations in the storage and distribution of medication and related products, but also by their attitude in the health team.
The aim is to use management methods that decrease costs and make available technical and management information to health teams. At the same time, modern information systems decrease hospitalization time and problems involving patients.

L13 - ADRIAMYCIN-INDUCED MITOCHONDRIAL CARDIOMYOPATHY

KENDALL WALLACE

Universit of Minnesota - Medical School, Duluth, MN, USA

Adriamycin (doxorubicin) is a broad-spectrum antineoplastic agent that is effective and potent in treating a variety of cancers including both solid tumors and leukemias. Unfortunately, the clinical usefulness is limited by a dose-dependent and irreversible dilated cardiomyopathy that occurs in patients receiving a cumulative dose exceeding 550 mg/m^2. The aim of our research these past several years, and the topic of my presentation, is to decipher the biochemical and molecular mechanisms underlying this drug-induced cardiomyopathy in hopes of discovering improved strategies for limiting this dose-limiting consequence of this highly effective therapy for several forms of cancer. In vitro experiments reveal that adriamycin undergoes a vicious univalent redox cycle to generate reactive species of oxygen (ROS), which are believed to mediate much of the immediate tissue damage caused by the drug. The rate-limiting step in this redox cycle is the initial univalent reduction of adriamycin by assorted cell oxido-reductases to generate the reactive semiquinone free radical species. This then dictates the subcellular localization of oxidative injury based on the preponderance and intracellular compartmentalization of the corresponding reducing enzymes. For example, the large endowment of hepatocytes with NADPH-dependent cytochrome P450 reductase may underlay the centrality of the endoplasmic reticulum in the toxicity of adriamycin in liver. In contrast, determinants of cardioselective toxicity of adriamycin may owe to the abundance of mitochondrial electron transport chains, combined with the disproportionately high oxygen consumption and deficient antioxidant defense mechanisms in cardiac tissue. Adriamycin undergoes a complex I-specific redox cycling on mitochondrial electron transport chains. This is associated with a stimulation of state 4 respiration and inhibition of state 3 respiration resulting in a 50% inhibition of mitochondrial respiratory control. These respiratory effects are associated with both acute and chronic drug treatment and can be prevented by co-administering selected antioxidant drugs in combination with adriamycin.

Of particular concern with adriamycin-induced cardiac injury is the persistent and progressive nature of the toxicity. Not only is the degree of damage a function of cumulative dose, but it persists and evolves long-beyond the discontinuation of drug treatment. Cardiac tissue harvested from rats 25 drug half-lives after the last dose exhibit similar degrees of histopathology, oxidative modification of mtDNA and protein, and mitochondrial dysfunction as tissues harvested immediately following the last dose. Such persistence exceeds that which can be attributed to drug half-life or to cell or mitochondrial lifespan. Instead, the persistent and progressive cardiomyopathy associated with adriamycin toxicity appears to reflect a molecular imprinting, wherein de novo mitochondria generated in the course of normal turnover is altered such that the newly formed mitochondrion is in-an-of-itself dysfunctional – poorly coupled and actively generating ROS. Thus, the etiology reflects back to interference with mitochondrial biogenesis itself.

A final note is the metabolic phenotype associated with adriamycin-induced mitochondrial cardiomyopathy, which we attribute to a regulated compensatory defense mechanism designed to sustain sufficient ATP synthesis in the face of failing mitochondrial oxidative phosphorylation. We came upon this hypothesis in response to our observation that isolated perfused hearts from adriamycin-treated rats are able to better withstand episodes of ischemia/reperfusion asystole. Unlike hearts from control rats that exhibit systolic constricture upon reperfusion, hearts from treated animals resumed near normal contractile function shortly after reflow perfusion with well-oxygenated medium. Such metabolic resiliency was hypothesized to reflect an acquired non-aerobic metabolic capacity in cells harboring drug-induced compromised mitochondrial function. This hypothesis was borne out by both genomic and metabonomic studies. Gene expression array analyses revealed a composite inhibition of fatty acid oxidation and stimulation of glucose oxidation pathways in cardiac tissue from adriamycin exposed rats. Half of the genes that were differentially expressed encoded proteins that related back to mitochondrial metabolism. This altered transcription was accompanied by a switch in preferred substrates for isolated perfused hearts – again from fatty acid oxidation to glucose oxidation. Interestingly, this altered metabolic phenotype was prevented by co-administering dexaroxane with adriamycin, implying a critical role for ROS in the pathological process.

To summarize the biochemical and molecular mechanisms underlying the pathogenesis of adriamycin-induced cardiomyopathy, we suggest that the initial triggering event involves redox cycling of adriamycin on complex I of the mitochondrial respiratory chain to liberate highly reactive free radicals of oxygen. It is determined that these ROS molecules mediate the biological changes critical to the structural, functional and metabolic phenotype of adriamycin cardiomyopathy. Of particular import, is that this cardiac mitochondrial phenotype is persistent and self-propagating and that transcriptional regulation of altered intermediary metabolism is critical to tissue survival. (supported by NIH HL-058016).

L14 - NATURAL PRODUCTS AS A RESOURCE FOR ANTICANCER DRUGS

MANOEL ODORICO MORAES

Laboratório de Oncologia Experimental, Universidade do Ceará, Fortaleza, CE, Brasil

The development of more effective drugs for treating patients with cancer has been a major human endeavor over the past 50 years, and 21st century now promises some dramatic new directions. Nature has provided many effective anticancer agents in current use, such as the microbial-derived drugs, dactinomycin, bleomycin, and doxorubicin, plant-derived drugs, vinblastine, irinotecan, topotecan, etoposide, and paclitaxel, and marine-derived drugs, citarabine and bryostatin. Therefore, search for novel antitumor agents continues providing convincing evidence that natural products could be a source of novel cancer chemotherapeutic agents and leads for synthetic modification. Although cancer drug discovery has been, and continues to be, a process of serendipity, "screening" natural products remains one of the most important methods in cancer drug discovery. More recently, progress in molecular pharmacology has demonstrated that each anticancer drug has a unique molecular target. Presently, drug development has focused on natural product compounds that specifically inhibit and/or modify tumor-specific molecular biological changes (target-based drug development). These compounds include angiogenesis inhibitors and matrix metalloproteinase inhibitors. In Brazil, there are many examples of plant and marine organisms-derived molecules screened in the Experimental Oncology Laboratory of the Federal University of Ceará, Brazil, with potential to be developed as new anticancer drugs.

L15 - MITOCHONDRIAL OXIDATIVE STRESS AND ATHEROGENESIS: A POSSIBLE CONNECTION

ANÍBAL EUGÊNIO VERCESI

Departamento de Patologia Clínica, Faculdade de Ciências Médicas, Universidade Estadual de Campinas, Campinas, SP, Brasil

Atherosclerotic disease remains a leading cause of death in westernized societies, and reactive oxygen species (ROS) play a pivotal role in atherogenesis. Mitochondria are the main intracellular sites of ROS generation and are also targets for oxidative damage. Here, we show that mitochondria from atherosclerosis-prone, hypercholesterolemic low-density lipoprotein (LDL) receptor knockout mice have oxidative phosphorylation efficiency similar to that from control mice but have a higher net production of ROS and susceptibility to develop membrane permeability transition. Increased ROS production was observed in mitochondria isolated from several tissues, including liver, heart, and brain, and in intact mononuclear cells from spleen. In contrast to control mitochondria, knockout mouse mitochondria did not sustain a reduced state of matrix NADPH, the main source of antioxidant defense against ROS. Experiments in vivo showed faster liver secretion rates and de novo synthesis of triglycerides and cholesterol in knockout than in control mice, suggesting that increased lipogenesis depleted the reducing equivalents from NADPH and generated a state of oxidative stress in hypercholesterolemic knockout mice. These data provide the first evidence of how oxidative stress is generated in LDL receptor defective cells and could explain the increased LDL oxidation, cell death, and atherogenesis seen in familiar hypercholesterolemia.

Supported by FAPESP and CNPq

L16 - DISCLOSING THE MEANINGS EMBEDDED IN PHARMACEUTICAL CARE PRACTICE

DJENANE RAMALHO DE OLIVEIRA

Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brasil

For the pharmacy profession to reach a deeper understanding of human phenomena, it needs to enter into and learn about the world in which we live as human beings, taking into consideration human experience as it is lived in social, cultural, historical, and political contexts. This study explored patients, practitioners and students' experiences within the historic-socio-cultural context of the promising pharmacy practice model known as pharmaceutical care. An ethnographic study was conducted for one year in nine clinics and one community pharmacy in the Twin Cities, Minnesota, U.S.A. Field observation, in-depth interviews, focus groups, and analysis of documents were conducted in order to uncover the practice as it is in the real world. The results of this project unveiled the meanings embedded in pharmaceutical care from the perspective of individuals who live it on a daily basis. The study uncovered the skills and knowledge required to be a patient-centered practitioner as well as provided an understanding of how to better prepare students for this role. Additionally, the findings point to the significance of the qualitative methodology to obtain a deeper understanding of patients' attitudes and behaviors with regards to medications. Lastly, this study was a crucial step in moving the pharmacy profession towards a more caring practice to better meet the medication-related needs of patients and serve a unique and vital role in society.

L17 - CUTANEOUS PERMEATION OF COSMETIC INGREDIENTS IN SAFETY AND EFFICACY STUDIES

JEAN PAUL MARTY

Dermopharmacology and Cosmetology Department, Faculty of Pharmacy, University Paris-South, France

Cosmetic products (formulations) are obtained by the superposition of numerous ingredients. Some have technical functions and are listed as "inactive ingredients" (preservatives, additives, tensioactives…), some are used for the effect they will produce on the skin or the hair and are defined as "active ingredients" (dyes, moisturizers, sunscreen, vitamins, alpha-hydroxy acids…). When applied on the skin each ingredient will have a specific behaviour linked to its own physico-chemical properties and to the other constituents present in the formulation. So, any compound can more or less penetrate the skin and have beneficial effects (i.e. a pharmacological activity) or deleterious effects (i.e. irritation, allergy, systemic toxicity). For the scientist in charge of developing a cosmetic product safety is the major objective. For the consumer efficacy is the major interest. The benefices and risks of cosmetics ingredients are linked to their capacity to penetrate and diffuse through the skin. The exposition to any particular ingredient is one of the key elements to consider when evaluating the probability to obtain any positive or negative effects. The particularities of the skin penetration of cosmetics will be reviewed according to these dual aspects.

L18 - SAFE MEDICATION PRACTICES

MICHAEL R. COHEN

Institute for Safe Medication Practices, Huntingdon Valley, PA, USA

This program will present information about the causes and prevention of medication errors. In the United States, health professionals may voluntarily report medication errors to a national error-reporting program operated since 1994 by the Unioted States Pharmacopeia and the Institute for Safe Medication Practices. Information is also shared with the US Food and Drug Administration. Information about medication errors and other adverse drug events, along with prevention recommendations, is also shared with the medical community through various journal and newsletter publications read by over 3 million health professionals in the US and worldwide. Ongoing communication occurs with regulatory authorities and standards setting organizations internationally. The program has impacted upon drug standards and federal regulations and has created a sense of awareness of the problem as a public health issue. The Joint Commission on Accreditation of Healthcare Organizations has incorporated many of the ISMP recommendations into required National Patient Safety Goals, which must be met by over 20,000 accredited healthcare organizations in the US to maintain accreditation status. One of the top public policy issues in the United States in recent years has been medical error and the need to improve the quality of care. A report from the Institute of Medicine's Committee on Quality of Healthcare in America has led to rigorous changes throughout the US health care system, including improvements in error reporting requirements and development of new tools and systems needed to identify errors and address persistent problems. This session will provide multiple examples of actual medical errors as well as crucial and timely information needed to address many of the most challenging issues. Advice will be provided about system-based causes of medication errors, the need for developing non-punitive reporting systems, and many other topics.

Objectives:
1. Provide background and share experience derived from ISMP participation as a cooperating agency in the operation of the Medication Errors Reporting Program in the United States.
2. Provide an analysis of common causes of medication errors and major recommendations for prevention.
3. Identify system enhancements needed to prevent medication errors, detect errors before they reach a patient, or minimize their consequences.
4. Identify proactive strategies to prevent errors with high-alert drugs, which consistently result in serious patient injuries.
5. Understand the value of focusing error reduction efforts on the system rather than individuals.
6. Learn strategies for implementing a non-punitive environment and a useful error-reporting program.

L19 - BIOTA/FAPESP - A MODEL FOR RESEARCH PROGRAMS ON THE CHARACTERIZATION, CONSERVATION AND SUSTAINABLE USE OF BIODIVERSITY

RICARDO RIBEIRO RODRIGUES

ESALQ/USP, Piracicaba, SP, Brasil

Carlos Alfredo Joly & Ricardo Ribeiro Rodrigues
Funding Agency: FAPESP/BIOTA

Officially created in March 1999, the Research Program on Characterization, Conservation and Sustainable Use of the Biodiversity of the State of São Paulo, called "BIOTA/FAPESP, The Virtual Institute of Biodiversity", is the result of three years of planning and the articulation of a group of researchers who, with FAPESP support, made the scientific community aware of the need for concrete actions to implement the Convention on Biological Diversity, signed by the Brazilian government during the 1992 Earth Summit in Rio de Janeiro. Nowadays, this wide-ranging research program on the conservation of biodiversity, which supports public environmental planning and sustainable development strategies, involves about 450 Ph.D. researchers from research institutions in the State of São Paulo, besides 70 researchers from other states and about 50 foreign research professionals. The projects of the BIOTA/FAPESP Program aim to study the biodiversity in the State of São Paulo in order to: a) understand the processes that create and maintain biodiversity, including those processes that can result in its noxious reduction; b) systemize the collection of relevant information for making decisions about priorities in the conservation and sustainable use of biodiversity; c) disseminate all information widely, rapidly and freely (public and free access to information); d) improve the quality of teaching at all levels and in all forms, about nature and the basic principles of conservation and sustainable use of biodiversity. The BIOTA/FAPESP projects were elaborated with a view to a significant increase in academic knowledge levels about the São Paulo State biota and, simultaneously, to produce results that support the definition or improvement of public policies related to the conservation and sustainable use of biodiversity.

L20 - EXTRACTS FOR PHYTOMEDICINE AND PHYTOCOSMETIC MARKET

LAURO E. S. BARATA

IQM/UNICAMP, Campinas, SP, Brasil

Brazil is rich in Biodiversity, Etnomedicine, scientific knowledge and technology domain for the production of Phytomedicines and Phytocosmetics. Nevertheless, it was only this year that the country has launched its first national medicine based on the traditional Brazilian medicinal plant Erva-Balieira (*Cordia verbenaceae)*. Standardized Extracts are essential for the production of high quality Phytomedicines and Phytocosmetics, yet they are practically non existent in Brazil. The market is basically occupied by small companies and informal street-markets and there is a lack of quality control and drug supervision. Despite these problems 85% of eight thousand Scientists that are annually produced are concentrated in Universities. On the other hand, there is a lack of R&D staff in the companies, which should be the innovation source. A partnership between the Companies and Universities can be the solution for these problems. The international pharmaceutical market sums up US$ 500 billion/year and Brazil contributes only with 2.5%. The Brazilian pharmaceutical market gross annual invoicing is about US$ 7.5 billion, US$ 500 million of which corresponds to medicines produced from plant, a market that grows 12%/year. Standard Extracts are also the base for the Cosmetic market that in Brazil achieved US$ 5.2 billion last year. Unfortunately the Academy is unaware of this market that could provide employment for the Doctors graduated at Universities.

L21 - TAILOR MADE RUTHENIUM NITROSYLS AS NITRIC OXIDE DONORS.

ELIA TFOUNI

Departamento de Química FFFCLRP/USP, Ribeirão Preto, SP, Brasil

Nitric oxide (NO) plays key roles in almost every function of mammalian species and high or low NO concentrations can be either beneficial or harmful and could accompany numerous pathological states. In this context, ruthenium nitrosyl complexes have shown to be very promising NO donors, chemically or photochemically, and some of them display biological activity, which are explained with the complexes properties. The release of NO can be induced by reduction or by irradiation with light, and the properties of the complexes such acidity and rates of release of NO. These complexes can also be supported in several matrices resulting in NO donor materials. The activated release of NO can be tuned by the adequate choice of ligands or matrices to suit a desired effect and target.
FAPESP, CNPq, CAPES.

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Symposia

SYMPOSIUM 1 - NATURAL PRODUCTS

S1.1 - BIODIVERSITY IN THE STATE OF SÃO PAULO AS A POWERFUL TOOL FOR A DRUG DISCOVERY INTEGRATED PROGRAM

VANDERLAN DA SILVA BOLZANI

Instituto de Química da UNESP, Araraquara, SP, Brasil

Certainly, the use of natural products has been the single most successful strategy in the discovery of novel medicines. Nowadays the most medical breakthroughs has been based on natural products, such compounds also represent a large share of the market. In 1999, half of the top 20 best-selling drugs were natural products, and their total sales amounted to US$ 16 billions. The importance of natural products is evidenced by the new chemical entities (NCE) approved by regulatory authorities around the world in the past decade. Of the ca. 500 NCE, nearly half are from natural resources. In 1999, the approval of the natural alkaloid galanthamine as a medicine to treat Alzheimer disease acclaimed definitively the potential of natural compounds, which will continue to reach the market.

The biodiversity found in Brazil makes it a very feasible source of biological active compounds and its preservation is an important goal both for the intrinsic value of this enormous biological resource and for its huge potential as a source of new pharmaceuticals, cosmetics, agrochemicals, nutraceuticals, and others uses. The preservation and sustainable use of this fantastic diversity is one of the greatest challenges nowadays facing the accelerated process of devastation of several Brazilian biomes, specially the Cerrado and Atlantic Forest.

Taking in account the importance of these biomes for the State of São Paulo, in March of 1999, officially was created the Research Program on Sustainable Conservation of Biodiversity, named Biota-FAPESP Program, which has as main objective to catalogue and characterize the remaining biodiversity of the State of São Paulo, and establishes the mechanisms for its conservation and sustainable use.

Our collaborative project at Biota-FAPESP "Conservation and Sustainable Use of the Diversity from Cerrado and Atlantic Forest: Chemical Diversity and Prospecting for Potential Drugs" was conceived to identify antioxidant, antifungal, anticancer, antimalarial and acetylcholinesterase inhibitor lead compounds from plant species and endophytic fungi of the Cerrado and Atlantic Forest. This project was the first tentative work at the Biota FAPESP that resulted in ca. of 1600 extracts obtained from 650 species. This amount of screened material is so far, little, if we consider that the angiosperm plant species are estimated at over of 8500 into São Paulo's State. Together with even less-investigated are the endophytic fungi, which have no data available yet, and the screening of these microorganisms also represents a powerful source of pharmaceutical leads.

The bioprospecting work in the Brazilian academia still been a challenge, and our proposal only was going on due to the structure of the Biota-FAPESP, which represents a new paradigm of research on biodiversity in Brazil. Even though, our bioprospecting work accomplished along of these five years can be considered excellent it stills far away of high throughput screening, that are be able to screen a thousands of samples in a few minutes. Additionally, the collaboration among botanist, chemist, biologist, pharmacologist and pharmacist professionals, in drug discovery, is fundamental for success of a bioprospecting program. With this objective, the subprogram BIOprospecTA was created aiming to establish a competitive bioprospecting program to screen thousands of samples using the local expertise to the new needs. [FAPESP, Biota-FAPESP, CNPq, CAPES].

S1.2 - INSTITUTE OF THE MILLENNIUM: INNOVATION AND DEVELOPMENT IN DRUGS AND MEDICINES

JOÃO LUIZ CALLEGARI LOPES

Faculdade de Ciências Farmacêuticas de Ribeirão Preto/USP, Ribeirão Preto, SP, Brasil

Medicines are essential instruments to the preservation, maintenance and promotion of health. The access to the medicines is an important issue for social inclusion, and the availability of drugs (pharmacologically active compounds) is essential for the preparation of medicines. The knowledge to obtain and prepare drugs and medicines is important for the feasibility of the public policies of health and sovereignty of a Nation. This proposal of the Institute of the Millennium Innovation and Development in Drugs and Medicines involves the following approaches: the process of rational discovery of drugs; screening of pharmacological activities, optimization of prototype compounds, scale-up, development of a pharmaceutical dosage form and analytical methodologies, clinical trails and regulatory submission for *generic* medicines, under the general coordination of Prof. Dr. Eliezer J. Barreiro (UFRJ). The use of products from the Brazilian biodiversity as source of prototype compounds is one of the aims of this project. The rational use of the biological properties of Brazilian plants depends on several aspects. The establishment of a screening program with a multidisciplinary team is extremely necessary to increase the efficiency of development of candidates to new drugs.

S1.3 - BIODIVERSITY AND PHARMACEUTICAL INNOVATION: A NEW MODEL FOR *EXTRACTA*

ANTONIO PAES DE CARVALHO

EXTRACTA Moléculas Naturais S/A, Rio de Janeiro, RJ, Brasil

The rapidly changing environment in Pharma business & innovation and in Brazilian biodiversity access regulation led EXTRACTA to diversify services and products. We used our in-house capacity to offer Brazilian Pharmaceutical Industry modern versions of classical and novel Brazilian Plant Drugs based on HTS screening proprietary results against six different primary targets assayed in a 40,000 compound NP library, each collection shown to be active “in vitro” on: (a) resistant nosocomial infections; (b) elastase inhibitors, a factor in the control of COPD; (c) Hepatitis C; (d) Chagas Disease; (e) Tuberculosis; and (f) Type II Diabetes. Clients can license anything from pure bioactive molecules to standardized certified crude extracts with QC markers to match their innovation pipeline planning and finances. This new R&D&I model helps to correct distortions presently found in sustainable exploitation of Brazilian biodiversity: nearly 60,000 plant species and only 1,400 with a written record of pharmaceutical usage.

SYMPOSIUM 2 - ADVANCES IN DIAGNOSIS AND CANCER THERAPY

S2.1 - TUMOR ANGIOGENESIS AND VASCULAR DEVELOPMENT – TWO RELATED PROCESSES?

CLAUDIA OLIVEIRA RODRIGUES, ELSIE L. WHITE AND JOHN L. CLEVELAND

St. Jude Children's Research Hospital, Memphis, Tennessee, USA

During vasculogenesis a primitive vascular network is established from newly differentiated endothelial cells that assemble into vascular tubes. After this initial step, angiogenesis or sprouting and remodeling of capillaries from pre-existing vessels occurs to ensure the delivery of oxygen, nutrients and growth factors to all the tissues in the body. In adulthood vasculogenesis and angiogenesis are tightly controlled and restricted to neovascularization during physiological processes such as ovulation, placental development and wound healing. Uncontrolled angiogenesis plays an important role in a growing list of pathological conditions that includes cancer, and have recently become a target for the development of drug therapy.
Tumor progression requires the development of an ample blood supply to ensure tumor maintenance and growth. We are interested in studying the relationship between tumor progression and angiogenesis, in particular the role of the proto-oncogene c-myc. Previous work from our group has shown that c-myc is essential for vasculogenesis and angiogenesis during development and tumor progression. However, the mechanisms by which c-myc control these processes are still not very clear. Studying the mechanisms involved in vascular development may help answering some questions as many of the signaling events that occur during embryonic development are activated during pathological conditions.
Knockdown of c-myc in *Xenopus laevis* causes embryos to develop edema and hemorrhage. *In situ* hybridization with endothelial cell markers show that blood vessels are present suggesting that c-myc is not required for specification of the endothelial cell precursors and that the vessels are probably leaky. When c-myc is overexpressed in these embryos, development is normal, but embryos show signs of hypervascularization. C-myc knockdown alters the expression of neural crest markers at migratory stages. Overexpression of the same neural crest markers rescues the vascular defect phenotype. Our results suggest that c-myc promotes angiogenesis by regulating the expression of neural crest markers.

S2.2 - DENDRITIC CELLS: AN EFFECTIVE TOOL IN CANCER IMMUNOTHERAPY

JOSÉ ALEXANDRE MARZAGÃO BARBUTO

Instituto de Ciências Biomédicas (ICB IV) - Unversidade de São Paulo, São Paulo, SP, Brasil

Dendritic cells (DC) are the most effective initiators of immune responses and their generation *in vitro* has renewed the interest in immunotherapy of cancer. Indeed, many promising clinical results have been achieved and much is still expected. Here we describe the results of a protocol using autologous tumor and allogeneic dendritic hybrid cell vaccination every 6 weeks, with at least two doses, for metastatic melanoma and renal cell carcinoma patients. Seventy patients were enrolled between March 2001 and December 2004. Half of the patients received the vaccine alone (until March 2003), and the other half received a single dose of cyclophosphamide before each vaccine dose and, after the second vaccine dose, a 5-day course of low dose IL-2 starting at the vaccination day. In each group 30 patients received the intended treatment of, at least, two vaccine doses. Response rates and patterns were not significantly different between the two groups. Though all patients included presented large tumor burdens and progressive diseases, 82% of them experienced clinical benefit from the vaccination, with disease stabilization up to more than 22 months. The median time to progression was 5.7 months and no significant untoward effects were noted. Furthermore, immune function, as evaluated by cutaneous delayed-type hypersensitivity reactions to recall antigens and by peripheral blood proliferative responses to tumor-specific and non-specific stimuli, presented a clear tendency to recover in vaccinated patients. Also, dendritic cell differentiation and function showed a significant recovery in the vaccinated patients. These data indicate that dendritic-tumor cell hybrid vaccination affects the natural history of advanced cancer and provide support for its study in less advanced patients, who should, more likely, benefit more from this approach**.**

S2.3 - MICROARRAY AS A TOOL FOR CANCER DIAGNOSIS AND PROGNOSIS

HELENA BRENTANI

Hospital do Câncer, São Paulo, SP, Brasil

We shall discuss some specific applications of cDNA microarrays as diagnostic or prognostic tools and, as examples, we will use some of the strategies we are currently applying to address two issues related to breast cancer. Clinical stage (CS) is an established indicator of breast cancer outcome and meaningful differences in prognosis are observed in CSII as compared to CSIII patients. We have used cDNA microarray profiling to identify molecular differences between these two clinical stages. We also will discuss trios of genes that could predict response to doxorubicin based primary chemotherapy in breast cancer patients. Response to chemotherapy was evaluated in 51 patients and based on RECIST guidelines, 42 who presented at least a partial response (≥30% reduction in tumor dimension), were classified as responsive. Gene profile of samples, divided into training set (n=38) and independent validation set (n=13) was used. Unsupervised clustering could correctly group all the resistant, as well as at least 85% of the sensitive samples. A classifier could correctly distinguish 95.4% of the 44 samples analyzed, with only two misclassifications, one, sensitive and another, resistant tumor.

SYMPOSIUM 3 - ENZYMES OF PHARMACEUTICAL INTEREST

S3.1 - ENZYMES FOR FOOD TECHNOLOGY

GLÁUCIA MARIA PASTORE

Faculdade de Engenharia de Alimentos - UNICAMP, Campinas, SP, Brasil

The majority of industrial enzymes using in food industries are from microorganisms due to the rapid growth rate of microorganisms and the enzymes yield. The most useful enzymes in food processing are: Carbohydrases, proteolytic enzymes and lipases. Among the carbohydrases the amylases in particular are applied to great advantage in the food industries. In special the baking industries to improve the loaf volume of the bread. Although other enzymes within this group, invertase, pectinase, cellulose, hemicellulase all have important roles in a large number of food processes. For istance, the fruit juice industries using pectinases to improve the extraction properties, to obtain a richer aroma compounds product. Proteases are utilized in the baking industry to cleave the gluten protein, which is responsible for the viscoelastic properties of flour, and any change in the rheological characteristics of the dougt will have a profound effect on its utilization. Lipases have the major role in cheese manufacture, and their hydrolytic activity produce several volatile compounds.
The pharmaceutical industry are using lipases to concentrate polyunsaturated fat acids as omega-3 from fish oil.

S3.2 - ENZYME THERAPIES IN THE EARLY YEARS OF THE 21st CENTURY

MICHAEL SIMON NOTHENBERG

Faculdade de Ciências Farmacêuticas-USP, São Paulo, SP, Brasil

The unique properties of enzymes – affinity and specificity toward substrates as well as catalytic behavior, each molecule being able to convert multiple target molecules – are highly desirable features for drugs. The evolution of recombinant technology promoted enzymes to increasingly relevant roles in cancer therapy (as antineoplastic agents or as prodrug activators); in replacement therapies for the management of genetic diseases, including severe combined immunodeficiency disease (SCID), lysosomal and mucopolysaccharide storage disorders, congenital sucrase-isomaltase deficiency (CSID), and phenylketonuria; and as clot busters, valuable agents against cardiovascular occlusions. Clinical research is underway with new and more efficient enzymes for traditional preparations like digestive aids and as wound debridement agents. Recent developments include anti-infective enzymes (enzbiotics) evaluated against protozoa, fungi, and bacteria; an uricolytic enzyme evaluated as a novel anti-gout agent; paraoxonases as atherosclerosis preventers, and butyrilcholinesterase in the management of cocaine overdosing. High treatment costs and risks of immunological reactions, two major obstacles for the expansion of enzyme therapies could be subdued with the implementation of so-called molecular farms, which contemplate mass production of protein drugs by transgenic animals and plants.

S3.3 - ENZYMES IN DERMO-COSMETIC AND PERSONAL CARE PRODUCTS

SURAIA SAID

Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

Enzymes have recently been of great interest to dermo-cosmetics and personal care products. The studies of enzymes in these kinds of products have to be view by two focuses: in the first the enzyme will be the active principle of the formulation and on the second inhibitors or activators of one target enzyme will be. But before enzymes could be applied in dermo-cosmetic and personal care products some technical problems have to be solved such as the stability of them in the formulations. Nowadays antioxidant enzymes are present in anti-aging cosmetics, proteases in exfoliatation or in skin smoothing treatments and inhibitors of enzymes, which prevent for example the hyperpigmentation have been intensively used. For each proposal many studies about the properties of the enzyme and its stability in the formulation or about its role in the skin are necessary what requests the integration of specialists from different areas. Here some enzymes and coenzymes, controlled release systems for enzymes as well as the allergenic potency of them will be discussed.

SYMPOSIUM 4 - ATHEROSCLEROSIS

S4.1 - INTERFERING WITH CD36 SCAVENGER RECEPTOR FUNCTION PROTECTS APOLIPOPROTEIN E-DEFICIENT MICE FROM DEVELOPING ATHEROSCLEROTIC LESIONS

SYLVIE MARLEAU

Sylvie Marleau[1], Diala Harb[1], Kim Bujold[1], Roberta Avallone[1], Annie Demers[1], Martin G. Sirois[2], Maria Febbraio[4], André Tremblay[3], Huy, Ong[1,2]
[1]Faculty of Pharmacy, Departments of [2]Pharmacology, [3]Obstetrics & Gynecology and Biochemistry, Faculty of Medicine, Université de Montréal, Québec, Canada
[4]Department of Cell Biology, Lerner Research Institute, Cleveland Clinic Foundation, Cleveland, OH, USA

CD36, a type B scavenger receptor expressed on macrophages, appears to play a major role in fatty streak formation through scavenging oxidatively modified lipoproteins in the arterial wall. We tested the hypothesis that growth hormone-releasing peptides (GHRPs) including hexarelin (HEX) and EP 80317 (EP), identified as CD36 ligands, exerted anti-atherosclerotic effects in apolipoprotein E-deficient mice fed with an atherogenic diet from 6 weeks old. Daily sc injections of HEX (100 mg/kg) or EP (300 mg/kg) were initiated at 6-, 10-, 12- or 14-weeks until sacrifice at 18 weeks. En face analyses of the aortic tree revealed a striking reduction of lesion formation, down to 28% (HEX) and 51% (EP) compared to vehicle-treated mice. Chronic treatment with EP was associated with a 30% decrease in total plasma cholesterol, suggesting potential effects on cholesterol metabolism at the intestine/hepatic levels. In macrophages, GHRPs up-regulated genes involved in cholesterol efflux including peroxisome proliferator-activated receptor g, liver x receptor a and the ATP-binding cassette transporters, supporting a role in regulating peripheral cholesterol trafficking. Importantly, the effects of GHRPs were shown to be CD36-dependent, inasmuch as no anti-atherosclerotic effects were observed in apoE/CD36 double-deficient mice. Our results suggest that GHRPs, as CD36 ligands, might be prototypes for a novel class of anti-atherosclerotic agents. Supported by Ardana Bioscience and CIHR.

S4.2 INFECTIOUS AGENTS AND ATHEROSCLEROSIS

MÁRIO HIROYUKI HIRATA

Faculdade de Ciências Farmacêuticas - USP, São Paulo, SP, Brasil

Infectious agents, such as *Chlamydia pneumoniae (Cp), Helicobacter pyroli (Hp)* and *Cytomegalovirus (CMV),* have been implicated in dysfunction of endothelial cells and injury of the arterial wall. The inflammatory response to these agents may be associated with instability of the atherosclerotic plaque that leads to coronary events as myocardial infarction. The aim of this speak is to discuss whether the infection caused by *CP*, *Hp* or *CMV* is associated with the expression of CD40L, a mediator of the inflammatory response, in the atherosclerotic plaque. The degree of inflammatory response in the plaque evaluated by histopathological examination can be correlated with *Cp*, *Hp* and *CMV* detection in the plaques and circulating cells, by PCR. Serum anti-Cp, anti-Hp, and anti-CMV antibodies can be used to detected with safety as diagnosis data?. CD40L mRNA expression can suggest as a inflammatory process if measured by RT-PCR, using G6PD as house keeping gene. Our studies showed that 62.2%, 67.6% and 18. 9% of the plaques were positive for *Cp*, *CMV* and *Hp*, respectively. While, in peripheral cells, the positivity dropped to 39.0%, 7.3% and 9.8%, respectively. In serum, anti-Cp was positive in 41.5% samples while anti-CMV and anti-Hp were positive in 92.6% and 78.0% samples, respectively. The histopathological results showed a positive correlation between the degree of inflammatory response and positivity for *Cp* ($p<0.021$) but not for *Hp* or *CMV*. The mRNA expression of CD40L was higher in *Cp*-positive plaques ($p<0.001$) than in *Cp*-negative ones. These results suggest that *Chlamydia pneumoniae* may induce the inflammatory response that leads to instability in atherosclerotic plaques, probably mediated by CD40L.

S4.3 - OXIDATIVE AND NITROSATIVE STRESS IN ATHEROSCLEROSIS

DULCINÉIA SAES PARRA ABDALLA

Faculdade de Ciências Farmacêuticas - USP, São Paulo, SP, Brasil

Atherosclerosis is actually considered as an inflammatory and autoimmune disease in which reactive oxygen and nitrogen species (RONS) may contribute to the generation of pro-inflammatory factors and to endothelial dysfunction. Lipoproteins may be modified by RONS and oxidatively modified low density lipoprotein (LDL) plays an important role in atherogenesis. In fact, electronegatively modified forms of LDL (LDL^-) exhibit impaired cell uptake and metabolism and are enhanced in patients with diabetes and coronary syndromes. Moreover, passive immunization with antibodies against LDL^- reduced the atherosclerotic plaque areas in atherosclerosis-prone LDLR-/- mice indicating that antibodies against LDL^- may play a protective role in atherosclerosis. Nitrosative stress mediated by nitric oxide-derived oxidants may also contribute to the atherosclerotic process. Indeed, nitrated and nitrosated compounds have been detected in biological fluids of dyslipidemic subjects. In contrast, nitrated lipids may also induce vasorelaxation what supports their role as endogenous sources of nitric oxide that may play a role in vasorelaxation. Thus, oxidative and nitrosative stress may represent important biochemical pathways in pathophysiology of atherosclerosis.

Supported by FAPESP and CNPq.

SYMPOSIUM 5 - PHARMACOGENETICS AND THE USE OF MEDICINES

S5.1 - IMPACTS ON PHARMACOGENETICS – SEARCHING FOR PERSONALIZED PRESCRIPTIONS

EDUARDO BARBOSA COELHO

Departamento Clinica Médica, Disciplina de Nefrologia, Faculdade de Medicina de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

The variability of the therapeutic response to drugs has implications for the efficacy of the treatment proposed and for the triggering of adverse effects. The clinical consequences range from patient discomfort through serious clinical illness to the occasional fatality. A recent US study estimated that 106 000 patients die and 2.2 million are injured each year by adverse reactions to prescribed drugs. Among the mechanisms involved in this variability is the influence of genetic factors. The pharmacogenetic use the information collected from genomic research to find new markers that could be used to design new drugs or new therapeutic approaches in order to minimize adverse effects and extract the maximal benefits of drugs. This presentation will introduce basic concepts of pharmacogenetic field and will discus advantages and limitations of such therapeutic approach.

S5.2 - PHARMACOGENETICS IN DYSLIPIDEMIAS

ROSARIO DOMINGUEZ CRESPO HIRATA

Faculdade de Ciências Farmacêuticas-USP, São Paulo, SP, Brasil

Cholesterol-lowering therapy is the central approach in the primary and secondary prevention of cardiovascular disease, the leading cause of death in industrialized countries. Statins are inhibitors of the 3-hydroxi-3-methylglutaryl coenzyme A reductase that are currently the most potent and widely used cholesterol-lowering drugs. Large-scale clinical trials have demonstrated the efficacy of statin treatment in reducing the risk for cardiovascular events. In general, statins are well tolerated, although some patients develop severe adverse effects such as myopathy or rhabdomyolysis.
On the other hand, not all patients respond to statin therapy with a reduction in coronary heart disease risk. It is therefore of interest to develop diagnostic test systems, which would allow to identify patients at increased risk of adverse drug reactions or patients with a lack of therapeutic effect. Genetic background is one of the factors that significantly modify drug responses. In this regard, the current knowledge of the genetic determinants of dyslipidemias and cholesterol-lowering therapy is summarized in this presentation.
Results from studies describing effects of polymorphisms in genes encoding proteins involved in cholesterol metabolism, and drug biotransformation and transport are discussed. Future implications of pharmacogenetics on clinical laboratory and pharmacological therapy are commented.

S5.3 - PHARMACOGENETICS, A FUNCTIONAL APPROACH: NITRIC OXIDE EXAMPLE

JOSÉ EDUARDO TANUS DOS SANTOS

Departamento de Farmacologia, Faculdade de Medicina de Ribeirão Preto - USP, Ribeirão Preto, SP, Brasil

Many factors including genetic background may influence drug response. Pharmacogenetics, a field aimed at elucidating the genetic basis for the differences in drug response that are commonly found in clinical practice, will probably generate clinically relevant information leading to improved therapy. Although the genetic component of the variability in drug response depends on the interplay of several gene products, genetic variations in genes encoding the most important regulators of the cardiovascular system are expected to have a major impact on cardiovascular drug response.
Nitric oxide (NO) plays a major role in the regulation of vascular homeostasis. The major source of NO is the endothelium and, as a consequence, many cardiovascular diseases may be related to abnormalities in the activity of endothelial nitric oxide synthase (eNOS), the enzyme that produces NO in endothelial cells. The pivotal role of NO in the regulation of the cardiovascular system has recently motivated a number of investigators to study whether polymorphisms in the eNOS gene are associated with cardiovascular diseases and drug response. Although inconsistent associations between these eNOS variants and cardiovascular diseases have been found, most of the studies associate eNOS gene variants with an increased risk of developing cardiovascular diseases. Importantly, recent studies show that eNOS gene variants are associated with significant differences in drug response. For example, estradiol decreases platelet aggregation in most subjects, but increases platelet aggregation in subjects who are homozygous for the eNOS less common variant in exon 7. Another study has shown that these individuals are at increased risk of developing essential hypertension. Moreover, hypertension is more frequently resistant to anti-hypertensive therapy in these subjects.
Although the study of the effects of different haplotypes and multi-locus genotypes on drug response is probably the best approach to the pharmacogenetic study of cardiovascular drugs, polymorphisms in eNOS gene may be of special importance in determining the response to drugs that depend on increased NO production to produce beneficial effects.

SYMPOSIUM 6 - TECHNOLOGICAL AND BIOLOGICAL ASPECTS OF DRUG DELIVERY SYSTEMS

S6.1 - DESIGN OF MICRO AND NANOPARTICLES DELIVERY SYSTEMS

OSVALDO DE FREITAS

Faculdade de Ciências Farmacêuticas de Ribeirão Preto/USP, Ribeirão Preto, SP, Brasil

The research for alternative materials from renewable natural sources has been increasing due to the constant need to modify chemical and physical properties of natural polymers and improve their functional characteristics or to look for new uses. Proteins and polysaccharides present a large potential use in pharmaceutical area, especially in the development of micro and nanoparticle delivery systems, due to the capacity of forming structured complexes. In our laboratory, we demonstrated the formation of an instable spherical organized system in a protein/polysaccharide dispersion (1:1), pH 8.0, with solids ranging 4-10%. The formation of microspheres could be attributed to the complexes formation between protein and polysaccharide; the protein hydrophobic domains were directed to inside of the particle and the hydrophilic domains to outside. At pH 8.0, the microspheres engulf solid or oil particles (fixed or volatile). The slow pH reduction up to 5.0 stabilizes the system, keeping the substances inside the microspheres. Additionally, they can be spray-dried without morphological alteration. The system described here could be safely used in the pharmaceutical, food and agricultural area, because it is obtained by wet chemistry using clean and mild conditions, without dangerous residues, and composed by protein and polysaccharide widely used in food industry.
Financial support: FAPESP.

S6.2 - MICRO- AND NANOPARTICULATE DRUG DELIVERY SYSTEMS: A VIEW ON PROCESS AND PRODUCT ENGINEERING

MARIA INÊS RÉ

Laboratório de Tecnologia de Partículas, Divisão de Química / IPT, São Paulo, SP, Brasil

Microencapsulation techniques are normally used to enhance materials stability, reduce adverse or toxic effects, or extend material release for different applications in various fields of manufacturing. For pharmaceutical applications, several techniques of microencapsulation are available and the choice of one depends on the physical and chemical properties of the polymer and the drug to be encapsulated, and the function and the desired size for micro or nanoparticles. A high ratio of drug to polymer is preferred to minimize the amount of mass that needs to be administered, without compromising the release kinetics. In addition, the microencapsulation technique must provide a pharmaceutically acceptable product relative to residual solvents, batch-to-batch reproductibility, ease of scale-up and high encapsulation efficiency and yields. For commercialization, cost-effectiveness is also an important requirement. A general overview of the existing micro- and nanoparticulate delivery systems enphasizing the various methods of preparation in the pharmaceutical area will be given here, focusing primarily on the advances in the production technology such as continuous microencapsulation processes ideally suitable for automation and aseptic manufacturing at larger scale.

S6.3 - MICRO- AND NANOSTRUCTURED DELIVERY SYSTEMS AND BIOLOGICAL APPLICATIONS

JOSÉ MACIEL RODRIGUES JÚNIOR

NANOCORE Biotecnologia Ltda. Ribeirão Preto, SP, Brasil

Micro- and nanotechnology emerges as an important tool for the development of intelligent therapeutics, which can act by a selective targeting to a specific tissue or cell and by reducing the drug toxicity. The confluence between nanotechnology and biology opens the doors to new opportunities for the development of therapeutics that can be administered by different routes and can also be directed to the target by physiological features or by external forces. Many applications have been described, going from the improvement of physical stability to gene transfer. One of the main applications is related to the cell transfection by means of non-live vectors. In this talk it will be presented new developments of micro and nanostructures used to improve the gene transfer in vaccines and gene therapy. Some pre-clinical and clinical results of our current work will be presented in the segments of Human and Animal Health. A recent survey of the Science and Technology Ministry identified the opportunities to Brazil and it will be discussed. As it is an emergent technology some opportunities to Brazilian companies will be presented.

SYMPOSIUM 7 - STRATEGIES FOR MEDICATION SAFETY

S7.1 - A SYSTEM-BASED APPROACH TO MEDICATION ERROR REDUCTION

MICHAEL R. COHEN

Institute for Safe Medication Practices, Huntingdon Valley, PA, USA

This program will present information about the causes and prevention of medication errors. In the United States, health professionals may voluntarily report medication errors to a national error-reporting program operated since 1994 by the Unioted States Pharmacopeia and the Institute for Safe Medication Practices. Information is also shared with the US Food and Drug Administration. Information about medication errors and other adverse drug events, along with prevention recommendations, is also shared with the medical community through various journal and newsletter publications read by over 3 million health professionals in the US and worldwide. Ongoing communication occurs with regulatory authorities and standards setting organizations internationally. The program has impacted upon drug standards and federal regulations and has created a sense of awareness of the problem as a public health issue. The Joint Commission on Accreditation of Healthcare Organizations has incorporated many of the ISMP recommendations into required National Patient Safety Goals, which must be met by over 20,000 accredited healthcare organizations in the US to maintain accreditation status. One of the top public policy issues in the United States in recent years has been medical error and the need to improve the quality of care. A report from the Institute of Medicine's Committee on Quality of Healthcare in America has led to rigorous changes throughout the US health care system, including improvements in error reporting requirements and development of new tools and systems needed to identify errors and address persistent problems. This session will provide multiple examples of actual medical errors as well as crucial and timely information needed to address many of the most challenging issues. Advice will be provided about system-based causes of medication errors, the need for developing non-punitive reporting systems, and many other topics.

Objectives:
1. Provide background and share experience derived from ISMP participation as a cooperating agency in the operation of the Medication Errors Reporting Program in the United States.
2. Provide an analysis of common causes of medication errors and major recommendations for prevention.
3. Identify system enhancements needed to prevent medication errors, detect errors before they reach a patient, or minimize their consequences.
4. Identify proactive strategies to prevent errors with high-alert drugs, which consistently result in serious patient injuries.
5. Understand the value of focusing error reduction efforts on the system rather than individuals.
6. Learn strategies for implementing a non-punitive environment and a useful error-reporting program.

S7.2 - EDUCATION OF MEDICAL STUDENTS TO REDUCE PRESCRIBING ERRORS

AJITH KUMAR SANKARANKUTTY

Departamento de Cirurgia e Anatomia da Faculdade de Medicina de Ribeirão Preto-USP, Ribeirao Preto, SP, Brasil

Medication safety use has to be the goal of every healthcare service. Studies have shown that, globally, we are far behind. Medication misuse and adverse effects are responsible for high morbidity and mortality rates, becoming a public health concern. Strategies to prevent and reduce medication problems are been developed. Study from World Health Organization has shown that medication prescribing presents inadequacies that lead to irrational medication use. It was developed guidelines for good prescribing. Implementation of rational prescribing practices is one of the strategies for medication safety. The Brazilian schools of Medicine were invited by the health authorities to promote the teaching on good prescribing as suggested by WHO. The detection of prescribing errors and the experience with 5th year medical students of the USP campus at Ribeirão Preto since 2003 will be described and discussed.

S7.3 - STUDIES ON MEDICATION ERRORS IN BRAZILIAN HOSPITALS

SILVIA HELENA DE BORTOLI CASSIANI

EERP-USP, Ribeirão Preto, SP, Brasil

The study analyzed the causes, types, administrative measures taken and suggestions concerning medication errors according to the perspective of professionals involved with the medication systems in four Brazilian hospitals. It is an exploratory survey-type multicentric study. The sample consisted of professionals from the medical clinic and pharmacy in the above-mentioned hospitals. Semi-structured interviews were used for data collection. Results showed that the most frequently error types mentioned by the professionals were related to medication ordering/transcription. Lack of attention, individual mistakes and problems in service management were the major causes of errors. Reports were the main measures taken in view of errors and changes in individual attitudes were the most frequently mentioned form to prevent them.

S7.4 - DATA ANALYSES OF *CPOE* SYSTEM FOR DETECTION OF POTENTIAL ADVERSE DRUG EVENT

DANIEL FÁBIO KAWANO

Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

In the last years, numerous studies in the patient safety area points out the high potential of medication errors to cause harm. Since 2003, our research group has been working on the detection of high-risk situations to patient safety analyzing data from the CPOE system in the “Hospital das Clínicas dapotential of information technology systems to reduce medication errors and patient injury. Specifically, our studies have been focused on the detection and prevention of harm associated to the use of high-risk drugs, including the benzodiazepine midazolam. We have analyzed every inpatient prescriptions supported by the CPOE system in a 12-month period and we have detected 26 situations in which the midazolam prescription resulted in the use of flumazenil, an antidote to benzodiazepine poisoning. CPOE seems to provide information to promote medication safety.

SYMPOSIUM 8 - APOPTOSIS

S8.1 - MECHANISMS OF CELL DEATH: CANCER AND THE APOPTOTIC MACHINERY

JOÃO GUSTAVO PESSINI AMARANTE-MENDES

Laboratório de Imunologia Celular e Molecular, Departamento de Imunologia - ICB -USP, São Paulo, SP, Brasil

Apoptosis is not the only type of cell death, but it is probably the most common and relevant to health care. It comprises a complex molecular program that is observed in many physiological and pathological conditions. A deregulation of the apoptotic machinery may result in pathologies such as autoimmune diseases, neoplasias, neurodegenerative and neuromuscular diseases, etc. The apoptotic process can be initiated by intrinsic or extrinsic signals. Extrinsic signals consist in the ligation of death receptors (DR) such as Fas, TNF-RI and DR3-5. When bound to their ligands, FasL and TRAIL (TNF Receptor Apoptosis Inducing Ligand), for instance, they recruit the adapter molecules TRADD and/or FADD and subsequently the pro-form of caspase-8. In certain types of cells caspase-8 directly activates the effectors caspases (caspases-3, -6 and -7). Intrinsic signals that induce apoptosis include changes in cytoskeleton, DNA damage and ER stress. In general, these diverse signals somehow converge to the mitochondria where the balance between pro- and anti-apoptotic proteins members of Bcl-2 family dictates the fate of the cell. Pro-apoptotic members of the Bcl-2 family include molecules such as Bax, Bak, Bad, Bid that are counteracted by the anti-apoptotic members Bcl-2, Bcl-x_L, Bcl-w, Mcl-1 and A1 molecules. If the apoptogenic signals are too strong, they result in the release of cytochrome c from mitochondria, which combines to APAF-1 in the cytosol and result in the activation of caspase-9. Finally, caspase-9 activates the abovementioned effector caspases, which are responsible for the cell deminse. Apoptotic cells must be recognized and removed in order to avoid inflammation. Proteins that inhibit apoptosis include FLIP (FLICE Inhibitory Protein) and the IAP (Inhibitor of Apoptosis) family, which are endogenous inhibitors of caspases. A complete understanding of the molecular mechanisms that control apoptosis is crucial to design of new drugs for neoplasic, autoimmune and neurodegenerative diseases.

S8.2 - PHARMACOLOGICAL INTERFERENCE WITH THE APOPTOSIS MACHINERY

FABÍOLA ATTIÉ DE CASTRO

Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

A retrospective look at the basis of human diseases almost always reveals an apoptotic component that either contributes to disease progression or accounts for it. In normal healthy tissues, equilibrium is established between cell death and cell survival. This equilibrium ensures that cells survive in the right milieu, but undergo programmed cell death (apoptosis) when damaged or when the environment is no longer supportive. Diseases are quite often the result of alterations in this homeostasis. The abnormal cell resistance to apoptosis may lead to the appearance of neoplasias and autoimmune diseases, and the exacerbation of cell death underlies some types of neurodegenerative diseases. Apoptosis may occur via a death receptor-dependent (extrinsic) or independent (intrinsic or mitochondrial) pathway. Apoptosis machinery could be modulated by numerous drugs. For example, chemotherapic drugs potentiate apoptosis by p53 oncogene pathway. The p53 plays a critical role in induction of apoptosis in response to cell stress. The p53 activation triggers apoptosis through multiple mechanisms, including mitochondrial and death receptor pathways, cytoskeleton changes, suppression of survival signaling, and induction of hypoxia. On the other hand, peptide-based caspase inhibitors may prevent neuronal loss in animal models of head injury and stroke, suggesting that these compounds may be the forerunners of non-peptide small molecules that halt the apoptotic process implicated in these neurodegenerative disorders. Our research group has been investigating the cytotoxic effect and the cellular and molecular mechanisms involved in cell apoptosis induced by commercial and new potential antineoplastic drugs on leukemic cell lines. Recently, we have been studying the apoptosis machinery alterations mediated by Glivec®, a Bcr-Abl (tyrosine kinase) inhibitor used in the treatment of chronic myelogenous leukemia (CML) patients. According to our results Glivec® abrogates *bcr-abl* expression and seems to modulate pro- and apoptotic genes expression on CML leukemic cells. We believe that the knowledge of the mechanisms involved in apoptosis regulation may bring advances in the field of cell death-based therapies and drug development.

S8.3 - CANCER IMMUNOTHERAPY: ON THE *TRAIL* OF A CURE?

THOMAS S. GRIFFITH

Department of Urology, University of Iowa, Iowa, IA, USA

Since its discovery in 1995, numerous studies have investigated the potential of using TRAIL (TNF-related apoptosis-inducing ligand) as an alternative cancer therapeutic, since it is a potent inducer of apoptosis in tumor cells but not in normal cells and tissues. As a consequence, a great deal is known about TRAIL/TRAIL receptor expression, the molecular mechanism of TRAIL receptor signaling, and methods of altering tumor cell sensitivity to TRAIL-induced apoptosis. Translating the preclinical TRAIL studies into the clinic is beginning, with the hope that TRAIL will retain all of its tumoricidal activity against human primary tumors in situ with no toxic side effects.

SYMPOSIUM 9 - PROBIOTICS

S9.1 - PROBIOTICS: CURRENT STATE AND PROSPECTS

SUSANA MARTA ISAY SAAD

Faculdade de Ciências Farmacêuticas - USP, São Paulo, SP, Brasil

The growing demand for 'healthy' foods is stimulating innovation and new product development in the food industry throughout the world. Foods that promote health in addition to providing basic nutrition are termed functional foods. The gut microbiota plays an important role in both human health and disease, and the supplementation of the diet with probiotics and prebiotics may ensure an appropriate equilibrium of this microbiota. Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. Prebiotics are nondigestible carbohydrates that beneficially affect the host by selectively stimulating the growth and/or activity of a limited number of bacteria present in the colon. A product referred as symbiotic is one in which probiotics and prebiotics are combined. A probiotic microorganism must survive the acidic conditions of the upper gastrointestinal tract and then proliferate and/or colonize the intestine. Bacteria belonging to the genera *Lactobacillus* and *Bifidobacterium* are most often used as probiotic supplements for food, and have been implicated in a variety of beneficial roles for the human body, including maintenance of the normal intestinal microbiota, pathogen interference, exclusion and antagonism, immunostimulation and immunomodulation, anticarcinogenic and antimutagenic activities, deconjugation of bile acids, and lactase release *in vivo*.

S9.2 - PROBIOTICS: STUDIES FROM ANIMAL MODELS AND CLINICAL TRIALS

JACQUES ROBERT NICOLI

Nicoli J.R.,[1] Vieira L.Q.,[2] Arantes R.M.E.,[3] Carmona D.C.[3], Penna F.J.,[4] Péret L.A.,[4] Figueiredo P.P.,[4] Bambirra E.A.[5]

Departments of Microbiology[1], Biochemistry and Immunology[2] and General Pathology[3], Institute of Biological Sciences and Departments of Pediatrics[4] and Anatomopathology[5], Medical School, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil.

The indigenous intestinal microflora offers three main beneficial functions to the health of its host: resistance against colonization, immunomodulation and nutritional contribution. It is important that this microflora rapidly colonizes the digestive tract of newborns and that, once installed, these functions be preserved. Cesarean delivery, type of feeding and premature birth disturb initial colonization as a antimicrobial treatment, and feeding changes and stress interfere in the maintenance of these functions. In these disturbance situations, using probiotics can offer a possibility of compensation. Probiotics are preparations containing live microorganisms which, when ingested, offer some kind of benefit to the host. Bacteria (*Lactobacillus, Streptococcus, Bifidobacterium, Escherichia coli*) and yeasts (*Saccharomyces boulardii*) are frequently used as probiotics. At the ICB/UFMG, the gnotobiotic animal model has been used to demonstrate and understand the mechanisms responsible for the protective effect of various probiotics against experimental infections by enteropathogens. Moreover, in collaboration with the UFMG Medical School Pediatrics Department, double-blind placebo-controlled clinical trials demonstrated a protective effect of probiotics against episodes of diarrhea in the newborn's first year of life and in the frequency of diarrhea associated with the use of antibiotics in children.

S9.3 – PROBIOTICS: AAPPLICATIONS IN CLINICAL PRATICE

CARLOS DANIEL MAGNONI

IMeN - Metabolism and Nutrition Institute, EPM - UNIFESP, São Paulo, SP, Brasil

Society has always worried about incorporating healthy food into its daily nutritional habits. Food is not only seen as a way of satisfying hunger, preventing diseases caused by a deficient diet and providing human beings with the nutrients needed for tissue construction, maintenance and reparation, but has also become the main vehicle towards good health and well-being[1]. In this context, consumers have shown their interest in how specific food items can benefit health through their physiological / biological activity, which are called functional food, designed food or nutraceutics [2,3]. Probiotics are thoroughly incorporated in this new phase of diet therapy. Recommended by evidence-based medicine, they clearly need to be included in routine health and nutrition prescriptions. Knowledge about this probiotic capacity plays an important role in the treatment of intestinal diseases, cancer and metabolic syndrome, among other clinical conditions. According to the Institute of Medicine of the U.S National Academy of Sciences, any food or ingredient that can exercise a beneficial effect on the organism can be considered as functional food [5]. The functional food concept was introduced in Japan in the mid 1980's [1] and remains the only country with a specific regulatory process for functional food, which is known as FOSHU - Foods for Specified Health Use. This food is qualified and receives a label of approval by the Japanese Ministry of Health and Social Security [2]. Nowadays, about 250 products possess a FOSHU license in Japan and, since 1999, this market has experienced immense growth, as a result of international companies and corporations' investments in publicity and educational projects [6,7]. Probiotics are one type of functional food. These are nutrients processed with live organisms that, when ingested, exert a benefic effect on the bacterial flora of their host. The first scientific studies on probiotics date back to the beginning of the last century. Metchnikoff, from the Pasteur Institute, claimed that probiotics benefited their host by working against noxious bacteria inside the intestinal tract [8,9]. The initial hypothesis on probiotics supposed greater benefits from bacterial strains that were able to attach more efficiently to the surface of the intestinal layer [10]. Probiotics were initially described as "live organisms that when ingested in a certain number or quantity exert beneficial effects to humans" [11]. Currently, probiotics are defined as: "live microbial food supplements that exert a benefic effect on their receptor, due to a positive balance of the intestinal microbial flora" [8,10]. Probiotics deserve special attention because studies prove their effect on the bacterial intestinal flora and, thus, their action in disease control [12]. Escherich affirmed the importance of the host-bacteria interaction and the essential role of intestinal microbiota competition for human health and well-being [13]. Probiotics can be added to industrialized foods and their use is increasing in leavened milk, yoghurt and other food products. They can also be found as powder or capsules in pharmaceutical products [14]. Probiotics are products that viably carry human intestinal bacteria for human consumption, as well as animal intestinal bacteria for consumption by this animal specie. These products' main aim is to maintain the intestinal microbiota that was somehow unbalanced through antibiotics treatment, chemotherapy, radiotherapy or metabolic stress situations [15]. Maintaining the intestinal microflora is related to opposing pathogenic agents, to the microbial barrier effect and to the modulation of immunological functions by the healthy intestine [10,11,16]. Probiotics must display specific features, such as: being normal inhabitants of the intestinal tract; rapid reproduction; producing antimicrobial substances; resistance to degradation between fabrication, commercialization and ingestion, as they have to ingested in live form [17,18]. In recent years, significant research efforts have allowed for a better understanding of the relations between intestinal microorganisms and health, proving that preparations with probiotics can alter the composition or activity of intestinal microflora. However, science still has a long way ahead, as no definitive conclusions have been reached about how probiotics act in cancer treatment, as well as how frequently and in what quantity they have to be ingested.

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SYMPOSIUM 10 - PATHOGENY AND THERAPY OF AUTOIMMUNE ILLNESSES MEDIATED BY IMMUNECOMPLEXES

S10.1 - PATHOGENESIS OF DISEASES CAUSED BY IMMUNOCOMPLEXES: ROLE OF NEUTROPHILS

YARA MARIA LUCISANO VALIM

Departamento de Física e Química da Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

Autoimmune disorders are classified into organ-specific and non organ-specific types. In organ-specific types, the reaction is directed against one particular organ-examples include Hashimoto´s thyroiditis (thyroid) and Addilson´s disease (adrenal glands). In non-organ-specific disorders, the effects are wide spread throughout the body, for example systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Grave´s Disease. Immune complexes are often associated with a systemic autoimmune disease. Immune complex deposition in tissues triggers the inflammatory cascade through a variety of mechanisms, including complement activation and phagocyte recruitment. Because immune complex tissue injury is largely PMN-mediated many studies have been dedicated to ascertain the mechanisms molecular that activate neutrophils in vivo in both infections and in inflammatory disease to determine if extracellular secretion of toxic mediators can be modulate or even inhibited without affecting phagocytosis and intracellular killing. We are discussed all these molecular events, because the selective inhibition of neutrophil function might be practical therapeutically in inflammatory diseases such as the ICs ones.

S10.2 - EXPERIMENTAL MODEL FOR ILLNESSES TRIGGERED BY IMMUNOCOMPLEXES

CLENI MARA MARZOCCHI MACHADO

Associação São Bento de Ensino, Araraquara, SP, Brasil

Illnesses triggered by immunocomplexes (IC) are generally associated to systemic infections and auto-immune illnesses of the connective tissue. IC deposition in tissues stimulates a local inflammatory response, that can lead to a lesion and consequently harms to the physiology of the organ. The IC production in vivo triggers molecular and cellular pro-inflammatory and anti-inflammatory mechanisms, through activation of the complement system and receptors for IgG (FcgR). Several experimental models have contributed for a better understanding of the clinical aspects of IC illnesses: a) Infusion of IgG aggregates triggers several disturbances that can lead to death due to lethal acute toxicity, mediated by the release of phagocytes under FcgR stimulation; b) Serum diseases has been used to investigate the active immunization, when huge amount of antigens are present in the circulation and the produced IC are located inside the small vessels. c) models used to evaluate structure and function of the receptors for complement and FcgR display the protective contribution of the complement system for an efficient removal of IC; and d) genetic linked or acquired deficiencies of complement enhance the risk of auto-immune diseases. So the challenge is to establish models that could show the signalization of receptors involved in these responses. The activation or inhibition of the FcgR, CR and cytokine receptors play a potential role for immunotherapy.

S10.3 - THERAPY OF AUTO IMMUNE ILLNESSES

EDUARDO ANTÔNIO DONADI

Departamento de Clínica Médica da Faculdade de Medicina de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

Besides genetic and environmental factors, several alterations of the immune system function have described that contribute to the pathogenesis of autoimmune diseases (AID). The humoral, cellular or both components of the immune response may be implicated in the production of localized or systemic AID. Among the humoral-mediated mechanisms associated with AID pathogenesis include the participation of autoantibodies , complement and circulating immunecomplexes, and among cellular-mediated mechanisms, B cells, T cells and Tcell subsets have been implicated. Several therapeutic approaches have been describe to treat these disorders, including the utilization of antiinflammatory, immunosuppressive and biological agents. Among immunosuppressive drugs, cyclophosphamide, methotrexate, azathioprine, chlorambucil, cyclosporin, mophetyl mycophenolate have been intensively used. Biological agents represent the ultimate approach to the treatment of these disorders, encompassing the use of monoclonal humanized antibodies against molecules that participate in the inflammatory and immune response processes. Monoclonal antibodies against cytokines or cytokine receptors, including tumor necrosis factor (TNF), IL-1, adhesion, costimulatory, and lymphocyte CD surface molecules have been introduced into the therapeutic arsenal. In addition to these agents, plasmapheresis and autologous stem cell transplantation have recently been introduced as new and powerful tools to reconstruct the immune system function

SYMPOSIUM 11 - CHALLENGES OF PHARMACEUTICAL CARE AND CLINICAL PHARMACY

S11.1 - PHARMACEUTICAL CARE: ADVANCES AND NATIONAL POLICY

NORBERTO RECH

Ministério da Saúde, Brasília, DF, Brasil

S11.2 - CHALLENGES AND PERSPECTIVES OF CLINICAL PHARMACY

JULIETA UETA

Faculdade de Ciências Farmacêuticas de Ribeirão Preto - USP, Ribeirão Preto, SP, Brasil

Along these last decades the pharmaceutical profession has changed all over. Pharmacists have taken the responsibilities to provide patients services and activities that should reflect on quality of care and in therapeutic outcomes provided by health professionals. Brazil is now been introduced to Clinical Pharmacy and pharmacists are becoming healthcare team member in hospitals and primary care services. Clinical pharmacy practice requires intense pharmacotherapy knowledge for the safe, appropriate and economic medication use, besides communication abilities, management, etc. Pharmacists need continuous education while in pharmacy schools a curriculum change is a demanding challenge. The changes should bring to modify the level of healthcare quality. The volume of knowledge requirements is shown in the pharmacy schools curricula succeed in preparing qualified clinical pharmacists. Without heavy investments and compromised changes the clinical pharmacy could be restrained to shy advances. However a solid academic formation integrated to healthcare services to consolidate SUS seeking for excellence in safe and rational medication use can define a outstanding future for the pharmacist.

S11.3 - CHALLENGES TO PHARMACEUTICAL CARE AND CLINICAL PHARMACY

DIVALDO PEREIRA DE LYRA JÚNIOR

Faculdade de Ciências Farmacêuticas de Ribeirão Preto USP, Ribeirão Preto, SP, Brasil

In the last fifteen years, the concept of Pharmaceutical Care has been defined by Hepler and Strand (1990), and significant progress has been achieved. It is estimated that millions of patients worldwide have been benefited by the Pharmaceutical Care practice. Studies on Pharmaceutical Care were begun in the United States in the early 1990s by groups in the University of Minnesota and University of Florida. According to analysis of the literature "*Pharmaceutical Care: 10 años"*, in the 1990s, a total number of 2,510 studies containing the key words "pharmaceutical care" were published and later indexed in the most frequently used secondary sources. In Brazil, the small number of investigations on Pharmaceutical Care places the country aside from the scientific development in that field as well as hinders the development of patient care methods that are directed to the national reality. As regards teaching, although the National Guidelines for Undergraduate Pharmacy Programs (2002) have included Pharmaceutical Care as a constituent element in the training of generalist pharmacists, most of the Brazilian Universities have not yet introduced in their curricula the competencies and skills that can prepare for the new professional profile.

S11.4 - PRATICES IN CLINICAL PHARMACY: AN ACADEMIC MODEL

DÍLSON BRAZ DA SILVA JR

Secretaria Municipal da Saúde de Cássia dos Coqueiros, Ribeirão Preto, SP, Brasil

Information on medicines is essential for their rational utilization. Clinical pharmacist is a unique health professional able to complement physician practices on individual care by applying evidence based pharmacotherapy associated to cost-effective prescribing. Clinical pharmacist interventions are proved to reduce medication inappropriateness and errors. Focusing on medication safety strategies to prevent errors and to improve prescription of medical students, the School of Medicine of Ribeirão Preto, with the participation of the School of Pharmacy of Ribeirão Preto, started three years ago the ministration of "Guidelines for Good Prescribing" discipline, according to WHO's model. As part of their training, the medical students are taken to an internship in Cássia dos Coqueiros (São Paulo State, Brazil) health care unit assisting the population for primary care needs. A pharmacist was included in the team responsible for students' activities there. The role of pharmacist has been assistance on general pharmacotherapeutic management associated with informal teaching. The most prevailing types of intervention have been comprehension and correction of prescriptions, suggestion for drug regimen changes, discontinuation or inclusion of a drug. The outcomes revealed the recognition of the pharmacist role in patient safety by medical staff and students, cost reduction and improved effectiveness and safety of medications.

SYMPOSIUM 12 - IMMUNE RESPONSE MODULATION

S12.1 - THE ROLE OF GANGLIOSIDES IN MODULATING THE FUNCTION OF IgE RECEPTORS

CONSTANCE OLIVER

Department of Cell and Molecular Biology and Pathogenic Bioagents, FMRP-USP, Ribeirão Preto, SP, Brazil

Mast cells exert their function through the liberation of mediators via activation of the high affinity IgE receptor (FcεRI) located in microdomains (lipid rafts) of the plasma membrane. Using a mast cell specific antibody, mAb AA4 that recognizes gangliosides present in lipid rafts, the role of the gangliosides in the activation of FcεRI has been investigated. When mAbAA4 binds to the surface of cultured rat mast cells, mediator release is inhibited in a time and dose dependent manner which is related to the capping of the gangliosides. *Lyn,* known to be associated with these gangliosides, is the first kinase activated following FcεRI stimulation. In unstimulated RBL-2H3 cells *Lyn* and the gangliosides are distributed along the plasma membrane, but rarely colocalize. Five min after stimulation, *Lyn*s colocalizes FcεRI with the gangliosides. After 24 hr incubation with mAb AA4 the gangliosides aggregate into a single cap. Under these conditions, in unstimulated cells, *Lyn* does not colocalize with the capped gangliosides. By 5 and 30 min after stimulation, *Lyn* colocalizes only with the gangliosides that are outside the cap and mediator release is reduced by 70%. The interaction between *Lyn,* FcεRI and the gangliosides is essential for mast cell degranulation.

S12.2 - NEW INSIGHTS INTO SIGNALING VIA IgE RECEPTORS

DAVID HOLOWKA

Department of Chemistry and Chemical Biology - Cornell University, Ithaca, NY, USA

Recent work in our laboratory to characterize the role of lipid segregation in IgE receptor signaling in mast cells has revealed a mechanism by which segregation of liquid ordered regions from disordered regions of the plasma membrane results in protection of the Src family kinase Lyn from inactivating dephosphorylation by a transmembrane tyrosine phosphatase. Antigen-mediated crosslinking of IgE receptors drives their association with the liquid ordered regions, commonly called lipid rafts, and this facilitates receptor phosphorylation by active Lyn in the raft environment to initiate the signaling cascade that leads to mast cell degranulation. Previous work showed that polymerization of F-actin regulates stimulated receptor phosphorylation and downstream signaling processes, and more recent work in our laboratory implicates cytoskeletal interactions with ordered lipid rafts and Lyn in this negative regulation. Recent work has also revealed that receptor-stimulated Ca^{2+} mobilization utilizes a novel membrane domain that contains Ca^{2+} channels and associated phospholipase Cγ. These and other results provide an emerging view of the complex role of membrane structure in orchestrating signal transduction mediated by immune and other cell surface receptors.

S12.3 - FUNCTIONAL GLYCOMICS - ROLE OF GLYCOCONJUGATES IN IMMUNITY AND DEVELOPMENT

RICHARD DALE CUMMINGS

University of Oklahoma, Oklahoma, USA

Ongoing studies are demonstrating that animal tissues contain thousands of glycoconjugates with multiple glycan structures in glycoproteins, glycolipids, and glycosaminoglycans. In addition, there are over a dozen classes of glycan-binding proteins (GBPs) that are important in recognizing self-glycans in development and cellular function and in recognizing foreign glycans in homeostasis and innate immunity. Understanding the structures and functions of the glycans and GBPs is within the area termed "Functional Glycomics". Defining the specificity and affinity of GBPs to glycoconjugates is important to understanding cellular communication in development and in disease processes. Our laboratory is part of the funded efforts in the U.S.A. from the National Institute of General Medical Sciences at the NIH that is supporting the *Consortium for Functional Glycomics* to develop high throughput, unbiased, global screening platforms for the analysis of protein-glycan interactions. The "glycan arrays" created through this effort are demonstrating the extraordinary specificity and recognition by GBPs from humans, animals, and pathogens. My group has studied specific roles of glycans and GBPs in animal development, cellular signaling, and vascular biology/inflammation. This presentation will focus on these recent studies with emphasis on the biological functions of O-glycans in cell adhesion and animal development, and the recognition of glycans by GBPs and antibodies important in both innate and acquired immunity to parasitic infections, such as schistosomiasis and intestinal nematodes.

SYMPOSIUM 13 - ANIMAL POISON TOXINS APPLICATIONS

S13.1 - EVOLUTIVE ASPECTS ON TOXINS AND IMMUNITIES

OSVALDO AUGUSTO BRAZIL ESTEVES SANT' ANNA

Laboratório Especial de Microbiologia, Instituto Butantan, São Paulo, SP, Brasil

Experimentation and the search for knowledge are intrinsic characteristics of the human specie in an attempt to understand, explain and express the causes and the effects between the multiple relations that exist in the natural world, in the universe. In science, repetitive correlations are associated to complexity of systems that lead to the notion of species, for example. The development of thinking will demand study and multiple reflections, therefore much more than the domination of a technique or a search for a new technology. The biological questions regarding the concepts of venoms, toxins or an antigen in the wide sense, on one side and receptors or effector molecules of the immune system, on the other side, are part of the evolutionary process that appears in the principle formulated by Dobzahansky: ***NOTHING IN BIOLOGY MAKES SENSE EXCEPT IN THE LIGHT OF EVOLUTION***. These principles are also part of the general concept of complexity, diversity and specificity, and of the functional network of the immune system proposed by Jerne. The definition of time, space, movement, energy dissipation, chaos and non-reversibility, gave us knowledge and today we start to notice them together; these concepts give us tools to the comprehension of the origin of life and its evolution. Toxins or immunity: in a broken mirror images and similarities, or non-similarities, acquire variable forms. The snakes and their immunities, the *Homo sapiens* and their toxins!

S13.2 - DESINTEGRINS: SNAKE VENOM TOXINS THAT AFFECT CELL PROLIFERATION AND ANGIOGENESIS

HELOISA SOBREIRO SELISTRE-DE-ARAÚJO

Departamento Ciências Fisiológicas, Universidade Federal de São Carlos, São Carlos, SP, Brasil.

Angiogenesis is the development of new capillaries from preexisting blood vessels. This is a key physiological process in development, wound healing and female reproduction. Undesirable angiogenesis may also occur, which facilitates the progression of solid cancer, metastasis and inflammation. Angiogenesis involves the proliferation of endothelial cells, a process mediated by growth factors including the vascular endothelial growth factor. Cell proliferation and angiogenesis depend on the interactions of cells with the extracellular matrix (ECM) through the integrins, a family of cell surface receptors for ECM components. The integrins $\alpha v\beta 3$ (vitronectin receptor) and $\alpha 2\beta 1$ (collagen I receptor) play an important role in endothelial cell proliferation and angiogenesis. Therefore, compounds that target to these integrins can be used to control both processes. Disintegrins isolated from snake venoms specifically bind to integrins therefore inhibiting ligand binding and integrin activation. Most disintegrins have the RGD sequence which is the structural adhesive motif recognized by the integrin, and these RGD-disintegrins induce cell apoptosis and inhibit experimental metastasis. Another class of disintegrin does not have the RGD motif and induces endothelial cell proliferation. The complexity of the structure and function relationship of disintegrins and the potential medical applications of these proteins will be discussed.

Support: FAPESP, CNPq, FINEP, International Foundation for Science

S13.3 - TOXINS FROM *TITYUS SERRULATUS* VENOM: MECHANISMS OF ACTION AND APPLICATIONS AS BIOLOGICAL TOOLS

ELIANE CANDIANI ARANTES

Departamento de Física e Química, Faculdade de Ciências Farmacêutica de Ribeirão Preto - USP, Ribeirão Preto, SP, Brasil

Scorpion venoms are a rich source of bioactive small proteins that have been used as specific tools for ion channels research. The best studied peptides are those that recognize K^+- or Na^+-channels. These neurotoxins affect the gating mechanism and ion permeability of excitable membranes, inducing an intense autonomic discharge, leading to a massive release of neurotransmitters. Voltage-gated Na^+-channel toxins are the most reactive of these proteins and the main responsible agents by the toxic effects of scorpion envenoming. They are composed of 60-76 amino acid residues stabilized by four disulphide bridges, and can be classified into two classes: α- and β-scorpion neurotoxins, which bind to external receptor sites 3 and 4 of voltage-gated Na^+-channels, respectively. This presentation will provide a comparison between TsTX-V (α toxin) and TsTX-I (β toxin) from *Tityus serrulatus* venom. K^+-channels are particularly important in electrically excitable cells and in synaptic transmission. The K^+-channels toxins contain from 22 to 47 amino acid residues tightly folded by 3 or 4 disulfide bridges and have been useful in probing the physiological roles of different subtypes of K^+-channels. We will discuss the ability of $\alpha KTx_{12.1}$ and TsTX Kα interact with a variety of K^+-channels. The *T. serrulatus* venom is also a source of components with action on complement system that can be involved in the inflammatory process induced by the venom.

Financial support: FAPESP, CNPq, CAPES.

SYMPOSIUM 14 - EMERGENT AND RE-EMERGENT DISEASES

S14.1 - DISRUPTION OF A HUMAN MALARIA PARASITE *Plasmodium falciparum* GENE LINKED TO MALE SEXUAL DEVELOPMENT CAUSES EARLY ARREST IN GAMETOCYTOGENESIS

TETSUYA FURUYA

Malaria Genomics Unit, Laboratory of Malaria and Vector Research, NIAID, NIH, Bethesda, MD, USA

The sexual stages are vital phases in malaria parasite transmission and are the targets of various interventions such as transmission-blocking vaccines. The molecular mechanisms underlying sexual development, however, remain poorly understood. Previously, a male gametocyte defect in the *Plasmodium falciparum* Dd2 parasite was discovered through the observation that all progeny clones in the Dd2 x HB3 genetic cross were the result of fertilization events between Dd2 females and HB3 male gametes. A determinant linked to this defect in Dd2 was subsequently mapped to an 800 kb segment on chromosome 12. Here we report mapping of the genetic determinant to an 82-kb region and the identification of a sexual stage-specific gene (*pfmdv-1*) that is expressed at a lower level in the Dd2 than in W2 parasite, its normal gametocyte-producing ancestor. Disruption of *pfmdv-1* results in a dramatic reduction in mature gametocytes, especially male gametocytes, with the majority of sexually committed parasites developmentally arrested at stage-I. The *pfmdv-1* knockout parasites show an enlarged nucleus, often with separation of the inner and outer nuclear membranes and presence of multi-membrane vesicles in red blood cell cytoplasm. Mosquito infectivity of the knockout parasites is also greatly reduced, but not completely lost, suggesting the presence of compensatory mechanisms in the sexual development pathways.

S14.2 - STRUCTURE-BASED DRUG DESIGN FOR TROPICAL DISEASES

MARIA CRISTINA NONATO

Laboratório de Cristalografia de Proteínas, Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

The repertoire of drugs to fight tropical diseases such as malaria, Chagas' disease, leishmaniasis, and African trypanosomiasis is usually inadequate. Chemotherapy to fight the mentioned diseases exists, but is plagued by high toxicity and increasing resistance. Genome sequencing and structural genomics projects enable molecular targets to be identified and characterized, providing incredible opportunities for the use of structure-based drug design approach against tropical diseases.
This technology, which is an integral part of drug discovery today, is based on a multidisciplinary approach that includes biological, physical and computational sciences, and allows us to identify the structural properties of the cellular receptor (target) such as size, shape and electrostatic properties and can enhance the understanding of chemical reactivity involved in the binding of a lead compound. These data, in turn, suggest ways to bind the lead compound to the target protein with greater selectivity, thus improving efficacy.
Here, we illustrate the application of structure-based drug design technology in progress in our laboratory as an important tool against tropical diseases.

S14.3 - STUDIES ON HANTAVIRUS CARDIOPULMONARY SYNDROME IN BRAZIL

LUIZ TADEU MORAES FIGUEIREDO

Departamento de Clínica Médica, Faculdade de Medicina de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

Firstly we will show why Hantavirus Cardiopulmonary Syndrome (HCPS) is an important emergent disease in Ribeirão Preto Region and in Brazil. We will show RT-PCRs used for diagnosis of HCPS in our laboratory and our phylogenetic studies on Araraquara Hantavirus detected in patients and wild rodents. Araraquara virus is the causative of HCPS in the Region of Ribeirão Preto. Finally, results of a serologic survey for Hantavirus infection carried out in a county near to Ribeirão Preto City will be shown as well as information on a N recombinant protein of Araraquara virus produced in our laboratory to be used as an antigen in ELISA tests and for studies on immune response and physiopathology of HCPS.

SYMPOSIUM 15 - METABOLISM REGULATION FOR ELDERLY

S15.1 - ENERGY METABOLISM AND BODY COMPOSITION IN THE ELDERLY

EDUARDO FERRIOLI

Departamento de Clínica Médica, Faculdade de Medicina de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

Body composition changes with usual ageing, with an increase in fat body mass and decrease in lean body mass. This is followed by a decrease in basal metabolic rate, which is partially due to body composition changes and partially due to changes in energy metabolism regulation itself. Recent studies have shown that adaptative changes in food intake after a period of under or overfeeding in elderly persons is impaired. Older volunteers maintain low caloric intake following a period of forced underfeeding in contrast to younger volunteers, who spontaneously increase their food intake until they regain weight. The opposite happens after a period of forced overfeeding. The effect of physical activity in energy metabolism has also been studied recently and the results show that it partially reverts the effects of aging in body composition and energy metabolism. Obesity is still a serious public health problem in old age, and recent studies of our group have shown a prevalence of obesity of 28% in our free-living elderly population. A study of body composition, energy expenditure and physical activity level in independent older persons of our population is being developed by our group at the School of Medicine of Ribeirão Preto – USP, and partial results will be presented at the Congress.

S15.2 - GLYCEMIC REGULATION ALONG THE AGEING PROCESS

PATRICIA MONTEIRO SERAPHIM

UNESP, São Vicente, SP, Brasil

Type 2 diabetes is a growing problem among the elderly population in the world. Since the population is ageing, it is not surprising that the elderly increasingly comprise a larger proportion of patients with newly diagnosed diabetes. The underlying defect that causes type 2 diabetes is insulin resistance in which the main feature is the unpaired glucose utilization by the target tissue of insulin. The effect of insulin on glucose homeostasis is largely mediated through the action of a family of membrane transport proteins called glucose transporters (GLUTs). GLUT4 is expressed in tissues that depend on insulin for their glucose utilization, like muscle and fat. In general, in the absence of insulin, GLUT4 is mostly excluded from the plasma membrane, and insulin reversibly stimulates the exocytosis of GLUT4-containing vesicles, thereby causing a translocation of GLUT4 to the cell surface. Various studies have demonstrated that ageing provokes a reduction in GLUT4 content in plasma membrane, collaborating for the insulin resistance installation. In this way, therapy that improves glucose transport in adipocyte and muscle, GLUT4 expression in plasma membrane and/or insulin signaling can contribute with glycemic homeostasis.

S15.3 - ADIPOSE TISSUE METABOLISM IN THE AGEING PROCESS

ANALÚCIA RAMPAZZO XAVIER

UNIRP, Faculdade de Farmácia, São José do Rio Preto, SP, Brasil

White adipose tissue now emerges as a pivotal organ controlling lifespan. The effect of adipose tissue reduction on lifespan could be due to the factors released of fat deposition acting on target tissues such as the brain, or due to the indirect prevention of age-related metabolic disorders like type 2 diabetes or atherosclerosis. Ageing rats have characteristically increased body weight, fat mass and a specific body fat distribution. In humans, increased fat mass (obesity), and in particular increases in abdominal obesity as a result of deposition of visceral fat, are associated with the metabolic syndrome of ageing. In advanced old age, fat depot size declines while lipid is redistributed to muscle, bone marrow, and other tissues. Redistribution of lipid to extra-adipose sites with aging could result from loss of lipid storage capacity in fat depots, altered fatty acid handling resulting in lipid accumulation, dysdifferentiation of mesenchymal precursors, or loss of free fatty acid utilization by lipoprotein lipase activity or a combination of these mechanisms. Fat tissue, however, plays a major role by secreting multiple metabolically active factors, which are potentially responsible for the common aging diseases. This abstract will focus on and review the potential cause-effect relation between increased fat mass, decreased fat depots and ageing process.

SYMPOSIUM 16 - ANIMAL HEALTH

S16.1 - ALTERNATIVE METHODS FOR ACUTE ORAL TOXICITY TESTING

EKATERINA AKIMOVNA B. RIVERA

UFG - Universidade Federal de Goiás, Goiânia, GO, Brasil

Acute toxicity studies in animals are usually performed to support the registration of chemicals (pharmaceutical, pesticides, and others) intended for the use of humans and animals. The main purpose of these studies is the human and animal safety and when possible scientific valid and feasible approaches must be put into practice.
Traditional methods for assessing acute oral toxicity use death of animals as an endpoint, but since 1984 a new approach to acute toxicity testing was suggested by the British Toxicology Society based on a fixed – dose procedure avoiding, thus, the death of animals as an endpoint.
The Directive 86/609/EEC specifically requires that "an experiment (on a laboratory animal) should not be performed if another scientifically satisfactory method, not entailing the use of an animal, is reasonably and practically available."
As stated by Dr. Michael Balls(ECVAM) "the law is on our side, and we need not be hesitant in demanding that scientifically valid and feasible non-animal methods and testing strategies should be incorporated into regulatory testing guidelines".
Since then many other acute testing have been proposed to replace the conventional LD50 test. Three of them have been published, validated and are accepted by the OECD (Paris, November 2000): the Fixed Dose procedure (guideline 420), Acute Toxic Class Method (guideline 423), and the Up and Down Procedure (guideline 425). In this lecture we will provide a summary of these methods , comparing them and also which organizations do not recommend the conventional acute oral toxicity test anymore.

1. OECD Guideline for the Testing of Chemicals – 2nd volume, November 2000.
2. ICLAS/CCAC International Symposium on Regulatory Testing and Animal Welfare, Quebec, 2002- Summaries of the Beakout Groups.
3. Alternative methods for acute oral toxicity testing: Practical Guidance for Implementation; Lab Animal Europe, Vol 2, No. 7-August/September 2002
4. An Industry/Animal Welfare Initiative to Minimise Dog Use in Preclinical Toxicology-Smith, D. et al. 9th FELASA Symposium, 14-17 June , 2004-Nantes, France

S16.2 - UTILIZATION OF FELINES IN SCIENTIFIC RESEARCHES: EMPHASIS IN POLICYSTIC KIDNEY DISEASE AND ITS USE IN HUMAN RENAL TRANSPLANT

ANDRÉ LUIZ LOUZADA MALDONADO

Vetimagem, São Paulo, SP, Brasil

Polycystic kidney disease (PKD) is a congenital disease characterized by the development of renal cysts that lead to chronic renal insufficiency (BILLER, 1994; BILLER; CHEW; DIBARTOLA, 1990; EATON et al., 1997; FELDHAHN, 1995; FISCHER, 1999; FORRESTER; LEES, 1998; GONZALEZ; FRÓES, 2003). It occurs in different breeds of cats, but prevalence rates are particularly high in the Persian breed, as well as in crossbreeds of Persian cats, such as the Himalaya and Exotic breeds (BECK; LAVELLE, 1999; BILLER; CHEW; DIBARTOLA, 1990; FELDHAHN, 1995; FISCHER, 1999; GONZALEZ; FRÓES, 2003). It has been proved that this disease is related to a hereditary autosomal dominant character (EATON et al., 1997; BILLER; CHEW; DIBARTOLA, 1990). EATON et al. (1997) observed the similarity between this disease and autosomal dominant polycystic kidney disease (ADPKD) in humans. In this context, cats are excellent experimental models. This disease has also been verified in mice, dogs from the Cairn Terrier, West Highland White Terrier and Bull Terrier breeds and ferrets (EATON et al., 1997; FORRESTER; LEES, 1998; MYLONAKIS; PATSIKAS; KOUTNAS, 1999; O´LEARY; MACKAY; MALIK, 1999). The development and growth of cystic structures in both kidneys, and occasionally in the liver and pancreas, are characteristic of ADPKD (EATON et al., 1997; GONZALEZ; FRÓES, 2003). In 1994, BILLER noted that the increase in the amount and size of renal cysts is accompanied by a progressive and bilateral increase of the organ. The cysts' compression of the renal parenchyma is the main factor in the pathogenesis of renal insufficiency, whose clinical signs vary individually in terms of manifestation age as well as duration (BILLER, 1994). Nowadays, PKD is considered an important cause of renal insufficiency. Studies on cats all over the world have proved that the disease is more frequent than previously imagined (CANNON et al., 2001; LYONS, 2000). Ultrasound imaging allows for the identification of positive animals, which used to be limited by the non-existence of a sensitive and non-invasive ante-mortem diagnostic method. Moreover, ultrasound allows for early diagnosis, that is, before renal insufficiency is developed, which is of basic importance in countries where renal transplants are an actual treatment alternative. The possibility of early and non-invasive diagnosis by means of ultrasound imaging should also be seen as a disease prevention and control strategy (BILLER, 1994). ETHIOPATHOGENY AND EPIDEMIOLOGY. In 1969, BATTERSHELL; GARCIA reported the first case of PKD in felines. In mankind, there exist two forms of inheritance: recessive and dominant, which used to be called infant

and adult PKD, respectively. This nomenclature is related to the manifestation age of clinical signs, and not to the age when renal injuries are developed (BILLER, 1994). Only one recessive case has been reported on in cats. Clinical signs were present and the animal died before seven weeks of life, and the macroscopic and microscopic alterations were correlated to recessive PKD (CROWELL; HUBBELL; KILEY, 1979). The most common genetic manifestation of polycystic renal disease in felines is the dominant form, which is more frequent in Persian cats and crossbreeds (BILLER, 1994; BILLER; DIBARTOLA; EATON, 1996). The hereditary autosomal dominant character is related to three types of gene forms. **P** represents the dominant form whereas **p** represents the recessive one. Each individual carries two genes in the locus for PKD, one maternal and another paternal, from which the following three combinations can emerge: **PP** as the genotypic form of positive homozygotes, **Pp** as the genotypic form of positive heterozygotes and **pp** as the genotypic form of negative homozygotes. As PKD is considered to be of dominant inheritance, the individual needs to possess the **P** gene to present the disease. Thus, phenotypically positive (with the disease) are considered to be those individuals who present the **PP** and **Pp** genotypes. However, positive homozygotic individuals (**PP**) are considered to be unviable, and kittens die soon after birth or even inside the mother's womb. To give an example, if the father were **Pp** and the mother **Pp**, this would result in 25% of **PP** animals, 50% **Pp** and 25% **pp** (phenotypically speaking, 75% of kittens would be positive and 25% negative). According to this theory, two parents who are genetically **pp** (recessive and negative) cannot produce positive kittens, unless there is a genetic mutation. PKD is called autosomal because it is unrelated to sex (BILLER; DIBARTOLA; EATON, 1996). Ultrasound imaging allows for 100% of specificity and 75% of sensibility after the thirteenth week of age, and 100% specificity and 91% sensibility after the thirty-sixth week (BILLER; DIBARTOLA; EATON, 1996). Other authors report that the use of 7.5 MHz transducers allows for a 98% sensibility level in cats older than ten months (LYONS, 2000).

S16.3 - THE ROLE OF THE PHARMACIST IN THE VETERINARY INDUSTRY

LUCIMARA CRISTIANE TOSO BERTOLINI

OUROFINO, Ribeirão Preto, SP, Brasil

• International and National Panorama of Veterinary Pharmaceutical Market .

• International Regulatory Requirements : an approach for reaching the Global Market

• Main Therapeutic classes involved in the Veterinary area.

• Pharmaceuticals Form: peculiarities and challenges in the Veterinary area.

• A new perspective for the Pharmacist Professional in the Veterinary Industry.

• Human Medicines x Veterinary Medicines: Parallel in the National Setting

• Bioequivalence: Case Study in the Veterinary area

SYMPOSIUM 17 - NEW PERSPECTIVES FOR THE TREATMENT OF INFECTIOUS DISEASES

S17.1 - NEW ANTI-INFECTIOUS AGENTS FROM BRAZILIAN MARINE INVERTEBRATES

ROBERTO G. S. BERLINCK, MIRNA H. R. SELEGHIM, SIMONE P. LIRA, MIRIAM H. KOSSUGA, ANDRÉA M. NASCIMENTO, TATIANA O. LIRA, MARIA FERNANDA DE OLIVEIRA, EDUARDO HAJDU, GUILHERME MURICY, ROSANA M. DA ROCHA, GISLENE G. F. DO NASCIMENTO, MARCIO SILVA, OTÁVIO THIEMANN, GLAUCIUS OLIVA, ANA O. DE SOUZA, PAULO R. R. MINARINI, CÉLIO L. SILVA, SOLANGE PEIXINHO

IQSC/USP, São Paulo, SP, Brasil

During the past 20 years, marine organisms including marine invertebrates and marine microorganisms, have proven to be an exceptional source of new secondary metabolites (natural products), with completely novel chemical structures and potent biological activities. We have screened over 500 samples of marine invertebrates, including marine sponges, ascidians, octocorals and bryozoans, searching for crude extracts active against antibiotic resistant bacteria, against *Mycobacterium tuberculosis* and as inhibitors of *Leishmania tarentolae* adenosine phosphorribosyl transferase (L-APRT). Several extracts displayed activities and were subsequently investigated toward the isolation of active compounds. The majority of the active compounds isolated were alkaloids, belonging to different structural classes, such as guanidines, alkylpyridines, alkylpiperidines, bromotyrosine derivatives and alkylaminoalcohols. Sulfated sterols and polyketides were isolated as inhibitors of L-APRT. The pharmacologicial evaluation of pure compounds demonstrated that various compounds presented activity in the range of nM-?M level. The results obtained reinforce the importance of the search for new biologically active compounds from natural sources that can be developed as new drug leads.

S17.2 - LEUKOTRIENES: NEW STRATEGY FOR IMMUNOLOGIC INTERVENTION IN THE ANTIMICROBIAL HOST DEFENSE

ALEXANDRA IVO DE MEDEIROS, CAMILA P. PERES, CÉLIO LOPES DA SILVA, LUCIA HELENA FACCIOLI

DACTB - Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

The resistance to *Histoplasma capsulatum* and *Mycobacterium tuberculosis* in mammals is dependent on a cellular immune response mediated by $CD4^+$ and $CD8^+$ T cells and mononuclear phagocytes which produce essential cytokines to control these diseases. We have recently demonstrated a protective role of endogenous leukotrienes (LTs) in animal models of *H. capsulatum* and *M. tuberculosis* infection. Leukotrienes were associated with a survived, clearance of microorganisms and essential cytokines production to control these diseases. Alternatively, tissue levels of LTs at the site of the infection might be amplified by their exogenous administration. In this scenario, LTB_4 would be the preferred candidate for exogenous delivery because of its broader antimicrobial activity and less propensity for myotropic and edemagenic effects. However, to increase the short biological half-life of LTB_4, several formulations and carrier systems have been developed using liposomes or microspheres. These carriers share some of the following properties: protection of leukotrienes degradation allowing its administration by different routes, including mucosal, and the ability to sustain the leukotrienes release over an extended period of time. These studies are important strategies for *in vivo* administration of LTB_4 in experimental model and may be used to treat human patients with histoplasmosis and tuberculosis.

S17.3 - THE CONTRIBUTION OF INTEGRONS TO THE DISSEMINATION OF EXTENDED-SPECTRUM - LACTAMASES (ESBL)

ELSA MASAE MAMIZUKA

Faculdade de Ciências Farmacêuticas-USP, São Paulo, SP, Brasil

Genes encoding ESBL are usually located on conjugative plasmids, although many of the most recently described ESBL genes are frequently found within integron-like structures. On the other hand, ESBL-producing isolates are usually resistant to other antibiotics such as aminoglycosides, tetracyclines, chloramphenicol, trimethoprim, sulfonamides, or quinolones, often due to the presence of different resistance genes on transferable elements such as plasmids, transposons, or integrons and/or genetic structures generated by combinatorial evolution of different interactive pieces. The fact that ESBL genes could be acquired by strains harboring particular integrons may enlarge the possibilities of selection of these isolates by a variety of different antimicrobials. Moreover, ESBL genes can be located on integrons, which may facilitate the spread of such genetic Integrons are natural highly efficient recombination and expression systems able to capture genes as part of genetic elements known as gene cassettes. The widespread presence of *GNB* containing Antimicrobial Resistant Integron observed among the community-based population indicates the existence of a substantial reservoir potentially feeding multidrug resistance in the nosocomial setting ESBL located on integron-like structures are also being increasingly reported worldwide.

SYMPOSIUM 18 - BRAZILIAN BIODIVERSITY

S18.1 - PLANT DIVERSITY MANTAININING METHODOLOGIES OF RESTORATION OF RIVERINE FORESTS USED BY THE LABORATORY OF ECOLOGY AND FOREST RESTORATION (LERF/ESALQ/USP)

RICARDO RIBEIRO RODRIGUES & SÉRGIUS GANDOLFI

LERF/ESALQ/USP, Piracicaba, SP, Brasil

Due to the legal and environmental questions, the restoration of degraded areas has nowadays mainly focused in the riverine environment. Although riverine forests have been protected by the legislation since almost a half of century, they were not saved from the degradation. With the fulfillment of the legal requirements by the supervisor agencies in the last decades, judicial collections compelling the conservation and restoration of riverine formations have become more and more frequent in the quality of the proposed actions. However many of these requirements did not find endorsement in the scientific area, leading to an increase in the research for riverine forests in the different fields of the research. Today a bulk of evidence concerning to distinct features of riverine forests has been obtained, such as geomorphology, grounds and hydrology as well as concerning to biotic such as the kind of flowers of these forests and its standards, the nomenclature of these formations, aspects off the dynamic of this vegetation, involving phenology, adaptative strategies, avifauna, ictiofauna, groups of mammals and insects. The significant knowledge concerning to tropical forests and mainly on the involved processes in its dynamic no mater if in preserved remaining areas as well as in the different grades and types of degradation, have led to a significant change in the orientation of programs of handle and forest restoration. Recently the most important discussion is concerned to the use of this knowledge in the different areas focusing the actions for conservation, handle and regeneration of the riverine forests. Some theoretician and methodological features concerning to forest restoration have been exhaustingly discussed and tested. One point of total agreement is that the success in the re-establishment of the biodiversity of the riverine forests involves not only the vegetation as well as the distinct groups of fauna and its ecological relationships. We briefly present the methodology of recuperation of degraded areas used by the Laboratory of Ecology and Forest Restoration (LERF/ESALQ/USP) which has three main issues: the first one is to re-establish the actions of recuperation, not forgetting the potential of auto recuperation of these areas; the second is that these initiatives can be done with high diversity, to guarantee the capacity of auto-perpetuation as well as to keep the restoration of the vegetal diversity; the third is that all actions allow an self-sufficiency of the executors permitting a permanent of recuperation of these areas. These concerns have as consequences the reduction of costs in the recuperation and mainly to guarantee the success of recuperation and perpetuation of the restored forests. It is worth to emphasize that although the success of the initiatives of recuperation of riverine forests, further advances must be taken in account, due to the presence of biological data from distinct species of these areas.
"Use of diversity in the creation and establishment of conservation units"

S18.2 - AMAZONIAN BIODIVERSITY - WHAT IS BEYOND FORMS AND COLORS?

ADALBERTO LUÍS VAL

Laboratory of Ecophysiology and Molecular Evolution, National Institute for Research in the Amazon, Manaus, AM, Brasil

Amazonian biodiversity is often referred to as panacea of this new millennium. In fact, it is more than a scientific or economic issue. Biological diversity (=biodiversity), in all of its manifestations, is an essential component of the quality of human life. As it encompasses all biological organization levels, from molecular to behavioral level, from species to populations, from habitats to ecosystems, biodiversity in the Amazon reach the climax. The characteristics of each of these levels have co-evolved and have been shaped during millions of years, preserving up to date, in many cases, the solutions developed by the organisms to face the regular natural constraints of their environment. Indeed, as biodiversity affects human life through enjoyment or through suffering, caused by the effects of pests and parasites or caused by reduction of food, the study of all dimensions of biodiversity is essential. In the Amazon, this is not a simple task. The Amazon region extends across several countries in South America, with an area equivalent to 7.5 million square kilometers, 65% of which located within the Brazilian territory. The biological diversity housed in this area has no parallel in the world. Examples are in excess as the new frontier in biology is hidden in delicates interactions of tropical organisms among themselves and with their environment. However, it is unknown what is beyond the forms and colors of Amazonian organisms. The few examples coming from plants and animals are exciting.
(Part of the examples to be shown is from original studies supported by CAPES, CNPq, FAPEAM and FINEP)

S18.3 – USE OF DIVERSITY IN THE CREATION AND ESTABLISHMENT OF PROTECTED AREAS

ADRIANO PAGLIA

Conservação Internacional – CI-Brasil, Belo Horizonte, MG, Brasil

Brazil is the 5th largest country in the world, with 3.5 million km^2 of coastal waters, 5 major terrestrial biomes and the 1st place in terrestrial biodiversity. We know about 1.8 million species. The country harbors 13% of all described amphibian species in the world, 10% of all mammals, and 19% of all plants. There are 9,126 endemic plant species and 179 endemic plant genera. Despite these impressive numbers, biodiversity in Brazil is in jeopardy. According to the official list of threatened species there are 633 animals and almost 1.500 plant species on the brink of extinction. The threat factors are habitat destruction, illegal hunting and harvesting and invasive species. One of the most efficient ways to prevent species extinction is the creation of Protected Areas (PAs). In Brazil, there are 468 Strictly PAs, covering ~37 million hectares (less than 4% of the country's territory). Knowing that the main goal of strictly PAs is biodiversity conservation, it is easy to conclude that the definition of new PAs must be done using the information on the distribution of threatened species. This premise was used in the Conservation Priority-setting Workshops promoted by Brazilian Ministry of Environment. More recently, other techniques such as Gap Analysis and Key Biodiversity Areas, based on more accurate data on distribution of threatened and endemic species, have greatly contributed to the process of creation and implementation of new Protected Areas.

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Round Tables

ROUND TABLE 1 - STEM-CELLS RESEARCH

RT1.1 - STEM CELL THERAPY: BIOLOGICAL AND ETHICAL ASPECTS

MARCO ANTONIO ZAGO

Faculty of Medicine and Center for Cell Therapy of Ribeirão Preto, SP, Brasil

Stem cells play a key role in cell therapy, although they are not the only agents for this type of treatment that includes also cells that modify the biological response such as dendritic cells and lymphocytes. They are classified as embryonic or adult tissue-specific stem cells that can be obtained from most of the human adult tissues (nervous system, muscles, epithelia, dental pulp); in the bone marrow there are two different types of stem cell: hematopoietic precursors and mesenchymal stem cells. In addition, embryonic stem cells lineages can be derived by the technique of the somatic nucleus transfer. A wide spectrum of diseases are candidate for treatment with cell therapy, although bone marrow transplantation is the only well consolidate form of stem cell therapy in human at present. In addition to the biological and technical difficulties related to the use of stem cells for therapy in humans, there are legal and ethical questions, owing to the fact that treatment or research with embryonic stem cells implies the destruction of the embryo in its early development stages.

RT1.2 - CELL THERAPIES IN NEUROLOGICAL DISEASES

ROSALIA MENDEZ-OTERO

Instituto de Biofísica Carlos Chagas Filho - UFRJ e Instituto do Milênio de Bioengenharia Tecidual, Rio de Janeiro, RJ,

Neurons in the Central Nervous System (CNS) do not regenerate after injury and functional deficits occurs after lesions of the CNS. This central dogma has been challenged by recent discoveries that neurogenesis and takes place continuously in the adult CNS. However, although present the neuronal regeneration is not sufficient to replace the neuronal loss and restore function after CNS lesions. Recently, several research groups are studying stem cells (ST) as potential sources for cell therapies to restore function in the CNS. Stem cells are defined by their capacity of self-renowal and for their plasticity. Embryonic stem cells are very potent in animal models but several questions have to be solved before clinical trials are available with these cells. The use of bone marrow stem cells for cell therapies has been widely investigated for treatment of cardiovascular and neurological diseases. Although less potent then the embryonic stem cells they are safer and their use do not involve ethical and legal issues. In this talk we will review the clinical protocols using bone marrow stem cells for neurological diseases.

RT1.3 - THERAPEUTIC APPLICATIONS OF STEM CELLS AND THE ROLE OF CLINICAL AND RESEARCH LABORATORY

JÚLIO CÉSAR VOLTARELLI

Bone Marrow Transplantation Unit and Center for Cell Therapy, University Hospital and Regional Blood Center, School of Medicine of Ribeirão Preto, University of São Paulo, Brazil

Hematopoietic stem cells from adult bone marrow have been employed for several decades to treat potentially fatal hematological diseases after high dose chemotherapy and/or radiotherapy. More recently, the same strategy has been used for severe/refractory autoimmune and inflammatory diseases such as systemic lupus erythematosus, multiple sclerosis and type I diabetes mellitus. The possibility that stem cells from embryonic tissues, adult bone marrow and even adult specialized organs can differentiate into functionally active somatic tissues opened a window for utilization of those stem cells in the regeneration of a variety of damaged organs. However, this issue is still very controversial and much laboratory research has to be done to characterize the various types of stem cells and their pathways of differentiation to functional tissues. Also, the clinical laboratory is very much involved in the collection, preservation and manipulation of stem cells to be utilized in therapeutic protocols.

ROUND TABLE 2 - BIOTECHNOLOGY, INDUSTRY AND UNIVERSITY

RT2.1 - BIOMEMBRANE® (BIOCURE) OF NATURAL LATEX FROM THE *Hevea brasiliensis* TREE: FROM THE BENCH TO THE PHARMACY SHELF.

JOAQUIM COUTINHO NETTO

Departamento de Bioquímica e Imunologia, FMRP-USP, Ribeirão Preto, SP, Brasil

The search for specific agents to improve healing is as old as the practice of medicine. Chronic, nonhealing wounds are an important cause of morbidity in surgical and medical patients. Wound healing cannot occur without angiogenesis, as the vasculature comprises up to 60% of repair tissue, and the denomination granulation tissue for the temporary organ of repair is derived from the prominence of its vessels. An abundant blood supply is obviously necessary to meet the enormous local metabolic demands of debridement and fibroplasia in the repair region. The most frequent common denominator in nonhealing wounds is the inadequate tissue oxygenation, which impairs normal healing and facilitate infection. The avaiability of substances capable of stimulating the process of wound repair is limited and potentiallly costly. In 1995, Fatima Mrue and I reported that the biomembrane prepared from the natural latex of the *Hevea brasiliensis* tree induces angiogenesis in many models of experimental animal, as cornea and the chorioallantoic membrane of embrionated chicken eggs and the rate of wound healing.
The beneficial effects from the topical application of the biomembrane as a new angiogenic dressing to treat chronic human ulcers and the significant advantages in terms of medical utilility will be discussed.

RT2.2 - RELATIONSHIP INDUSTRY-UNIVERSITY: A POSITIVE ALLIANCE

ANA LÚCIA DELGADO ASSAD

YBIOS, Barueri, SP, Brasil

Public policies have encouraged and promoted actions aimed at developing integrated projects between universities and companies, in the attempt to find products and processes of social benefit. If these actions are to turn into positive results, each of the agents has to act according to its specific vocations, which are summarized below:
• The function of universities and research institutes is to create knowledge, ideas and innovations and to educate and train human resources in different knowledge areas;
• companies are responsible for scale up, investments in R&D, innovative processes and the production of goods and services;
• the government is responsible for establishing guidelines and public policies, stimulating research and development and educating the human resources the country needs, as well as to regulate relations and how products are put on the market.
Can a relation be constructed in which all parties receive benefits? Are there any bottlenecks to be overcome? Can we point out positive results?
These are some of the questions to be discussed during CIFARP, with a view to broadening the debate and contributing to the development of Pharmaceutical Sciences and to the creation of new pharmaceutical products and processes.

RT2.3 - THIRD MILLENNIUM ALCHEMY: HOW TO CHANGE LEAD INTO GOLD IN HEALTH SCIENCES.

PIERRE SIROIS

Institute of Pharmacology of Sherbrooke-Medical School-Université de Sherbrooke, Sherbrooke, Quebec, Canada

The steps leading from the creation of an innovative University Hospital (CHUS) to a biomedical park will be presented. The School curriculum was elaborated in the early 60ies, putting forward novel teaching approaches, and state-of-the-art research facilities were built. At the beginning of the 90ies, planning was done to develop into a biomedical park. The Institute of Pharmacology of Sherbrooke (IPS) (7500m2) and the Clinical Research Center (7000m2) were built and connected to the Medical School. These 2 entities have been equipped with the latest technologies and staffed with first class expertise. The 3rd floor of the IPS (2500m2) was kept as an incubator for biotech companies in which 5 companies are already growing. Overall, the whole complex has more than 100,000m2 of research and patient care facilities all interconnected. Recently another larger incubator (6,000m2) was built to help for secondary incubation. I created 2 companies in the IPS; one called IPS Therapeutique is a Contract Research Organization focusing on the cardiotoxicity of novel drugs before entering clinical trials. Another called IPS Pharma is developing new drugs and innovative therapeutic approaches for targeted pathologies in inflammatory and cardiovascular diseases. One of our approaches is focused on the treatment of vascular and neuropathic complications associated with diabetes. Our lead compound (Intrakin), a first-in-a-class brakykinin B1 receptor antagonist, enters phase 1-a clinical trials. The B1 receptors were discovered by Regoli et al in the early 80ies and the technology was transferred by the University of Sherbrooke to IPS Pharma who exploits it under a licensing agreement. In brief the B1 receptor is absent in healthy individuals and animals but is newly expressed in inflammatory conditions including diabetes and increases microvascular permeability in selected tissues. Protein and enzyme leakages from the microcirculation have deleterious effects and are responsible for the diabetic complications including painful neuropathy, nephropathy, retinopathy and cardiomyopathy. The company has benefited from various investments from VC to get started, has now 24 employees and is growing. Information and comments will be presented regarding the organization, financing, development of biotechs within University structure and mission as well as prerequisites such as technological platforms with an adequate market, University structures and commitment, local financial organizations, roles of Governments, and very importantly, “transgenic” researchers with an entrepreneurial spirit and motivation.

ROUND TABLE 3 - DRUGS DEVELOPMENT

RT3.1 - THE ROLE OF SMALL COMPANIES ON THE DEVELOPMENT OF PHARMACEUTICALS

JOSÉ MACIEL RODRIGUES JÚNIOR

NANOCORE Biotecnologia Ltda. Incubadora SUPERA, Ribeirão Preto, SP, Brasil

The introduction of new pharmaceutical and biotech products in the market is becoming more and more difficult, due to the costs to develop new drugs and to prove safety statements. In the Brazilian context, the recently recognized Intellectual Property Law imposes the need of innovation, leading the Brazilian companies to reorganize themselves in order to introduce new products in the market. Among the existent alternatives to accelerate this process, we can point out the introduction of R&D departments in the companies and/or the establishment of partnership with Academy and Institutes of Technology. In both situations it is important to emphasize the need of changes in the way of work, the need of well trained Human Resources and, face to the legal statements, which difficult the interactions of public institutions with the private sector, many obstacles are still in the roadmap. That is indeed remarkable that for both situations the success can be reached in the medium or long term. It is very recent the introduction of small technology companies in this context and it is presented as alternative for reduce the timing of success and to reach new products in the market by contract services. In this talk, the experience of a technology based small company, which is developing high tech R&D projects in partnership with national and transnational companies, will be presented. The business and professional opportunities will be discussed.

RT3.2 - MEDICINES IN THE SUS: INNOVATION AND ITS CHALLENGES

JOSÉ DA ROCHA CARVALHEIRO

FIOCRUZ - Fundação Oswaldo Cruz, Rio de Janeiro, RJ, Brasil

The elements of the Health Industrial Complex can be grouped in two segments: one related to medical services, and another to the production of health products (vaccines; blood products; medicines; diagnostic reagents and kits; surgical medical equipment). Medicines in particular present a special character: they are both an therapeutic instrument and also a merchandise. This dialectic relation has been extensively explored by private producers and by the State. Is frequent to consider that the State has the access as main concern, while the private producers make of the profit its main motivation. Being a great purchaser the State is an important factor that can facilitate the development of innovations ("pull"). The development complexity is generally presented by the "big pharma" as an argument for the raised unitary prices of its products. They argue with extremely high costs and with long lasting periods to transform an invention into innovation (product in the market). In particular the final stage of evaluation of the innovations (clinical trials) is pointed as an important factor in the increase of the costs and delaying the release by regulatory agencies. For this reason, countries with an Universal Health System presents competitive advantages in the introduction of innovations. The typical example is the National Health System in UK, and could be our SUS in Brazil.

RT3.3 - TRAINING AND PREPARATION OF TECHNICIANS FOR THE PHARMACEUTICAL INDUSTRY

JOÃO BATISTA DE OLIVEIRA

Ministério da Saúde, Brasília, DF, Brasil

The academic training of technicians for employment in the pharmaceutical industry is complicated by the differing requirements by the university and commercial environments. The university may sometimes feel disinclined to invest in programs that are vocational rather than academic in nature, and that demand practical training tailored to the specific needs of employers. Moreover, the modern technician must adapt to the needs of the 21st century where self-motivation and ethical considerations also enter. He must have good communication skills and should inspire others with an example of independence and self-starting enthusiasm. The pharmaceutical industry may require skills in areas as diverse as quality control management, drug regulation, pharmacotechnical development, automation, project management, production engineering, maintenance, computation of project costs, etc.
The program for training of pharmaceutical technicians, including seminars and workshops, is supported by the Ministry of Health in partnership with ANVISA, ABIQUIF, FEBRAFARMA, ALFOB, ISPE and participating universities.

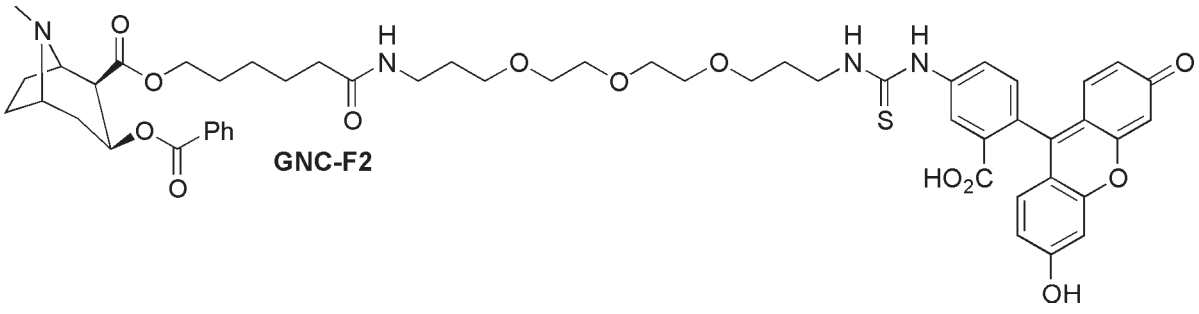
ROUND TABLE 4 - DESIGNS OF NEW DRUGS

RT4.1 - SYNTHESIS AND PROPERTIES OF FLUORESCENT COCAINE PROBES: TOOLS FOR THE HIGH-THROUGHPUT SELECTION OF COCAINE BINDING ANTIBODIES

MICHAEL M. MEIJLER
Michael M. Meijler, Gunnar F. Kaufmann, Longwu Qi, Masayuki Matsushita and Kim D. Janda

The Scripps Research Institute, La Jolla, CA, USA

Cocaine is a highly addictive drug and despite intensive efforts, effective therapies for cocaine craving and addiction remain elusive. In recent years, we and others have reported advances in anti-cocaine immunopharmacotherapy based on the generation and/or administration of antibodies capable of sequestering the drug before it reaches the brain. In an effort to identify high affinity therapeutic cocaine antibodies, either whole IgGs, or other antibody constructs, fluorescence spectroscopic techniques could provide a means of implementing molecular engineering selection strategies. We report the synthesis of a series of cocaine fluorophore conjugates (GNC-F1, GNC-F2, GNC-I). The functional evaluation of these compounds against antibodies generated via crystallographic analysis/molecular engineering and commercially available anti-cocaine antibodies with a wide range of binding affinities for cocaine. From these studies we found that GNC-F2 fluorophore faithfully reproduces affinity constants obtained using tritium-labeled cocaine. We anticipate that GNC-F1 because of its ease of synthesis and luxury of being non-radioactive material will find use both as a tool for bioimaging and high-throughput engineering of therapeutically interesting antibodies for the drug of abuse.



GNC-F2

RT4.2 - MOLECULES ARE LIKE HUMANS - THE REPRESENTATION OF MOLECULES IN DRUG DESIGN

JOHANN GASTEIGER

Computer-Chemie-Centrum, University of Erlangen-Nürnberg, Erlangen, Germany

The international language of chemistry is a two-dimensional structure diagram. However, molecules are three-dimensional objects much like human beings. Molecules have surfaces, are flexible, and can show chirality. Computational approaches to the generation of 3D molecular models, [1] to the calculation of molecular surface properties, to the generation of multiple conformations, and to the quantification of molecular chirality will be presented. It will be shown how these structure representations can be applied to ligand-based drug design, to the separation of molecules with different biological activity, to finding new lead structures, to the definition of the diversity of a library, and to the analysis of high-throughput screening data.[2]

[1] http://www2.chemie.uni-erlangen.de/software/corina and: http://www.mol-net.de
[2] *Chemoinformatics – A Textbook,* J. Gasteiger, T.Engel, Editors, Wiley-VCH, Weinheim, 2003

RT4.3 - CURRENT TRENDS IN MOLECULAR MODELING APLLIED TO DRUG DESIGN

CARLOS HENRIQUE TOMICH DE PAULA DA SILVA

Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

Medicinal chemistry is a science that investigates bioactive substances in respect to discovery, design and development of novel drugs. Current trends in drug design involve molecular modeling as a crucial step. Recent efforts provide compelling evidence that molecular modeling is a power-and successful tool when practiced in an integrated fashion involving structural and molecular biology, organic synthesis and biochemistry in the drug discovery process. Treatments of important diseases have been improved with majority participation of molecular modeling. Theoretical methods include homology modeling of target proteins, electronic properties of whole proteins, design and optimization of ligands, pharmacophore modeling, screening lead compound scaffolds, novel quantum methods for calculating binding energies, virtual high-throughput screening, structure-based drug design, quantitative structure-activity relationship (QSAR) studies, and screening methods for predicting properties such as ADMET, water solubility, Rule of 5 and others. Recent progress and significant contributions in computer-aided drug design are discussed.

ROUND TABLE 5 - RESEARCH AND DEVELOPMENT OF VACCINES

RT5.1 - RESEARCH AND DEVELOPMENT OF DNA VACCINES

CELIO LOPES SILVA, KARLA M LIMA, JOSE MACIEL RODRIGUES JUNIOR, LÚCIA H FACCIOLI, ANDREY LAGE.

[1] FMRP-USP, [2] Nanocore Biotecnologia Ltda, [3] FCFRP-USP, [4] FMV-UFMG.

During the past 20 years, the technologies applied to vaccine development have radically changed from using the pathogen itself to harnessing the developments of a variety of technologies to use new forms of antigens (such as the gene encoding an antigen – DNA vaccines), new adjuvants, new delivery systems and the prime-boost concept. Despite the successful development of many vaccines, it has not been feasible in many cases to simply use the same approaches to make new vaccines. When the concept of a DNA vaccine first popped onto the scene in the early 1990‘s, it seemed too simple and too easy to be true. DNA vaccines rely on a plasmid to encode an antigen that when taken up by the immune system, elicits a response strong enough to protect against infectious disease3. Such plasmids can hold multiple genes for multiple antigens and recombinant DNA technology offers an easy way to mix-and-match antigens in new combinations. Experimental data showed for several years that rodents injected with foreign genes expressed antigens, produced antibodies, stimulated cell mediated immune response and achieved a protective and long-lasting immune response. The excitement waned, though, as products moved into primate studies and human safety trials. In the jump to primate immune systems, Naked DNA failed to make the grade, generating little-to-no response. Similar results were observed in our own work. We have previously demonstrated that a DNA vaccine encoding the mycobacterial 65kDa heat shock protein (hsp65) was able to protect mice and guinea pigs from challenge infection with a virulent strain of *Mycobacterium tuberculosis* and also able to cure previously infected mice when administered as Naked-DNA by intramuscular injection. We also showed that the therapeutical use of DNAhsp65 in combination with antimycobacterial drugs shortens the duration of tuberculosis (TB) treatment, improves the treatment of latent TB infection and is effective against multi-drug resistant TB. When we tested the same preparation of Naked-DNA in cattle to prevent these animals against TB infection, it was not able to induce immunogenicty as observed in mice. Thus, several strategies were introduced in our work to overcome this situation. We will show here the development of a simple technology based on a single dose/prime-boost formulation to eficiently immunize large animals with a DNA vaccine.

RT5.2 - IMMUNOBIOLOGICAL SELF-SUFFICIENCY INCLUDED IN THE BASIC SCHEDULE OF VACCINATIONS

AKIRA HOMMA

FIOCRUZ - Fundação Oswaldo Cruz - Diretor , Bio-Manguinhos, Rio de Janeiro, RJ, Brasil

The National Self-sufficiency of vaccines is included in the basic calendar of immunization. Amongst the governmental programs, prevention – control and eradication of immunopreventable diseases – it is regarded as the best cost-benefit. The implementation of right policies and strategies, continuously and systematically for years, resulted in the eradication of smallpox in the 70s, eliminated poliomyelitis 14 years ago, and measles 4 years ago; and the other immunopreventable diseases have had the lowest notification of the Public Health history in Brazil. In this context, vaccine-manufacturing laboratories have played a strategic role producing the vaccines required by the National Program of Immunization (PNI). Three public laboratories (Bio-Manguinhos/ Fiocruz, Butantan, and Tecpar) and a private one (FAP) produce or are in the process of incorporation of production technologies of all vaccines included in the basic calendar of PNI. In order to reach this level, the vaccine-manufacturing laboratories had governmental support, but they also had to gain PNI and public reliability and credibility assuring the supply of high quality vaccines in amounts and time due. Technological innovation activities, which are essential for the future of the country in this area, have also been supported by governmental agencies of foment, which allow us to foresee the development of some vaccines and immunobiologicals that are important to the country.

RT5.3 - THE SOCIAL ROLE OF NATIONAL PRODUCTION OF DRUGS AND VACCINES

ISAIAS RAW

Fundação Butantan, São Paulo, SP, Brasil

Vaccination is a public health program that must cover each family. Butantan produces more than 80% of the vaccines for children, young adults and over 60 years, at cost that makes possible public free immunization, creating technology and innovation competency. A rotavirus vaccine that covers all continent serotypes and freely supply of lung surfactant for premature, at a third of the price of the imported equivalents, is expect to reduce by half one year old child mortality.
It is a shocking experience to witness old people and a large proportion of the population with an income of US$ 100 per month, spending half to fill a basket with drugs, most of them they do not required, and part without any therapeutic value. Today the Government supplies all AIDS patient with the required drugs. Formulation by public pharmaceutical companies at reduced cost allows for free distribution drugs and will make possible in the near future to cover other chronic diseases, like hypertension, diabetes and hepatitis.
The introduction of generics in Brazil was an important conquest. Treatment requires an effective medicine, which is not always the “new” products, announced in the media (“ask your doctor”). The hundred different drugs for hypertension are not better than some of the old diuretics that cost hundred times less.

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Courses

COURSE 1 - CHRONIC LYMPHOPROLIFERATIVE ILLNESSES

C1.1 - GENERAL ASPECTS OF THE LYMPHOPROLIFERATIVE ILLNESSES AND THEIR CLASSIFICATION

MARIA DE LOURDES LOPES FERRARI CHAUFFAILLE

Fleury - Centro de Medicina Diagnóstica, São Paulo, SP, Brasil

Chronic lymphoproliferative disorders originate from B or T lymphocytes and present different morphological and clinical features. The most frequent are: chronic lymphocytic leukemia (CLL), follicular lymphoma, mantle zone lymphoma and large cell lymphoma. CLL is a neoplastic disorder characterized by the accumulation of small mature lymphocytes in peripheral blood, bone marrow and lymphoid tissues. It is the most frequent leukemia in adults in the Western world and most of the cases occur in elderly patients. Immunephenotyping is important for the characterization of this disease and as well as to differentiate it from other malignant lymph proliferations. Mature B cell disorders are characteristically CD 19, CD 5 and CD 23 positive. Cytogenetics helps in diagnosis, allowing the differentiation of CLL from other lymph proliferations as mantle zone lymphoma, but the greatest interest in identifying chromosomal abnormalities is for prognostic reasons, better sub-classification and to direct the most appropriate therapeutic choice. Chromosomal anomalies have been described in 30 to 50% fo CLL cases. The most frequent abnormality seems to be trisomy 12, an unfavorable abnormality, followed by deletion 13q that is considered indicative of longer survival. Deletion 11q is related more advanced disease while deletion 17p with shorter survival. FISH, a molecular cytogenetic technique helps to improve the rate of abnormality detection.

C1.2 - LABORATORIAL DIAGNOSIS OF CHRONIC LYMPHOPROLIFERATIVE ILLNESSES

SÉRGIO LUÍS RAMOS MARTINS

Fleury - Centro de Medicina Diagnóstica, São Paulo, SP, Brasil

Chronic lymphoproliferative disease can develop from B and T cell lymphocytes, those origin wide spectrum of distinct clinical and morphologic entities. B cell mature lymphocytes are the most frequent disorders. In this group, the most important diseases are chronic lymphocytic leukemia (LLC), follicular lymphoma, mantle cell lymphoma, and diffuse large B cell lymphoma.
LLC is a malignant disorder characterized by accumulation of small and mature lymphocytes in the peripheral blood, bone marrow, and lymphoid tissue. LLC is the most frequent leukemia among adults, and the majority of all cases occur in elderly. The diagnostic of LLC was improved by immunophenotypic studies. Currently, immunophetype allow us to distinguished LLC of others chronic proliferate diseases, such as follicular lymphoma, mantle cell lymphoma, lymphoplasmacitic lymphoma, and large B cell lymphoma. LLC has a mature B cell phenotype, expressing CD20, monotype immunoglobulin light chain, CD23, and co-expression of CD5 on membrane. Cytogenetic study is auxiliary to diagnose, and it is remarkably important to differentiated LLC of mantle cell lymphoma. In addition, cytogenetics findings can stratify LLC in different prognoses groups. Chromosomes abnormalities have been detected by classical citogenetics at 30 to 50% of cases of LLC. The most common finding described by several authors is a presence of trisomy of chromosome 12, followed by Del 13q that indicates a good prognosis. The Del 11p is related with disease at stage more advanced, while Del 17p is associated with worse prognosis.

COURSE 2 - AN INTRODUCTION TO CHEMILUMINESCENT DETERMINATIONS IN THE MICROPLATE

PAUL HELD

Bio Tek, Winooski, VT, USA

Microplate readers were first developed in the early 1970's primarily to measure the color change produced by enzymatic reactions, such as those taking place in enzyme-linked immunosorbent assays (ELISAs). Microplates provide a compact, standardized format for 96 samples, offering advantages over conventional tube based assay methodology, based primarily on an increased sample throughput, which facilitates the automation of ELISAs. Over the past 30 years, assays have evolved from those based on simple absorbance measurements to those based on the more sensitive fluorescence and luminescence methods. In parallel, microplate readers have been developed to perform these different tasks in the standardized 96 and 384 well formats. Here we describe the use of microplate readers to make chemiluminescent determinations. An overview of some of the molecular basis of the chemistries involved in the generation of luminescence will be presented. In addition, a comparison of luminescence to absorbance and fluorescence techniques in regards to advantages and disadvantages will presented along with some example data. Along with a brief overview of instrument design, several different examples of luminescent techniques will be discussed and how they are accomplished in microplates.

COURSE 3 - PHARMACEUTICAL CARE: KNOWLEDGE IN COMMUNICATION AND THERAPEUTICS

DÍLSON BRAZ DA SILVA JR, DIVALDO P. DE LYRA JÚNIOR, JULIETA UETA

Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

The objective of this course is to introduce the audience in the concepts, philosophy and cases of pharmaceutical care practice. After some introductory knowledge to be presented at the beginning of each session, cases and Drug Related Problems identification and solution will be simulated and dramatized using communication and clinical skills to illustrate the practice of pharmaceutical care in different healthcare settings.

COURSE 4 - DRUG SURVEILLANCE IN BRAZIL

NAIR RAMOS DE SOUZA

Unidade de Farmacovigilância da ANVISA, Brasília, DF, Brasil

Brazil has 178 million inhabitants in over 5,500 municipalities, is among the 10 largest pharmaceutical markets in the world with: 4,700 drug registration holders, 52,000 drug presentations, 10,000 pharmaceutical products and annual sales estimated at approximately US$4.8 billion in 2003. In addition, Brazil has a social and cultural diversity that makes drug market regulation a more complex issue. In 1999, the Brazilian National Health Surveillance Agency started the consolidation process for the National Pharmacovigilance System, after establishing the National Centre for Drug Monitoring, headquartered at ANVISA's Pharmacovigilance Unit and created by Ministerial Decree MS no. 696, of 7 May 2001. In August of the same year, Brazil was included in the International Drug Monitoring Programme co-ordinated by the WHO Collaborating Centre for International Drug Monitoring, Uppsala, Sweden. One of the difficulties to face is the lack of tradition among health professionals and service directors of notifying the occurrence of drug adverse events. By June 2005, CNMM had received 4,876 notifications, which provided important information for the decision making process concerning pharmaceutical market regulation. Through the analysis of ADR notifications, it is possible to detect signs, assess the post-market benefit/ risk ratio of drugs, favouring the development of Pharmacovigilance at regulatory level.

COURSE 5 - USE OF LC-MS^n IN PHARMACEUTICAL SCIENCES

NORBERTO PEPORINE LOPES

Departamento de Física e Química, Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

Analytical methods are available to detect and quantify drugs, natural products and synthetic compounds by high performance liquid chromatography (HPLC) with UV-VIS detection. The photodiode array detection assisted by spectral data is the most applied analytical procedure. However, identification of several organic compounds is limited since a complete chromatographic resolution for all chromophores compounds is required to assure a similarity conclusion. On the other hand, liquid chromatography with photodiode array detection combined with tandem mass spectrometry (LC-MS/MS) is a powerful analytical technique for qualitative and quantitative analyses for several classes of compounds. Advances in the development MS^n and the elucidation of new ionization processes and gas-phase fragmentation chemistry are now aiding in the characterization and analysis of new compounds and complex mixtures. The aim of this work was to illustrate the possibilities to investigate the quantification and identification of know and unknown co-metabolites in small amount of biological material by LC-sequential mass spectrometry (LC-MS^n), performed on an ion trap mass spectrometer. Ion trap mass spectrometry allows the efficient trapping of ions, and multi-stage collision fragmentation experiments and provides detailed structural information, which is not obtainable from MS/MS.

SINK DO BRASIL

COURSE 6 - TECHNOLOGICAL INNOVATIONS IN COSMETIC RESEARCH AND DEVELOPMENT

IDALINA M.N.S. SANTOS
EVIC do BRASIL, São Paulo, SP, Brasil

JEAN PAUL MARTY
Faculty of Pharmacy - University of Paris, France

PATRÍCIA MARIA BERARDO GONÇALVES MAIA CAMPOS
Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, Ribeirão Preto, SP, Brasil

The development of modern cosmetic formulations requires a good mix of science and art. Products are now far more efficient, cost effective, elegant and safe than the choices available a few short years ago. Thus, the success of a cosmetic product mostly depends on the cares observed in its development. The technological advances on the last decade are well-standardised natural products with improved efficacies that contain flavonoids, polyphenols, vitamins and antioxidants. These constituents improve collagen synthesis, skin hydration, firmness and reduce appearance of the lines on the face and neck. In addition, delivery systems and devices that are used to improve and control the delivery of many active substances to the skin are among the new technological advances. In this course the speakers will describe the technological innovations in cosmetic research and development. Finally, some examples of efficacy tests will be presented and equipments normally used for them will be either discussed.

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Posters

Análises Clínicas / *Clinical Laboratory Analysis* (AC)

AC001-CORRELATION BETWEEN CHOLESTEROL LEVELS AND THE PERIODS OF ANDROPAUSE AND MENOPAUSE

JÚLIO CÉZAR ARAÚJO DO ESPÍRITO SANTO (IC)[1]; ADRIANA DE FIGUEIREDO (IC)[1]; DANIELE BEZERRA(IC)[1]; MURILO FERRERA DE SOUZA (IC)[1].

[1]UNIGRAN

Introduction - Andropause and menopause are important life events in which occurs hormonal rearrangement, in respectively men and women, that leads to a malfunctioning of the cholesterol metabolism in the organism. The atherosclerosis is the obstruction of the blood's flow in the circulatory system due to the formation of atheroma plaque composed by cholesterol molecules, precursors of hormones. Objective – To know if there is correlation between cholesterol levels and the periods of andropause and menopause. Methodology - A study of the cholesterol levels of 43 men and women from three age classes (51 to 60, 61 to 70, and 71 to 80 years old), based on the biochemical blood analysis and anamnesis, was carried out at an asylum of Dourados, MS, Brazil. Results - Despite of the sex, high levels of ateroschlerotic diseases were observed in the 61- 70yr old class. Conclusions - It is suggested that there is a possibility that the formation of the atheroma plaque occurs during andropause and menopause due to disturb in the cholesterol metabolism during these periods, leading to the so called atherosclerotic diseases (thrombosis, stroke, and infarction).

Financial support: UNIGRAN
Advisor: Ayd Mary Oshiro

AC002-USE OF THE TRIPHENYL TETRAZOLIUM CHLORIDE (TTC) TEST TO DETECT ASYMPTOMATIC BACTERIURIA

TATIANA ZAMPIERO RAMOS (PG)[1]; ELISABETH LOSHCHAGIN PIZZOLITTO (PQ)[1]; ANTONIO CARLOS PIZZOLITTO (PQ)[1]

[1]Faculdade de Ciências Farmacêuticas do Campus de Araraquara/SP-UNESP

Introduction. Urinary infection is generally defined as the presence of 10^5 or more CFU/mL in the urine, revealed without contamination, with or without symptoms. It is a major clinical problem. Using conventional methods, laboratory examination of urine is expensive, time-consuming and labour-intensive. The need for a simple test capable of detecting significant numbers of bacteria in the urine is well established. Objective. Reevaluate the triphenyl tetrazolium chloride (TTC) test, with modification of the reagent. Methodology. The 458 urine specimens were collected aseptically. Quantitative urine culture was performed using a dipslide (URILAB), with two different agar types: CLED and MacConkey. Colonies were counted after 18-24h of incubation at 37ºC. The finding of 10^5 or more CFU/mL of the same microorganism constituted a positive culture. To perform the TTC test, 4 mL of the urine were mixed with 1 mL of the TTC (Mallinckrodt) 1% aqueous sterile solution and incubated at 37ºC for 4h. A positive result was shown by a red precipitate. A comparison between the quantitative culture and the TTC test were made, for the evaluation of the test. Results. The results show that the TTC test has sensitivity 84.3%, specificity 96.5%, positive predictive value 94.6% and negative predictive value 96.7%. Conclusions. The TTC test can be use as a laboratory trial, especially in health care programs, to detect asymptomatic bacteriuria of pregnancy, childhood and elderly.

Financial Support: FUNDAP
Supervisor: Antonio Carlos Pizzolitto.

AC003 - INCIDENCES OF ASSYNTOMATICS CARRIERS OF *STAPHYLOCOCCUS AUREUS* IN *TECHNICAL NURSING COURSE AND NURSING PROFESSIONAL* OF THE HOSPITAL OF DOURADOS (MS)

ROSIMAR ODETE CORREIA DE SOUZA (IC) [1]; ADRIANA MARY MESTRINER FELIPE (PQ)[1]

[1] Centro Universitário da Grande Dourados -UNIGRAN

Text: Introduction: Infections caused by *Staphylococcus aureus* normally occur on the skin and mucous membranes of humans and is the causer too of the hospital infections had its high frequency and in immunodeficiency individuals. Objective: The objective of this work was to discover the incidences of assyntomatics carriers in nurses of the "Hospital of Dourados" determining the small farm of bigger prevalence of the microorganism in orofaringeal and/or nasofaringeal, as well as, in order to alert them on the risk of this bacterial in the hospital environment. Methodology: The study was made of the 2004 in hospital of Dourados (MS) and f*orty individuals participated in the study. The samples were collected from their nasal cavity and orofaringeal* with swabs and transported in transport agar. The bacterial identification was carried through using itself: coloration of GRAM, and the tests biochemists as: test of catalase, coagulase and Dnase. Results and conclusions: The analysis of the results shows that 31 (77,5%) were nasal assyntomatics carriers of *S. aureus* and he biggest farm of prevalence was in nasofaringe.

Financial Support: UNIGRAN
KEYWORDS: *Staphylococcus aureus*, carrying assintomatic, nurses, hospital, environment

The authors did not follow the Scientific Committee's suggestion for an English language review

AC004-STUDY OF β-LACTAM RESISTANCE IN STAPHYLOCOCCI MEDIATED BY *MECA* AND *BLAZ* GENES

AMANDA REHDER [(1)] (PG); IZABEL C. V. PALAZZO[(1)] (PQ); ANA LÚCIA C. DARINI[(1,3)] (PQ)

(1) Faculdade de Ciências Farmacêuticas de Ribeirão Preto – USP

S. aureus and CNS are frequently resistant to β-lactam antibiotics due to the production of β-lactamase and/or production of a penicillin binding protein with low affinity to β-lactam, PBP2a. The minimum inhibitory concentrations to oxacillin and penicillin were determined by the agar dilution method and E-test. β-lactamase production was determined by nitrocefin. The strains were characterized as β-lactamase hyperproducer using amoxicillin discs plus clavulanic acid. The presence of the *blaZ, mecA* and *coa* genes were detected by polymerase chain reactions. Among 150 CNS isolates, 84% were resistant to oxacillin and 52% to penicillin. Of 121 *S. aureus* strains, 98,3% were resistant to penicillin and 44,5% were resistant to oxacillin. In this study, 84% and 99,2% of the CNS and *S. aureus* respectively harbored the *blaZ* gene; *mecA* gene was detected in 64% of the CNS and 54,6% of the *S. aureus*. Sixty-five percent and 93,2% of the CNS and *S. aureus* strains were β-lactamase producer. Only one CNS was β-lactamase hyperproducer. Some strains showed discrepant results in the phenotypic and genotypic methods and the genetic changes responsible for that discrepance are being investigated.

Financial support: FAPESP (03/3800-3)
(3) Principal Investigator

AC005-EVALUATION OF THE VTEC SCREEN ASSAY FOR THE DETECTION OF SHIGA TOXIGENIC *ESCHERICHIA COLI*

SÔNIA MARIA DE SOUZA SANTOS FARAH (PG)[1]; EMANUEL MALTEMPI DE SOUZA (PQ)[1]; FÁBIO DE OLIVEIRA PEDROSA (PQ)[1]; LIU UN RIGO (PQ)[1]; MARIA BERENICE REYNOUD STEFFENS (PQ)[1]; KINUE IRINO (PQ)[2]; OCTAVIANA FIALHO (G)[1]; CYNTIA FADEL PICHETH (PQ)[1].

[1]Universidade Federal do Paraná; [2]Instituto Adolfo Lutz.

Introduction: Shiga Toxigenic *E. coli* (STEC) can cause diarrhea, hemorrhagic colitis and uremic hemolytic syndrome. STEC are characterized by the production of Shiga toxin, being bovine cattle its main reservoir. The reference method for STEC detection is the citotoxicity assay in Vero cells, which is not practical for routine. Easy to perform immunological assays for STEC detection are commercially available, but their performance has not been well studied. Objective: To evaluate the performance of the immunological assay VTEC Screen Seiken (Denka Seiken Co. Ltd, Japan) using *E. coli* strains previously identified as STEC by the citotoxicity assay. Methodology: Sixty-two strains of STEC were grown in TSA medium and the VTEC Screen assay was carried out as recommended by the manufacturer. Results: Only 48 (77.4%) of the 62 strains tested were identified as STEC by the VTEC Screen, yielding 33% of false negatives. Conclusion: Given the potential danger of false negative result, the VTEC Screen cannot substitute the citotoxicity assay as a routine method for STEC detection.

Supervisor: Cyntia Fadel Picheth

AC006-EFFECTS OF GRANDISIN ON HEMATOPOIESIS IN MICE

RITA DE CÁSSIA FIGUEIREDO(PG)(1); ZITA MARIA DE OLIVEIRA GREGÓRIO (PQ)(1); SÉRGIO DE ALBUQUERQUE(PQ)(1); ANA MARIA DE SOUZA(PQ)(1).

(1)Fac. Ciências Farmacêuticas de Ribeirão Preto-USP

Introduction: *Virola surinamensis* popularly know as ucuúba branca is a tree which grows frequently on Amazon forest. The bark resin is used in folk-medicine for the treatment of erysipelas and the tea prepared from leaves in colic and dyspepsia. Previous studies revealed that different constituents of plant were actives against *Schistosoma mansoni*, *Plasmodium falciparum* and *Leishmania donovani*. Before therapeutic use of plant is essential to evaluate the possible adverse effects. Objective: evaluate the effects of grandisin, a lignana isolated from *V. surinamensis,* on hematopoiesis in mice. Methods: grandisin was administered intraperitoneally, in concentrations of 25, 50 and 100mg/g (single dose) being the animals sacrificed after 7 and 14 days (d) of treatment. We have determined the parameters: erythrocytes and leukocytes in peripheral blood (PB); differential leukocyte count in PB; total cell count in bone marrow (BM) and spleen (S). Results and Conclusions: the administration of grandisin (100mg/g) significantly lowered the leukocyte and lymphocyte counts (7 and 14 d); total cell count increased in BM and reduced in S (14 d); this suggest that grandisin affect production and/or distribution of leukocytes.

Supervisor: Profª Drª Ana Maria de Souza

AC007-MEDICINAL PLANTS-MEDIATED IMMUNOMODULATION

JULIO CESAR MACHADO JR (PG); *ANGELA FLORÃO (PG); **FABIANA HERRERA ROCHA (IC) ALMERIANE MARIA WEFFORT-SANTOS (PQ)

Programa de Pós-graduação em Ciências Farmacêuticas – UFPR – Curitiba, Brazil

INTRODUCTION/OBJECTIVE: Cell culture techniques are useful for investigating the biological activities of herbal plants used in the folk medicine. The effects of the extracts prepared from the plants popularly known as equinácea, Brazilian ginseng, escada-de-macaco, pequizeiro and its fruit pequi, canela-de-veado, camomila, agoniada, cipó-suma, and pau-pra-tudo on the spontaneous and phytohemagglutinin-stimulated blastic transformation and proliferation of human lymphocytes were studied. METHOD: Peripheral blood mononuclear cells (MNC, >95% lymphocytes) treated with increasing concentrations of plant extracts (1-1000ug/ml) were induced to proliferate for 5 days, at 37°C, and 5% CO_2, with or without mitogen, and the cells behavior was analyzed by flow cytometry. RESULTS: The equinácea, chamomile, ginseng, and escada-de-macaco extracts were stimulants for the proliferation of lymphocytes, while the pequi, pequizeiro and canela-de-veado ones were ineffective. In contrast, agoniada and cipó-suma extracts were inhibitors, probably because of their cytoxicity. Pau-pra-tudo extract showed a significant inhibitory effect, acting probably on the lymphocyte activation mechanisms.

Financial support: *CAPES; **Fundação Araucária
Supervisor: A.M. Weffort-Santos

AC008 - COMPARATION OF METHODOLOGIES DIAGNOSTIC APPLIED TO *GIARGIA LAMBLIA* IN FECES OF CHILDREN FROM REGION OF ARARAQUARA, SP. BRAZIL

JOSÉ GUSTAVO DONATO GARCIA(PG)[(1)];MARIA JACIRA SILVA SIMÕES(PQ)[(1)];VERA LUCY DE SANTI ALVARENGA(PQ)[(1)]

[(1)] State University of São Paulo(UNESP)-Araraquara, SP. BRAZIL;

Introduction
The protozoan *Giardia lamblia* has been chosen to study because it is an enteric parasite of significant worldwide prevalence.
Objectives
The present essay aims to study the diagnostic reproductibility of the following methods: Direct, Faust and Contributors, Coprotest, and Iron Hematoxylin. It also describes the presence of *Giardia lamblia* according to the association of some population characteristics, such as: age group and gender.
Methods and Results
Two hundred stool samples of children from the region of Araquarara, Sao Paulo State, were analyzed. The four diagnostic methodologies were applied and then compared. The results obtained pointed out that *Giardia lamblia* was the most frequent parasite, representing 8.0% of the cases; there was no association with gender, and regarding age the more cases occurred in the 3 to 5 year-old group.
Conclusion
It has been concluded that the best approach to diagnose Giardia lamblia is the association of at least two connected methodologies of excellent reproductibility which in this study are: Coprotest-Faust, Direct-Faust, and Coprotest-Direct (k>0, 81).

Supervisor: Profa. Dra. Maria Jacira Silva Simões
Co-Supervisor: Profa. Dra. Vera Lucy de Santi Alvarenga

AC009-SHORT-TERM LEVELS OF SERUM INSULIN AND LEPTIN LEVELS FOLLOWING GASTRIC BYPASS SURGERY

MÁRCIA R A ABREU (PG)[1]; ADRIANA P PINHO (PG)[1,2]; REGINA C VENDRAMINI (PG)[1]; IGUATEMY L BRUNETTI (PQ)[1]; MARIA T PEPATO (PQ)[1].

[1] Depto Análises Clínicas-FCF-UNESP-Araraquara-SP, [2] Curso de Ciências Farmacêuticas - UNAERP

Introduction: There exists an association between obesity and high serum levels of insulin and leptin. Objective: To estimate insulin and leptin levels before and a short time after gastric-bypass bariatric surgery (BS). Methodology: We measured plasma glucose, serum insulin and leptin and insulin resistance indices (HOMA) of 14 men and women, before and 1 and 3 months after BS. Results: Body weights fell (p<0.05) by 14.3 and 25.7 kg (1 and 3 months after BS). Before BS, patients exceeded reference values for glucose (119.7±49.7mg/dL), HOMA (5.49±4.39 mol/dL×μU/mL) and leptin (men 75.4±7.8, women 122.4±19.4ng/mL) but had normal insulin (18.3±8.4μU/mL). Intra-group analysis showed post-BS values were lower than pre-BS values (p<0.05), after 1 and 3 months respectively, in glucose (94.2±20.1 and 89.2±21.7 mg/dL), HOMA (2.2±0.94 and 2.6±3.3 mol/dL×μU/mL), leptin (men 43.5±14.3 and 39.7±8.3; women 66.3±28.1 and 51.5±27.8 ng/mL) and insulin (9.8±3.5 and 10.3±9.1μU/mL). Conclusion: The weight reduction promoted by BS corrected carbohydrate metabolism and leptin levels in the short term.

Financial support: FUNDUNESP and and PADC-Araraquara
Supervisor: Maria T. Pepato.

The authors did not follow the Scientific Committee's suggestion for an English language review

AC010-MOLECULAR CHARACTERIZATION OF ENTEROCOCCI WITH GENOTYPE AND PHENOTYPE INCONGRUENCE RELATIVE TO GLYCOPEPTIDES RESISTANCE

PRISCILA MORAES HENRIQUE [1] (PG); IZABEL CRISTINA V. PALAZZO [1] (PQ); ROSEMAIRE C. ZANELLA [2] (PQ); ANA LÚCIA DA COSTA DARINI [1] (PQ)

[1] Instituition: Faculdade de Ciências Farmacêuticas de Ribeirão Preto- USP
[2] Instituition: Instituto Adolfo Lutz- SP

VanA and VanB phenotypes are the most common glycopeptide resistance among enterococci. The VanA phenotype is characterized by vancomycin and teicoplanin resistance and it has been predominant in enterococci isolated in Brazil. Three *Enterococcus faecalis* with *van*A genotype that are susceptible to teicoplanin (VanB phenotype-*vanA* genotype) were analyzed using molecular methods as pulse field gel electrophoresis (PFGE), polymerase chain reaction (PCR), hybridization with van*A* probe and plasmid profile. According to the results obtained, two enterococci strains isolated in one hospital have the same PFGE profile and other strain was found to be unrelated. All enterococci strains harbored the van*A* gene only into the chromosome. The VanA element in these strains showed a deletion on right terminal with loss of *vanZ* gene, and it can be responsible by teicoplanin susceptibility.

Supervisor: Ana Lúcia da Costa Darini

AC011-EFFECTS IN THE LEUKOCYTES LEVEL OF WISTAR RATS SUBMITTEDTO PNEUMOPERITONEUM WITH CO_2 AND PERITONITIS

AMÁLIA CINTHIA MENESES DO RÊGO(IC)[1]; RENAN ARAUJO GOIS(IC)[1]; IRAMI ARAÚJO FILHO(PG)[1]; ALDO DA CUNHA MEDEIROS(PQ)[1]

[1]Universidade Federal do Rio Grande do Norte

Introduction: In laparoscopic surgery is not expected a significant increase in the peripheral leukocytes like in opened technique procedures, but the use of peneumoperitoneum with CO_2, sugestes influence in the immune responses. Objective: Analyze the leucogram of rats under the effect of peneumoperitoneum with CO_2 and peritonitis. Methodology: 18 male rats Wistar was divided in 3 groups of 6 animals. Groups: (1), control, rats anaesthetized; (2) rats submited to open laparotomic and peritonitis; and (3), rats with peritonitis associated to the peneumoperitoneum with CO_2. All groups used the anaesthetic Tiopental 20mg/K. After 24 hours were collected samples of blood of the animals for accomplishment of the leucograma. Results: Leukocytes: Group 1 (4,55K/µL), Group 2 (11,2K/µL) and Group 3 (3,71K/µL); monocytes and lynphocytes: Group 1 (10,2%; 32,5%), Group 2 (6,4%; 10,3%) and Group 3 (7,8%; 23,0%); eosinophils, basophils and neutrophils: Group 1 (4,0%; 1,4%; 51,75%), Group 2 (0,7%; 2,5%; 80,2%) and Group 3 (2,0%; 6,2%; 60,85%). Conclusion: After the analysis of the results, the pneumoperitoneum with CO_2, in rats causes alteration in the leukocytes cells trending the leucopeny.

Supervisor: Aldo da Cunha Medeiros

AC012-HL A LINKAGE DISEQUILIBRIUM IN DIFFERENT ETHNIC GROUPS FROM NORTH AND NORTHWEST OF PARANÁ, BRAZIL.

SELL, ANA MARIA [1]; TATEYAMA, SILVANA AKEMI (IC) [2];

Universidade Estadual de Maringá.
[1] Docente do DAC-UEM, [2] Acadêmica do curso de Farmácia.

Introduction: Linkage disequilibrium is the non-random association of alleles at two or more linked loci. At equilibrium the association of allele in gametes is random and the frequency of the allelic combination of gamete is equal to the product of the alleles frequencies. Objective: The aim of this study was to analyze the linkage disequilibrium of HLA A/B, A/DRB1 and B/DRB1 haplotypes. Methods: Healthy and unrelated individuals (1000 White individuals from north, 1000 White from northwest, 216 Orientals, 277 Mulattos and 215 Blacks) were selected. The HLA typing was conduced by PCR-SSP (SSP™ DNA, One Lambda, Inc). Alleles and haplotypes frequencies were determined by Arlequin 1.1 Program package. Fisher's exact test was used to calculate the significance of the linkage disequilibrium. Results: Analyses of linkage disequilibrium revealed significant results ($p<0,001$). The most significant disequilibrium were HLA A*01/B*08 and B*08/DRB1*03 for White and Mulattos individuals; HLA A*24/B*52, B*52/DRB1*15 and B*07/DRB1*01 for Orientals and HLA B*08/DRB1*03 for Blacks. Conclusion: The populations were in Hardy-Weinberg equilibrium. The results were found as expected and racial admixture was observed.

Supervisor: Ana Maria Sell

AC013-QUANTIFICATION OF SERUM IMMUNOGLOBULINS AND SUBCLASSES IN ADOLESCENTS WITH DIFERENT DEGREES OF IRON DEFICIENCY

JILMARA B. DE OLIVEIRA CODARIN (PG)[1,2]; ANA MARIA DE SOUZA (PQ)[1]; GERSON C. CROTT(PQ)[2]; LUCIANA SIMON P. CROTT (PQ)[1]

[(1)]DACTB-FCFRP-USP; [(2)]Universidade de Ribeirão Preto

Introduction: Iron plays essential roles in immune function. Iron deficiency is common in adolescents, ranging from depletion to anemia. Objective: We aimed to evaluate the association between iron deficiency and humoral immune response parameters. Methodology: Levels of iron deficiency were determined by erythrogram, sTfR, and serum ferritin, and quantification of serum immunoglobulins and IgG subclasses was performed by nephelometry in 80 adolescents from both sexes. Results: 12.5% of the adolescents were iron depleted and 13.75% had iron deficiency, being classified as normal (N), iron depleted (DEP) and iron deficient (DEF) adolescents. There were no statistical differences in the IgG, IgA, IgM, and IgG subclasses among those groups. However, when two groups of female adolescents were analyzed, group DEP+DEF demonstrated higher levels of IgG2 and IgG4 and lower levels of IgG1 compared to the control group (N). Conclusions: Iron deficiency could conduct to alterations in important parameters of humoral response, like IgG subclasses, that could explain, at least in part, the susceptibility to infections of these individuals.

Apoio financeiro: UNAERP; USP
Supervisor: Profa. Dra. Luciana Simon P. Crott

AC014-SENSIBILITY OF DIFFERENT TESTS USED IN DIAGNOSTIC OF AMERICAN CUTANEOUS LEISHMANIASIS

MAÍRA PERES FERREIRA(PG)[1]; MARGARIDA M.P.NASCIMENTO(PQ)[1]; ANA MARIA F.ROSELINO(PQ)[2]; JULIANA M. AYRES (PG)[2]; JOSÉ FERNANDO CASTRO FIGUEIREDO(PQ)[1].

Division of Infectious and Tropical Molests [1] and Dermatology[2], Department of Internal Medicine, Faculty of Medicine of Ribeirão Preto of University São Paulo, Brazil

Introduction: The diagnosis of American Cutaneous Leishmaniasis (ACL) is usually suspected by the characteristics of the cutaneous lesions and confirmed by laboratory tests. Usually, several laboratory methods may be used for the diagnosis of ACL, with different sensitivity among them. Objectives: To compare the sensitivity of Enzyme-linked Immunosorbent Assay (ELISA) using *L. braziliensis* crude antigen, Indirect Immunofluorescence Reaction (IIR), Montenegro skin test, Polymerase Chain Reaction (PCR) in biopsy of skin or mucous membranes and visualization of parasites in biopsies. Methods: all tests were performed in a population of patients with ACL (n=53), and the sensitivity of each test in this population was analyzed individually. Results and Conclusions: The sensitivity of each method was: ELISA 85%, PCR 81%, Montenegro skin test 64,4%, IIR 58% and presence of parasites in biopsy, 34%. The ELISA test showed the highest sensitivity in the population studied, better than IIR and PCR.

Supervisor: José Fernando de Castro Figueiredo

AC015-ZINC AND BONE: EFFECTS OF ZINC SUPPLEMENTATION IN OVARIECTOMIZED RATS

ELAINE CRISTINA SILVA FERREIRA(PG)[1]; MARCELA ABBOTT GALVÃO URURAHY(IC)[1]; TERESA CRISTINA PAIVA SILVA(PG)[1]; BRUNO CUNHA MEDEIROS(IC)[1]; LUCIANA AUGUSTO REZENDE(PQ)[2]; ALDO CUNHA MEDEIROS(PQ)[1]; JOSÉ BRANDÃO NETO(PQ)[1]; MARIA DAS GRAÇAS ALMEIDA(PQ)[1]; ADRIANA AUGUSTO REZENDE(PQ)[1]

[1]Universidade Federal do Rio Grande do Norte, Centro de Ciências da Saúde, Natal/RN, Brasil; [2]Universidade de Ribeirão Preto, Ribeirão Preto/SP, Brasil.

INTRODUCTION: Zinc plays an important role in bone growth and mineralization. OBJECTIVE: The aim of the present study is to evaluate zinc supplementation effects on circulating bone markers in a post-menopausal model, over 45 days. METHODOLOGY: Female Wistar rats were divided in 3 groups: control, ovariectomized (OVX) and OVX with zinc supplementation (OVX-Zn). Biochemical parameters were measured using Kits Labtest analyzed in spectrophotometer RA 50 (Bayer). RESULTS: Serum alkaline phosphatase activity increased significantly in OVX when compared to control, and decreased in OVX-Zn when compared to OVX. Serum ionized Ca decreased and urinary Ca increased significantly in OVX when compared with other groups. Serum phosphorous decreased and tibia zinc increased significantly in OVX-Zn when compared with the other groups. CONCLUSION: Results suggest that zinc supplementation improved bone formation.

Financial Support: PIBIC, CNPq/UFRN
Supervisor: Adriana Augusto Rezende

AC016-SODIC HEPARIN AS IN VITRO ANTI-COAGULATE CAN INTERFERE WITH THE LABORATORIAL DIAGNOSIS OF ACUTE MYOCARDIUM INFARCTION (AMI)–PRELIMINARY RESULTS

GABRIEL DE SOUZA LIMA OLIVEIRA(PQ)[1]; MARIA DE LOURDES NUNES KONO (PQ)[1]; CARLOS EDUARDO DOS SANTOS FERREIRA (PQ)[1]; CRISTOVÃO LUIS PITANGUEIRA MANGUEIRA(PQ)[2]

[1]Dante Pazzanese Institute of the Cardiology; [2]Israelite Albert Einstein Hospital;

Introduction: AIM is diagnosed by chest pain, electrocardiographic changes and elevations of myocardial injury markers. Objective: To verify the interference of sodium heparin contained in the blood collecting tubes on the measurents of total CK (CK), CK-MB activity (CK-MBa), CK-MB mass (CK-MBm) and Troponin I (cTnI) in patients with AMI. Methods: We measured the level of cardiac markers of 50 patients with a cTnI above 1ng/mL during hospitalization. Samples of peripheral blood were collected simultaneously in a *Vacuntainer BD*® tube with 72 USP units of heparin and in dry tube. The CK was measured by CK NAC method and CK-MBa by immunoinhibition in the *Hitachi 912* analyzer *Roche*®. The cTnI and CK-MBm measurements were done by immunometric assay from *Immulite DPC*® analyzer. All tests were performed within the same analytical run. Results: There were significant low levels of cTnI, CK and CK-MBa in the plasma samples ($p<0,001$). Not statistical difference in CK-MBm levels ($p=0,412$) was found. There was an average reduction of 1,77ng/mL for cTnI, 2,8U/L for CK and 1,48U/L for CK-MBa in the plasma compared to the serum. Conclusions: These data suggest that only serum should be used for measuring these analytes in patients under AMI evaluation. These data needs to be reevaluated in a bigger sample to know the clinical implications of these results.

AC017-PRODUCTION OF LIPID BODIES, CYTOKINES AND LEUKOTRIENES IN ALVEOLAR MACROPHAGES, BY GALECTIN-1 INDUCTION.

LÍLIAN CATALDI RODRIGUES(PG)[1]; CARLOS ARTEIRO SORGI (PQ)[1]; LÚCIA HELENA FACCIOLI(PQ)[1]; MARCELO DIAS BARUFFI(PQ)[1].

[1]Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP.

INTRODUCTION: Galectin-1 (Gal-1) is a lectin family member, which recognizes β-galactosides and is involved in several biological processes, including the modulation of inflammatory response. Gal-1 is supposed to stimulate cytokines release that could be important to the defense mechanism of infections. Data from our lab suggest alveolar macrophages stimulated by immunogenic agents induce lipid bodies related to increase of LTB_4 production.
OBJECTIVE: Determination of cytokines, leukotrienes production and formation of lipid bodies in alveolar macrophage by stimulation with gal-1.
METHODOLOGY: Quantification of LTB_4, LTC_4 and presence of lipid bodies in these cells challenged by purified Gal-1 (LPS free). Determination of IL-1-α, IL-6, IL-10, IL-5, IL-12, IFN-γ e GM-CSF cytokines of alveolar macrophage *in vitro* (with/ without Gal-1 treatment).
RESULTS AND DISCUSSION: We have found that Gal-1, have induced, *in vitro*, lipid bodies in alveolar macrophages of C57/ BL6 mice experimental group. This result suggests that Gal-1may contribute for a better understanding of the immunomodulatory role of these mediators in infectious disease processes like Histoplasmosis.

Supervisor: Prof. Dr. Marcelo Dias Baruffi.

AC018 - INVESTIGATION OF NADPH-OXIDASE PARTICIPATION ON BIOLOGICAL GAL-1 FUNCTIONS IN NEUTROPHILS: PHOSPHATIDYLSERINE EXPOSURE AND PHAGOCYTOSIS BY MACROPHAGES.

JULIANA DA SILVA OLIVEIRA (PG)[1]; LILIAN CATALDI RODRIGUES (PG)[1]; MARLISE BONETTI AGOSTINHO MONTES (PQ)[1]; MARCELO DIAS-BARUFFI (PQ)[1].

[1] Faculdade de Ciências Farmacêuticas de Ribeirão Preto.

INTRODUCTION: Galectin-1 (Gal-1) recognizes β-galactosides and this relation is involved in several biological processes like modulation of inflammatory response. Gal-1 participates on phagocytosis process by induction of phosphatidylserine (PS) on neutrophil surface, beyond NADPH-oxidase activation. However, Gal-1 does not promote apoptosis. Correlation between apoptosis and Reactives Oxigen Species (ROS) in neutrophil homeostasis is not well elucidated.
OBJECTIVE: Impact of ROS production, in neutrophil cells treated or not with Gal-1, on activities promoted by this lectin: PS exposure and their phagocytosis by macrophages.
METHODOLOGY: PS exposure using stain cells with AnnexinV-FITC and DNA degradation by TUNEL, both measured by Flow Cytometry. ROS by chemiluminescence.
RESULTS AND DISCUSSION: Neutrophils treated with Gal-1 released ROS. However, neutrophils pre-treated with DPI (NADPH-oxidase inhibitor) and induced with Gal-1 have not released ROS. This result may be interesting for investigation of NADPH-oxidase participation on biological function of Gal-1 in neutrophils.

Supervisor: Prof. Dr. Marcelo Dias Baruffi

AC019-EFFECTS OF PNEUMOPERITONEUM WITH CO_2 ON INTRAPERITONEUM CYTOKINES

AMÁLIA CINTHIA MENESES DO RÊGO (IC) ([1]); THIAGO VICTOR CIRNE DE OLIVEIRA (IC) ([1]); IRAMI ARAÚJO FILHO (PG) ([1]); ALDO DA CUNHA MEDEIROS (PQ) ([1])

([1])Universidade Federal do Rio Grande do Norte

Introduction: The pneumoperitoneum with CO2 is a technique required to laparoscopic surgery, which causes local and systemic effects, like an alteration in the immune and inflamatory response to the trauma and septicemy. Objective: To observe the concentrations of TNF-α, IL-1 and IL-6in the presence of pneumoperitoneum with CO2. Methodology: 12 male Wistar rats were divided in 2 groups of 6 animals each. In group 1, control, the animals were just anaesthetized, in group 2 was done pneumoperitoneum with CO2 with pressure of 2mmHg during 30 minutes. After this period, rat's intraperitoneum liquid were collected and centrifugated. From the supernatants acquired, it were determinated the concentrations of TNF, IL-1 and IL-6 by ELISA. Results: Group 1: 161,8pg/mL (±10) of TNF- α, 172pg/mL (±11) of IL-1 and 225pg/mL (±33); Group 2: 148pg/mL (±23) of TNF- α, 112pg/mL (±7) of IL-1 and 160pg/mL (±21) of IL-6. Conclusion: After analysis of the files, we can suggest that the pneumoperitoneum with CO2, provoke the diminished on the levels of TNF- α, IL-1 and IL-6, related to the control group.

Supervisor: Aldo da Cunha Medeiros

AC020-OPTIMIZATION OF INDIRECT ELISA USING TC85-11 PROTEIN FOR THE SEROLOGICAL DIAGNOSIS OF CHAGAS' DISEASE.

THALITA B. ZANONI[(1)]; ANTONIO A. PUPIM FERREIRA (PG)[(2)]; IRACILDA Z. CARLOS (PQ)[(3)]; JOÃO O. TOGNOLLI (PQ)[(2)]; HIDEKO YAMANAKA(PQ)[(2)]

[(1)] Centro Univ. Barão Mauá, Fac. Pharm. Sciences, Ribeirão Preto (SP), Brazil; [(2)]Unesp, Inst. Chem., Araraquara (SP), Brazil; [(3)]Unesp, Fac. Pharm. Sciences, Araraquara (SP), Brazil.

Chagas' disease is caused by the *Trypanosoma cruzi (T.cruzi)* and the detection of anti-*T. cruzi* antibodies in the serum is a method for diagnosis of the disease. In this work, indirect ELISA was optimised for detection of serum antibodies of patients with Chagas' disease using Tc85-11 protein (Ag) from the trypomastigote surface of the parasite. The full factorial design for optimization of the experimental conditions was carried out for the incubation time, dilutions of Ag (0,08 mg mL^{-1}), primary antibody (Ac) and anti-IgG conjugated with peroxidase (Ac*) parameters. The best results were obtained with the following conditions: 0,14 μg Ag/well, 60 min incubation time, dilutions of 1:35 and 1:1000 for Ac and Ac*, respectively. The cut off value was A_{495nm} = 0,371. Tc85-11protein, which is involved in the adhesion of the parasite to host cell, is also suitable for serological diagnosis of Chagas´ disease.

Financial support: FAPESP
Donation of the Tc85-11: W. Colli, M. J. M. Alves, D. R. Oliveira

AC021-CLEANUP OF PLASMA SAMPLES USING POLYMERS COMPARED WITH DESPROTEINIZATION METHODS

GABRIELA SCHMITT[(1)](PG); SILVANA BOEIRA[(1)](IC); JULIANA VICENTINI[(1)](PQ); DENISE BOHRER[(1)](PQ).

[(1)] Universidade Federal de Santa Maria

Inroduction: Proteins must be removed of plasma samples to medicament quantification before analysis by HPLC because they can precipitate or form irreversible linkings with the stationary phase, harming the analysis and reducing the time of useful life of the chromatographic column. Objective: Comparison of effectiveness by extraction liquid-solid with 7 polymers, deproteinization with trichloroacetic acid (TCA 10 and 15%) and sulfosalicilic acid (SSA 10, 15 and 20%) and organic solvents as methanol and cold ethanol. Methodology: Columns with differents polymers (cellulose acetate, polytetrafluoroethylene, polybutadiene, polyurethane and polyethylene (medium and high density and ultra-high molecular weight) were confectioned with tips, forming a column and 500mL plasma were eluited with a peristaltic pump. Deproteinization: acid dilution 1:1 and solvents 1:2. After sample were centrifugated. Residual proteins were measured with Coomassie test. Results: Acids TCA and SSA (independently of the concentration used), high density polyethylene and polytetrafluoroethylene presented protein levels < 4 mg/L. Conclusion: Both polymers can be used as an alternative method to cleanup in plasma samples without pH modifications.

Financial Support: FIPE
Supervisor: Solange Garcia[(1)]

AC022-LABORATORIAL DIAGNOSIS OF CHAGAS' DISEASE DUE THE INGESTION OF SUGAR CANE JUICE

KARINE VIEIRA GASPARETO[1]; DAYANNE TOZATTO WAKIMOTO[1]; PAULO DONIZETI ZANZARINI[2]; THAÍS GOMES VERZIGNASSI SILVEIRA[2]; MARIA VALDRINEZ CAMPANA LONARDONI[2]; SANDRA MARA ALESSI ARISTIDES ARRAES[2].

[1] Students of Pharmacy - Universidade Estadual de Maringá (UEM)
[2] Departamento de Análises Clínicas - UEM

Introduction: Chagas' disease caused by *Trypanosoma cruzi* is transmitted by stool of triatomine insect, containing parasites. An outbreak was reported in March of 2005 by the authorities of Santa Catarina State. The transmission was probably by ingestion of sugar cane juice contaminated with the parasites. Objective: To diagnostic the Chagas' disease in inhabitants of Maringá, Paraná State, who had been in the coast of Santa Catarina in February of 2005 and had presented symptoms of acute phase of Chagas' disease. Methodology: Samples of blood had been collected and conducted to the Laboratório de Ensino e Pesquisa em Análises Clínicas (LEPAC/UEM). Results: Of the 139 immunofluorescence tests (IFT) for research of IgG and IgM anti-*T. cruzi,* one presented titers of IFT-IgG 320 and negative IFT-IgM and another case, presented negative IFT-IgG and IFT-IgM 40. Conclusion: The presence of IgG characterizes the chronic phase and IgM represents recent infection, therefore it was not possible to confirm recent infection, since the significant titer for IFI-IgM is 80.

Supported by LEPAC/UEM
Supervisor: Sandra Mara Alessi Aristidef Arref.

The authors did not follow the Scientific Committee's suggestion for an English language review

AC023-OCCURRENCE OF SYPHILIS IN DIFFERENT POPULATIONS IN MARINGÁ, PARANÁ

DAYANNE TOZATTO WAKIMOTO[1]; KARINE VIEIRA GASPARETO[1]; PAULO DONIZETI ZANZARINI[2]; THAÍS GOMES VERZIGNASSI SILVEIRA[2]; MARIA VALDRINEZ CAMPANA LONARDONI[2]; SANDRA MARA ALESSI ARISTIDES ARRAES[2]

[1] Students of Pharmacy – Universidade Estadual de Maringá (UEM)
[2] Departamento de Análises Clínicas – UEM

Introduction: Syphilis is a sexually transmissible disease caused by *Treponema pallidum*, characterized for primary injury, that later can became systemic. Objective: To evaluate the occurrence of syphilis in different populations in Maringá. Methodology: In December of 2004, 486 blood samples were collected. 240 of them were obtained in the masculine penitentiary, 177 were collected in the Raposo Tavares Square and 69 were colleted from of the university community (UEM). The laboratory diagnosis of syphilis was carried out at the Laboratório de Ensino e Pesquisa em Análises Clínicas (LEPAC/UEM), using VDRL (non-treponemic test) to evidence anti-cardiolipin antibodies. Results: Of the 240 samples collected in the penitentiary, 3 (1,25%) presented titers 1/2. Of the 177 samples collected in the square, 3 (1,70%) showed titers 1/1, 1/8 and 1/32. Of the 69 samples collected at UEM, none presented positive result. These results need to be confirmed by treponemic test. Conclusion: The results show the necessity of more effective educational programs to control sexually transmissible diseases.

Supported by LEPAC/UEM.
Supervisor: Sandra Mara Alessi

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Assistência e Atenção Farmacêutica/*Pharmaceutical Assistance and Pharmaceutical Care* (AF)

AF001-POPULATION PERCEPTION AND ANALYSIS RELATED TO PHARMACEUTICAL ASSISTANCE – CONCHAL (SP)

A. L. GUIMARÃES[1](IC); F. P.. PIVA[2](PQ); F. P. G. CARAVANTE JÚNIOR[3], J. C. FACHINELLI[4] (PQ)

[(1,2,3,4)] Centro Universitário Hermínio Ometto – UNIARARAS

Brazil is 5th producing and consuming of medicines in the world. However the distribution of this consumption is diversified with high concentration in the A and B social classrooms. Add to it high degree of lack of information to the majority of the population on the medicine use. In this direction, prospective study has been performed, in the city of Conchal (SP), using systematic sampling for conglomerates being the domicile the sampling unit. An open and closed questionnaire was applied in 100 domiciles to the home responsible person for medicines, to knowledge about the indication, the orientation on the use and the pharmacist activities. From the total interviewed domiciles, 80% have presented the family mother as responsible, 21% have gone to the pharmacy instead of the doctor when they are sick, 26% have not been guided about the use and 42% have been confused or they do not know the pharmaceutical profession. The analysis concluded that are necessary institutional actions for information about the pharmaceutical paper, beyond necessity of increase relative information about medicines use, confirming the necessity to construct new practices as the Pharmaceutical Attention.

Financial Support: Antibioticos do Brasil Ltda.
Supervisor: Francisco de Paula Garcia Caravante Junior

AF002-PHARMACEUTICAL CARE: FROM UTOPIA TO REALITY

MARIANA LINHARES PEREIRA (PG) [(1)]; DJENANE RAMALHO DE OLIVEIRA (PQ) [(2)]; MARCELLA GUIMARÃES ASSIS TIRADO (PQ) [(3)]

[(1)] Farmácia Universitária, UFMG; [(2)] Departamento de Farmácia Social, Faculdade de Farmácia, UFMG; [(3)] Departamento de Terapia Ocupacional, Escola de Educação Física, Fisioterapia e Terapia Ocupacional, UFMG.

Introduction: Pharmaceutical care is a practice model developed within the pharmacy profession in 1990. It is a patient-centered practice whose goal is to prevent and resolve drug therapy problems. Even though pharmaceutical care was accepted by the profession of pharmacy as its new professional mandate, for the most part, there is much more discourse than practice as it relates to taking care of real patients. Objetive: to understand, from the perspectives of pharmacists, the importance of working directly with patients to acquire a deeper comprehension of the patient care process in pharmaceutical care, to incorporate its philosophy of practice and to advance it. Methodology: this study used qualitative methodology and the methods of participant observation and semi-structured interviews. Results and conclusions: The results of this study show the importance of taking the first step in the direction of working with patients. The experience of pharmacists with the practice indicates a significant transformation in their attitudes, behaviors and level of responsibility as they start taking care of people.

Supervisor: Profa. Dra. Djenane Ramalho de Oliveira

AF003-INFLUENCE OF PHARMACIST INTERVENTIONS TO IMPROVE THE QUALITY-OF-LIFE OF ELDERLY OUTPATIENTS IN RIBEIRÃO PRETO (SP), BRAZIL

DIVALDO PEREIRA DE LYRA JÚNIOR (PG)[(1)]; JULIANA PALMA ABRIATA (IC)[(2)]; IRENE ROSEMIR PELÁ (PQ)[(1)]

[(1)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto, USP, SP, Brazil; [(2)]Curso de Ciências Farmacêuticas da Universidade de Ribeirão Preto, UNAERP, SP, Brazil.

Introduction: Drug-related morbidity and mortality are growing up between the elderly, reducing their quality of life (QoL). Objective: To assess the influence of pharmacist interventions on the QoL of elderly outpatients assisted by the Basic Health Care Unit (UBDS) Dr. Ítalo Baruffi in Ribeirão Preto (SP). Methodology: 30 elderly participated in a prospective longitudinal study from July 2003 to July 2004. During the study, the drug therapy of each patient was evaluated. The instrument of QoL SF-36© was administrated at baseline and after 12 months. Results: In this group, the inadequate drug therapy gave rise to 92 drug-related problems (DRP). The interventions based on critical consciousness development optimized the use of medication, resulting in the solution and prevention of 70% of the DRP. Consequently, the QoL instrument observed significant improvement ($p<0.05$) for six of the eight domains under study. Conclusion: In this UBDS, the pharmacist interventions were associated with significant improvements in QoL of elderly outpatients.

Financial Support: CAPES
Supervisor: Irene Rosemir Pelá

AF004-DIAGNOSIS, TREATMENT AND ACCOMPANIMENT OF SPONGED CHILDREN OF THE INFANTILE EDUCATIONAL CENTER SÃO JOSÉ IN THE CITY OF CASCAVEL- PR

SÔNIA DE LUCENA MIORANZA(PQ)[1]; OSVALMIR SÁ DA SILVA(IC)[1]; MARIA DAS GRAÇAS TAKIZAWA(PG)[1]; THAIS CHUNG(IC)[1]; MARCO YAMAGUCHI(IC)[1]; YASKARA LÜERSEN(IC)[1], CLÁUDIA GOBBI(IC)[1]; MELINA MELITO(IC)[1] ; LARISSA MALLMANN(IC)[1]; ANA PAULA SANTI(IC)[1].

[1] State University of the West of Paraná - Cascavel - PR

Introduction: The diagnosis, treatment and sponged individuals' accompaniment constitute valuable indicators in epidemic studies. **Objectives:** Verify the parasitic disease prevalence, accomplish lectures, treatment and to accompany the adverse effects of the medicines. Materials and Methods: The samples were obtained in the period of October to December of 2004 with children zero to eight years from both sexes. By the method of Hoffmann, Pons and Janer 58 fecal samples were analyzed and 61 by Graham. Took place treatment of the positive cases and their adverse effects, coming the medicines from the Basic Drugstore of the Municipal district. **Results:** For HPJ the results were of 39,66%, happening a larger prevalence of *Ascaris lumbricoides* (13,79%) and *Giardia lamblia* (12,07%), having most of children many parasites (65,22%). In relation to Graham's technique, it was obtained a result of 44,26%, and 25 samples were positive for *Enterobius vermicularis* (92,59%) and 2 for *Ascaris lumbricoides* (7,41%). Five of the six children that underwent the treatment with albendazol and metronidazol, presented diarrhea, and one diarrhea and vomit. **Conclusion:** It was observed high index of parasitism, adverse reactions and the participants' larger interest on prevention measures and treatment of the parasitic diseases.

Supervisor: Sônia de Lucena Mioranza

The authors did not follow the Scientific Committee's suggestion for an English language review

AF005-PATIENT COMPLIANCE AND CURE PERCEPTION AMONG ANTIBIOTIC USER IN COMMUNITY PHARMACY

PAOLA BARRICHELO (PG)[1], PAULA ROSSIGNOLI (PG)[1], CASSYANO J. CORRER (PQ)[2], FERNANDO FERNÁNDEZ-LLIMÓS (PQ)[3], ROBERTO PONTAROLO (PQ)[1]

[1] Federal University of Paraná(Brazil)
[2] Positivo University Center(Brazil)
[3] Pharmaceutical Care Research Group.University of Granada(Spain)

Introduction: Improper use (including patient non-compliance) of antibiotics is producing resistances. *Objective*: To observe antibiotic treatment non-compliance among customers from a community pharmacy, so as to observe their cure perception from health problem origin of their antibiotic prescription. *Methods*: Observational study including patients presenting an antibiotic prescription. *Results*: 118 patients concluded the study (64.4% were women). Average age was 38 years old (SD=15.6). 118 antibiotics were prescribed, with a duration average of 6.3 days (SD=3.6). Penicillins were the most prescribed (41.5%). Main health problems were respiratory tract (46,6%), and genitourinary (22%). At the end of the treatment, 72.9% of patients self-considered as cured. After the pill-count, 65.3% of patients were considered as non-compliers. Among compliers, 80.5% self-considered as cured (chi-square=0.176).*Conclusions*: there was not any relation between cure self-perception and treatment compliance, what has to be taken into account in education for compliance.

Own finantial support
Supervisor: Roberto Pontarolo

AF006-PHARMACEUTICAL CARE (PC) FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

ANA PAULA HELFER (IC)[1]; JUCIANE A. FRANCO (IC)[1]; ANDRÉA L.G. SILVA (PQ)[1]; ANDRÉIA R. M. VALIM (PQ)[1]

[1] UNISC

Introduction: The patients with COPD use many drugs and pharmacotherapy follow-up can be very helpful. PC is defined as a set of attitudes, behaviors, ethical values, knowledge and responsibilities of the pharmacist, aimed at contributing towards the obtainment of the desired therapeutic results and improvement of the patients quality of life. **Objective:** The aim of this study was to do pharmacotherapy follow-up of COPD patients preventing drug therapy problems (DTP). **Methodology:** Dader method was used following the 3 major phases: pharmaceutical anamnesis, analysis of date and patients instructions. **Results:** Between the 4 patients enrolled in the study 100% were male sex, the mean age was 67 years and all had smoked for long periods. 100% of the patients used budesonide/formoterol, the majority used 3 or more medicines inhaled and they didn't describe DTP. However, we detected poor use of inhaler maneuvers in 50% of them, reducing the effectiveness of pharmacotherapy. **Conclusion:** Instruct the patients to use inhalers is important. If not taken properly, the drugs may never reach the lungs. The PC using Dader in patients with COPD is a good option to carry out drug therapy follow-up and reach better pharmacotherapy results.

Financial Support: UNISC
Supervisor: Andréia R. M.Valim

AF007-SILDENAFIL USER'S PROFILE IN A DRUGSTORE IN THE CITY OF SÃO PAULO

FRANCISCO RONDINELE BARROS DE OLIVEIRA(IC), FABIANA GATTI DE MENEZES, MICHELE MELO ANTONIALLI, JORGE WILLIAN LEANDRO NASCIMENTO(PQ)

Departamento Ciências da Saúde, Curso Farmácia e Bioquímica - UNINOVE

Introduction: Sildenafil (phosphodiesterase 5 inhibitor) has been used worldwide to treat erectile dysfunction. Objective: To evaluate the profile of the users of sildenafil. Methodology: Were applied 360 questionnaires to the clients of a drugstore in São Paulo (Brazil) who had bought sildenalfil. Results: The distribution of the users in age group presented 28,4% between 40-49 years old, 23,5% between 50-59 years old and 17,2% between 30-39 years old. A total of 55,6% obtained this drug without medical prescription. According to reason of the use, 45,7% of the interviewees informed that was using to treat erectile dysfunction, 30% to increase the sexual potency and 22,8% by curiosity. According to use frequency, 41,8% answer that use one or more times a week, 34,7% once a month and 23,5% eventually. According to day of the week, Friday (22%) and Saturday (23%) were the days with high sale and Sunday (6%) and Monday (7%) the days with low sale. Conclusion: Our results showed that many users obtain sildenafil without medical prescription and they use even without diagnostic of erectile dysfunction.

Financial Support: UNINOVE
Supervsor: Jorge Willian Leandro Nascimento

AF008-THE CONTRIBUITION OF A NEW MODEL OF STORAGE OF MEDICINES FOR AID TO THE PHARMACEUTICAL PRACTICE

KYRLAH JERONYMO (PG)[1]; ÉRICA FERREIRA MENDES (PQ)[1]

[1]Academical Center Newton Paiva

Introduction: The pharmacist plays promoter´s role in the orientation on medicines in community drugstores and educator in centers of academic formation in academical drugstores. Independent of the establishment the stages of the pharmaceutical attendance should be accomplished in a systematic and articulate way. The storage of medicines, disregarded stage of the process, was developed under new optics in the School Drugstore Newton Paiva, Belo Horizonte, to contribute with the academic´s formation and to promote a rational dispensing. The form of organizing the shelves was based on the classification Anatomical Therapeutical Chemical (ATC) in which the medicines are contained in agreement with the system where it will exercise pharmacological activity. Metodology: To organize the storage of the medicines, an adaptation of ATC was created. To evaluate the understanding of this organization and the implantation possibility in any drugstore, a questionnaire was applied in the trainees. **Results:** 57 academis were interviewed and it was observed that the classification is comprehensible, it aids in the professional formation and it propitiates a rational dispensing. Conclusion: The innovative form of storing medicines could be used by any drugstore contributing to the guided dispensing.

Supervisor: Kyrlah Jeronymo

AF009-OUTCOME OF PHARMACOLOGICAL TREATMENT OF PATIENTS HARBORING PROLACTINOMA - ROLE OF PHARMACEUTICAL CARE.

CRISTIANE FÁTIMA GUARIDO(PG); ANA VALÉRIA BARROS DE CASTRO(PQ)

Faculdade de Medicina - UNESP – Botucatu, Departamento de Clínica Médica

Pituitary adenomas secreting prolactin (prolactinomas) are relatively common tumors. The first-line of treatment for these tumors consists of dopaminergic agonist administration, usually associated with other drugs. This association potentially increases the risks of drug interactions (DI), adverse drugs reactions (ADR) and problems related with drugs (PRD). The objective of this study was to investigate and describe possible DI, ADR and PRD of patients harboring prolactinomas by applying Dader Methodology of Pharmaceutical Care (PC). PC was applied to ten patients for 3.9±1.6 months, 8 treated with bromocriptine and 2 with cabergoline, 1 with associated hormonal replacement (thyroxin and testosterone). The prolactinemia levels were 64.0±101 ng/dL; 50% of patients presented DI; 20% of patients presented with unexpected ADR; 80% presented PRD; 80% were self-medicated. After pharmaceutical intervention, the prolactinemia levels decreased to 34.6±45.3 ng/dL; 75% had no DI; 83% had no ADR; 87.5% had no PRD and 87.5% stopped self–medication. We concluded that PC increased the security of treatment and improved the outcome of patients harboring prolactinomas.

Supervisor: Prof. Dr. Ana Valéria B. de Castro

AF010-PHARMACEUTICAL SUPERVISION OF THE ANTIMICROBIALS USE IN A MATERNITY-SCHOOL IN FORTALEZA/CE

HANNAH I. DIAS(IC)[1;3];MARTA C. C. PINHEIRO(PG)[1;2];MARIANA O. B. SOUZA(PQ)[1;2];JULIANE R. AGUIAR(IC)[1];MYLENNE B. JÁCOME(IC)[1];GISLEI F. ARAGÃO(PG)[1]

[1]Assis Chateaubriand Maternity School(MEAC)/Federal University of Ceará(UFC);[2]Post Graduation in Pharmaceutical Science(UFC)/;[3]Pharmacy Course(UFC)

Introduction: The follow up of the antimicrobials use is an important tool in the bacterial resistance control. Objective: To delineate the profile of antimicrobials (atm) use for obstetric and gynecological patients in meac from january to october of 2003; to register and to characterize the occurrences related to the atm use and the pharmaceutical interventions made. Methodology:daily follow up of the atm dispenses with the occurrences registration and the pharmaceutical interventions made. Results:from 827 patients who had used atm, 74% remained in use for up to 4 days and 39% changed of the drug plan at least once. From 1226 antibiotic therapy (atbt) identified, 71.7% corresponded the monotherapy and 87.1% lasted up to 2 days. The more prescribed atm were cefalotin and ampicillin. It was registered 181 occurrences with 128 pharmaceutical interventions made, being respected 47.7%. **Conclusion:** The great variety of atbt indicates inexistence of protocols of treatment. The raised number of occurrences show the necessity of a bigger action, bringing together the pharmacy and the health professionals.

Supervisor: Mariana O. B. Souza

AF011-RESEARCH ON SELF-MEDICATION WITH PHYTOTHERAPICS AND THE IMPORTANCE OF PHARMACEUTICAL CARE IN PHYTOTHERAPY.

RALPH SANTOS OLIVEIRA (PQ) [1] ; SIMONE COULAUD-CUNHA(PQ) [2]

[1] Professor FF/UFF, UNIG-RJ e UNIVERSO-RJ
[2] Professora ad hoc da UNIG-RJ

Introduction: The self-medication has one cultural meaning in brazil. In the case of medicinal plants and phytotherapics it has an aggravation, because of the acquisition easiness and the sale exempts indiscriminate. The pharmacist must inform the patients that these "products" are medicines, and for that, the improper use can be dangerous. Objective: To evaluate the degree of the population information about phytotherapics and to present proposals for the rational use of medicinal plants through the clarification of basic concepts. Methodology: a research was carried through, in the city of rio de janeiro, where 80 people had been interviewed using strategies of classification of the sample, in age, school degree, and sex. Results: 86% of the interviewed affirmed that already used phytotherapics, 94% of these had not presented contraindications and 57% are unaware the necessity of communicate to the doctor the use of phytotherapics. Conclusion: The work obtained to evaluate the lack of information of the population in relation to phytotherapics. It also serves to enhance the great necessity of the insertion of the phytotherapics in the context of the medicine politics and the pharmaceutical assistance.

AF012-UNRAVELING THE PATIENT LIVED EXPERIENCE WITH PHARMACEUTICAL CARE: A QUALITATIVE APPROACH

ERIKA LOURENÇO DE FREITAS (PG) [(1)]; DJENANE RAMALHO DE OLIVEIRA (PQ) [(1)]; EDSON PERINI (PQ) [(1)]

[(1)] Faculdade de Farmácia da UFMG.

Introduction: Pharmaceutical care, as proposed by Hepler & Strand in 1990, emerged as a possible answer to the social need for a more rational use of medicines. **Objective:** To comprehend patients' experiences with the pharmaceutical care services offered in a community pharmacy in Belo Horizonte, MG. Methods: Semi-structured interviews with patients and a reflexive journal were used. Data were analyzed using the phenomenological-hermeneutical approach proposed by Max Van Manem. Results: Themes that emerged from the data, based on patients' experiences, include increase of patients' perception of safety in using their medications, lack of more incisive actions of the pharmacist related to the patient's pharmacotherapy, deterioration of the patient-health professional relationship and the need of a new approach to medication use. **Conclusions:** The comprehensive understanding of the meanings emerged from the patient lived experience with pharmaceutical care practice can grant pharmacists with new possibilities for caring in a more successful manner. A better understanding of the life world of patients followed-up by pharmacists can contribute to improve this new professional practice.

Financial support: CAPES
Supervisor: Dr. Djenane Ramalho de Oliveira

AF013-PHARMACEUTICAL CARE IN PATIENTS WITH HIGH BLOOD PRESSURE IN A SCHOOL OF PHARMACY OF SOUTH BRAZIL

JAQUELINE CAPELARI (IC) [1]; JULIANA ROMAN (PG)[1]; JANE MARLEI BOEIRA (PQ) [1]

[1] Universidade Regional Integrada do Alto Uruguai e das Missões, URI, Campus de Erechim, RS, Brazil

Hepler and Strand (1990) proposed a new professional experience called Pharmaceutical Care where pharmacists, students and patients discussed drugs and health problems related and tried to solve them. The aim of this study was to implant pharmaceutical care at the Pharmacy School in a University in Brazil (URI, Campus Erechim, RS) in patients with high blood pressure. For this, fifteen patients were observed during a semester. The study was developed by Dáder methodology. In the first interview 36 Medicines Related Problems (MRP) were detected and 41,67% of them were related to the high pressure blood pharmacological therapy. In addition to this, the pharmacists and students reviewed drug-use-profiles and blood pressure monitoring. 30 pharmaceutical interventions were realized and 21 of them were solved or minimized. These results indicate the adverse reactions, the lack of adhesion to the pharmacological treatment and the self-medication were the most frequent causes of the MRP. Moreover, pharmaceutical care provided an improvement of the patients quality of life after having solved the MRP.

Financial support: URI, Campus Erechim, RS
Supervisor: Jane Marlei Boeira

AF014- ECONOMIC IMPACT OF THE IMPLANTATION OF A SATELLITE PHARMACY IN THE SURGICAL SECTOR OF A MATERNITY IN FORTALEZA/CE

MARTA C.C. PINHEIRO(PG)[1,2];MARIANA O.B. SOUZA(PQ)[1,2];HANNAH I. DIAS(IC)[1,3];IANA L. FERNANDES(IC);[3]GISLEI F. ARAGÃO(PG)[1]

[1]Assis Chateaubriand Maternity School(MEAC)/Federal University of Ceará(UFC);[2]Post Graduation in Pharmaceutical Science/ UFC;[3]Pharmacy Course/UFC

Introduction:The satellite pharmacy implantation is useful in strategical sectors which posses raised supplies, high materials consumption, drugs of high unitary cost and need of special care in the storage of some products. Objective:To determine the economic impact of the satellite pharmacy implantation in the surgical floor of MEAC, from August to December of 2004. Methodology:Elaboration of spare lists of each sector and anesthetics and obstetric kits; withdrawal of the carryover stocks of drugs and correlates and weekly pharmaceutical supervision in the units; calculation of the costs for attendance to the sectors and of the value of returns to the pharmacy, and comparison to the same period of the previous year. Results:It was observed a reduction of 6,8% in the expenses to attend the units and an increase of 315,6% in the financial equivalent of the returns to the pharmacy. **Conclusion:** The satellite pharmacy implantation in the surgical floor of MEAC provided to the institution a significant economy, besides having implemented the pharmaceutical assistance in each sector attended.

The authors did not follow the Scientific Committee's suggestion for an English language review

AF015-MEDICATION NONCOMPLIANCE IN OUTPATIENTS WITH CHRONIC KIDNEY DISEASE: PRELIMINARY STUDY

LEONARDO B. MOREIRA (PG)[(1)]; PAULA F. C. B. C. FERNANDES (PQ)[(1)]; PABLO S. P. SILVA (IC)[(1)]; ROSA S. MOTA (PQ)[(1)]; FRANCISCA S. MONTE (PQ)[(2)]; QUEIROZ M.G(PQ)[(1);] ALICE M. C. MARTINS (PQ)[(1)]

[(1)] Universidade Federal do Ceará; [(2)] Universidade Potiguar

Introduction:Medication noncompliance in chronic kidney disease(CKD)can adversely affect the treatment outcomes, taking to increase of end-stage renal disease incidence.Objective: Identify and analyze factors related with medication noncompliance in CKD outpatients of the Academicals Hospital Walter Cantídio, in Fortaleza (CE).Methodology: This is a preliminary cross-sectional study with 11 CKD outpatients, at least 18 years old, taking some self-administered antihypertensive or immunosuppressive agent and not being submitted to renal replacement therapy.Compliance was measured by interview, physician assessment and outcome methods.The statistical tests used in the bivariate analysis were Mann-Whitney test, Fisher exact test and chi-square test ($p<0.05$).Results:Noncompliance was detected by any method in 5 patients (45.5%).The number of prescribed medicines was significantly ($p=0.03$) greater in the noncompliant group (5.00 ± 2.45x2.17 ± 0.98) and the number of daily doses was significantly ($p=0.03$) greater in the noncompliant group (8.00 ± 4.63x$2,83 \pm 1.17$) than in the compliant.Conclusions:These are preliminary results. A new stage of the work, with more patients, is being developed and will allow a more appropriate analysis of the determining factors and consequences of the medication noncompliance in CKD outpatients.

Supervisor: Alice M. C. Martins

AF016-ANTI-HYPERTENSIVES IN THE HIGH RISK PREGNANCY AND THE IMPACT IN THE HOSPITAL COSTS

TATIANA XAVIER DA COSTA-PG[1]; TAYNE ANDERSON CORTEZ DANTAS-PG[1]; ELAINE CRISTINA ALVES-PG[1]; IDYLLA SILVA TAVARES-IC[2]; GIOVANA RODRIGUES ARAÚJO-IC[2]; MIGUEL ADELINO DA SILVA FILHO-IC[2]; MARIA EMÍLIA PEREIRA PINHEIRO-IC[2]

[1]Pharmacist Maternidade Escola Januário Cicco - Universidade Federal do Rio Grande do Norte; [2]Trainee Maternidade Escola Januário Cicco - Universidade Federal do Rio Grande do Norte

Introduction: The hypertensive disease of the pregnancy is characterized by high level tensions being responsible by 35% (140-160 /100.000 maternal death born in Brazil), being confirmed as the major cause of the fetal obit. To control the blood pressure of the patient, decreasing the syntomatology and the possibility of convulsive crisis, are used especific medicines. Goal: Evaluate the hospital impact of the costs of the standard antihypertensives used by the pregnancy and the prevalence of the method. Methodology: The data was obtained from the medical prescription farmacy copyes referring to the patients interned in the "Unidade de Cuidados Intensivos da Maternidade Escola Januário Cicco-UFRN" in the period: June to December/2004. Results and Conclusions: The antihypertensives represent 0.75 % of the cost with medicines; the use of methyldopa being the remedy in the choice of pregnancy, corresponds to 69,4 % of the consume of hypertensives.

Supervisor: Tatiana Xavier da Costa

AF017-PATIENT PROFILE IN DRUG INFORMATION CENTER OF UFRJ

CARLA EDIALLA F. ZAIRE(IC)[1]; ISABEL GALDINO (IC)[1]; MÁRCIA M. B. PASSOS (PQ)[1]; NÁIRA V. B. VIDAL (PQ)[1]

[1] Farmácia Universitária – FF-UFRJ

Introduction: The Drug Information Regional Center (CRIM) of Rio de Janeiro has been funded in 1996 and our mission is answer the informations requires about drugs, helping the racional use of drugs with scientific-technical information. Objective: Evaluate the patient profile who required a information in CRIM, on last three years (2002, Jan to 2004, Dec). Methodology: Analysis data of solicitation recorders. Results: In the distribution of frequency of the kind of users was observed that pharmacist (48,48%); others (18,74%); patients (17,33%); students (8,20%); nurses (3,51%); doctors (3,04%) and teachers (0,7%). The age´s patients frequency: 82,0% adult (19–65 years), 8,0% seniors (65 years or more), 6,0% teenages (12-18 years) and 4,0% infants (0-12 years). Upon analyzing the nature of the information requested by the patient: others subjects (40,8%); drugs adverse reactions (19,7%); drugs interactions (8,4%), pharmacology (15,4%), stability (3,0%), technology pharmaceutical (2,0%); pharmacokinetic (2,8%) and dosage (1,4%). Conclusion: The results of this study show that the patient is the kind of user that requires the information center with frequency, what suggests that is a potential user of CRIM.

Financial Support: CRF-RJ
Supervisor: Márcia M. B. Passos

AF018-DESIGN OF AN INSTRUMENT FOR ASSESSMENT OF PHARMACEUTICAL SERVICES IN MUNICIPAL DISTRICTS

MAÍRA MELARÉ RAMOS DOS SANTOS(IC)[1]; SILVIO BARBERATO FILHO(PQ)[1]

[(1)]University of Sorocaba, Brazil

[Introduction] Pharmaceutical services encompass a group of activities related to medication and intended to provide support for the health care activities required by a community. [Objective] To design an instrument for assessing activities related to the provision of pharmaceutical services in municipal districts. [Methodology] The instrument was based on a literature review and on several inspection standards of the Brazilian National Agency for Sanitary Surveillance (Anvisa), publications of the World Health Organization (WHO), the Pan-American Health Organization (PAHO) and the Brazilian Ministry of Health. [**Results**] In addition to municipal district characterization, parameters were proposed to evaluate activities that involve pharmaceutical services, such as drug selection, programming, procurement, storage, distribution and dispensation. In order to provide elements for the analysis of data obtained with the new instrument, each parameter was classified as Indispensable (I), Necessary (N), Advisable (A) or Informative (INF). [Conclusion] Although validation has not been carried out, the instrument is expected to contribute to the evaluation and improvement of pharmaceutical services in municipal districts.

Supervisor: Silvio Barberato Filho

AF019-PROFILE OF DRUG UTILIZATION IN A BASIC HEALTH UNIT OF RIBEIRÃO PRETO, SP.

L.H.T. RODRIGUES PEREIRA (PQ)[1]; M.A. MORAIS (PQ)[1]

Municipal Health Service of Ribeirão Preto[1]

The pharmacy of Basic Health Unit Sérgio Arouca, Ribeirão Preto, attends the mean of 700 users/day. The objective of this study was to evaluate the profile of this pharmacy users as well as the most prescript and the most dispensed drugs. All the prescriptions were evaluated in relation to medical attendment divided into adults programmed consultation and emergence, and pediatric and in relation to the drugs prescript. The prescription analysis showed that 45% of the pharmacy attendment proceeds from the adults programmed consultation, 34% of the emergence and 21% of the pediatric. 68% of the users attended in the programmed consultation use drugs to the chronic diseases treatment (hypertension, diabetes and/or dyslipidemia). In the emergencial attendment prescription only 4% contained drugs to the chronic diseases treatment while the analgesic, anti-inflamatory and antipyretic agents were the most prescript drugs (53%) followed by the antibacterial agents (34%). In the pediatric, 35% of the consults resulted in antibacterial prescription. The evaluation showed that the adult population is the principal users of the service, the chronic diseases incidence is high in this adult population (57%) and is high the antibacterial utilization by the adults and children.

AF020-RATIONAL USE OF ANTIBIOTICS: EVALUATION ON QUALITY USE IN A BRAZILIAN CITY.

FERNANDO DEL FIOL(PQ)[1]; FERNANDA SALTO(IC)[1]; VANESSA MAGALHÃES(IC)[1]; ELISABETHE MARVULLE(IC)[1].

(1) University of Sorocaba

Introduction: The indiscriminate use of antibiotics has contributed significantly to increase the antimicrobial resistance around the world. Objective: This study observes the quality of the antibiotics use (prescription, orientation and patients' use) in a Brazilian city. Methodology: A survey containing 50 questions were divided in three parts: 1) questions about medical appointment and prescription; 2) questions about patients' pathology; 3) questions about the level of information of the patient regarding antibiotics. The patients answered this survey right before they received the antibiotics. Three pharmacies is in the sample: a) commercial; b) public and; c) University's pharmacy. Results and Conclusions: Forty percent of all users have been using other drugs that could cause drug interactions and induce therapeutic failure. Almost 40% of the patients did not complete the antibiotic course due to economical reasons and 20% due to disappearance of symptoms. The information level of the patients regarding antibiotics was 50% of correct answers, which shows the deficiency of knowledge of regarding this issue. We concluded that the necessity of educational campaigns is very urgent in order to promote the rational use of antibiotics and to inhibit the bacterial resistance.

Financial Support: FAPESP - The State of Sao Paulo Research Foundation.
Supervisor: Fernando Del Fiol.

AF021-THE ROLE OF THE ONCOLOGIC NURSE AND THE PHARMACIST IN CHEMOTHERAPY

PAULA ELAINE DINIZ DOS REIS (PG)[1], EMÍLIA CAMPOS DE CARVALHO (PQ)[2], ADRIANNE R. C. M. B. FERREIRA DE SANTANA[3]

[1, 2, 3] Ribeirão Preto Nursing School - USP

The antineoplasics are considered risk medications that may cause genotoxicity, carcinogenicity and teratogenicity, which makes complying with the regulation of norms for the chemotherapy services and the delegation of competencies for the oncologic team mandatory. The present study aimed at comparing the present practice of the nurses and pharmacists who act in chemotherapy with the minimum requirements established by the first Technical Regulation for the Functioning of the Antineoplasic Therapy Services, which is part of RDC Resolution # 220 dated September 21 2004, from the National Sanitation Watch Agency (ANVISA), which will be in force in September 2005. This is a descriptive study on the practice of these professionals in the chemotherapy services, identifying theoretical and legal elements that support their actions. It is believed that this study can contribute to a better performance of the nurses and pharmacists in both chemotherapy-related assistance and the biosafety of the users and health professionals involved.

The authors did not follow the Scientific Committee's suggestion for an English language review

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Bioquímica / *Biochemistry* (BQ)

BQ001-ENZYMATIC CHARACTERIZATION OF BJUSSUMP-II, A NEW PROTEASE FROM *BOTHROPS JARARACUSSU* SNAKE VENOM.

[2] SILVANA MARCUSSI (PG); [3] CAROLINA DALAQUA SANT'ANA (PG); [1] RAFAEL SPINOLA CAMBRAIA (IC); [3] MAURÍCIO VENTURA MAZZI (PG); [2] JOSÉ ROBERTO GIGLIO (PQ); [3] ANDREIMAR MARTINS SOARES (PQ).

[1]UNAERP; [2]FMRP; [3]FCFRP-USP, RIBEIRÃO PRETO-SP, BRASIL.

Introduction: Proteases are abundant in snake venoms and can affect the hemostatic system. Objective: A metalloprotease (BjussuMP-II) was isolated from *B. jararacussu* snake venom and functionally characterized. Methods and results: It was obtained through chromatography on CM-Sepharose in 0,05M AMBIC, pH 8.1, using a concentration gradient up to 1M, followed by Phenyl-Sepharose in 0,05M Tris-HCl, pH 7,4, using a decrescent gradient of NaCl from 4 to 0M. Its *Mr* by SDS-PAGE was around 24,000. Its enzymatic activity was evaluated spectrophotometrically upon casein, BAPNA and TAME as well as upon fibrinogen after previous incubation followed by SDS-PAGE at different concentration, reaction times, temperatures, pHs and presence of several ions and inhibitors. BjussuMP-II did not show any activity upon BAPNA or TAME, but was proteolytic upon casein or fibrinogen. It was kept stable at pH from 2,5 to 10,0 and showed to be sensible to heparin, EDTA, Co^{2+}, Mg^{2+}, Zn^{2+} and Ca^{2+}. It was neither hemorrhagic nor myotoxic but showed procoagulant effect upon plasma. Conclusion: BjussuMP-II represents a promising biotechnological potential to be used as a tool in future studies.

Financial support: FAPESP, CNPq, CAPES.
Supervisor: Andreimar Martins Soares

BQ002-N-ACETYLCYSTEINE (NAC) EFFECTS ON OXIDATIVE STRESS AND LIPIDEMIC PROFILE IN RATS WITH HIGH-SUCROSE INTAKE

KATIUCHA ROCHA (IC); YEDA DINIZ (PG); GISELE SOUZA (IC); CRISTIANO MACHADO GALHARDI (PG); LUCIANE FAINE (PG); HOSANA RODRIGUES (PG); GEOVANA EBAID (IC)

Depto. Química e Bioquímica,IB/UNESP/Botucatu

INTRODUCTION: Recently, much attention has been taken to new antioxidant compounds. **OBJECTIVE:** Thus the aim of the present study was to determine the effects of NAC on oxidative stress and lipid profile in rats fed high-sucrose diet. METHODS: 15 male Wistar rats (200g), divided into 3 groups (n=5): control C; S group drinking 30% sucrose (SAS) and (SNAC) treated with 2g/L NAC and SAS. Statistical: ANOVA and Tukey, $p<0.05$. **RESULTS AND DISCUSSION:** S group had higher body weight gain (119.1±10.7g), VLDL (37.0±9.9mg/dL) and triacylglycerol (TG) (185.0±46.7mg/dL) than the others groups. S (7.7±0.6%) and SNAC (6.6±0.4%) had lower alimentary preference than C (12.4±0.7%). SNAC had lower alimentary efficient (29.1±7.5g/Kcal) than C group(47.4±8.7g/Kcal). No alterations were observed in cholesterol, HDL, hidroperoxyde and oxidized-LDL (Ox-LDL) in S rats. SNAC had no effects on cholesterol, HDL, VLDL, but decreased the Ox-LDL (SNAC=30.2±8.6; S=38.9±5.5nmol/mg), when compared to S group. CONCLUSION: NAC had beneficial effects inhibiting the body weight gain induced by high-sucrose intake and an antioxidant effect decreasing the Ox-LDL.

Financial Support: FAPESP,CNPq
Supervisor: Ethel Novelli

BQ003-EFFECTS OF VITAMIN C IN INSULIN-DEPENDENT DIABETES MELLITUS: LIPID AND SERUM GLUCOSE PROFILES

RAQUEL VOLPATO BEDONE(IC)[(1)]; RAFAEL L. SAKAI(IC)[(1)]; RONALDO R. S. OLIVEIRA(IC)[(1)]; CRISTIANO M. GALHARDI[(2)]; ETHEL L. B. NOVELLI(PQ)[(2)]; ANA ANGÉLICA H. FERNANDES(PQ)[(2)]

[(1)]FMB/UNESP; [(2)]IB/UNESP

INTRODUCTION: Insulin-dependent diabetes mellitus (IDDM) is characterized by increased oxidative stress and a disturbance in glucose metabolism. Vitamin C, an important antioxidant, plays a role in preventing the development of atherosclerosis. **OBJECTIVE:** To evaluate the effects of vitamin C through parameters biochemists in diabetic rats. **METHODS:** 20 male rats (± 200g) were used in the experiment and distributed in: G1- untreated control; G2- normal rats receiving vitamin C (250mg.kg^{-1}); G3-untreated diabects and G4-diabects rats receiving vitamin C (250mg.kg^{-1}). Diabetes was induced by intraperitoneal injection of streptozotocin (60 mg.kg^{-1}). The animals received vitamin C daily, during 30 days. RESULTS: It resulted in a significant decrease in the levels of Triglycerides and VLDL-Cholesterol for the groups G2 and G4 in comparison to the G3. The serum cholesterol in the G3 group were higher then the others groups. Vitamin C did not modify the serum HDL-Cholesterol level, but it reduced ($p<0.05$) the glycemia in diabetic rats (G4=153,00±18,69 mg/dL). **CONCLUSION:** Vitamin C improved the lipid profile and demonstrated a hypoglycemic effect in diabetic rats.

Supervisor: Ana Angélica H. Fernandes

BQ004-BEHIND THE LIPID PROFILE: DIET, EXERCISE AND OXIDATIVE STRESS

REGINA M BURNEIKO (PG)[1]; IVANIA GARAVELLO (PQ)[1]; LUCIANE FAINE (PG)[2]; CRISTIANO MACHADO GALHARDI (PG)[2]; YEDA DINIZ (PG)[2]; HOSANA RODRIGUES (PG)[2]; GEOVANA EBAID (PG)[2]

[1] Dep Fisioterapia da Faculdade de Ciências e Tecnologia, UNESP, Presidente Prudente, SP
[2] Dep Química e Bioquímica, IB, UNESP, Botucatu, SP

Introduction: Intense exercise associated to dietary nutritional inadequacy is the result of many lifestyle disorders. **Objective:** The present study evaluated the effect of hypercaloric diet (HD) and physical exercise (PE) on lipid profile (LP) and oxidative stress (OS) in rat myocardium. **Methods:** Male Wistar rats (200g) were supplied with control (C:3.0kcal) and hypercaloric diet (HD:4.5kcal) and divided in sedentary (SC, SH) and exercised (CE, HE) subgroups. Serum samples and cardiac tissue were obtained after 9weeks. **Results:** PE reduced the final body weight. SH rats showed increased TG-C (68%), VLDL-C (69%), LDL-C (62%) and reduced HDL-C (23%). HD had no effect on hidroperoxide (HP) serum, although antioxidant property was increased. Association between PE and HD increased myocardium HP (43%). The benefic effect of PE was demonstrated by increased citrate synthase myocardial levels (84%). **Conclusion:** HD induced alters LP in SC and CE groups, although reverting. However, this condition induced myocardial OS. LP analysis itself did not indicate molecular myocardium injury.

Financial Support: FAPESP
Supervisor: Ethel Novelli

BQ005-CAN MAYTENUS ILICIFOLIA AQUEOUS EXTRACT ACT OVER OXIDANT SPECIES AND PEROXIDASES?

JOSÉ CARLOS R. VELLOSA(PG)[1,2]; VANESSA F. BARBOSA(IC)[1]; IGUATEMY L. BRUNETTI(PQ)[2]; OLGA M. M. F. OLIVEIRA(PQ)[1].

[1]Instituto de Química, UNESP-Araraquara; [2]Faculdade de Ciências Farmacêuticas, UNESP-Araraquara

Introduction: MPO, a neutrophil peroxidase, participates in highly oxidative species generation (e.g. hypochlorous acid-HOCl) and is involved in many diseases (e.g. Atherosclerosis, Alzheimer disease). **Objective:** evaluate if *M. ilicifolia* root bark aqueous extract (CMICRE) work as antioxidant and as peroxidase inhibitor. **Methods:** i)CMICRE and Trolox were assayed over HOCl-22µM (TNB oxidation: Phosphate buffer 50mM, pH7,0 and TNB-80µM) and their IC50 values were calculated; ii) CMICRE (10µg/mL and 1µg/mL) was evaluated in peroxidase assay: PBS-D buffer, guaiacol(2mM), peroxidase-HRP (7nM) and H_2O_2(0,1mM); initial velocities (sec^{-1}) were calculated. Results (media±SD; n=3; $p<0,05$): i)IC50 (µg/mL) over HOCl: 1,9±0,2 for CMICRE; 3,1±0,3 for Trolox; ii)peroxidase assay (v0 values): 0,014±0,001(control), 0,009±0(CMICRE 10µg/mL) and 0,012±0(CMICRE 1µg/mL). Conclusions: *M. ilicifolia* extract were better antioxidant than Trolox and it inhibited the peroxidase activity; these are really important results because oxidant species and peroxidases are essentials components on different oxidative damages.

Financial support: FAPESP and CAPES
Supervisor: Olga M. M. F. Oliveira

BQ006-FUNCIONAL CHARACTERIZATION OF BJUSSUSP-I, THE NEW THROMBIN-LIKE ISOLATED FROM *B. JARARACUSSU* VENOM.

CAROLINA DALAQUA SANT'ANA (PG)[1]; SILVANA MARCUSSI (PG)[2]; FÁBIO K. TICLI (PG)[1]; MAURÍCIO V. MAZZI (PG)[1]; JOCIVÂNIA O. DA SILVA(PG)[1]; JOSÉ R. GIGLIO (PQ)[2]; ANDREIMAR M. SOARES (PQ)[1]; SUELY V. SAMPAIO (PQ)[1]

[1] FCFRP/USP; [2] FMRP/USP- BRAZIL

Introduction: Serine proteases are enzymes present in snake venoms, responsible for *in vitro* blood clotting activity. Objective: To characterize enzymatic and pharmacologically a thrombin-like from *B. jararacussu* venom, named BjussuSP-I. Methods: Following evoluation of the minimal coagulant dose able to clot plasma in 1 min. at 37ºC. The coagulant and fibrinogenolytic activity of BjussuSP-I was evaluated under different conditions of temperature, pH and inhibitors or ions. The proteolytic activity was measured on different substrates such as casein, fibrinogen, fibrin and BAPNA. Assays were carried out to evaluate its ability to induce hemorrhage, edema and myotoxicity in mice. Results: BjussuSP-I showed a high coagulant activity upon plasma, high stability, which decreased only at low pH and high temperatures. The ions Fe^{2+}, Ca^{2+}, Mn^{2+} and Zn^{2+}, and the inhibitors PMSF and leupeptin, decreased its activity. BjussuSP-I displayed proteolytic activity upon the several substrates assayed, except for casein. BjussuSP-I did not show hemorrhagic and myotoxic activity but was only able to induce a moderate edema inducing effect at high. Conclusion: BjussuSP-I, a glycoprotein from *B. jararacussu* snake venom, is a thrombin-like, relatively stable under different temperature and pH, with no toxic effect.

Financial support: FAPESP and CAPES
Supervisor: Suely Vilela Sampaio

BQ007-MONOSODIUM GLUTAMATE, METABOLIC SYNDROME AND OXIDATIVE STRESS IN RATS

YEDA DINIZ (PG); CRISTIANO MACHADO GALHARDI (PG); GISELE SOUZA (IC); LUCIANE FAINE (PG); HOSANA RODRIGUES (PG); GEOVANA EBAID (IC); REGINA M. BURNEIKO (PG); ANTONIO CICOGNA (PQ)

Departamento de Química e Bioquímica,IB/UNESP/Botucatu,SP.

INTRODUCTION:Dietary monosodium glutamate (MSG) addition may induce hyperphagia and some metabolic changes. OBJECTIVE:The objective of this study was to determine the MSG effects in standard and in fiber-rich diet, on serum glucose, lipid profile and oxidative stress in rats. METHODS: Male Wistar rats (65±5g; n=8) were fed control standard diet (C), standard diet with 100g MSG/kg (MSG), fifer-rich diet (F), fiber rich diet 100g MSG/kg (MSG-F). Treatment was 45 days. Statistical-ANOVA and Tukey ($p<0.05$). RESULTS AND DISCUSSION: Food intake was increased (16%) in MSG rats. MSG group had increased glucose (14.8%), triacylglycerol (TG,13%), insulin (95%), leptin (79%) and homeostasis model assessment (78%) than C. These effects were related to the imbalance of oxidant/antioxidant systems. MSG group had higher lipid hydroperoxide (58%) than C. TG was decreased in F (27%) and MSG-F (14%) rats. CONCLUSION: MSG in standard diet enhanced the food intake. The overfeeding induced metabolic disorders associated with oxidative stress. Fiber-rich diet is beneficial, avoiding overfeeding and improving oxidative stress induced by MSG.

Financial Support: FAPESP, CNPq
Supervisor: Ethel Novelli

BQ008-SYNTHESIS AND INHIBITORY EFFECT OF D-GALACTOSE AND LACTOSE DERIVATIVES ON HEMAGLUTINATION INDUCED BY THE *RICINUS COMMUNIS* TOXIC LECTIN

DIOGO TEIXEIRA CARVALHO [(1)] (PG); ANNA PAOLA BUTERA [(2)] (PG); RUTE CUNHA FIGUEIREDO [(1)] (PG); MARIA ANGÉLICA NUNES [(1)] (IC); LUIZ CARLOS ALVES DE FARIA [(1)] (IC); RICARDO JOSÉ ALVES [(1)] (PQ); MARIA AUXILIADORA FONTES PRADO [(1)] (PQ); MILTON HERCULES GUERRA [(3)] (PQ); ALEXANDRE GONÇALVES DOS SANTOS [(3)] (IC).

[(1)] Faculdade de Farmácia - UFMG; [(2)] Instituto de Ciências Exatas - UFMG; [(3)] Instituto de Ciências Exatas e Biológicas - UFOP.

INTRODUCTION
Lectins are proteins that bind sugars specifically. This binding plays an important role in cell adhesion processes which can be involved in several diseases. Among plant lectins, much attention has been focused on ricin, a toxin from *Ricinus communis*.
OBJECTIVE
Synthesis and evaluation of inhibitory activity of D-galactose and lactose derivatives on ricin-induced hemaglutination.
METHODOLOGY
D-galactose and lactose derivatives were synthetized by classical carbohydrate chemistry reactions and characterized by infrared and ^{1}H and ^{13}C NMR spectrometry. Inhibitory effect on hemaglutination was performed by standartized protocols.
RESULTS AND CONCLUSIONS
Fourteen compounds were synthetized and tested. D-galactose and lactose were used as reference compounds. galactose aromatic glycosides were better inhibitors than the other derivatives.

Financial Support: Fapemig; CNPq
Supervisor: Ricardo José Alves

BQ009-EFFECTS OF DIGITONIN ON DISLIPIDEMIA INDUCED BY TIME-RESTRICTED DIETARY INTAKE

GEOVANA EBAID(IC); CRISTIANO MACHADO GALHARDI(PG); LUCIANE FAINE(PG); HOSANA RODRIGUES(PG)

Departamento de Química e Bioquímica, IB/UNESP, Botucatu

INTRODUCTION:Much attention has been given to antioxidants intake on heart diseases prevention. **OBJECTIVE:**Thus, the aim of the present study was to determine the effects of digitonin on dislipidemia induced by time-restricted dietary intake. **METHODS:** Male *Wistar* rats, 60d old, were divided into 4 groups of 6 rats each. Control *ad lib.* diet (C). Time-restricted group (R) received the amount of diet given to C group for 1 hour (9-10h). Group CD received 10% digitonin solution and *ad lib.* diet. Group RD received the amount of diet consumed by group CD for 1 hour and digitonin. Statistical:ANOVA and Tukey, $p<0.05$. **RESULTS AND DISCUSSION:** R and RD groups had lower final body weight (C=354±14g; R=194±47g; CD=362±28g; RD=215±26g). No alterations were observed in serum protein, HDL and total cholesterol. R group presented elevation in LDL (C=34±8mg/dL; R=48±6mg/dL) and LDL/triacylglycerol (C=0.4±0.1; R=0.8±0.1). Group CD presented elevation on HDL/LDL (C=1.5±0.4; CD=1.9±0.5). No differences were observed on lipid profile on RD compared with R. **CONCLUSION:** Digitonin improved the lipid profile of C group. However, digitonin was not sufficient to prevent dislipidemia induced by time restricted dietary intake.

Financial Support: CNPq, FAPESP
Supervisor: Ethel Novelli

BQ010-ACTION OF NICOTINE ON SERUM ACETYLCHOLINESTERASE (ACHE) AND BUTYRYLCHOLINESTERASE (BCHE) ACTIVITY

FABIANE SÔNEGO (IC) [(1)]

[(1)]Universidade Federal de Santa Maria

INTRODUCTION: Serum cholinesterase has been used as marker of exposure to some compounds. Previously we showed that nicotine inhibits the activity of AChE from plasma of humans.
OBJECTIVE: To evaluate nicotine effects on the AChE and BChE activities from serum of rats, and to determine the sensitivities of both activities to this compound.
METHODS: AChE and BChE activities were determined according to *Ellman's* method, using acetylthiocholine (ATC) and butyrylthiocholine (BTC) as substrates, respectively. The final concentrations of nicotine ranged 0 to 5.0 mM. Ethopropazine 0.01mM was used to inhibit the BChE activity.
RESULTS: Nicotine caused a greater inhibition on AChE than on BChE activity in the absence of ethopropazine. Ethopropazine caused inhibition of 15.54% on AChE activity and 82.22% on BChE. The inhibitory effect of nicotine on these activities in the presence of ethopropazine revealed that only the hydrolysis of ATC was inhibited by nicotine. The residual BChE activity, after inhibition by ethopropazine, remained unaltered.
CONCLUSION: These results show that only serum AChE activity was inhibited by nicotine, and suggest that the serum BChE can not be used as a marker of exposure to nicotine.

Financial Support: FAPERGS
Supervisor: Maria Ester Pereira

BQ011-STUDYING THE INTERACTION OF S(-)BUPIVACAINE AND BETA-CYCLODEXTRIN BY HPLC

CAROLINA M. MORAES (IC)[1]; PRISCILA ABRAMI (IC)[1]; ENEIDA DE PAULA (PQ)[2]; LEONARDO F. FRACETO (PQ)[1,2]

[1] Univ. Sorocaba; [2] Dep. Biochem./Unicamp

Introduction: S(-)Bupivacaine, S(-)BVC, is a local anesthetic that is used worldwide due to its long action and high potency. Cyclodextrins (CD) can be used as a drug-carrier system since they are able to form inclusion complexes with many drugs, modifying their physic-chemical properties. Objectives: The aim of the present study was to prepare and to characterize inclusion complexes of S(-)BVC in CD, using HPLC.
Method: The retention behaviour of S(-)BVC, CD and of the complex has been analyzed in a wide temperature range (25-45ºC) using a reverse-phase C_{18} column, using methanol/5mM phosphate buffer, pH 7.4 (70/30, v/v) as the mobile phase in which CD was incorporated as an additive (in a range of 0-30 mM).
Results: The decrease in the S(-)BVC retention time as a function of CD concentration allowed the determination of the association constant (K) while temperature variation allowed the measurement of thermodynamic parameters using the van't Hoff plot. The values of K, determined between S(-)BVC and CD were 13.4, 5.2, 4.9 and 3.6 M^{-1} at 25, 35, 40 and 45ºC, respectively.
Conclusion: The K values and thermodynamic parameters determined by HPLC confirmed the formation of a S(-)BVC:CD complex.

Financial Support: FAPESP/UNISO
Supervisor: Leonardo F. Fraceto

BQ012-DIFFERENTIAL INTERACTION BETWEEN TWO CLINICALLY USED LOCAL ANESTHETICS AND CYCLODEXTRIN

PRISCILA ABRAMI (IC)[1]; CAROLINA M. MORAES (IC)[1]; ENEIDA DE PAULA (PQ)[2] & LEONARDO F. FRACETO (PQ)[1,2]

[1]Univ. of Sorocaba; [2]Dep. Biochemistry/Unicamp

Introduction: Bupivacaine (BVC) and Lidocaine (LDC) are drugs-of-choice for clinical procedures and have different physico-chemical properties. Hydroxypropyl beta-cyclodextrin (HP-bCD) is used as a drug-carrier system in order to increase drug bioavailability. Objectives: The aim of this work was to prepare and to characterize inclusion complexes between local anesthetic and HP-βCD. Methodology: The complexes were prepared at different BVC (or LDC) and HP-βCD molar ratios. For equilibrium of the complex formation, the samples were shaked up to 24h. The systems were studied relatively to their kinetics of complexation and release as well as to phase solubility, by spectrophometry. Results: The kinetics of complexation revealed that 8 h is enough for stabilization of the anaesthetics' absorbance. The affinity constants determined at pH 10.5 were 96.1±11.8 M^{-1} and 35.7±4.7 M^{-1} for BVC and LDC, respectively. The release kinetics experiments showed that BVC released 24% while LDC released 88% after 180 minutes, at pH 7.4. Conclusion: Chemical structure and pH play an important role in the complexation and release profile of BVC and LDC complexes with HP-βCD.

Financial Support: FAPESP/UNISO
Supervisor: Leonardo F. Fraceto

BQ013-GLYCERONEOGENESIS (G3P*NEO*) IS DECREASED IN ADIPOSE TISSUE (WAT) FROM RATS ADAPTED TO A HIGH CALORIC DIET (HCAL)

VALÉRIA E. CHAVES[(1)](PG) DANÚBIA FRASSON[(1)](PG) M.EMÍLIA SM SANTOS[(2)](PG) RENATA P BOSCHINI[(1)](PG) MARIA AR GARÓFALO[(1)] ISIS C KETTELHUT[(2)](PQ) RENATO H MIGLIORINI[(2)] (PQ)

Departments of [(1)]Physiology and [(2)]Biochemistry FMRP USP

INTRODUCTION Glycerokinase (GyK) activity is low in WAT, the only recognized source glycerol-3-phosphate (G3P) for triacylglycerol synthesis being glucose (*via* glycolysis). G3Pneo (G3P synthesis from three carbon compounds) has been little investigated. AIM To investigate the effect of HCAL on WAT G3P*neo* METHODS Rats were fed for 24 days a HCAL or control diet. The contribution to G3P formation by each pathway was evaluated by:a)incorporation of ^{14}C-pyruvate or ^{14}C-glycerol into TAG-glycerol from epididymal(nmol.10^6cells^{-1}.hour^{-1});b)determination of GyK and p-*enol*pyruvate-carboxykinase(PEPCK) activities(nmol.mg protein^{-1}. min^{-1});c)*in vivo* glucose uptake using 2-deoxy[^{14}C]-glucose(ng.mg tissue^{-1}.min^{-1}) RESULTS WAT from HCAL-fed rats showed: a)an increased glucose uptake(2.7±0.4vs1.8±0.2); b)increased GyK activity(1.5±0.1vs1.1±0.1) and incorporation of ^{14}C-glycerol into TAG-glycerol(25.1±0.1vs14.7±0.9); c)decreased in PEPCK activity(1.9±0.2vs3.0±0.2) and incorporation of ^{14}C-pyruvate(5.0±0.8vs16.7±0.7) into TAG-glycerol. CONCLUSION The G3P-generating pathways are adjusted to maintain an adequate supply of G3P.

Financial support: FAPESP, CNPq
Supervisor: Renato H. Migliorini

BQ014-ANTIOXIDANT PROPERTIES AND FATTY ACIDS CONTENTS OF THE BRAZILIAN ALGAE *HYPNEA MUSCIFORMIS*

THAIS GUARATINI (PG)[1]; DAYANA R. GOUVEA (IC)[2]; ERNANI PINTO (PQ)[3]; NORBERTO P. LOPES (PQ)[2]; PIO COLEPICOLO (PQ)[1]

[1]Dep. Bioquímica, IQ-USP;
[2]Dep. Química e Física, FCFRP-USP;
[3]Dep. Análises Clínicas e Toxicológicas, FCF-USP

Introduction: Many studies have focused on the search of active compounds extracted from red algae for different purposes. Among the most encountered and studied compounds we can include fatty acids and antioxidants agents.
Objective: Evaluation of the antioxidant activity of *Hypnea musciformis* extracts and quantification of its fatty acids.
Methodology: Algae were extracted, fractionated according polarity, and the extracts were dried. The antioxidant activity was evaluated through the vitamin E equivalent antioxidant capacity. Fatty acids were extracted and methylated for analysis by GC and GC-MS.
Results: Increasing concentration of the extracts showed a linear dose-response curve of scavenging activity. An antioxidant capacity of approximately 1.5%, related to the vitamin E antioxidant capacity was obtained. Among the fatty acids quantified, it was found high amounts of lauric, miristic, palmitic, stearic and oleic acids.
Conclusion: These results suggest that the extracts studied may present potent antioxidant capacity, and adds valuable information on lipid composition of this alga, for pharmaceutical applications.

Support: FAPESP, CAPES, CNPq
Supervisor: Prof Dr Pio Colepicolo

BQ015-PENTOXIFYLLINE TREATMENT DECREASES MUSCLE WASTING IN DIABETIC RATS.

AMANDA M. BAVIERA(PG)[(1)]; NEUSA M.Z. RESANO[(1)]; LUIZ C.C. NAVEGANTES(PQ)[(1)]; RENATO H. MIGLIORINI(PQ)[(1)]; ISIS C. KETTELHUT(PQ)[(1)].

[(1)]Departments of Physiology and Biochemistry, Faculty of Medicine, USP, Rib. Preto, Brazil

INTRODUCTION: It is well known that diabetic rats lose body weight mainly due to enhanced skeletal muscle proteolysis. Pentoxifylline (PTX; cAMP-phosphodiesterase inhibitor) has been used to treat cachectic animals to prevent muscle mass loss. **OBJECTIVES:** Investigate the effect of PTX treatment on muscle protein breakdown of diabetic rats. METHODS: Male Wistar rats (70-80g) were injected with streptozotocin (135mg STZ/kg, *i.v.*). Three days after STZ and four days after PTX treatment (100mg/kg, *s.c.*) diabetic and normal rats (saline and PTX-treated) were killed and *extensor digitorum longus* (EDL) incubated. The rates of overall proteolysis and of the proteolytic systems (lysosomal, Ca^{2+}- and ATP-dependent) were determined by measuring the rates of tyrosine release. **RESULTS:** The increase in the activity of Ca^{2+}- and ATP-dependent proteolytic systems in EDL from diabetic rats was prevented by PTX treatment, which promoted decrease in total rates of protein breakdown (~21%) and in proteolytic pathways (47%, Ca^{2+}- and 23%, ATP-dependent). CONCLUSION: Probably PTX decreases the rates of Ca^{2+}- and ATP-dependent proteolysis by increasing intramuscle cAMP levels.

Financial Support: CNPq, FAPESP
Supervisor: Isis C. Kettelhut

BQ016-IN VITRO ASSAYS FOR STUDYING THE EFFECT OF XENOBIOTICS ON THE ACTIVITY OF HUMAN NEUTROPHIL MYELOPEROXIDASE AND NADPH OXIDASE

YARA M. LUCISANO-VALIM (PQ)*; ANDREA S.G. FIGUEIREDO (IC); JOEL G. SOUZA (IC); ALEXANDRE KANASHIRO (PG); LIVIA M.C. SIMÕES-AMBROSIO (PG); LUCIANA M. KABEYA (PG); ANA CRISTINA M. POLIZELLO (PQ); ANA ELISA C.S. AZZOLINI (PQ).

Depto. Física e Química, FCFRP/USP, *yaluva@usp.br

Neutrophils (PMNs) play an essential role in the defense of the organism against invading microorganisms, throughout generation of reactive oxygen species (ROS). This function is mediated by NADPH oxidase complex (NADPH-ox), which reduces molecular oxygen to superoxide anion radicals, and myeloperoxidase (MPO), which converts hydrogen peroxide to the strong oxidant hypochlorous acid. Despite its beneficial effects, PMNs-derived ROS has also been implicated in the pathogenesis of many inflammatory diseases. In this work, the experimental conditions for *in vitro* studies of xenobiotics effects on human PMNs enzymes were established. NADPH-ox activity was evaluated by oxygen consumption, measured with Clark electrode. MPO was extracted from PMNs and the enzyme activity was evaluated by luminol-enhanced chemiluminescence. Additionally, quercetin activity was assessed, and it had a concentration-dependent inhibitory effect on both enzymes. The proposed methods may be useful for investigating the mechanism of action of xenobiotics that modulate PMNs oxidative metabolism.

Support: FAPESP, CNPq
Supervisor: Yara M. Lucisano-Valim

BQ017-PARACOCCIDIOIDES BRASILIENSIS ALTENATIVE OXIDASE HETEROLOGOUS EXPRESSED GENERATES CYANIDE RESISTANT RESPIRATION IN E. COLI

VICENTE DE PAULO MARTINS (PG) [(1)]; FREDERICO MARIANETI SORIANI (PG) [(1)]; TAISA MAGNANI (PG) [(1)]; VALÉRIA GOMES TUDELLA (PG) [(1)]; GUSTAVO HENRIQUE GOLDMAN (PQ) [(2)]; SÉRGIO AKIRA UYEMURA (PQ) [(1)].

Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP: [(1)] DACTB; [(2)] DCF

P. brasiliensis, a thermically dimorphic fungus, is the etiological agent of paracoccidioidomycosis one of the most prevalent human systemic mycosis in Latin America. An alternative respiratory pathway besides the cytochrome *c* pathway has been well described in some fungi and protists. This alternative pathway is comprised of a single protein, alternative oxidase (Aox), that is a potential target for chemotherapy. Thus, the Aox cDNA clone of *P. brasiliensis* (*aoxPb*) was subcloned into the *E. coli* expression vector [pET28a(+)] and heterologous expressed in Rosetta™(DE3)pLysS *E. coli* strain. Functional characterization of the AoxPb was carried out measuring the oxygen uptake by bacteria with a Clark-type electrode. The oxygen uptake by control cells [*E. coli* and *E. coli*/pET28a(+)] were totally inhibited by KCN, on the other hand the respiration of *E. coli*/pET28a(+)-*aoxPb* was partially inhibited by KCN and inhibited by KCN plus SHAM. These data show *aoxPb* gene can be functionally expressed conferring cyanide resistant respiration to Rosetta™.

Support: Fapesp and CAPES
Supervisor: Sérgio A. Uyemura

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BQ018-COMPARISON BETWEEN WATER-SOLUBLE AND WATER-INSOLUBLE POLYSACCHARIDES FROM THE ROOT OF ANGICO BRANCO

FLÁVIA C. MATTANA(IC)[(2)]; ANA P. BOMBARDA(IC)[(2)]; MARINA K. KADOWAKI(PQ)[(2)]; RICARDO WAGNER(PG)[(1)]; GUILHERME L. SASSAKI(PQ)[(1)]; CLARICE A. OSAKU(PQ)[(2)]

[1]Departamento de Bioquímica – UFPR–PR
[2]Centro de Ciências Médicas e Farmacêuticas – UNIOESTE-PR.

Introduction: Angico branco is a leguminose tree and it was studied for you immunological properties and can be used in respiratory problems. Objective: Isolation and characterization of polysaccharides. Methodology: The polysaccharides were obtained by extraction with water and different concentration of the aq. KOH at 80°C under reflux. The KOH extracted was dialyzed and the polysaccharides were obtained by precipitation with excess EtOH and then submitted to freeze-thawing, giving a water-soluble(S) and water-insoluble(I) fractions. The monosaccharides components of this fractions were analyzed by GC-MS. Results: The fraction 1FS had glc:ara:gal:xyl:galA (79,3:5,5:4,8:1:9,4 molar ratio) and 1FI had glc:fuc:ara:rha:xyl (95,9:2,1:1,1:0,5:0,3). The fraction 4FS had glc:xyl:ara:gal:galA (68,7:15,1:3,2:1,9:11) and 4FI glc:xyl:rha:ara:fuc:gal (45,8:28,3:11,2:6,7:5,3:2,7). The fraction 7FS had xyl:glcA (60:40) and 7FI had xyl:gal:rha:glc:ara:man (84,7:7,0:3,0:2,0:1,7:1,6). Conclusion: The freeze-thawing process shown different polysaccharides from the root of angico branco.

Financial Support: PIBIC-UNIOESTE/PR
Supervisor: Clarice A. Osaku

BQ019-ANTIOXIDANT POTENCIAL OF DIPHENYL DISELENIDE: STUDIES ON THE EFFECT OF LONG TERM DIET SUPPLEMENTATION IN RABBITS

ANDREZA FABRO DE BEM(PG)[1]; ANDRESSA SAUSEN DE FREITAS(IC)[1];RAFAEL PORTELLA(IC)[1]; JULIANA DE LONGHI(IC)[1];MARTA DUARTE(PG)[1]

[1]Universidade Federal de Santa Maria

Many diseases are accompanied by oxidative stress which is characterized by a situation that more oxygen species are formed.Based on fact that diphenyl diselenide demonstrated protection against lipid peroxidation we appraised the antioxidant role of this organodiselenide compound. Twenty rabbits were used in the present study,divided into four groups and were fed with commercial diet supplemented with 0,3, 3 or 30ppm of diphenyl diselenide and the control group only with commercial diet for eight months.Biochemical profile, TBARS, CAT, GPx, ascorbic acid, ALA-D and SH were measured in liver and kidney of this rabbits. There were not significant difference in the level of TBARS and in the enzyme activities of GPx,CAT and ALA-D in liver and kidney of all animals.However,there were a significant increase in SH level in liver of animals treated with diphenyl diselenide and a decrease in the ascorbic acid levels in kidney and liver of all animals in a concentration dependent manner. The results of this study indicates that chronic administration of diphenyl diselenide may pose no toxicological effect, suggesting this compound may be a promising antioxidant.

Supported by: CNPq,CAPES
Supervisor: João Batista T. Rocha

BQ020-OPTIMIZATION OF EXTRACELLULAR XYLANASE PRODUCTION BY *FUSARIUM HETEROSPORUM*

CAROLINE HENN (IC)[(1)]; ANGÉLICA R. CAPPELLARI(IC)[(1)]; VIVIANE C. H. SILVA(IC)[(1)]; ADRIANA ZILLY(PQ)[(2)]; CLARICE A. OSAKU(PQ)[(1)]; MARINA K. KADOWAKI(PQ)[(1)].

[(1)]Centro de Ciências Médicas e Farmacêuticas – UNIOESTE-PR
[(2)]Departamento de Ciências Biológicas –UNIAMÉRICA- PR

Introduction: Xylanases, are used in the biobleaching of kraft pulps, reducing the emanating of chlorine; in food processing, clarifying juices, in treatment of animal feed; generation of biological fuels, and other chemicals from agricultural wastes. Objective: Study some properties of the xylanolytic system from *Fusarium heterosporum.* Methodology: The enzymatic production was carried out in liquid media, supplemented with 1,5 % of corn straw. After 7 days of incubation at 25ºC in static conditions, the xylanolitic activity were determined by hidrolysis of xylan and the reducing sugar were then quantified by 3,5 dinitrosalicylic acid. Results: The best culture medium to the enzymatic production was the Khanna modified, when the fungus showed activity xylanolytic of 1,61 U/mg of protein. Crude cellulase-free xylanase showed a high termal stability at 55ºC, in pH 6,5, maintained levels of activity around 5.43 U/mg after 3 hours. Conclusion: *Fusarium heterosporum* was capable to produce stable extracellular xylanase that hydrolyze the xylan from corn straw, promising to be useful in industrial applications.

Supervisor: Marina K. Kadowaki

BQ021 - HYPOCHLOROUS ACID SCAVENGING PROPERTIES OF DRUGS WITH TERTIARY AMINE FUNCTIONAL GROUPS

NAJEH MAISSAR KHALIL(PQ)[1]; JOSE CARLOS REBUGLIO VELLOSA(PQ)[2]; IGUATEMY LOURENÇO BRUNETTI(PQ)[1]; VALDECIR FARIAS XIMENES(PQ)[1]; LUIZ MARCOS DA FONSECA(PQ)[1]; OLGA MARIA MASCARENHAS DE FARIA OLIVEIRA(PQ) [2]

DAC-FCF/UNESP[1]; DBT-IQ/UNESP[2]

Introduction:The generation of hypochlorous acid (HOCl) through myeloperoxidase (MPO) catalyzed Cl^- oxidation is involved in antimicrobial activity. Tertiary amines (R_3N), as quinine (QUI), ranitidine (RAN) and trimethylamine (TMA) are able to react with HOCl leading to the highly reactive quaternary chloramonium ions. Objective: Study the effect of R_3N on HOCl generated by MPO/H_2O_2/Cl^- system. Methodology:The production of HOCl was monitored by taurine/tetramethylbenzidine (TMB) coupled assay. MPO (2.5 nM) was incubated at 37 °C in PBS buffer (0.05M, pH 6.0, NaCl 0.14M) with H_2O_2 (0.1mM) and taurine (1mM), in the presence or absence of R_3N by 15 minutes. The reaction was stopped by adding catalase (0.03 mg/ml) and revealed by adding TMB (2.4mM). HOCl was detected by TMB oxidation which was measured at 652 nm. Results and concluions:The effect of the R_3N (1000, 100, 10 and 1 μM) as scavenger of HOCl was quantified and the % of inhibition calculated from the control (RAN: 98±2.8, 98±3.2, 90±0.7 and 53±4.9; QUI: 81.3±1.8, 30±0, 0±0 and 0±0; TMN: 42±4.2, 42±4.9, 22±3 and 20±0.1). The results showed that RAN but not QUI or TMN is an efficiently scavenger of HOCl generated by MPO/H_2O_2/Cl^-.

Supervisor: Olga Maria Mascarenhas de Faria Oliveira

BQ022-PURIFICATION AND CHARACTERIZATION OF AN ANGIOGENIC PROTEIN FROM THE NATURAL LATEX OF RUBBER TREE (*HEVEA BRASILIENSIS)*.

RICARDO J. MENDONÇA (PG) [1]; VANESSA B. MAURÍCIO (PG) [1]; MARIA LETÍCIA P. AGOSTINI (PG) [1]; JOAQUIM COUTINHO-NETTO (PQ) [1]

[1] Department of Biochemistry, FMRP, USP

Introduction: The angiogenesis is an important event to the wound repair and healing. It is also important on tumoral growth and revascularization of tissues submitted to ischemia. It has been suggested that the latex from *Hevea brasiliensis* posses angiogenic activity, leading us in this work to initiate the purification of active(s) compound(s) and to characterize it, in order to demonstrate its angiogenic activity and its effects on vascular permeability and wound healing.
Objectives: Isolation of the angiogenic factor from natural latex of rubber tree (*H. brasiliensis)*
Methodology: The crude latex was fractionated by chromatography and activity analyzed by Miles' test (vascular permeability) and chorioallantoic membrane eggs assays (angiogenicity).
Results: Angiogenic protein was isolated by chromatography (two steps) and the purification efficiency was demonstrated by PAGE-electrophoresis and isoelectric focusing.
Conclusions: An angiogenic protein (referred to as hevenina) was isolated and it can be the responsible for the wound healing activity of natural latex of rubber three.

Financial Support: CAPES
Supervisor: Joaquim Coutinho Netto

BQ023-COMPARATIVE STUDY OF ISOLATION PROCEDURES TO OBTAIN HUMAN NEUTROPHILS OF PATIENTS WITH RHEUMATOID ARTHRITIS

ADRIANA BALBINA PAOLIELLO PASCHOALATO (PG)[1]; MIRIAN RIBEIRO MOREIRA (PG)[2]; DAIANI CRISTINI DE OLIVEIRA ANDRADE (PG)[1]; ANA CRISTINA M. POLIZELLO (TC)[1]; ANA ELISA C. S. AZZOLINI (TC)[1]; YARA MARIA LUCISANO-VALIM(PQ)[1]

[1]Depto. de Física e Química, FCFRP-USP; [2] Depto. de Bioquímica, FMRP- USP; [3] Depto. de Imunologia Básica , FMRP-USP.

Neutrophils are essential to host defense against bacterial and viral infection. They are also involved in the pathology of several inflammatory diseases. Studies with neutrophils frequently employ these cells for understand processes to cell biology through the investigation of substances that neutrophlis produce after their estimulation. Techniques for neutrophils purification are very important to study the characteristics of these cells. However, many of the currently available methods for isolation do not combine the rapidity, purity, reliability and inexpensiveness needed for routine of laboratory. The present work compares three isolation methods to separate human neutrophils, frequently used and cited in the literature. The effectiveness of each method was measured through chemiluminescence assay.

Financial Support: CAPES
Supervisor: Yara Maria Lucisano-Valim

The authors did not follow the Scientific Committee's suggestion for an English language review

BQ024-GLYCERONEOGENESIS (G3P*NEO*) AND GLUCOSE UPTAKE IN DENERVATED ADIPOSE TISSUE (WAT)

DANÚBIA FRASSON(PG)[1]; VALÉRIA E CHAVES(PG)[1]; M.EMÍLIA SM SANTOS(PG)[2]; RENATA P BOSCHINI(PG)[1]; MARIA AR GARÓFALO[1]; ISIS C KETTELHUT(PQ)[2]; RENATO H MIGLIORINI(PQ)[2]

Departments of [1]Physiology and [2]Biochemistry FMRP USP

WAT G3P*neo* [synthesis of glycerol-3-P(G3P) from 3 carbon compounds] increases in situations of reduced glucose utilization, such as fasting, suggesting that G3P*neo* compensates the decreased G3P production via glycolysis.AIM:To investigate the effect of sympathetic denervation on WAT G3P*neo* and glucose uptake in fed or 48 hr-fasted rats.METHODS:Retroperitoneal WAT was denervated unilaterally, and the contralateral depot used as control. Seven days after surgery G3P*neo* was evaluated by the incorporation of ^{14}C-pyruvate into glyceride-glycerol(nmol/cells.h) and the activity of p-enol-pyryvate carboxylase(PEPCK)(nmol/mg prot.min);in vivo glucose upatake was measured with 2-deoxy-14C-glucose(ng/mg.min). RESULTS:Norepinephrine content, assayed by HPLC, was 68% lower in denervated WAT. Fasting decreased glucose uptake (0.8±0.1vs fed2.6±0.3), and increased 14C-pyruvate incorporation (19.2±1.4vsfed5.6±1) and PEPCK activity (13.9vs2.3).Denervation increased glucose uptake (1.3vs4.2), and decreased incorporation of^{14}C-pyruvate (12.2vs2.3) and PEPCK(5.5.vs1.5). CONCLUSION: The data confirm the idea of an inverse relation between WAT glucose utization and G3P*neo* activity.

FAPESP, CNPq
Supervisor: Renato H. Migliorini

BQ025-LIVER GLYCEROKYNASE (GYK) IN RATS FED A HYPERCALORIC DIET: EFFECT OF DENERVATION

M.EMÍLIA S.M. SANTOS[1](PG); VALÉRIA E. CHAVES[2](PG); DANÚBIA FRASSON[2](PG); RENATA P. BOSCHINI[2](PG); MARIA A.R. GARÓFALO[2]; ISIS C. KETTELHUT[1](PQ); RENATO H. MIGLIORINI[1](PQ)

Departments of Biochemistry-Immunology[1] and Physiology[2] - FMRP USP.

Introduction: Because liver has high levels of GyK and also produces glycerol-3-phosphate (G3P) from glucose, via glycolysis, the activity of GyK is not judged limiting for the supply of G3P needed for triglyceride synthesis, and has therefore been little studied. Aim: To verify the effect of a HCAL diet on the GyK activity of intact or denervated liver. Methods: Rats were fed a HCAL(0.7 Kcal. g $bw^{-1}.day^{-1}$) or control diet (0.5). For denervation 85% phenol was gently swabbed around the hepatic artery and the portal vein in the hilum. After 24 days on the diets, intact rats, or rats denervated or sham-operated 7 days previously, were killed and liver norepinephrine (NOR), assayed by HPLC, and GyK activity (nmol.mg $protein^{-1}.min^{-1}$), assayed by standard technique, were determined. **Results:** Denervation caused a 90% decrease in liver NOR content The HCAL diet induced in intact rats an increase in Gyk activity(28.5±0.8vs22.7±0.5) that was blocked by denervation (23.0±0.7 vs. 28.3±1.3 in sham-operated rats). Conclusion: The data suggest that the HCAL diet-induced increase in liver GyK activity is mediated by the sympathetic system.

FAPESP, CAPES
Supervisor: Renato H. Migliorini

BQ026-ANTIOXIDANT ACTIVITY OF FLAVONOIDS ON ISOLATED MITOCHONDRIA

DANIEL J. DORTA(PG)[(1)]; ANAISA F. CALGARO HELENA(PG) [(1)]; CLAUDIA M. SIQUEIRA(IC) [(1)]; ANTONIO C. SANTOS(PQ) [(1)]; CARLOS CURTI(PQ) [(1)]

[(1)] FCFRP-USP

Mitochondria are important intracellular sources and targets of ROS. A fraction of O_2 available to the respiratory chain may undergo incomplete reduction giving rise to the superoxide radical ($O_2^{\cdot-}$), which is dismuted to hydrogen peroxide (H_2O_2). In presence of iron, a hydroxyl radical ($^{\cdot}OH$) is produced, causing oxidation of proteins and lipid peroxidation (LPO). Therefore, mitochondria may be regarded as intracellular target of agents protecting against ROS, such as flavonoids. Objective: The present study addressed the antioxidant activity of flavonoids on mitochondria/mitochondria-free systems, concerning scavenging activity, protection against *t*-BHP-elicited H_2O_2 accumulation and Fe^{2+}/citrate-mediated LPO. Results: Quercetin and galangin showed to be more potent in affording protection against H_2O_2 accumulation and LPO, although quercetin, but not galangin, was an effective scavenger of $DPPH^{\cdot}$ radical and $O_2^{\cdot-}$. **Conclusions:** The results suggest that the 2,3-double bound in conjugation with the 4-oxo function in the structure, is a major determinant of the their antioxidant activity on mitochondria; the presence of an *o*-di-OH structure on the B-ring favors this activity *via* $O_2^{\cdot-}$ scavenging, while the lack of this structure, favors it *via* mitochondrial uncoupling.

Financial support: CNPq, FAPESP
Supervisor:: Carlos Curti

BQ027-PARTIAL PURIFICATION AND BIOLOGICAL EFFECTS OF THE HYDROALCOHOLIC FRACTION FROM *TAMARINDUS INDICA* L. FRUITS

JENNIFER M. CHAUCA YOKOYA (IC)[1]; ANA ISABEL DE ASSIS-PANDOCHI (PQ)[1]; ANA ELISA SEIXAS AZZOLINI (PQ)[1]; IEDA RAZABONI PRADO (PQ)[1]; SÉRGIO AKIRA UYEMURA (PQ)[2]; CAREM GLEDES VARGAS-RECHIA (PQ)[1]

[1]DFQ and [2] DACTB – FCFRP-USP

Recent studies showed that the crude extract of fruits from *Tamarindus indica* (tamarind) inhibits colon carcinogenesis, decreases blood levels of cholesterol and have antiinflamatory activity in experimental models. Here we performed isolation of carbohydrate fraction of hydroalcoholic extract of this fruit pulp, the chemical characterization of these compounds, and a preliminary evaluation of its activity on the human complement system. Crude tamarind fruits were extracted with ethanol 70%. The hydroalcoholic extract was fractioned using a sequence of solvents: hexane, chloroform, ethyl acetate and water. The aqueous fraction (total sugar 35%, protein 0.2% and phenolic compounds 1.2%) was partially fractionated according to molecular weight in a Biogel P2 column. The major subfraction (FI) was assayed for sugar, protein and phenolic compounds, and analyzed by TLC, HPLC (size determination) and GLC (monosaccharide composition). The monosaccharide components of FI were mannose (24.3%) and glucose (75.7%) and the fraction was free of protein and phenolic compounds. FI showed decrease of activity on complement system, from normal human serum.

Financial support: CNPq
Supervisor: Carem Vargas-Rechia

BQ028-CITOTOXIC ACTIVITITY OF BTHTX-I CROTAMINE FROM *BOTHROPS JARARACUSSU* AND *CROTALUS DURISSUS TERRIFICUS* SNAKE VENOM ON SARCOMA 180 AND MACROPHAGES

LUIZ CARLOS GEBRIM DE PAULA COSTA (PQ)(1) ; CARLA DA SILVA RODRIGUES DE MENEZES (PQ) (1); [1];LUIZ FERNANDO MOREIRA IZIDORO (PG); VERIDIANA DE MELO RODRIGUES ÁVILA (PQ)(1); ANDREIMAR MARTINS SOARES (PQ)(2); AMÉLIA HAMAGUCHI (PQ)(1); MARIA INÊS HOMSI BRANDEBURGO (PQ)(1).

(1) Instituto de Genética e Bioquímica, UFU; (2) Faculdade de Ciências Farmacêutica de Ribeirão Preto-USP-Ribeirão Preto.

Introduction: BthTX-I and crotamine are non enzymatic myotoxins isolated from *Bothrops jararacussu* venom and *Crotalus durissus terrificus* respectively. Objective: The aim of this work was to evaluate the action of BthTX-I and crotamine (*in vitro*) on Sarcoma 180 (S180) and macrophages. Methodology: the action of BthTx-I and crotamine was determined using MTT conversion in order to verify the cell viability of S180 and macrophages. Results: The assay showed that BthTX-I and crotamine incubated separately in different concentrations with S180 and macrophages, reduced the cellular viability in a dose dependent manner. BthTX-I (1µg/µL) produces 90% in macrophages and S180. Crotamine (1mg/mL) showed of 75% on S180 and 20% on macrophages. Conclusions: These results demonstrate that BthTX-I and crotamine possess high cytotoxic activity on the cellular lines tested *in vitro.*

Financial Support: CAPES, CNPq and Fapemig.
Supervisor: Maria Inês Homsi Brandeburgo.

BQ029-THE EFFECTS OF CUBEBIN DERIVATIVES ON MITOCHONDRIAL RESPIRATION

JULIANA SARAIVA(PG)[1]; CLAUDIA M SIQUEIRA(IC)[1]; VALERIA G TUDELLA(PG)[1]; ROSANGÊLA SILVA(PG)[2]; MARCIO L A SILVA(PQ)[3]; PAULO M DONATE(PQ)[2]; JAIRO K BASTOS(PQ)[1]; SÉRGIO A UYEMURA(PQ)[1]; CARLOS CURTI(PQ)[1]; SERGIO DE ALBUQUERQUE(PQ)[1]

[1]Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP; [2]Faculdade de Filosofia, Ciências e Letras-USP; [3]Universidade de Franca

Introduction: The structures of cubebin derivatives resemble the classical inhibitor of mitochondrial respiratory chain NADH. Objective: Evaluate the effects of these compounds on mitochondrial respiration. Methods: Hamster liver mitochondria were energized by the site I substrates-glutamate/malate or the site II substrate-succinate, followed by addition of ADP (resting respiration) and of each compound. Results: None of compounds stimulated the resting respiration. Five of the compounds substantially (IC_{50} bellow 100 μM) inhibited glutamate/malate-supported respiration: metoxi-methylpluviatolide>dimethylethylamino cubebin>hydroxi-methylpluviatolide>metoxinitro methylpluviatolide>cubebin and only dimethylethylamino cubebin inhibited succinate-supported respiration. Conclusions: The compounds are not uncouplers and excepting one that inhibit respiratory chain at the complex II all inhibit respiratory chain only at the complex I level. Structure-activity relationship is discussed.

Financial Support: Fapesp
Supervisor: Sérgio de Albuquerque

BQ030-EVALUATION BIOCHEMIST SERICA OF ANIMALS DEALT WITH COPAIBA OIL

JOSIANE BUENO (IC)[1];CLAUDIA CONSUELO DO CARMO OTA(PQ)[1]; KARIN CRISTINA DUARTE SAIF(IC)[1]; KARLA AZUMA(IC)[1]; ROSELI CORREA SILVA(IC)[1]

[1]Universidade Tuiuti do Paraná. Paraná, Brazil

INTRODUCTION: Among the medicinals plants most used by amazon people, Copaiba is being viable. It is a big tree from the Caesalpinacea family. The Copaiba trees are ramified and reach 18 to 30 meters height. The used material is the oil with is inside the tree trunk. OBJECTIVE: This work has the aim to realize de biochemical evaluation of triglicerides, total cholesterol levels, LDL, HDL. METHODOLOGY: It was used 80 rats Wistar, mouthly treated with the oil at 450, 700 and 900mg/kg in a period of 28 days. For obtaining the samples, the animals were decapitated and the blood collected in sterile falcon tubes containing EDTA. The tubes were centrifuged and collected serum. **RESULTS:** In the groups control, 450, 700, 900 the total cholesterol was value 148±11,1; 155±9,4; 160±9,1; 166±7,2, respectively. The concentration of was LDL 107±7,0; 113±12; 121±12,0; 125±9,8; for triglicerides was 59±5,1; 56±3,1; 64±5,1; 76±6,5 For HDL it happened a minor value. The control present result of 297±3,1; at the group of 450mg/kg was 28±3,1; at the 700mg/kg the value was 25±3,4 and for 900mg/kg value was 24,5±3,4. CONCLUSION: The Copaiba oil is capable of serics levels change of HDL, LDL, total cholesterol, triglicerides.

Supervisor: Claudia C. C. Ota.

The authors did not follow the Scientific Committee's suggestion for an English language review

BQ031-PHOTODYNAMIC ACTIVITY OF ZINC PHTHALOCYANINE INCORPORATED INTO LIPOSOMES ON SHEEP RED BLOOD CELLS: EFFECTS OF CHOLESTEROL

MIRIAN R. MOREIRA(PG)[1]; FABIANA C. SANTOS (IC)[2]; THIAGO PADOVANI (PG)[2]; ANTONIO E. DA HORA MACHADO (PQ)[2]; CARLOS ALBERTO DE OLIVEIRA(PQ)[2]

[1] Universidade de São Paulo, [2] Universidade Federal de Uberlândia

Zinc phthalocyanine (ZnPc) was recently introduced in clinical trials of photodynamic therapy (PDT). Because ZnPc is insoluble in water, it must be transfered to the target cells by delivery systems, such as liposomes. In this work we prepared liposomes, containing ZnPc and cholesterol by the ethanol injection method. The procedure is simply and does not expose lipids or entrapped materials to deleterious conditions. We have used sheep erythrocytes (SRBC) as target cells for to study the photodynamic activity of ZnPc. A solution of phospholipids, containing 2.5umols.L of ZnPc in ethanol, was injected rapidly into an excess of saline. SRBC at 0,4% in saline was incubated with liposomes containing ZnPc and cholesterol and photoirradiated for 15 minute. The amount of haemoglobin and K^+ ions released were spectrofotometrically measured. We observed that the photodynamic activity of ZnPc on SRBC was strongly dependent of the presence of cholesterol in liposomes. The photohaemolysis were more intense at the Epikuron/cholesterol ratio of 2:1, 3:1 and 5:1. We believed that cholesterol participate directly in the ZnPc transfer from liposomes to target cells.

Supervisor: Prof. Dr. Carlos Alberto de Oliveira

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Biotecnologia / *Biotechnology* (BT)

BT001- ANTIDERMATOPHYTIC ACTIVITY OF *BOTHROPS JARARACUSSU* SNAKE VENOM.

[3] SILVANA MARCUSSI (PG); [4] RAFAEL SPINOLA CAMBRAIA *(*IC); [3] JOSÉ ROBERTO GIGLIO (PQ); [2] JOSÉ ODAIR PEREIRA (PQ); [2] SPARTACO ASTOLFI-FILHO (PQ); [1] ANDREIMAR MARTINS SOARES (PQ).

[1]FCFRP; [2] UFAM-Manaus-AM; [3]FMRP-USP; [4] UNAERP; Ribeirão Preto-SP, Brasil.

Introduction: Snake venoms and their isolated proteins have been used for different therapeutic applications in search of new bioactive agents. Objective: The effect of *B. jararacussu* snake venom on *Trichophyton metagrophyte* fungi (ATCC 11480), a dermatophyte of relevant veterinarian interest in the northern region, was evaluated after being grown in Sabouraud Dextrose at 28ºC for 6 days. Methods and results: The inoculum was prepared by homogenization in tween 20 (0,1%), diluted 1000X and quantified. Incubations were carried out with 50µL of inoculum in different venom concentrations, for 30min at 37ºC, followed by seeding and colony counting. *B. jararacussu* venom strongly inhibited the fungi growth at 1.500, 2.500 and 5.000µg. Other snake venoms were assayed and did not show any effect. Conclusion: These results may rise suggestions in the action mechanism of the venom proteins which act as fungicide, bactericide and even as cytotoxin, thus opening field for the search of new drugs.

Financial support: FAPESP, CNPq, CAPES.
Supervisor: Andreimar Martins Soares

BT002-ANTI-OPHIDIAN AGENTS ISOLATED FROM *CASEARIA SYLVESTRIS* AND *ANACARDIUM HUMILE.*

[2] PAULO SÉRGIO PEREIRA (PQ); [3] SILVANA MARCUSSI (PG); [2] MÔNICA CURTARELLI (IC); [1] CAROLINA DALAQUA SANT'ANA (PG); [2] RAFAEL SPINOLA CAMBRAIA (IC); [1] ANDREIMAR MARTINS SOARES (PQ).

[1]FCFRP; [2]UNAERP; [3]FMRP-USP; Ribeirão Preto-SP, Brasil.

Introdution: Several plants popularly quoted as anti-ophidian have been investigated regarding their effects against envenomation. **Objective:** Crude aqueous extracts from *A. humile* (stem inner bark) and *C. sylvestris* (leaves) displayed total or partial inhibition of myotoxic, PLA_2, hemorrhagic, edema inducing, coagulant and lethal activities induced by different snake venoms. **Methods and results:** Fractionation of the extracts was carried out on Sephadex LH-20 (*A. humile*) or Sephadex G-25 (*C. sylvestris*) and the resulting fractions were submitted to the PLA_2 inhibition assay after previous incubation for 30' at 37ºC at 1:50 ratio. The indirect hemolysis method was used, were the substrate is egg yolk supplemented with human erythrocytes diluted in PBS and semi-solidified with agar. Evaluation of results was performed, 12h after incubation, by measuring hemolysis halo diameters on the gel. Fractions S3, S4, S5 S6 and S7 from *A. humile* totally inhibited the enzymatic activity induced by *B. jararacussu*, *B. neuwiedi*, *B. moojeni*, *C. d. terrificus*, crotoxin and PLA_2 (both isolated from *C. d. terrificus* venom). *B. alternatus* venom was totally inhibited by fraction S3 only. Methanolic fractions from *C. sylvestris* partially inhibited the PLA_2 activity of *B. jararacussu* and *C. d. terrificus* venom at 1:50 ratio. The major inhibition was shown by the first eluted fractions (tubes 1-18). **Conclusion:** These results confirm the anti-ophidian activity of both plants.

Financial support: FAPESP, CNPq, CAPES.
Supervisor: Andreimar Martins Soares

BT003-ANALYSIS OF FUNGICIDAL ACTIVITY OF *BAUHINIA FORFICATA* CALLUS EXTRACTS.

NATÁLIA G. P. NOGUEIRA(PG)[1] MARCUS V. P. RODRIGUES(PG)[1] ; JULIANA A. MAZZINI(IC) [1]; FERNANDA S. LEITE(IC)[1]; ANA MARISA F. ALMEIDA(PQ)[1]; MIRIAM V. LORENÇO(PQ)[1]; SUZELEI DE C. FRANÇA(PQ)[1] ; ANA HELENA JANUÁRIO(PQ)[1]; ROSEMEIRE C. L. R PIETRO(PQ)[1,2]

[1]Universidade de Ribeirão Preto-UNAERP, Ribeirão Preto, São Paulo, Brasil; [2]Universidade Estadual Paulista-UNESP, Araraquara, São Paulo, Brasil.

The incidence of fungicidal infection has increased the need to develop new anti-fungicidal drugs. The phytochemical studies performed with *Bauhinia forficata* showed the presence of steroids, flavonoids and tannins in the leafs and flowers of that species. The goal of the present study was to evaluate the fungicidal activity of MeOH (B1) and $CHCl_3$ (B2) extracts of aerial parts and the callus culture *in vitro* of *Bauhinia forficata*. The fungicidal activity was evaluated by the microdilution method using the ATCC and wild of *Candida* ssp. The extracts were not efficient against ATCC strains. On the contrary, the results demonstrated that the MeOH and $CHCl_3$ extracts from the callus culture were fungicidal to the wild strains. The data suggest that the extracts from the callus inhibited the growth of strains isolated from patients, therefore it requires further investigation of this activity.

Financial Support: UNAERP
Supervisor: Rosemeire C. L. R. Pietro

BT004-CYTOTOXIC ACTIVITY OF THE MELANIN EXTRACTED FROM *ASPERGILLUS NIDULANS*

RITA DE CÁSSIA R. GONÇALVES (PG)[1], ROGRIGO R. KITAGAWA (PG)[1] , MARIA STELLA G. RADDI (PQ)[2], SANDRA R. POMBEIRO-SPONCHIADO (PQ)[1]

Instituto de Química – UNESP – Araraquara [1], Faculdade de Ciências Farmacêuticas – UNESP – Araraquara[2]

The fungal melanin has biotechnological interest because various studies demonstrated that this pigment plays various biological activities including antioxidant, photoprotective and anti-inflammatory. In early studies, we showed that the melanin from *Aspergillus nidulans* is a potential HOCl scavenger in the concentration of 100 µg/ml and may be considered a promising material for the cosmetic industry. However, it is important to evaluate the cytotoxicity of this substance before they are used for practical applications. In the context, the aim of the present study was to determine the cytotoxic index (IC_{50}) of the melanin extracted from highly melanized strain from *A. nidulans*. The cytotoxic activity was evaluated by neutral red assay in McCoy cell line, using different concentrations of melanin (31,2 to 500 µg/mL). The quantification spectrophotometric, realized in 540/620 nm, showed a cytotoxic index around the 375 µg/ml. This result indicated that the melanin from *A. nidulans* don't damage components cellular in concentration of 100 mg/ml and, therefore, be used with security in formulation of creams that protect the skin against possible oxidative damage.

Supervisor: Dra. Sandra Regina Pombeiro Sponchiado.

BT005-BIOCHEMICAL CHARACTERIZATION OF INTRACELLULAR XYLANASE OF *FUSARIUM HETEROSPORUM*

VIVIANE C. H. DA SILVA(IC)[1]; CAROLINE HENN(IC)[1]; ANGELICA R. CAPPELLARI(IC)[1]; ADRIANA ZILLY(PQ)[2]; CLARICE A. OSAKU(PQ)[1]; MARINA K. KADOWAKI(PQ)[1].

(1)Centro de Ciências Médicas e Farmacêuticas – UNIOESTE-PR
(2)Departamento de Ciências Biológicas –UNIAMÉRICA- PR

Introduction: Xylanolytic enzyme from microrganisms have biotecnological potential in various industrial process such as food, feed, pulp and paper industries. **Objective:** To investigate the biochemical characterization of intracellular xylanase of *Fusarium heterosporum*. **Methodology:** The fungus was inoculated in Khanna liquid media with 1,5% of corn straw, incubated at 25°C for 7 days under static conditions. The xylanolitic activity was determined by hidrolysis of xylan and the reducing sugar by the dinitrosalicylic acid method. **Results:** The fungus produced cellulase-free intracellular xylanase with 0,7 U/mL. The optimum pH and temperature of xylanase were 6,0 and 45°C, respectively. The enzyme exibited high thermal stability when incubated at 40ºC, 45ºC and 50ºC, it retained 75%, 54% and 42% of its activities for 60 minutes. The analysis of the products of xylanase hydrolysis in paper chromatography resulted only xylose, after 5 hours. **Conclusion:** The production of xylanas by *F. heterosporum* can be improved by optimization of growth conditions using cheap media containing lignocellulosic source.

Supervisor: Marina K. Kadowaki

BT006-ANTI-TOXIC ACTIVITY OF SNAKE VENOM CROTOXIN ASSOCIATED WITH PLANT EXTRACTS

GOMES, O.A. (PQ) [1]; PAIVA, R.P. (IC) [1]; FURLAN. M.V. (IC) [1]; CHAHUD, F. (PQ) [1]; PEREIRA, P. S. (PQ) [2]; SOARES, A. M. (PQ) [3].

[1]FM-UNAERP; [2]UB-UNAERP; [3]DACTB, FCFRP-USP.

Crotoxin is one of the major neurotoxic constituents of the venom of the rattlesnake *Crotalus durissus terrificus* . The aim of this work was to evaluate histopathologically the effects of crotoxin associated with plant extracts. Mice were injected with Crotoxin isolated from *C. d. terrificus* venom by molecular exclusion chromatography, SDS-PAGE analyzed for determination of purity, associated to aqueous extracts of *Casearia sylvestris*, *Mikania glomerata* and *Mandevilla velutina. S*ections of heart muscle, skeletal muscle, lung, liver, brain, spleen and kidney were red-faced with H&E. The association of crotoxin to *Casearia* for 6 h promoted inflammatory infiltrates with necrosis in liver and lung sections besides cerebral edema, inducing animals to death in less than 02 days; while Mandevila for 6 h caused a diffuse edema in liver and brain besides necrosis and renal atrophies leading to death in 03 days; however Mikania partially neutralized the toxic effects of crotoxin, despite of showing discreet hepatic and cerebral edema accompanied of lung necrosis at the end of 03 days. Obtained results confirm the systemic toxicity of crotoxin increased by the association of *Casearia* and *Mandevilla*, and the potential anti-toxic property of *Mikania* extract.

Financial Support - FAPESP and UNAERP
Supervisor: A. O. Gomes

BT007-PRACTICAL TWO-STEP PURIFICATION OF RECOMBINANT HUMAN PROLACTIN AND TWO ANALOGOUS EXPRESSED BY CHINESE HAMSTER OVARY (CHO) CELLS

CARLOS ROBERTO JORGE SOARES(PQ); SUSANA DA ROCHA HELLER(IC); JOÃO EZEQUIEL DE OLIVEIRA(PG); JOSÉ MARIA DE SOUSA (PQ); PAOLO BARTOLINI (PQ)

IPEN/CNEN-SP, São Paulo - Brasil - Biotechnology Department – CBM

Human prolactin (hPRL) promotes the proliferation and differentiation of mammary epithelial cells during mammary gland development and has been linked to breast tumor development. In the last years the development of hPRL analogous antagonists has been an emerging field of research. The two prolactin antagonists more studied in the literature are G129R-hPRL and S179D-hPRL. The hPRL and its two antagonists were synthesized by our group in CHO cells. For the purpose of their characterization a practical two-step purification process was set up: SP-Sepharose FF followed by a size exclusion chromatography employing a high-performance size-exclusion chromatography (HPSEC) as a preparative column. An extensive physico-chemical characterization was thus carried out including SDS-PAGE analysis, MALDI-TOF-MS, HPSEC and reversed-phase high-performance liquid chromatography (RP-HPLC). In conclusion, this practical purification process provided sufficiently pure material, which was extremely helpful for the comparison and proper characterization of these hPRL analogous.

Financial Suport: Suported by FAPESP and Biolab-Sanus/Hormogen.
Supervisor: Carlos R.J. Soares

BT008-AUTOMATING THE ESTABLISHMENT OF THE DIAGNOSIS HYPOTHESIS OF LEUKEMIA BY MEANS OF LOGISTIC REGRESSION

MARCO AURÉLIO SICCHIROLI LAVRADOR (PQ)[(1)]; ANA MARIA DE SOUZA (PQ)[(1)]; ANDRÉ LUIS PEREIRA MANTOANI (PQ)[(1)]

[(1)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto da Universidade de São Paulo

Nowadays a great variety of mathematical, statistical and artificial intelligence models have been used as decision support tools for the establishment of pathology diagnostics. On the other hand the precocious diagnosis for leukemia can improve the effectiveness of the treatment.
The present work seeks to use a model known as logistic regression as a decision support tool to the establishment of the hypothesis of diagnosis of acute lymphocytic leukemia.
Some few variables of blood count were used as the independent variables that fed the model. The model was implemented as a computational program developed in C++ language. Blood counts of healthy people and bearers of acute lymphocytic leukemia were used for estimatating the parameters of the model. The study included 115 people of which 92 were healthy and 23 were leukemic.
The final log-likelihood of the model resulted in -26.475 and the corresponding estimate for the miss-classification rate resulted in 0.0522.
This result attests a good performance of the model for the proposed objective.

BT009-PREPARATION OF NEW METABOLITES FROM LAMIVUDINE BY FILAMENTOUS FUNGI BIOCONVERSION

LEONARDO EULÁLIO DA SILVEIRA DIAS (IC) [1]; CAROLINA HORTA ANDRADE (IC) [1]; FRANCINE PAZINI (PG) [1]; (PG) [1]; VALÉRIA DE OLIVEIRA (PQ) [1]

[1] Faculdade de Farmácia,Universidade Federal de Goiás-UFG

Despite considerable research effort in the development of other dideoxynucleoside analogues and also therapies involving different mechanisms of action to the reverse transcriptase inhibitors, the understanding of their metabolism is still incomplete. In order to find novel or specific metabolites of lamivudine with a modified biological profile, a selected set of microorganisms with already known bioconversion talent was screened for their ability to transform lamivudine. By screening of five filamentous fungi, all strains tested were able to metabolize lamivudine within a 1 to 5 day period, producing in the incubation medium variable amounts of ten differents metabolites completely separated by HPLC and easily detected by its characteristic in the UV-absorbance. These results demonstrate the interesting potential of such methods for preparation of functionalized derivatives compared to chemical methods.

CNPQ; SECTEC
Supervisor: Valéria de Oliveira

BT010-PREPARATION OF ZIDOVUDINE AND STAVUDINE DERIVATIVES BY MICROBIAL BIOTRANSFORMATIONS

DIOGO PASSOS RIOS (IC) [1]; HÉRICA N. C. CIRILO (PG) [1]; FRANCINE PAZINI (PG) [1]; TATIANA CAIXETA FERREIRA GOMES (IC) [1]; VALÉRIA DE OLIVEIRA (PQ) [1]

[1] Faculdade de Farmácia,Universidade Federal de Goiás-UFG;

Owing to existing worldwide requirement for antiviral agents, there has been an increased interest in ways to synthesize novel nucleosides for use in chemotherapeutic screening. Microorganism metabolic reaction diversity enables the production of new derivatives of this compounds some of which can demonstrate higher activity, improved bioavailability or reduced toxicity compared to zidovudine and stavudine. An exhaustive screening of fungal and microbial strains allowed select the best microorganism to produce new derivatives in order to obtain significant amounts to pharmacological and toxicological studies. The antiretroviral was incubated in a liquid medium with various strains of filamentous fungi and at least nine different derivatives were separated by HPLC from the incubation supernatants. As the distribution of the metabolites observed in each strain was different, it was possible to select the best strain for the production of each derivative. Among the strains tested, *Cuninghamella echinulata* ATCC 9244 and *Mortierella isabelina* NRRL 1757was the most active producers of zidovudine and stavudine derivatives respectively.

CNPQ; SECTEC
Supervisor: Valéria de Oliveira

BT011-SELECTIVE EXTRACTION METHOD OF SOYBEAN KUNITZ TRIPSIN INHIBITOR (SKTI) USING ALCOHOLIC BUFFER

EDUARDO J. DE ARRUDA (PQ)[1]; EMILI S. BREDER (IC)[1]; ANIELLY B. DA C. BARBOSA (IC)[1]; TÂNIA R. DA SILVA (PQ)[1]; LINCOLN C. S. DE OLIVEIRA (PQ)[1].

[1]Pharmacy, MSMT – UCDB, C.G, MS

Introduction: Seeds of plants contain several biologically active proteins that play specialized functions, including defense mechanisms. Most of these compounds are currently acknowledged to have biological activities in the pharmacological, medical, and cosmetics fields. The present interest for trypsin inhibitors arises from their ability to suppress carcinogenic transformation, as detected *in vitro* and *in vivo* models. **Objective:** Description of a simple method for extraction and/or purification of the SKTI from deffated soybean powder. **Methods:** Extraction of the SKTI at a 1:10 proportion w/v of soybean powder to acetate buffer solution (100mM, pH of 5,4, 40% v/v MeOH or EtOH). Results: The SDS-PAGE electrophoresis shows the viability and selectivity of the SKTI extraction using different alcoholic concentrations. The protein pattern from the IAC-PL1 and Bünge Foods Co. soybean powder were similar. **Conclusion:** The MeOH and EtOH extractions were more selective than the isopropilic's and propilic alcohol's, as well as the low molecular weight PEG's. Results suggest that the MeOH extraction is more selective and has a higher yield of the SKTI.

Financial Support: FUNDECT/MSMT-UCDB
Supervisor: Eduardo J. de Arruda.

BT012-A NOVEL CYCLODEXTRIN GLYCOSYLTRANSFERASE ISOLATED FROM BRAZILIAN SOIL MICROORGANISM

CRISTIANE MORIWAKI (PG)[(1)]; GLAUCIANE DE LARA COSTA (IC)[(1)]; RUBIA PAZZETTO (IC)[(1)]; FRANCIELE BROL (IC)[(1)]; GISELLA MARIA ZANIN (PQ)[(2)]; FLÁVIO FARIA DE MORAES (PQ)[(2)]; MÁRCIA PORTILHO (PQ)[(1)]; GRACIETTE MATIOLI (PQ)[(1)].

[(1)]Pharmacy and Pharmacology Department, [(2)]Chemical Engineering Department, State University of Maringá,

Cyclodextrins (CDs) are cyclic oligosaccharides composed of 6 or more glucose units. They possess a hydrophilic surface and a hydrophobic central cavity. They are capable of forming inclusion complexes and stabilizing many substances. This research aimed to study the pH and temperature effect on the activity of the cyclodextrin glycosyltranferase (CGTase) of alkalophylic bacilli strain and to determine its activation energy (E_a) using Arrhenius equation. A novel CGTase was obtained from an alkalophylic microorganism isolated from Brazilian soil of oat culture, using a high alkaline pH medium containing 1% Na_2CO_3. The enzyme was characterized in soluble form, using as a substrate maltodextrin solution in 50 mM Tris-HCl buffer and 5 mM $CaCl_2$. The optimum temperature for the enzyme activity was 50°C and it was most active at pH 6.0. Activation energy for the production of beta-CD was 9.4 kcal/mol. The characteristics of the novel CGTase obtained in this work showed to be close to those observed in the literature.

Financial Support: CNPq
Supervisor: Graciette Matioli

BT013-DETERMINATION OF ALBENDAZOLE-β-CYCLODEXTRIN COMPLEX BY NUCLEAR MAGNETIC RESONANCE

RUBIA PAZZETTO(IC)[1]; GLAUCIANE DE LARA COSTA(IC)[1]; CRISTIANE MORIWAKI(PG)[1]; GRACIETTE MATIOLI(PQ)[1].

[1]Universidade Estadual de Maringá

Albendazole (ABZ) is a benzimidazole derivative with a broad-spectrum activity against human and animal helminth parasites. Cyclodextrins (CDs) are capable of forming inclusion complexes and improving the physiochemical substances properties. Nuclear Magnetic Resonance of proton (NMR-H^1) and of carbon 13 (NMR-C^{13}) is efficient for the identification of inclusion complexes with CDs. This work had for objective to analyze the formation of the complex albendazole-b-cyclodextrin (ABZ-βCD) by NMR spectrums. The studies of the ABZ-βCD complex formation were accomplished with the following molar ratios: 1:1, 1:2, 1:4, 1:6, 1:8 and 1:10. Each molar ratio was maintained under agitation to 175 rpm and 37°C/5 days. The suspensions were filtered, the supernadants were diluted in water and after drying by evaporation. The samples were dissolved in deuterade dimethylsulfoxide. The complexes assumptions were analyzed in NMR spectrophotometer. There were band enlargement and change of peak intensity (molar ratio 1:8) in relation to the standards ABZ and CD in NMR-H^1, which no seen through NMR-C^{13}. The result by NMR-H^1 supplied a good indication of this molecular inclusion and possibility of its use to increase the ABZ bioavailability.

Financial Suport: CNPq
Supervior: Graciette Matioli

BT014-SYNTHESIS OF BIODEGRADABLE POLYESTERS OF LACTIC ACID

AMANDA QUEIROZ SOARES (IC) [(1)]; DENILSON RABELO (PQ) [(1)]; APARECIDO RIBEIRO DE SOUZA (PQ) [(1)]; LEONARDO FRANÇOIS DE OLIVEIRA (IC) [(1)].

[(1)] Universidade Federal de Goiás

Introduction: The poly(lactic acid) (PLA) is relatively hydrophobic and biodegradable to atoxic products. The PLA can be prepared in the form of homopolymer or glycolic acid copolymer poly(lactic-co-glycolic acid) (PLGA). These polymers have application in the medical and pharmaceutical areas, mainly in the context of drug delivery. Objective: In this work, PLA and PLGA were produced using the sulfonic styrene-divinylbenzene copolymer as catalyst. Mothodology: Two methodologies of polymerization were used:1) previous esterification of monomers followed of polycondensation with ethanol elimination, 2) direct polycondensation with water elimination. PLA and PLGA were characterized by viscometry and FT-IR. Results: The previous esterification prevents the oxidation of the acid groups, during polycondensation reaction. The esterification also increased polymers viscosity, suggesting the production of higher molecular weight. The presence of ester axial deformation in the FT-IR spectra proves the characteristic link of polyesters. Conclusions: It was concluded that the previous esterification was a better methodology to produce light colorated PLA and PLGA with high molecular weight.

Financial Support: CNPq:
Supervisor: Denilson Rabelo

BT015-FORECASTING R-R INTERVALS USING RECURRENT NEURAL NETWORKS

FÁTIMA MARIA HELENA SIMÕES PEREIRA DA SILVA(PQ)[1];ANTÔNIO CARLOS DA SILVA FILHO(PQ)[2]; LOURENÇO GALLO JÚNIOR(PQ)[3]; FABIANO GUASTI LIMA(PQ)[4]; MARCO AURÉLIO SICCHIROLI LAVRADOR(PQ)[1]; JÚLIO CÉSAR CRESCÊNCIO(PG)[3];RENATA TORRES KOZUK(PG)[3]; MAURÍCIO MILANI(PG)[3].

[1]Faculdade de Ciências Farmacêuticas de Ribeirão Preto da USP;[2]Universidade de Ribeirão Preto;[3]Faculdade de Medicina de Ribeirão Preto da USP;[4]Centro Universitário de Franca

Introduction. R-R intervals are important variables extracted from ECG. Using them one can get information about a human physiology and pathology and foresee the heart behavior in future moments. Objective. The main goal of this research is to explore the possibility of using a Recurrent Neural Network model in order to obtain forecasts to R-R intervals. Methodology. We analyzed 12 healthy men in rest position. For each one, we collected around 1000 values, using 600 to train and validate the network and forecast from 2 to 100 values. Main Results. The used statistics were: TIC varying, typically, from 0.057578 to 0.214722; MAPE varying from 9.2090 to 41.4075; the Pearson Coefficient varying from -1 to -0.331760; the enveloping from 100% to 86.67%. Conclusion. For a few steps ahead, the approach is very good but as the number of steps increases (from 20) the forecasts values diverge more and more from the real ones.

Financial Support: Fapesp

BT016-ULTRASONIC FREQUENCY AND POWER EFFECTS IN LIPOSOME SIZE

MILENE HELOISA MARTINS (PG)[1]; FRANCISCO B.T. PESSINE (PQ)[1]

[1]Instituto de Química/UNICAMP

Several techniques can be used to decrease the size/polydispersity of liposomes, sonication being one of them. In this work one investigated the influence of ultrasonic frequency/power in liposomes formed by soy hydrogenated phosphatidylcholine (HPC) and/or cholesterol (CHOL). The size/polydispersity were measured by Quasi Elastic Light Scattering using PCS. We prepared 3 extruded (~1μm) formulations of HPC:CHOL 6mg/mL (3:1; w:w-F1); HPC 6mg/mL-F2 and HPC 30mg/mL-F3. These formulations were sonicated at 65ºC using the ultrasonic bathes: 25kHz/100W; 25kHz/240W, and 47kHz/240W. After 60min of sonication one observed: 1) using a fixed frequency of 25kHz and power of 100W and 240W a decrease of 10% and 20% in the diameter for F1; 25% and 40% for F2 and 37% and 49% for F3, respectively; 2) using a fixed power of 240W and frequency of 25kHz and 47kHz a decrease of 20% and 76% for F1; 40% and 83% for F2 and 49% and 80% for F3, respectively. Conclusions: a) frequency is more important than power in decreasing the liposome size/polydispersity; b) the vesicles containing CHOL were more resistant to sonication due to bilayers rigidity c) the larger effect of power in F3 is due to probability of cavitation implosions to occur in the neighborhood of the more vesicles.

Financial Support: CNPq
Supervisor: Francisco B. T. Pessine

BT017-SUGAR CONTENT IN NECTAR FLOWERS OF CONVENTIONAL AND TRANSGENIC ORANGE TREES

VALÉRIA RODRIGUES CELLOTO[1], VALENTIM SALA JUNIOR[1], JOSÉ EDUARDO GONÇALVES[2], ARILDO JOSÉ BRAZ DE OLIVEIRA[1], REGINA APARECIDA CORREIA GONÇALVES[1]

[1]Laboratório de Química Farmacêutica, Depto. de Farmácia e Farmacologia. Universidade Estadual de Maringá - Av. Colombo 5790, 87020-900, Maringá, PR, Brasil; [2]Centro Universitário de Maringá- CESUMAR. E-mail: racgoncalves@uem.br

The orange is important Brazilian export product; the citric chancre is its main disease, for that the gene of the sarcotoxin was inserted to the genome of the plant with objective of increasing its resistance the curse. The chemical composition of the floral nectar of conventional orange tree and transgenic was used to evalue the effect of the new on the composition of the sugars. The total sugar concentration was 1.79 to conventional and 2,48mg/flower to transgenic orange tree, respectively. It was also determined individual sugars concentrations (sucrose:glucose:fructose) using spectrophotometry. The relatives rates were 4:3:24 for conventional and 5:3:28 for transgenic. There is a difference between total nectar sugar in the conventional and transgenic orange tree but there is a small variation on individual sugars proportions. This can indicate that the genetic transformation interferes in the production of sugars for the orange tree.

Financial Support: Fundação Araucária; CAPES
Supervisor: Regina Aparecida Correia Gonçalves

BT018-CAN FOURIER TRANSFORM IMPROVE NEURAL NETWORKS FORECASTING OF R-R INTERVALS?

ANTÔNIO CARLOS DA SILVA FILHO(PQ)[(1)]; FÁTIMA MARIA HELENA SIMÕES PEREIRA DA SILVA(PQ)[(2)]; LOURENÇO GALLO JÚNIOR(PQ)[(3)]; FABIANO GUASTI LIMA(PQ)[(4)]; MARCO AURÉLIO SICCHIROLI LAVRADOR[(1)]; JÚLIO CÉSAR CRESCÊNCIO(PG) [(3)]; RENATA TORRES KOZUK(PG) [(3)]; MAURÍLIO MILANI(PG) [(3)]

[(1)]Universidade de Ribeirão Preto;[(2)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto da Universidade de São Paulo;[(3)]Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo;[(4)]Centro Universitário de Franca

Introduction. Fourier analysis and Neural Networks work together in a try to improve forecasts of R-R intervals. The R-R interval is the time interval between two heartbeats. Objective. To verify if the use of a Fourier analysis can improve the results achieved by recurrent neural networks in forecasting R-R intervals. Methodology. We analyzed 12 healthy men in the resting position. For each, we collected approximately 1000 values and used only 600. We computed the FFT and used the new values to train and validate the network. Then, we forecast from 2 to 100 values. Finally, we computed the inverse FFT. Main Results. Comparing the statistics with and without FFT we can see that: TIC varied a maximum of 1%, MAPE a maximum of 5% and Pearson Coefficient a maximum of 3%. Conclusion. Fourier transform, although an important tool in periodicity analysis, did not improve forecasts of the recurrent neural network to R-R intervals.

Financial Support: Fapesp

BT019-ACCUMULATION OF 7-HYDROXY-4',6-DIMETHOXY-ISOFLAVONE IN *DIPTERYX ODORATA* CELL SUSPENSION CULTURES

MIRIAM V LOURENÇO (PQ); RENATA S FERNANDES(PG); PATRÍCIA G ROBERTO(PQ), JOSÉ F LIMA(IC), SARAZETE IV PEREIRA(IC), SUZELEI C FRANÇA(PQ), ROSEMEIRE C. L. R. PIETRO(PQ), ANA H JANUÁRIO(PQ).

Biotecnologia - UNAERP- Ribeirão Preto- SP

Dipteryx odorata (Fabaceae) is a rich source of isoflavonoids, which are related to diverse therapeutic properties, like antioxidant, estrogenic, antinflammatory, antimicrobial, and anticancer. The yield of 7-hydroxy-4',6-dimethoxy-isoflavone (isoflavone 1) during the growth cycle of cell suspension cultures of *D. odorata* was evaluated. Friable callus from root explants of *D. odorata* cultured in MS semisolid medium supplemented with 2,4-D 2,0 mg/L plus 6-BAP 0,5 mg/L and sucrose 30 g/L were transferred to liquid medium, same composition, to establish fine suspension cultures. After three 30-day subcultures of cell suspensions, samples were collected at five-day intervals and submitted to selective extraction procedures in order to obtain fractions rich in isoflavones. HPLC-DAD analysis showed that accumulation of isoflavones occurs concurrently with the growth circle. After 15 days, cells accumulate the highest level (54,9 mg/gPS) of isoflavone 1, sustaining the production around 48 mg/gPS till the 30th day. Results indicate that this bioproduction under monitored conditions represents a continuous source of active isoflavonoids of pharmaceutical interest.

Instituition: UNAERP

BT020-CITOTOXIC AND MELANOGENIC ACTIVITY OF *BROSIMUM GAUDICHAUDII* EXTRACT OVER B16F10 MURINE MELANON CULTURE.

ROSA, F. C.[(1)] (PG); NOMIZO, A[(2)] (PQ); COUTO, L. B [(1)] (PQ); LOURENÇO, M. V[(1)] (PQ); DE MARCO [(2)] (IC); FRANÇA, S.C [(1)] (PG).

[(1)]Depto. Biotecnologia, UNAERP; [(2)]Depto.Toxicológicas, FCFRP-USP.

B.gaudichaudii is a native plant from the Brazilian cerrado. The present study was carried out to evaluate the melanogenic and "in vitro" citotoxicity of crude water extracts of *B. gaudichaudii*, over murine melanoma cultured cells B16F10. Cells were cultured with different concentrations of the extracts for 48-72h. The melanin contents were measured by spectrometric analysis at 450nm. Citotoxic activity was investigated according colorimetric method MTT. Obtained results showed that fractions of *B. gaudichaudii* extracts and one of its isolated compound the bergapten within the range 0.5-0.1 mg/mL and 50-100 µg/mL, induced melanogenesis. Fractions of extracts, at concentration over 0.1mg/mL were citotoxic for tumoral cells while the hydro soluble fraction at concentration lower than 0.01mg/mL induced proliferation of melanom. That 25-200 µg/mL of bergapten induced dose dependent proliferation of melanom. Overall data confirm the efficacy of extract to treat pigmentation skin diseases, due to its property to enhance melanin production.

Finantial support: CAPES and UNAERP.
Supervisor: Suzelei C. França

BT021-ANTI-TUMORAL ACTIVITY OF THE L-AMINO ACID OXIDASE FROM *BOTHROPS JARARACUSSU* VENOM *(*BJUSSULAAO)

FABIO KISS TICLI(PG); ANA PAULA SILVA OLIVEIRA(IC); ANDREIMAR MARTINS SOARES(PQ); AURO NOMIZO(PQ); SUELY VILELA SAMPAIO(PQ).

Departamento de Analises Clinicas, Toxicológicas e Bromatológicas – FCFRP-USP.

Introduction: The L-amino acid oxidase (LAAO) was described firstly by Zeller & Maritz in 1944. This protein is present in several snake venoms. The purification of venom's LAAOs has been describing by several researchs. LAAOs of differents origins show differents biological and toxic activities. The pharmacological effects this enzyme like citotoxicity, platelet aggregation, bactericide and leishmanicid, has the unknown mechanism. Objective: The present work studied the BjussuLAAO action upon tumoral cells, using human tumoral lines, SK-BR-3, C-8161 and JURKAT. Results and Conclusions: All doses showed anti-tumoral effects, the higher dose (0.5 mg) presented citotoxic activity on normal cells, but the minor dose (0.05 mg) displayed better results, with an excelent anti-tumoral action and was not presented high citotoxicity on normal cells. Methrotexate was used how drug control on the anti-tumoral action.

Supported by Fapesp and CNPq.
Supervisor: Suely Vilela Sampaio

BT022-IN VITRO STUDY OF LEUKOTRIENE B_4 RELEASE FROM BIODEGRADABLE PLGA MICROSPHERES

[1]ROBERTO NICOLETE(PG); [2,3]KARLA M. LIMA(PQ); [2,3]JOSÉ M. R. JÚNIOR(PQ); [1]MARCELO D. BARUFFI(PQ); [1]ALEXANDRA I. MEDEIROS(PQ); [2]CÉLIO L. SILVA(PQ); [1]LÚCIA H. FACCIOLI(PQ). [1]FCFRP-USP, [2]CPT, FMRP-USP E [3]NANOCORE BIOTECNOLOGIA LTDA., RP- SP, BRASIL.

Introduction Leukotriene B_4 (LTB_4) is a potent stimulant of phagocytosis, chemotaxis, chemokinesis and aggregation of PMNs. However, some characteristics about leukotrienes like poor solubility in water and chemically labiling difficult their *in vivo* administration. Objective To develop LTB_4-loaded microspheres, which sustain the *in vivo* release of this mediator. Methodology The lipid-loaded microspheres were prepared by oil/water extraction-evaporation technique. The *in vitro* characterization of microspheres consisted in diameters determination, entrapment efficiency and cumulative release of LTB_4 by EIA. Also chemotaxis assay was conducted in a modified Boyden microchamber. Results Mean particle size of LTB_4 microspheres was 5.8 ± 0.3 μm. The encapsulation efficiency was 50% and cumulative *in vitro* release of LTB_4 during 24 hours was 75% (r^2 = 0,9946). LTB_4-loaded microspheres showed a high chemoattractant activity (48 ± 4 cells, n=10) when compared to blank microspheres (3 ± 1.8 cells, n=10). Conclusion The method allowed the preservation of LTB_4 activity and may represent an alternative strategy to treat infections.

Financial Support: FAPESP, CNPq
Supervisor: Lúcia Helena Faccioli

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Biologia Molecular / *Molecular Biology* (BM)

BM001-LPS, GM-CSF AND CONTACT SENSITIZERS ACTIVATE NUCLEAR FACTOR NF-kB AND STIMULATE NITRIC OXIDE PRODUCTION BY A SKIN DENDRITIC CELL LINE

MARIA TERESA CRUZ(PQ)[1,2]; MARGARIDA GONÇALO(PQ)[3]; CARLOS B. DUARTE(PQ)[2]; MARIA CELESTE LOPES(PQ)[1,2]

[1]Faculdade de Farmácia; [2]Centro de Neurociências e Biologia Celular; [3]Serviço de Dermatologia, Hospital da Universidade de Coimbra; Universidade de Coimbra, Coimbra, Portugal.

Introduction Dendritic cells (DC) capture antigens and mature to become potent immunostimulatory cells. Objective To study cellular events, namely nitric oxide synthase (iNOS) expression and nuclear factor kappaB (NF-kB) activation in DC, after exposure to stimuli that induce DC maturation. Methodology A fetal skin-derived dendritic cell line (FSDC) was used as an experimental model of DC. We evaluated the effect of lipopolysaccharide (LPS), granulocyte macrophage-colony stimulating factor (GM-CSF) and three contact sensitizers, 2,4-dinitrofluorbenzene (DNFB), nickel sulphate and paraphenylenediamine (PPDA), on iNOS expression (immunocytochemistry and Western blot assays), NO production (Griess assay) and NF-kB activation (EMSA assay). Results LPS, GM-CSF, PPDA and nickel increased iNOS protein expression, whereas DNFB had no effect. All the stimuli tested activated the transcription factor NF-kB. Conclusions The NF-kB signalling pathway is involved on iNOS expression and DC maturation.

Financial Support: FCT (Portugal)
Supervisor: Maria Celeste Lopes

BM002-GLYCOSAMINOGLYCANS AND HEPARANASE: MARKERS FOR COLORECTAL CANCER

ANA PAULA CLETO MAROLLA (PG)[1]; PATRICIA SEMEDO (PG)[3]; THAÍS PERETTI (PG)[1]; RITCHELLI RICCI (PG)[1]; ANGELA NOHARA (IC)[3];JACQUES WAISBERG (PQ)[2]; MARIA APARECIDA DA SILVA PINHAL (PQ)[3]

[1] Depto. de Clínica Médica-UNIFESP, SP; [2] Depto. de Morfologia-FMABC, SP; [3] Depto. de Bioquímica-UNIFESP, SP – E-mail: amarolla@gmail.com

INTRODUCTION: Heparanase cleaves carbohydrate chains of heparan sulphate proteoglycans and is an important component of the extracellular matrix. OBJECTIVE: To determine the relation between heparanase and glycosaminoglycans expression with colorectal cancer and prognosis of patients. METHODS: The study included patients who underwent colorectal resection by immunohistochemistry and biochemical analysis. Immunohistochemistry assay was performed using polyclonal antibody HPA-C17 (Santa Cruz Biotechnology). The determination of glycosaminoglycans profile and quantification were performed by agarose gel electrophoresis from different regions of patients' biopsies. RESULTS: We observed a difference for heparanase expression between colorectal tumors (129,27 ± 47,5) and normal tissues (85,3 ± 40,65). The biochemical study showed colorectal tumors expressed more glycosaminoglycans than transient and normal tissues. CONCLUSIONS: Glycosaminoglycans and heparanase expressions were significantly higher in colorectal cancer.

Supported by CAPES
Supervisor: Maria Aparecida da Silva Pinhal

BM003-EXTRACTION AND PURIFICATION OF MTDNA FROM *PARACOCCIDIOIDES BRASILIENSIS*

MARIA ANGÉLICA GARGIONE CARDOSO (PG); FRANCISCO GORGÔNIO DA NÓBREGA (PQ).

Laboratório de Genética Molecular e Genomas, IP&D, Univap.

Introduction: Paracoccidioidomycosis is a systemic mycosis caused by the thermo-dimorphic fungus *Paracoccidioides brasiliensis* (Pb). The yeast and pathogenic phase grows at 36°C and a mycelial phase at room temperature (25°C). The mitochondria seem to be involved in the transition of phase induced by temperature shift when ATP and respiration rates decline and growth is adapted to temperature. Objectives: We have developed an optimized methodology to obtain a purified mtDNA from Pb. Methodology: Cells were maintained in solid medium (36°C) and cultivated in liquid YPD to improve the cellular mass. A stainless-steel blender cup with liquid nitrogen was used to disrupt cells. The ground and frozen yeast powder was stirred in buffer and the organelle fraction was centrifuged twice. MtDNA was separated by a CsCl solution containing Hoeschst 33258. Results: Purified mtDNA was digested using restriction enzymes *Eco*RI e *Hin*d III. We observed a different restriction pattern between isolates 18 and 339, analyzing resulting bands in agarose gels. Conclusion: This methodology optimizes the extraction resulting in good yield. Additionally, a specific restriction pattern seems to be a good option for the diagnostic of the disease.

Financial support: FAPESP
Supervisor: Francisco G. Nóbrega

BM004-EXTRATION AND PURIFICATION OF GENOMIC DNA OF ABIOTICS STRAINS OF *HAFNIA ALVEI*.

MARCUS V. P. RODRIGUES(PG)[(1)]; ANA MARISA F. ALMEIDA(PQ)[(1)]; NATÁLIA G. P. NOGUEIRA(PG)[(1]; EDNA BALDIALE(PQ)[(1)]; BIANCA W. BERTONI(PQ)[(1)]; SUZELEI C. FRANÇA(PQ)[(1)]; ROSEMEIRE C. L. R. PIETRO(PQ) [(1,2)]

[(1)]Universidade de Ribeirão Preto-UNAERP, Ribeirão Preto, São Paulo, Brasil;
[(2)]Universidade Estadual Paulista-UNESP, Araraquara, São Paulo, Brasil

Hafnia alvei is a member of the family *Enterobacteriaceae* that has been associated with sporadic cases of diarrhea in humans. The ability of *Hafnia* species to cause attaching and effacing (A/E) lesions in the host epithelial cells is now identified as a virulence factor. The use of molecular techniques for epidemiologic inquiry based on molecular profiles has risen. The aim of the present study was to describe a cheap, rapid and of easy execution protocol for extraction and purification of genomic DNA of *Hafnia alvei* isolated from abiotic sources. The methodology using SDS (Sodium Dodecil Sulfate) described by KEN and CHUO (1993) with a lise buffer modified for genomic DNA extraction in *H. alvei* and an additional precipitation worked properly. Results denoted that the new extraction method is reproducible and easier to perform than the conventional one. The recovered DNA reached satisfactory amounts and demonstrated to be suitable for several applications including RAPD.

Financial Support: UNAERP/CAPES
Supervisor: Rosemeire C. L. R. Pietro

BM005-RAPD-PCR ANALYSIS OF *SALMONELLA* ENTERITIDIS STRAINS ISOLATED FROM DIARRHEA OUTBREAKS.

SÍLVIA MORSOLETTO TOZETTO (PG)[(1)]; SÔNIA MARIA SOUZA SANTOS FARAH (PG)[(1)]; CYNTIA FADEL PICHETH (PQ)[(1)].

(1) Universidade Federal do Paraná.

Introduction: *Salmonella* Enteritidis is the most common cause of diarrhea outbreaks in the state of Paraná. Random Amplified Polymorphic DNA-Polymerase Chain Reaction (RAPD-PCR) is a method for subtyping bacterial species that is useful for outbreak analysis. Objective: To analyze *Salmonella* Enteritidis strains isolated from diarrhea outbreaks in Campo Mourão, Lapa and Curitiba using RAPD-PCR. Methodology: Bacteria were grown in MacConkey Agar and the DNA extracted using SDS and Proteinase K. The RAPD reactions were performed in a 20µL volume containing 25ng of DNA, 8µL of Master Mix (Eppendorf), $MgCl_2$ 3mM and 50pmol of one of a set of 6 primers. Amplification program was: 94°C for 4 min (1X); 94°C for 1 min, 35°C for 2 min, 72°C for 2 min (30X); and 72°C for 5 min (1X). The product was analyzed by gel electrophoresis. Results: Identical RAPD-PCR patterns were observed for strains isolated from the same outbreak. Two of the six primers (5‘-AATCGGGCTG-3‘ and 5‘-CCGAAGCTGC-3‘) made it possible to distinguish between strains from the different outbreaks. Conclusion: The RAPD-PCR results suggest that the *Salmonella* Enteritidis strains responsible for the outbreaks belong to three different subtypes.

Supervisor: Cyntia Fadel Picheth.

BM006-FUNCTIONAL EXPRESSION OF A MITOCHONDRIAL ALTERNATIVE OXIDASE FROM *ASPERGILLUS FUMIGATUS,* IN *S. CEREVISIAE*

TAISA MAGNANI (PG)[1]; VICENTE DE PAULO MARTINS(PG)[1]; FREDERICO MARIANETTI SORIANI(PG)[1]; VALÉRIA GOMES TUDELLA(PG)[1]; CARLOS CURTI(PQ)[2]; SÉRGIO AKIRA UYEMURA(PQ)[1]

FCFRP-USP, (1)-DACTB, (2)-DFQ

A. fumigatus is a human pathogenic fungus capable of inducing a range of disease in immunocompromised patients and has become one of the most important fungal pathogens. In addition to the cytochrome respiratory pathway, higher plants, protists and fungus exhibit a cyanide-insensitive respiration and some report suggested the presence of this alternative pathway in *A. fumigatus*. A cDNA fragment of alternative oxidase was cloned in an expression vector (pYES2) and transformed in *S. cerevisiae* (INVSc1). Protein expression was induced by 2% galactose, at 30ºC for 24 hours. After that, mitochondria were isolated and disrupted in SDS-PAGE sample buffer. Western blot analysis, using the monoclonal antibody against AOX protein, reveled a 37 kD protein, suggesting that AOX was highly expressed in *S. cerevisiae*. Functional expression was demonstrated polarographically by measurements of oxygen consumption in *S. cerevisiae*. Addition of KCN 1 mM inhibited the oxygen uptake and this activity was completely inhibited by salicylhydroxamic acid 2.5 mM, showing that AOX*Af* confer a cyanide-resistance respiration in *S. cerevisiae.*

Financial Support: FAPESP; CNPq
Supervisor: Sérgio Akira Uyemura

BM007-RESEARCH ON DNA-HPV BY SECOND GENERATION HIBRID-CAPTURE ON SEXUALLY ACTIVE FEMALE ADOLESCENTS AND YOUNG ADULTS: A CASE STUDY

PATRICIA MARÇAL DA COSTA(PG)[2]; JOSÉ ELEUTÉRIO JUNIOR(PQ)[2]; MARIA ANGELINA MEDEIROS(PQ)[1]; PAULO MICHEL PINHEIRO FERREIRA(PG)[2]; FERNANDO ANDRÉ VIANA(PG)[2]

[1]Universidade de Fortaleza; [2]Universidade Federal do Ceará

Introduction: Injuried caused by HPV infection in adolescents are more aggressive than in older women. Objective: Evaluate a case study on 195 sexually active women with suspicion of HPV infection. Methodology: The sampled women were divided according to age in two groups, 16-24 (group 1–n = 52) and 25-60 (group 2–n = 153 - control), and submitted to DNA-HPV HC II exams proceeding as described by the Digene®**.** Results: On group 1, 44.3% were found to be positive for high cancer-risk HPV (HR-HPV), 3.8% were positive for high and low-risk HPV and 1.9% for low cancer-risk HPV. On group 2, 25%, 4.4% and 4.4% were positive for high, high and low and low-risk HPV, respectively. On group 1, clinical indications for HC II were, in majority, based on colposcopic suspicion (38%) while in group 2, the test was a better indicative for disease control (36%), suggesting better relation between HPV positivity and clinical suspicion. Conclusion: The age interval from 16 to 24 years proved to be the most frequently infected for HR-HPV, corroborating the association of infection with the beginning of early sexual behavior.

Supervisor: Maria Angelina Medeiros

BM008-ANALYSIS OF THE MRNA EXPRESSION OF PROTEINS INVOLVED IN ANGIOGENESIS, CELL CYCLE CONTROL, INVASION AND MIGRATION OF C6 RAT GLIOMA CELLS TREATED WITH GAMMA-LINOLENIC ACID *IN VITRO*

MARCEL BENADIBA (PG) [1], ALISON COLQUHOUN (PQ) [1]

(1)Biomedical Sciences Institute – Cell and Developmental Biology Department, University of São Paulo, São Paulo, Brazil.

Introduction: Malignant gliomas are primary brain tumours with characteristic resistance to standard radiotherapy and chemotherapy treatments. The search for effective new drugs inhibiting both glioma cell proliferation and disease progression has identified polyunsaturated fatty acids as possible candidates, including gamma-linolenic acid (GLA).
Objectives: The mechanism(s) of action of GLA upon the cell cycle have not been clearly defined and are the subject of this study.
Methods: C6 cell culture ± GLA, RNA extraction and reverse transcriptase – polymerase chain reaction for proteins involved in cell cycle control, angiogenesis and invasion.
Results: Alterations in nm23 alpha, cyclin D1 and pRb gene expression were found after 24h GLA treatment. Conclusion: GLA inhibits C6 cell proliferation and was found to alter the mRNA expression of several proteins involved in the cell cycle.

Financial Support: FAPESP
Supervisor: Alison Colquhoun

BM009-EXPRESSION, PURIFICATION AND IMMUNOLOGICAL STUDIES OF GST-HCV CORE PROTEIN

SANDRA ANTONIA TAGLIAVINI SANTOS (PG) [1]; ANGELA YUMICO MIKAWA (PG) [2] FLÁVIO HENRIQUE DA SILVA (PQ) [3] ; LUIS FERNANDO REYES (PG) [3]; PAULO INÁCIO COSTA (PQ) [1]

(1) IQ-UNESP; (2) FCF-UNESP; (3) UFSCar

INTRODUCTION. Hepatitis C virus (HCV) is the major causative agent of viral hepatitis, which may provoke a hepatocellular carcinoma. The HCV-core antigen is highly conserved in all viral subtypes, being commonly used during the screening viral infection.OBJECTIVE. To express a fragment of core antigen and to assay its immunological reactivity.METHODS. A 408 bp (1-136 aa) fragment HCV core gene was cloned into the pET-42a vector and expressed in fusion with the glutathione-S-transferase (GST) protein into *E. coli* BL-21. Purified recombinant protein was used in immunoblot and ELISA assays with sera from HCV infected and non-infected patients. Positive sera for hepatitis B, HIV, HTLV, Chagas'disease and rheumatoid factor were also assayed to test the cross reactivity.RESULTS. The purified GST-HCV core protein was reactive with HCV-positive serum. None of the negative serum samples showed any reactivity against the recombinant protein. This same result was obtained in the cross reactivity test.CONCLUSIONS. Since the fusion protein presented reactivity for HCV-positive sera and any cross reactivity, its expression and purification may be useful for diagnostic purposes.

Financial Support: CAPES
Supervisor: Paulo I. Costa

BM010-MOLECULAR CHARACTERIZATION OF THE *BHC4-1* RING GLAND ACTIVATOR IN TRANSGENIC *DROSOPHILA*

TATHIANE MAISTRO MALTA (IC) (1); NADIA MONESI (PQ) (1)

(1) Departamento de Análises Clínicas, Toxicológicas e Bromatológicas, FCFRP-USP, Ribeirão Preto, SP.

The *Bradysia hygida BhC4-1* gene is expressed in fourth instar larvae salivary glands. The mechanisms that control *BhC4-1* expression in the salivary gland are conserved in transgenic *Drosophila*. The analysis of lines transformed with progressive deletions of the *BhC4-1* promoter revealed gene expression in another organ, the ring gland. Functional studies resulted on the identification of a 67 bp (-253/-187) ring gland activator. Here we extend the characterization of the ring gland activator. Five constructs comprising distinct mutants of the 67 bp activator were cloned upstream the *Fbp1* miminal promoter, in the pCaSper-AUG-β-gal vector. At least five independent transgenic lines were obtained for each construct. Third instar larvae were assayed for reporter gene expression. The preliminary results indicate that the mutations in the MUT3, MUT4 and MUT5 constructs abolish gene expression in the ring gland, whereas in the case of mutations MUT1 and MUT2 the levels of reporter gene expression are reduced, when compared to the wild type activator. Reporter gene expression analysis will be extended to other developmental stages in order to further characterize the 67 bp ring gland activator.

Financial Support: FAPESP
Supervisor: Nadia Monesi

BM011-MOLECULAR CHARACTERIZATION OF CHALCONE SYNTHASE CDNA RELATED TO ANTIOXIDANT ISOFLAVONE FROM DYPTERIX ODORATA CELLS.

PATRÍCIA GARNICA ROBERTO(PQ); RENATA SANTOS FERNANDES(PG); JOSE FRANCIRALDO LIMA(TC); MIRIAN VERGINIA LOURENÇO(PQ); ROSEMEIRE C. L. R. PIETRO(PQ) ANA HELENA JANUÁRIO(PQ); SUZELEI CASTRO FRANÇA(PQ).

UNAERP

Chalcones are precursors of flavonoid-derived plant natural products and can be converted to isoflavones by coordinated activation of enzymes regulating the central and the isoflavonoid branches of the phenylpropanoid biosynthesis pathway. Metabolome studies showed the presence of antioxidant and potential estrogenic isoflavones in cell cultures of *D. odorata* indicating that the phenylpropanoid pathway is activated in those cells. In this work, molecular approaches were conducted to isolate and characterize CHS cDNA related to the production of isoflavones by D. odorata cultured cell. Total RNA was extracted and reversibly transcribed using SuperScript kit. RT-PCR procedure was conducted with degenerated primers based on conserved sequences of plant CHS already described and the products were then cloned in TOPO TA vector. Automated sequencing further identified the obtained plasmids. *In silico* analysis of nucleotide sequences of a CHS clone (600bp) was performed through the multiple sequence alignment method CLUSTAL. Sequence Matrix Identity among the putative CHS of *D. odorata* and CHS sequences of 12 plant species ranged from 80,5 to 91,2%.

SUPPORT: FAPESP, CNPq

BM012-THE ROLE OF THE *E74* EARLY GENE ON *BHC4-1-LACZ* REGULATION IN THE RING GLAND

MARCOS DE CAMPOS NEVES (IC) [(1)]; NADIA MONESI (PQ) [(1)]

[(1)] *Departamento de Análises Clínicas, Toxicológicas e Bromatológicas, Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo*

In transgenic *Drosophila* the DNA puff *BhC4-1* gene is expressed in the salivary gland and in the ring gland in a developmentally regulated manner. Previous studies have shown that *BhC4-1-lacZ* expression in the salivary gland is reduced in the absence of the early gene products E74A and E74B. Here we investigate the role of the *E74* gene on the regulation of *BhC4-1-lacZ* in the prepupal ring gland through genetic interaction experiments. Animals with one copy of the *BhC4-1-lacZ* transgene in chromosome II and one of the *E74* mutant alleles over a deficiency in chromosome III were analyzed by assaying β-galactosidase activity. The results reveal that *BhC4-1-lacZ* expression in the prepupal ring gland is not affected in the absence of the *E74* gene products. Furthermore, the results confirm that the *BhC4-1-lacZ* expression in the salivary gland is reduced in the absence of the E74A isoform, as verified by the histochemical assay. In this way, these results provide further evidence that the factors that regulate *BhC4-1-lacZ* expression in the ring gland are distinct from those that regulate its expression in the salivary gland.

Financial Support: FAPESP
Supervisor: Nadia Monesi

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Ciência dos Alimentos e Nutrição / *Food Science and Nutrition* (AN)

AN001-EFFECTS OF SUCROSE INTAKE IN EXPERIMENTAL METABOLIC SYNDROME EVALUATION

CRISTIANO MACHADO GALHARDI (PG); HOSANA RODRIGUES (PG); GEOVANA EBAID (IC); KATIUCHA ROCHA (IC); LUCIANE FAINE (PQ); YEDA DINIZ (PQ); REGINA M. BURNEIKO (PQ); ANA ANGÉLICA H. FERNANDES (PQ)

Departamento de Química e Bioquímica, IB, UNESP, Botucatu, São Paulo

Introduction: Metabolic syndrome (MS) is associated with the incidence of cardiovascular damage, and inadequate food intake. Objective: The present study evaluated the body mass index (BMI), length (L), triacylglicerol levels (TG) and abdominal circumference (AC) in animals submitted to sucrose intake. Methods: Male *Wistar* rats, 24 animals (222.6±16.4g) were divided into two groups (n=6): (A) group received basal diet and (B) high-sucrose intake (30% of sucrose aqueous solution-SAS) plus basal diet during 30 days. Statistical analysis: T-test, $p<0.05$. Results: B group presented elevation in TG concentrations (244.75±31.01mg/dL) in comparison with the animals of the A group (139.33±27.35mg/dL). No significant differences were observed in L and BMI among the groups. The AC was higher in B group (20.67±1.47cm) than in A group (19.17±0.98cm). Conclusion: In conclusion, the addition of SAS to the diet, had no effects on BMI or L of the animals but, induced elevation in TG concentration and altered the phenotypic inducing hypertriglyceridemic waist as observed in MS condition.

Financial Support: FAPESP
Supervisor: Ethel Novelli

AN002-INORGANIC NUTRIENTS IN RICE AND BEAN

ISAURA AKEMI OKADA (PQ)[1]; MARIA CRISTINA DURAN (PQ)[2]; MÁRCIA LIANE BUZZO (PQ)[2]; ALICE MOMOYO SAKUMA (PQ)[2]; SÉRGIO DOVIDAUSKAS (PQ)[1]; ODAIR ZENEBON (PQ)[2]

[1]Instituto Adolfo Lutz – Lab. I de Ribeirão Preto; [2]Instituto Adolfo Lutz – Lab. Central – São Paulo

Introduction: the white rice and bean simultaneous ingestion is an important food intake in Brazil; however the composition tables reveal different contents of inorganic nutrients for those types of food. Objective: determination of inorganic nutrients in white rice and bean, and comparison of the obtained data with various food composition tables. Methodology: 40 samples of white rice (*Oryza sativa*) and 40 samples of bean (*Phaseolus vulgaris*) commercialized in São Paulo State (Brazil) were treated by a new wet ashing validated procedure (HCl hydrolisis in open vessels); the quantification was carried out by inductively coupled plasma atomic emission spectrometry (ICP AES). Results: in contrast to white rice results, bean samples showed high contents of Ca, Fe, K, Mg, Cu, Zn, and P. In another hand, the results for Ca, Fe, and Na do not corresponded to food composition tables declared values. Conclusions: since white rice and bean inorganic nutrients contents depend on a large number of factors (like climate, soil, and variety), the use of food composition tables should be judicious.

Financial support: Instituto Adolfo Lutz
Supervisor: Odair Zenebon

AN003 - INFLUENCE OF AN EGGPLANT (*SOLANUM MELONGENA*) PREPARATION ON CHOLESTEROL METABOLISM IN HUMANS.

ANTONIO VIEIRA DE FARIA JUNIOR(IC)[(1)] ; JULIANA DA SILVA AGOSTINI(PQ) [(1)]

[(1)] Unigran - MS

Introduction: The study of functional food has been the researchers' great interest, mainly food which action prevents the development of chronic diseases, such as diabetes, cardiac problems, high blood pressure, etc. The great variety of food avalilable in Brazil makes possible the discovery of new products with funcional property. The eggplant has been largely used to control the level of cholesterol, although its efficiency has not been proved yet. Objective: To check one's real probability of reducing the cholesterol levels (total and LDL) by having a diet based on eggplant, and so confirm its functional property. Methodology: Observing 257 people's cholesterol level (total, LDL, HDL and VLDL), 28 of them had shown the highest levels of total cholesterol, those people had gone on a diet based on eggplant and orange juice for 25 days and then, a new laboratory experiment had been done to evaluate the cholesterol metabolism. Main results: The research has shown that the use of eggplant juice during 25 days had no effect on the reduction of the cholesterol levels. Conclusions: New studies are necessary to be maden using a prolonged diet and a larger amount of people.

Financial support: Unigran
Supervisor: Juliana da Silva Agostini

AN004-QUANTIFICATION OF NITRATE, OXALIC ACID AND PHENOLIC COMPOUNDS IN TAIOBA´S LEAF

THIAGO DE MELO SILVA (IC)[1]; MAURO RAMALHO SILVA (IC)[1]; CLINASCIA RODRIGUES ROCHA (IC)[1]; YARA PIMENTA SOUZA (IC)[1]; RENATA SILVA DINIZ (IC)[1]; TASSIA CASSIMIRO VIGATO (IC)[1]; NÍSIA ANDRADE VILLELA DESSIMONI PINTO (PQ)[1]

[(1)] FACULDADES FEDERAIS INTEGRADAS DE DIAMANTINA

The vegetables contain an extensive metabolism, being able to synthesize a complexity of chemical products that can originate poisonous reactions when ingested in significant amount by human beings. The leaves of vegetables are able to accumulate high concentrations of those substances. So, the purpose of the present work is to determine the levels of nitrate, oxalic acid and phenolic compounds present in taioba´s leaf, *Xanthosoma sagittifolium*, looking for its consumption with respect to alimentary safety. The leaves were submitted to three drying conditions. Nitrate and phenolic compounds analysis was done using colorimetric methods, while oxalic acid was determined by titration, being all methods described in literature. All the numerical results obtained were inferior to that found in others conventional vegetables researched in literature. Therefore, it is concluded that taioba contains acceptable levels of nitrate, oxalic acid and phenolic compounds, and can be included in the population's diet without risks.

Financial Support: CNPq / FAFEID
Supervisor: Nísia Andrade Villela Dessimoni Pinto

AN005-DIETETIC FIBER AND CHEMICAL COMPONENTS IN LEAVES OF TAIOBA

MAURO RAMALHO SILVA (IC)[1]; MAITÊ DA COSTA SILVA (IC); THIAGO DE MELO SILVA (IC)[1]; CLINASCIA RODRIGUES ROCHA (IC)[1]; ANA ISAURA ARAUJO (IC)[1]; MARCELO MANDACARU SOUZA (IC)[1]NÍSIA ANDRADE VILLELA DESSIMONI PINTO (PQ)[1]

(1) Faculdades Federais Integradas de Diamantina

Due to an increasing interest on healthy and alternative foods, it is important to know their chemical composition. So the objective of this work was to characterize the chemical composition and the dietary fiber content in the leaves of the taioba. The samples were submitted to three drying conditions. The chemical composition was determined according to AOAC (1990); the fibers, AFD (acid fiber detergent) and NFD(neutral fiber detergent) were quantified through gravimetric analysis, while the pectins were determined using colorimetric method. The samples of taioba showed levels high of the qualitified fibers and which compared others convencional vegetables, cited in the literature. In conclusion, the leaves of taioba presented considerable fiber contents, able to cntribue in diets present a low caloric value and habits healthy.

Financial Support: CNPq / FAFEID
Supervisor: Nísia Andrade Villela Dessimoni Pinto

AN006- ACTIVITY TRYPSIN INHIBITORY AND VITAMIN C OF THE LEAVES OF TAIOBA (*XANTHOSOMA SAGITTIFOLIUM*)

CLINASCIA RODRIGUES ROCHA (IC)[1]; HELTON PINTO DE MATTOS (IC)[1]; MAURO RAMALHO SILVA (IC)[1]; THIAGO DE MELO SILVA (IC)[1]; HARA RODRIGUES DE MOURA(IC)[1]; DIACONIS JOSSELY SOARES ALMEIDA (IC)[1]; FELIPE ZILLE DE ALMEIDA (IC)[1]; NÍSIA ANDRADE VILLELA DESSIMONI PINTO (PQ)[1]

(1) Faculdades Federais Integradas de Diamantina

The taioba is not-convencional vegetable with high nutrition value, easily cultivated, a low cost and availability in areas where there is lack in foods. So, the purpose of this work was of quantifying levels the vitamin C and of trypsin inhibitor activity in the leaves of taioba, seeking as source of of nutrients and of alimentary safety. The leaf was dry and analyzed by the method enzymatic colorimeter and titration, for the trypsin inhibitors and vitamin C, respectively. The levels of vitamin C found in the taioba's leaves was close of the orange, melon and guava, mentioned in the literature. The taioba leaves presented levels of trypsin inhibitor below of others conventional vegetables, mentioned in the literature. It was concluded that the taioba leaves are viable sources of vitamin C and they not present negative effects to the absorption of proteins.

Financial Support: CNPq / FAFEID
Supervisor: Nísia Andrade Villela Dessimoni Pinto

AN007-DETERMINATION OF TRANS FATTY ACIDS IN ADIPOSE TISSUE OF OBESES INDIVIDUALS.

JOSIANE W. BORTOLOTTO(PG)[(1)]; ÂNGELA FERREIRA(IC) [(1)]; SIRLEI COSTA(PQ) [(2)]; CLÁUDIO C. MOTTIN(PQ) [(3)]; ANDRÉ A. SOUTO(PQ) [(4)]; REGINA MARIA GUARAGNA(PQ) [(1)]

[(1)]Depto Bioquímica, UFRGS; [(2)]CCR, RS; [(3)]COM, PUCRS; [(4)]Instituto de Química, PUCRS

INTRODUCTION: Trans fatty acids (TFA) are suspected to be one of heart disease risk factors. Humans consume TFA in different food (bakery foods, milk, hydrogenated vegetal fat) OBJECTIVE: The purpose of our study was to describe the total content of TFA in subcutaneous, retroperitoneal and visceral fat of obese and no obese patients as an indicator of dietary expose. METHODOLOGY: The adipose tissues (15 g) were obtained by surgery. Lipids were extracted, saponificated and esterificated. The TFA measured was doing by ATR-IR spectroscopy (correlation coefficient 0.9994). RESULTS: TFA averages found in obese patients was 6,3% (retroperitoneal) and 8,7% (visceral). For no obese patients 6,9% (subcutaneous) and 9,3% (visceral). There was no difference in both groups. However, TFA depot in the visceral fat was higher than others fats tissues ($p<0.001$) for obese and no obese ($p<0.05$). Our values of TFA content in all fat depots are higher than others countries (3-6%). CONCLUSIONS: These levels of TFA in adipose tissue presumably reflect the higher dietary intake of TFA by the Brazilian people.

SUPPORT BY: CNPq, FAPERGS, UFRGS, PUCRS.
Supervisor: Regina Maria Guaragna

AN008-LYCOPENE PROTECTION AGAINST CHROMOSOMAL DAMAGE INDUCED BY THE CHEMOTHERAPIC AGENT CISPLATIN"

MILENA CRISTINA SENDÃO (PG)[1]; ESTELA BEATRIZ BEHLING (PG)[1]; LUSÂNIA MARIA GREGGI ANTUNES(PQ)[2]; MARIA DE LOURDES PIRES BIANCHI (PQ)[3]

[1] Depto. Alimentos e Nutrição, FCFAR/UNESP; [2] Depto. Ciências Biológicas, FMTM; [3] Depto. Anal. Cli., Toxicol e Bromatol., FCFRP/USP

The use of cisplatin (cDDP) has limitation since it has been observed some side effects such as induction of chromosomal aberrations. Lycopene (L) is a natural carotenoid whose biological function is related to the ability of scavenging free radicals. The aim of this study was to investigate the possible protective effect of the antioxidant L on the cisplatin-induced chromosomal aberrations. The animals were divided into 10 groups: negative control, solvent, three doses of L (0.5; 1 and 1.5 mg/kg b.w.), cDDP (5 mg/kg b.w.), solvent associated with cDDP, and L and cDDP associations. L was given by gavage 72, 48, 24 and 1h before the cDDP intraperitoneal injection. The number of altered metaphases was reduced to 61.2%, 33.8%, 36% and the amount of chromosomal aberrations was reduced to 66.3% 29.1%, 33.1% in animals treated with L (0.5, 1 and 1.5 mg/kg) and cDDP, respectively, compared to animals treated with cDDP alone. This protective effect of L on the cDDP-induced chromosomal damage can be attributed to the ability of this carotenoid to scavenge free radicals.

Financial Support: CAPES
Supervisor: Maria de Lourdes Pires Bianchi

AN009-PHYSICAL PROPERTIES OF STRUCTURED LIPIDS FROM LARD AND SOYBEAN OIL

ROBERTA CLARO DA SILVA (PG)[1];LUIZ ANTONIO GIOIELLI[1]

[1]Biochemical Pharmaceutical Technology

Introduction:Human milk has characteristics of great importance for term infants, providing protection against infections and allergies. Therefore, the fatty acid composition and distribution in the triacylglycerol chain must be object of studies in infant formulas. Objective: The objectives of this paper were to obtain structured lipids from lard and soybean oil by chemical interesterification that have similar characteristics to human milk fat. Methodology:Binary mixtures of lard and soybean oil in different ratios (80:20, 60:40, 50:50, 40:60, 20:80) were submitted to chemical interesterification with the purpose of producing a structured lipid that mimic human milk fat. The fatty acid composition, iodine value, solid fat content, and consistency were analyzed. Main Results:The solid fat content and consistency of lard decreased by the addition of soybean oil. Chemical interesterification modified the behavior of lard and its binary mixtures with soybean oil, in all ratios, possibly in function of the increase of di and trisatured triacylglycerols produced by the randomic effect. Conclusion:The ratio 80:20 was similar to human milk fat composition and the interactions between lard and soybean oil presented a monotectic effect before and after chemical interesterification.

Financial Support:Capes
Supervisor:Luiz Antonio Gioielli

AN010-DIFFERENTIAL SCANNING CALORIMETRY ANALYSIS OF BINARY AND TERNARY MIXTURES FROM CHICKEN FAT, ITS STEARIN AND MEDIUM CHAIN TRIACYLGLYCEROLS (MCT)

MING CHIH CHIU (PG)[(1)]; RENATO GRIMALDI (PQ)[(2)]; LUIZ ANTONIO GIOIELLI (PQ)[(1)]

[(1)]Departamento de Tecnologia Bioquímico-Farmacêutica, FCF/USP; [(2)]Laboratório de Óleos e Gorduras, FEA/UNICAMP

Differential Scanning Calorimetry (DSC) is used for monitoring changes in the physicochemical properties of edible oils and fats by directly measuring their specific heat with high sensitivity and accuracy. In this study a three-component mixture experiment (7 runs) was employed to determine the interactions between abdominal chicken fat, stearin, and medium chain triacylglycerols (MCT), using a DSC-7 calorimeter (Perkin-Elmer Corp.), equipped with a thermal analysis data station. Chemical composition of fatty acids, softening, and melting points analysis were also used to complement the DSC data. A mathematical model of multiple regression (triangular diagrams) was applied to optimize the responses of each parameter of analysis. The results showed no significant ($p<0.05$) interactions between the components but was observed a synergic effect for the softening point. DSC could also provide information about the nature of triacylglycerol interactions.

Financial Support: CAPES
Supervisor: Luiz Antonio Gioielli

AN011-COFFEE BREW PREVENTS THE GENOTOXIC EFFECT OF CYCLOSPHOPHAMIDE IN RATS

STELLA MARIS DA SILVEIRA DUARTE(PQ)[1]; CELESTE MARIA PATTO DE ABREU(PQ)[2]; FERNANDA BORGES PAULA(PQ)[1]; CIBELE MARLI CAÇÃO PAIVA GOUVÊA(PQ)[3]

[1]Efoa/Ceufe – Dep. Análises Clínicas; [2]UFLA – Dep. Ciências Alimentos; [3]Efoa/Ceufe – Dep. Ciências Biológicas.

Introduction: Coffee is one of the most popular beverages consumed, but its anti-genotoxic effect is not clear. Objective: The aim was to test if the coffee brews prevent genotoxic effects. Methodology: The effect was evaluated against cyclophosphamide (CP) in the rat bone marrow micronucleus test (MN). Rats ingested 280 mg/kg/day of coffee brew for 7 and 30 days, and 24 h after CP ingestion (50 mg/kg), the bone marrow cells were collected and analyzed. Results: The coffee brews were tested over a broad dose range MN assays and no indication for genotoxic effects was seen, when administered for 7 or 30 days ($p<0.001$). The ingestion of coffee brews for 7 and 30 days decreased, significantly MN frequency formation ($p<0.01$), by 1.5 folds. However, there was no significantly difference between the percentage of MN decreasing, when 7 (31.09%) or 30-day-treatment (31.08%) were compared. Conclusions: The results indicate that the ingestion of coffee brew prevented the genotoxic effect of the CP, which could be due to the inhibition of CP biotransformation or the reduction of DNA alkylation by CP.

Financial Support: Capes, Efoa/Ceufe, UFLA
Supervisor: Cibele Paiva Gouvêa

AN012-*IN VIVO* ANTIOXIDANT ACTIVITY OF COFFEE BREWS PREPARED WITH PEELED ARABICA

STELLA MARIS DA SILVEIRA DUARTE (PQ)[1]; CELESTE MARIA PATTO DE ABREU (PQ)[2]; SELMO DE ÁVILA LIMA (PQ)[1]; JOSÉ ANTONIO LEITE (PQ)[1]; CIBELE MARLI CAÇÃO PAIVA GOUVÊA (PQ)[3]

[1] Efoa/Ceufe – Dep. Análises Clínicas; [2]UFLA – Dep. Ciência dos Alimentos; [3] Efoa/Ceufe – Dep. Ciências Biológicas.

Introduction: Coffee is one of the most popular beverages consumed daily. It is a very complex mixture of several chemicals which are either naturally occurring or induced by the roasting process, which account for its biological activity. Objective: The aim was to verify the effect of filtered coffee brew, prepared with peeled arabica, in rat lipid peroxidation. Methodology: Rats ingested 280 mg/kg/day of coffee brews for 7 days (acute treatment) and 30 days (chronic treatments). We determined if the coffee brew reduced the oxidative stress analyzing the brain lipid peroxidation as TBARS. Results: The ingestion of coffee brew for 7 and 30 days inhibited, significantly the TBARS formation ($p<0.01$) as compared to the control. However, there was no significantly difference ($p>0.05$) between the percentage of lipid peroxidation, when acute (48.6%) or chronic (53.4%) treatments were compared. Conclusions: The results indicate the beneficial health effect of moderated filtered coffee brew ingestion, as it inhibited lipid peroxidation.

Financial Support: Capes, Efoa/Ceufe, UFLA
Supervisor: Cibele Marli Cação Paiva Gouvêa

AN013-BIOLOGICAL CONTROL OF SALMONELLOSIS IN CHICKEN

ELIANE DE CARLI(PG)[1]; PAULO CEZAR CAMPAGNOL(PG)[1]; BIBIANA DOS SANTOS(IC)[1]; LEADIR FRIES(PQ)[1]; NELCINDO TERRA(PQ)[1]; CATIÚSCIA PADILHA DE OLIVEIRA(IC)[1]; ARIANE FURTADO(PG)[1]; DALVAN VEIT(PQ)[1]; DIALA URNAU(PQ)[1]

[1]Universidade Federal de Santa Maria

Salmonellosis is an infectious disease responsible for vast economical losses in the Brazilian poultry industry. This work aimed to evaluate the effect of the probiotic *Lactobacillus paracasei* in *Salmonella enteritidis* control. Three treatments were utilized as: treatment 1 (L1) the chickens were treated with water and ration; treatment 2 (L2), *L. paracasei* was added in the drink water and treatment 3 (L3), *L. paracasei* was added in the drink water and the chicken´s esophagus was inoculated with *Salmonella enteritidis*. Lactic acid bacteria counts and *Salmonella* spp were analyzed weekly for 42 days. It was observed the presence of *Salmonella* in L1 while in the L2 was not found and in the L3 the absence of *Salmonella* occurred only at 32 and 42 days. Therefore, the results showed that the utilization of probiotic *L. paracasei* inhibited the growth of *Salmonellas* species naturally present in the chicken's intestine, indicating a protective effect. It is concluded that the *Lactobacillus paracasei* can be an important tool in the control of salmonellosis in chickens.

Financial Support: Cnpq, PIBIC
Supervisor: Leadir Fries

AN014-EFFECT OF THE PROPOLIS HYDRO ALCOHOLIC EXTRACT IN THE DEVELOPMENT OF MOULDS IN SALAMI

ROSIELE LAPPE(PG)[1]; PAULO CEZAR CAMPAGNOL(PG)[1]; ERNESTO KUBOTA(PQ)[1]; NELCINDO TERRA(PQ)[1]; ANDRÉIA PAULA ILKIV(IC)[1]

[1] Universidade Federal de Santa Maria

The growth of some moulds on the surface of salamis can cause problems related to discoloration and off-flavour. This work aimed to study the effect of the utilization of propolis hydro alcoholic extract in the development of moulds in salami. Salamis produced in pilot scale were treated with four different propolis hydro alcoholic extract concentrations (0, 0.5, 1, 2 and 4%). Moulds and yeasts were evaluated during the maturation. The sensorial analysis was carried out at the end of the trial. The treated samples with 2 and 4% showed, to the term of the period of ripening, a decrease in the tally of moulds and yeasts of two logarithmic cycles in relation those not treated. On the sensorial evaluation no differences were observed between the treated samples and the control salami. It is concluded that the use of propolis hydro alcoholic extract decreased the growth the moulds and yeasts and it did not affect the sensorial characteristics of the salamis.

Financial Support: Capes
Supervisor: Ernesto Kubota

AN015-ADHERENCE OF LACTIC ACID BACTERIA AND *LISTERIA MONOCYTOGENES* TO STAINLESS STEEL COUPONS

REGIANE PRISCILA RATTI (PG)[1]; RAFAEL CHACON RUIZ MARTINEZ (PG)[1]; VANESSA MACIEL (PQ)[1]

(1) FCFRP-USP

Introduction: *L. monocytogenes* is a bacterium able to adhere to abiotic surfaces and may contaminate foods during manufacturing. *Leuconostoc*. sp. is a lactic acid bacterium (LAB) commonly found in foods and may present antilisterial activity. Objectives: To evaluate the capacity a bacteriocin-producing *Ln. mesenteroides* (bac^+) active against *L. monocytogenes*, a non bacteriocin-producing *Ln. mesenteroides* (bac^-) and *L. monocytogenes* to adhere to stainless steel coupons, in pure or mixed-cultures. Methods: *Ln. mesenteroides* bac^+ and bac^- were inoculated alone in BHI (Brain-Heart Infusion) and their adherence to stainless steel coupons was determined after 3h, 24h and 48h. Co-inoculation with *L. monocytogenes* was also tested, using selective culture media and analysis by scanning electron microscopy. Results: *Ln. mesenteroides* bac^+ lonely did not adhere to stainless steel coupons, differently from *Ln. mesenteroides* bac^-. In the tests with co-culture, *Ln. mesenteroides* bac^+ adhered to stainless steel coupons after 3h. LAB did not interfere with *L. monocytogenes* adherence in any test. Conclusion: The BAL used in co-culture were not capable to reduce *L. monocytogenes* adherence to stainless steel coupons.

Finnancial Support: CNPq
Supervisor: Elaine Cristina Pereira De Martinis (PQ)[1]

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Controle de Qualidade / *Quality Control* (CQ)

CQ001-VALIDATION OF A MICROBIOLOGICAL ASSAY FOR LOMEFLOXACIN IN COATED TABLETS

GREICI CRISTIANI GOMES TOZO (PG) [1] ; HÉRIDA REGINA NUNES SALGADO (PQ)[1]

[1] Programa de Pós-graduação em Ciências Farmacêuticas - Faculdade de Ciências Farmacêuticas, UNESP, Rodovia Araraquara-Jaú, km 1, Araraquara- SP - CEP 14801-902, Brazil.

Lomefloxacin (CAS 98079-52-8), a third generation fluoroquinolone, is 1-ethyl-6,8-difluoro-1,4-dihydro-7-(3-methyl-1-piperazinyl)-4-oxo-3-quinolone. No official method is available for the assay of pure drug and its formulations. In this work experimental 3 x 3 design using three dose levels for each standard and sample were used following the procedure described in Brazilian Pharmacopoeia. The calculation procedure normally assumes a direct relationship between the observed zone diameter and logarithm of applied dose. The calibration curve for lomefloxacin was constructed by plotting log of concentrations *versus* zone diameter and showed good linearity on the 2.0 - 8.0 $\mu g.mL^{-1}$ range and the linear equation for lomefloxacin was $y = 0.0839x - 0.703$ with coefficient of regression of $r^2 = 1.0000$; was used a strain of *B. subtilis* ATCC 9372 as the test organism. The assays were validated by means of the analysis of variance. The method validation showed that is linear precise (CV = 1.15) and accurate. We conclude that the microbiological assay is precise, accurate and satisfactory for quantification of lomefloxacin in tablets.

Financial Support: CAPES, CNPq-Brazil, INTECQ, Pfizer-Pharmacia Brazil.
Advisor´s Name: Hérida Regina Nunes Salgado

CQ002-INFLUENCE OF SOLVENTS ON SPECTROPHOTOMETRIC QUANTIFICATION OF RUTIN: PRE-VALIDATION ASSAY

ANDRÉ ROLIM(PG); CAROLINA MORAES MACIEL(IC); VIVIAN ZAGUE(PG); CLAUDINÉIA SALES DE OLIVEIRA PINTO(PG); TELMA MARY KANEKO(PQ); MARIA VALÉRIA ROBLES VELASCO(PQ)

Department of Pharmacy, School of Pharmaceutical Sciences, University of São Paulo

Introduction: Rutin is used as treatment of venous insufficiency. Analytical validation must guarantee that a method meets requirements of its application. Sources of inaccuracies in analytical methods are: impure standards; poor precision/accuracy and unsuitable techniques. Objective: This research evaluated inappropriate data of pre-validation precision and accuracy for rutin with different solvents. Methods: Absorbances were performed at 361.0 nm. Ethanol/acetic acid (99:1) [A], ethanol/distilled water (1:1) [B] and ethanol/distilled water/acetic acid (50:49:1) [C] were used as solvents for rutin. Calibration curves achieved the range 5-15 $\mu g.mL^{-1}$. Interval was assessed by precision/accuracy. LOD and LOQ were estimated by mean standard deviation and slopes. Results: [A] resulted R^2 (0.9995), suitable precision (0.3%) and accuracy (110.1%). [B] and [C] resulted unacceptable accuracies. LOD and LOQ for [A] were 0.09 and 0.27 $\mu g.mL^{-1}$. Conclusions: Ethanol/acetic acid (99:1) provided higher absorbances, precision/accuracy; linearity and low LOD and LOQ for rutin.

Financial support: CNPq, PIBIC, MCT/CNPq
Supervisor: Prof.ª Dr.ª Maria Valéria Robles Velasco

CQ003-THERMAL STUDIES OF PHARMACEUTICAL DRUGS

LUIZ MAMEDE(PG); BRUNO L. CAETANO(PG); LUCAS A. ROCHA(PG); EDUARDO FERREIRA(PG); CAMILA R. KFOURI(PG); EDUARDO J. NASSAR(PQ); KATIA J. CIUFFI(PQ); PAULO CALEFI(PQ).

Universidade de Franca, Av. Dr. Armando Salles Oliveira, 201 – CEP 14404-600 Franca/SP

Introduction: Thermal analysis technique can be used to characterize the materials and applications for the pharmaceutical and biotechnology industry. Pharmaceuticals compounds have a propensity to exist in different structural or morphological forms and this gives rise to concerns over processing, long-term stability, aging, and biodelivery. The development and manufacture of drugs requires that close attention be paid to purity, quality, stability and safety in order to ensure that the drug performs as intended. The successful formulation of a stable and effective solid dosage form depends on careful selection of the excipients used to make administration easier or more suitable, improves patient compliance, promote release and bioavailability of the drug and protect it from degradation. Objective: In this work we used thermal analysis to study the possible interaction between drugs and excipients. Methodology: The drugs were obtained commercial and the thermal analysis results compared with pure drugs. Results and Conclusion: The different composition percentage of aspirina and AAS drugs and different excipients existent in the formulation can promote change in physical properties.

Financial Support: FAPESP e CAPES
Supervisor: Eduardo Nassar

CQ004-FLOW INJECTION SPECTROPHOTOMETRIC DETERMINATION OF FUROSEMIDE IN PHARMACEUTICALS BY THE BLEACHING OF A PERMANGANATE CARRIER SOLUTION

FELIPE SILVA SEMAAN(PG)[1]; ROGÉRIO ADELINO DE SOUSA(PG)[2]; ÉDER TADEU GOMES CAVALHEIRO(PQ)[1]

[1]IQSC-USP, Av. Trabalhador Sãocarlense, 400, São Carlos - SP, CEP 13560-970; [2]DQ-UFSCar, Rod. Washington Luís, Km 235, São Carlos - SP, CEP 13565-905

Introduction: Few methods are described concerning furosemide (FR) determination, most of which time and reagent consuming. Objective: This work intends to develop a faster procedure for FR determination. Methodology: A flow injection spectrophotometric procedure based on FR reaction with $KMnO_4$ is described using a 50 cm sample loop and a 100 cm reactor at 50°C, in a flow rate of 2.2 ml min^{-1} (3.0 x 10^{-4}mol l^{-1} $KMnO_4$ carrier solution). The analytical signal was the bleaching of the carrier solution and the detection at 550 nm presented a linear range from 1.0 to 6.0 x 10^{-4}mol l^{-1}, obeying the linear equation $y = 587.5[FR] + 0.09$ ($r = 0.995$, $n = 6$), detection limit was 10^{-5} mol l^{-1}. Results and Conclusions: The proposed flow procedure was applied to four commercial samples (tablets and ampoules) from three different suppliers. It presented an adequate analytical frequency (40 measurements/hour). The results are in agreement with both labeled and a UV-Vis comparative procedure values within 95% of confidence.

Financial Support: FAPESP (04/08550-0)
Supervisor: Prof. Dr. Éder T. G. Cavalheiro

CQ005-DEVELOPMENT AND VALIDATION OF A HIGH PERFORMANCE LIQUID CHROMATOGRAPHIC METHOD FOR QUANTIFICATION OF ISOFLAVONE AGLYCONES IN HYDROLYSED SOY EXTRACTS

ISABELA C. CÉSAR (PG); FELIPE A. CONDESSA (IC); THIAGO A. F. BARBOSA (IC); CRISTINA D. VIANNA-SOARES (PQ); FERNÃO C. BRAGA (PQ); ELZÍRIA A. NUNAN (PQ); GERSON A. PIANETTI (PQ); LIGIA M. MOREIRA-CAMPOS (PQ)

Faculdade de Farmácia, UFMG

Isoflavones have widely been used as an alternative to conventional hormone replacement therapy due to their estrogenic activity and reduced adverse effects. The most common isoflavone aglycones in soy extracts are genistein, daidzein and glycitein, also found in glycosidic forms. Soy dry extracts are used as pharmaceutical raw materials to produce capsules and tablets. The aim of this study was to develop and validate a HPLC method for simultaneous quantification of the three aglycones in soy dry extracts after acidic hydrolysis. The samples were submitted to 3,0 mol L^{-1} ethanolic hydrochloric acid at steam bath for 40 min to yield the aglycone forms. Their separation and quantification was achieved using a C_{18} endcapped column, a mobile phase constituted of 0,1% acetic acid and methanol (52:48), at 1,0 ml/min flow rate and DAD detection at 254 nm. The method was linear, precise, accurate, robust and specific, thus can be used to quantify the three isoflavone aglycones in raw materials and pharmaceuticals.

Financial Support: FAPEMIG, Farmacopéia Brasileira.
Supervisor: Ligia M. MOREIRA-CAMPOS

CQ006-THE CUTANEOUS PROTECTIVE EFFECT OF TOPICAL FORMULATIONS CONTAINING QUERCETIN (QC) AGAINST UVB INDUCED OXIDATIVE STRESS IN HAIRLESS MICE

RÚBIA CASAGRANDE(PQ)[1,2]; SANDRA R. GEORGETTI(PG)[2]; WALDICEU A. VERRI, JR(PG)[3]; MARIA J.V. FONSECA(PQ)[2]

[1]Department of Food and Drugs Technology, CCA-UEL
[2]Department of Pharmaceutical Science, FCFRP–USP
[3]Department of Phamacology, FMRP–USP

Introduction: Antioxidants from natural products present novel possibilities for the treatment and prevention of oxidative stress-mediated skin diseases. Flavonoids such as QC may delay oxidative injuries by scavenging oxygen radicals. Objective: The aim of this study was to investigate the photoprotective effect of topical formulations containing QC. Methodology: Oxidative stress was induced in hairless mice by UVB irradiation. The leukocyte migration to the skin was evaluated with the myeloperoxidase kinetic-colorimetric assay and the glutathione (GSH) skin levels were determined using o-phthalaldehyde as a fluorescent reagent. Results: Above 1.23 J/cm^2, the neutrophil migration to skin was significantly increased, and GSH levels decreased after 2.46J/cm^2 UVB irradiation. Topical application of formulations containing QC before UVB irradiation significantly decreased the neutrophil migration as well as prevented GSH depletion. Conclusion: These results suggest QC as a promising drug for the treatment of photooxidative skin damages.

Financial Support: Capes and Fapesp
Advisor: Maria J.V. Fonseca

CQ007-DETERMINATION OF GLIMEPIRIDE IN PHARMACEUTICAL FORMULATION BY DERIVATIVE SPECTROPHOTOMETRY

REGINA CELLI ESPIRES-CARRION(PQ) [1], JOÃO FERNANDES MAGALHÃES [2]

[1]Universidade Estadual de Maringá. [2] Universidade de São Paulo.

A simple first-derivative spectrophotometric method was developed and validated for determination of glimepiride (GP) in pharmaceutical formulation. The quantification of GP can be carried out using 0.1M NaOH solution by heating at 80-90°C for 5-10 minutes for solubilization the drug from formulation and subsequently was evaluated directly by zero-crossing point method at 251 nm, where the interference from lactose, present in GP samples, was eliminated. The calibration graph was linear in the range from 3.0 and 30.0 µg/mL of GP with a correlation coefficient of 0.9999. Limits of detection and quantification are in the order of 5,86 µg/mL and 19,55 µg/mL of GP, respectively. The substitution of lactose for magnesium carbonate in simulated samples permitted determination of GP with direct spectrophotometry at 230 nm. The statistical results obtained with method described showed good accuracy, precision and linearity at determined conditions. The excipients commonly found in commercial pharmaceutical formulations do not interfere. The advantages of this method are simple analytical procedures, stable, inexpensive and it is suitable for routine pharmaceutical analysis.

Financial support: CAPES/UEM
Supervisor: João Fernandes Magalhães

CQ008-COMPARATIVE STUDIES OF THE ANTIOXIDANT ACTIVITY AND THE POLIPHENOL CONTENT IN EXTRACT OF GREEN PROPOLIS

YRIS MARIA FONSECA(PG)[1], FRANCIANE DELFIN MARQUELE(PG)[1] e MARIA JOSÉ VIEIRA FONSECA(PQ)[1]

(1)Department of Pharmaceutical Science – University of São Paulo – Ribeirão Preto

Introduction: Green propolis is constituted for several phenolic compounds, such as flavonoids. Studies suggest a significative contribution of these phenolic compounds for the antioxidant and anti-inflammatory activities. Objective: Compare the antioxidant activity and the poliphenol and flavonoid content of the fluid and dry extracts of green propolis. In addition, it was intended to verify the best solvent to solubilize the dry extract without losing the antioxidant activity. Method: The poliphenol and flavonoid determinations were performed as the method described for Kumazawa, 2004. The antioxidant activity was performed against the $DPPH^{\cdot}$ radical. Results: The results showed that the fluid extract presented IC50 of 0.07mg/mL, corresponding to 1.25µg/mL and 0.16µg/mL of poliphenol and flavonoid contents. The best solvent to solubilize the dry extract without losing the activity was the hidroalcoholic solution (80%), showing the same IC50 as the fluid extract. Conclusion: The results suggest that the activity antioxidant is dose dependent and the solvent used may decrease the antioxidant activity.

Financial Support: FAPESP and CAPES
Supervisor: Maria José Vieira Fonseca

CQ009-X-RAY SCATTERING AS A NEW METHODOLOGY IN QUALITY CONTROL OF SIMILAR, GENERIC AND NON-GENERIC DRUGS

SIMONE SOARES DE OLIVEIRA BORGES[1] (PG); MARIA IZABEL MARETTI SILVEIRA BUENO[1] (PQ)

[1]IQ - UNICAMP - CP 6154 - CEP 13084-971 - Campinas - SP - Brasil

INTRODUCTION
This work uses X-ray spectroscopy to control the quality of similar, generic and non-generic drugs, by a simple, fast, non-destructive technique, with no residue generation and low cost.
OBJECTIVE
To control the quality of drugs by X-ray fluorescence, with no pre-treatment.
METHODOLOGY
Three drugs (based on dipirone, amoxilin and diclofenac), in three distinct physical states and from different trademarks were processed. The equipment was EDX 700, Shimadzu. Conditions: irradiation time-100 s, beam collimation-10 mm, X-ray source-Rh tube, voltage-50 kV. The spectra were treated by Principal Component Analysis, considering mainly the Compton and Rayleigh scattering regions, which are susceptible to variations in sample content, morphology and structure.
RESULTS
A clear separation among the drugs was observed in their respective PC1XPC2 scores plots, promoted (1) by their physical states, (2) by their formulations and mainly (3) by their similar, generic and non generic classifications.
CONCLUSION
The physical-chemical parameters that promote the separations are being evaluated through chromatography, infrared absorption and moisture content. Even grain sizes can alter drug absorption, essential parameter for drug bioequivalence.

Financial support: FAPESP
Patent pending, INPI P10500753
Supervisor: Profa. Dra. Maria Izabel M. S. Bueno

CQ010-EVALUATION OF THE ANTIOXIDANT AND PHYSICAL STABILIY OF TOPICAL FORMULATIONS CONTAINING STANDARDIZED BRAZILIAN PROPOLIS EXTRACT

FRANCIANE D. MARQUELE (PG)[1]; MARIA JOSÉ V. FONSECA (PQ)[1]

(1)Institution:Faculty of Pharmaceutical Science-University of São Paulo

Introduction:The search for antioxidant substances has increased since the excess of free radicals in skin have been related to skin damages, such as cancer. Thus, propolis as an important antioxidant could be successfully added to topical formulations. Objectives:To develop a gel-cream (F1) and a cream (F2) formulation containing propolis extract and to study the pH, the drop area and the antioxidant activity stability. Methods:The antioxidant activity was assessed using chemiluminescence. The drop area was assessed by microscopy. Formulations were stored at room temperature and at 40º C/70% RH for nine months. Results:The stability of the antioxidant activity was maintained for F2, but F1 lost more than 20% of its activity stored for 270 days in both temperatures. The instability of F1 was also observed physically since the drop area increased in the same period. The presence of the extract in both formulations maintained the pH during the whole study, however the extract free-formulations had their pH decreased during the study. Conclusion:The cream formulation showed to be more stable than the gel-cream formulation during the period of study.

Financial Support: CAPES
Supervisor: Profa. Dra. Maria José V. Fonseca

CQ011-CITOTOXICITY STUDY OF *PSIDIUM GUAJAVA* L. ETHANOLIC EXTRACT

SILVIA MITIE IHA (IC) [(1)] ; ROSEMEIRE C. L. R. PIETRO (PQ) [(1, 2)]; VERA L. B. ISAAC (PQ) [(1)] ; HÉRIDA R. N. SALGADO (PQ) [(1)]

[(1)] Universidade Estadual Paulista–UNESP – Araraquara, São Paulo; [(2)] Universidade de Ribeirão Preto – UNAERP – Ribeirão Preto, São Paulo; Brasil.

The ethanolic extract of *Psidium guajava* L. (Myrtacea), popularly known as guajava tree, is shrub or evergreen tree, sometimes reaching 8 m of height, that occurs of Mexico until São Paulo. The determination of the citotoxicity index (IC) or viability was carried out using the Alamar Blue. This compound acts as indicating generality of cellular growth and/or viability. The technique consisted of collecting cellular strains for tripsinization, centrifugation and counting of the number of cells adjusting for 1x 10^5 cells/mL in RPMI culture medium. These cells had been incubated in 37ºC in atmosphere of 5% of CO_2 for 24 to 48 hours. Thus had been prepared dilutions of the samples to be tested, which had been added to the cells after the withdrawal of the culture medium, being again incubated in 37ºC in atmosphere of 5% of CO_2 for 24 hours. The cells that had been used in the development of this work are macrophages of the J774 ancestry. The ethanolic extract of fruits of *P. guajava*, assayed in accordance with the described methodology, did not present citotoxicity for the J774 strain. The accomplishment of the cytotoxic activity is very important to develop new formulations.

Financial Support: CNPq-Brasília, PADC-FCF-UNESP
Supervisor: Hérida Regina Nunes Salgado

CQ012 - SIMULTANEOUS DETERMINATION OF A MIXTURE DIPYRONE AND PAPAVERINE IN PHARMACEUTICAL FORMULATION BY USING UV SPECTROPHOTOMETRY AND PARTIAL LEAST SQUARES REGRESSION

ANDRÉIA P. DO NASCIMENTO[1] (PG), MARCELLO G. TREVISAN[2] (PG), ERIKA R. M. KEDOR- HACKMANN[1] (PQ), RONEI J. POPPI[2] (PQ)

1- Departamento de Farmácia – Faculdade de Ciências Farmacêuticas – Universidade de São Paulo.
2- Departamento de Química Analítica - Instituto de Química – Universidade Estadual de Campinas.

The combination of dipyrone and papaverine is used as an analgesic and antispasmodic drug. A simple and rapid procedure was proposed for simultaneous determination of these drugs in pharmaceutical formulation (Melpaz®) based on multivariate calibration and UV spectrophotometric measurements in the range of 218.5 to 300 nm. The calibration set was constructed with twenty-five solutions in the concentration ranges from 15.0 to 35.0 mg mL^{-1} for dipyrone and from 0.5 to 1.5 mg mL^{-1} for papaverine in methanol. The relative standard deviation (RSD) was 1.04 % for dipyrone and 1.56 % for papaverine in the pharmaceutical formulations. The percentage recovery was 96.1% for dipyrone and 96.5% for papaverine. The excipients did not interfere in the analysis. The results showed that this method can be used for rapid and simultaneous determination of dipyrine and papaverine in pharmaceutical formulation with adequated precision, accuracy and specificity.

Financial Support: FAPESP and CNPq.
Adviser: Erika Rosa Maria Kedor- Hackmann

CQ013-DEVELOPMENT OF ALTERNATIVE PROCEDURE TO QUANTIFY SIMETHICONE USING FT-IR

FÁBIO SEIGI MURAKAMI (PG)[1]; AUREANNA NEGRÃO (IC)[2]; PAULO ROBERTO JANISSEK (PQ)[2].

[1]Universidade Federal de Santa Catarina; [2]Centro Universitário Positivo - Curitba-Pr

Simethicone is indicated to relieve flatulence and abdominal discomfort due excess of gastrointestinal gas. Infrared Spectroscopy (IR) has been used to quantify the amount of simethicone in oral dosage forms such as tablets and capsules. A toluene solution is used in the analysis, as described on the United States Pharmacopeia. In order to eliminate the organic solvent, a KBr disk technique was evaluated as alternative procedure. A mixing of 2% KCN in KBr was prepared and 200 mg were used to obtain the pressed-disk. The KCN was used as internal standard. A relationship was established based on the peak areas of simethicone area1 (1220–1300 cm-^{1}) and KCN area2 (2020–2140 cm-^{1}), R=(area1/area2). The simethicone in the samples were calculated by the formula: $C=(R_1*SC/R_2)$, in which C is the sample concentration, SC is the standard concentration, R_1 and R_2 are the relationship of the sample and standard respectively. The standard Dow Corning simethicone was used to obtain the R_2 relationship. The results obtained for commercial formulations by this procedure were equivalent to those obtained by using the USP methodology, with the advantageous of removing a toxic solvent.

Supervisor: Dr. Paulo Roberto Janissek, e-mail pjanissek@unicenp.br

CQ014-DEVELOPMENT OF ANALYTICAL METHODS FOR AZADIRACTIN A DETERMINATION IN NEEM (*AZADIRACHTA INDICA*) HYDROALCOHOLIC LEAVES EXTRACT

PRISCILA D. ALVES (PG); MARIA G.L. BRANDÃO (PQ); CRISTINA D. VIANNA-SOARES (PQ)

Faculdade de Farmácia, UFMG

The use of natural products in plagues and diseases control in agriculture has been a long time practice until the development of synthetic products. The use of synthetic pesticides causes great problems to the environment and to the farm employees' health, due to their extreme toxicity. The Neem (*Azadirachta indica*), a tree originated from India, is known for its activity against 400 insect pests. Azadirachtin A (aza-A) is the main active ingredient, abundant in the seeds and, in less amount in the leaves. We propose to study the neem leaves extracts because of the difficult seed extraction process and also for economical reasons of the more abundant aerial parts. A spectrophotometric method for aza-A determination in the hydroalcoholic leaves extract was developed with measurements in the ultraviolet third order derivate (229,4 nm). In an HPLC method, the extract was assayed in the acetonitrile and water (40:60 v/v) mobile phase at 1 ml/min flow rate with detection at 214 nm and AZA retention time around 11 minutes in a C_{18} 250 x 4 mm Merck column. Both methods have been evaluated for validation features. Accelerated stability studies will also be investigated to determine the best storage conditions.

Supervisor: Cristina D. Vianna-Soares

CQ015-STANDARDIZATION OF THE EXTRACT OF *SYZYGIUM CUMINI* (L.) SKEELS FRUITS THROUGH THE ANTIMICROBIAL ACTIVITY

KETYLIN FERNANDA MIGLIATO(PG)[1];MARCOS ANTONIO CORRÊA(PQ)[1];MARIA JOSÉ S. MENDES GIANNINI(PQ)[1];ANA MARISA FUSCO ALMEIDA(PG)[1];ANTONIO CARLOS PIZZOLITTO(PQ)[1];JOÃO CARLOS PALAZZO DE MELLO(PQ)[2];JOÃO OLÍMPIO TOGNOLLI(PQ)[3];HÉRIDA REGINA NUNES SALGADO(PQ)[1]

[1]Faculdade de Ciências Farmacêuticas–UNESP–Araraquara–SP;[2]Universidade Estadual de Maringá-UEM-PR;[3]Instituto de Química–UNESP–Araraquara–SP.

The fruits used for the present study were *S. cumini* (Myrtaceae) popularly known as 'jambolão'. The first and important step is the extraction of active substances from a complex pool. The extracts were obtained from a dry fruit powder granulometry of 0.302 mm, by turboextraction, percolation and maceration 5 days and 10 days. By using antimicrobial activity assessment methodology, a factorial analysis was accomplished. The extractor liquids were ethanol 50ºGL, 70ºGL or 96ºGL. The extract tested in this study was screened three times against each organism. The microorganisms *S. aureus*, *S. epidermidis*, *P. aeruginosa*, *C. albicans*, *C. krusei* and *C. parapsilosis* were used to determine the antimicrobial activity. The results indicated percolation as the best extraction method, and the mixture ethanol: water (50:50) as the best solvent concentration. An important antimicrobial activity was observed by extracts.

Financial Support:CNPq-Brasília,PADC-FCF-UNESP,CAPES
Adiviser: Hérida Regina Nunes Salgado

CQ016-CRYSTALIZATION AND CHARACTERIZATION OF SOLID PHASES OF ANTIRETROVIRALS LAMIVUDINE AND NEVIRAPINE

BRUNO G. PEREIRA (PG)*; FÁBIO D. FONTE BOA (IC)[1]; MARIA IRENE YOSHIDA (PQ)[2]; GERSON A. PIANETTI (PQ)[1]; CRISTINA D. VIANNA-SOARES (PQ)[1]

[1]Departamento de Produtos Farmaceuticos, Faculdade de Farmácia, [2]Departamento de Química, ICEx, UFMG

Pharmaceutical dosage forms containing a solid active ingredient requires the drug release as an important step to achieve drug bioavailability and bioequivalence. Polymorphism of the drug substance may influence the intrinsic dissolution profile, besides other physical-chemical properties. It may affect the drug solubility and therefore its bioavailability. In this work, lamivudine and nevirapine, used for AIDS treatment, were crystallized by different traditional methods, the antisolvent, the temperature lowering and solvent evaporation. In order to attempt different polymorphs crystallization, solvents were mainly selected by observing their dielectric constant, proton donation and acceptance properties. Solids of different morphology and particle size, hydrates and anhydrous have been produced. They have been characterized by optical microscopy, powder and single crystal X-ray diffraction, thermal analysis (TGA, DSC) and spectroscopic methods (IR, RAMAN). A method to study the influence of crystals polymorphism in the intrinsic dissolution profile is being developed.

Financial Support: CAPES, FAPEMIG.
Supervisor: Cristina D. Vianna Soares

CQ017-EVALUATION OF DIFFERENT PACKAGING FOR CAPTOPRIL TABLETS

PRISCILA MUNARO DE CASTRO (IC) [(1)]; GUSTAVO MATHEUS PRATI (IC)[(1)]; NILSON CESAR PEREIRA(IC)[(1)]; CRISTIANE MORIWAKI (PG)[(1)]; SÓSTENES ROSA VALENTINI (PQ) [(1)]; GRACIETTE MATIOLI (PQ) [(1)]; ELZA KIMURA (PQ) [(1)]

[(1)] Universidade Estadual de Maringá

Captopril (CPT) is a medicine that undergoes a rapid degradation when in contact with the humidity, requiring a packaging that assures isolation from the environment. To evaluate different types of packaging for the protection of CPT tablets this study was carried out. CPT tablets were packed in aluminium or PVDC blisters, or aluminium or polyethylene-Kraft envelopes. All the packagings were immersed in 0.1% methylene blue dye to check the sealing and infiltration. The approved packagings were submitted to stability tests at 30, 40 and 50ºC submersed in water, and the content of CPT and CPT disulfide were quantified. The Kraft envelopes did not pass the infiltration test. The $t_{10\%}$ at 30, 40 and 50ºC for the CPT packed in aluminium envelops (398, 237, 138 days) and blisters (353, 268, 239 days) submersed in water were equivalent, and for PVDC blister was 61 days at 40ºC. The content of CPT disulfide in aluminium packaging was higher than 3 % after 227 days for envelopes and 310 days for blisters, and 17 days for PVDC blisters when submersed in water at 40ºC. The aluminium blisters were more efficient for protecting the tablets.

Financial support: LEPEMC
Advisor: Elza Kimura

CQ018-PHARMACOGNOSTIC STUDY ABOUT *PIMENTA PSEUDOCARYOPHYLLUS* (GOMES) L.R. LANDRUM LEAVES - MYRTACEAE

JOELMA ABADIA MARCIANO DE PAULA(PG)[(1,2)]; JOSÉ REALINO DE PAULA(PQ)[(3)]; MARIA TERESA FREITAS BARA(PQ)[(3)]; MARIA HELENA REZENDE(PQ)[(4)]; HELENO DIAS FERREIRA(PQ)[(4)]

[(1)]Prog. Pós-graduação Biologia - ICB/UFG; [(2)]Univ. Estadual de Goiás; [(3)]Fac. Farmácia/UFG; [(4)]Inst. Ciênc. Biológicas/UFG

Introduction: The savannah inside the Brazilian biodiversity is fountain of many vegetable species that naturally play a strong influence in the folk medicine. Objective: To obtain quality control parameters for the identification of the plant drug of *Pimenta pseudocaryophyllus* (Gomes) L. R. Landrum that occurs in Brazilian savannah. Methodology: Two samples were collected, one in Minas Gerais (UFG Herbarium 27159), and the other one in Brasilia (EPH Herbarium 21745-0). Part of the botanical material in both samples was prepared for microscopic analysis. The other one was air-dried, crushed to powder and used for phytochemical screening. Results: The study has shown that *P. pseudocaryophyllus* (Gomes) L. R. Landrum leaves are hypostomatic, there are abundant unicellular trichomes in abaxial surface and epidermal cells have thick wall. Tannins, phenolic compounds and flavonoids were detected in the phytochemical screening. Conclusion: The results have provided important parameters for the quality control of this plant drug.

Financial Support: FUNAPE/UFG, SECTEC/CNPq, UEG
Supervisor: José Realino de Paula

CQ019-VALIDATION OF THE ANTI-FACTOR XA AND ANTI-FACTOR IIA ASSAYS FOR THE POTENCY ASSESSMENT OF NADROPARIN

MAXIMILIANO SANGOI(IC)[1]; ROSSANA FRIEDRICH(IC)[1]; SILVIA MASIERO(PG)[1]; SILVANA VACCARI(PQ)[1]; SÉRGIO LUIZ DALMORA(PQ)[1]

[1]Department of Industrial Pharmacy, Federal University of Santa Maria, Santa Maria-RS, Brazil

INTRODUCTION: Nadroparin calcium is a low molecular weight heparin (LMWH) with molecular weight of 4,300 Da and is used clinically for the prevention and treatment of thrombosis.
AIMS: The aims of the present work were to validate the anti-factor Xa and IIa assays for the potency assessment of nadroparin in pharmaceutical formulations.
METHODS AND RESULTS: The anti-factor Xa and IIa assays were validated and applied for the potency evaluation of the pharmaceutical formulations against the 2nd International Standard of LMWH. The biological assays incorporated a chromogenic end-point and detection at 405 nm. The data validation show that the methods are accurate and possesses good linearity (r^2>0.99), robustness and precision characteristics (RSD<1.65%). Calcium nadroparin pharmaceutical products were evaluated by both assays giving potencies between 93.86% and 109.88%, with an anti-factor Xa/anti-factor IIa ratio between 3.2 and 4.0.
CONCLUSION: The results of the validation parameters demonstrated that the assays can be applied for the routine quality control of nadroparin in pharmaceutical formulations.

Financial Support: FAPERGS
Advisor: Sérgio Luiz Dalmora

CQ020-DISSOLUTION STUDIES AND DETERMINATION OF VALDECOXIB IN PHARMACEUTICAL PRODUCTS BY RP-HPLC

MARCIO FRONZA(PG)[1]; LIBERATO BRUM JUNIOR(PG)[1]; MICHELI WRASSE(IC)[1]; FELIPE BIANCHINI D'AVILA(IC)[1] AND SÉRGIO LUIZ DALMORA(PQ)[1]

[1]Department of Industrial Pharmacy, Postgraduate Program in Pharmaceutical Science, Federal University of Santa Maria, Santa Maria-RS, Brazil.

INTRODUCTION: Valdecoxib is a non-steroidal anti-inflammatory drug that represents a second-generation of cycloxygenase-2 inhibitors.
AIMS: Develop and validate an RP-HPLC method for the dissolution rate studies and quantitative determination of valdecoxib in solid dosage forms.
METHODS: RP-HPLC separation was carried out on a Synergi fusion C_{18} column (150mm x 4.6mm ID), held at 30ºC. The mobile phase consisted of water, pH 7.0/acetonitrile (52:48, v/v), run at a flow rate of 1.0 mL min^{-1} and with UV detection at 210nm. The dissolution test conditions and the medium were chosen as 0.5% of sodium lauryl sulfate in water at a stirring rate of 75 rpm.
RESULTS: The data validation show that the RP-HPLC is accurate, robust and possesses excellent linearity (r^2=0.9999) and precision. This method has been successfully used on the quantitation of valdecoxib in dissolution studies.
CONCLUSION: The method was applied for the analysis of the pharmaceutical formulations assuring the quality and efficacy of the product under investigation.

Financial Support: Pfizer Laboratories, FIPE-UFSM and FAPERGS
Advisor: Sérgio Luiz Dalmora

CQ021-EVALUATION OF THE *IN VITRO* AND *IN VIVO* ANTIOXIDANT ACTIVITY OF THE GINKGO BILOBA ESTANDARDIZED EXTRACT

VIVIANE CRISTINA BRONZATI[(1)]; CARLA Y. YOKOYAMA[(1)]; MARIA JOSÉ VIEIRA FONSECA[(1)]

[(1)] University of São Paulo

Introduction:The standardized *Ginkgo biloba* extract has in its composition poliphenolic compounds, such as flavonoids. Studies indicate that flavonoids have an important role preventing the oxidative damage in skin. **Objective:** Based on this fact, this work has the objective of evaluating the *in vivo* and *in vitro* antioxidant activity of the standardized *Ginkgo biloba* extract.**Methodology:** The *in vitro* antioxidant activity was assessed by the oxidizing activity inhibition of the stable DPPH radical and by lipid peroxidation inhibition. The *in vivo* antioxidant activity was assessed by inhibiting the depletion of endogenous GSH levels in skin caused by UV radiation.**Results:** Concernig the *in vitro* antioxidant activity, it was obtained IC_{50} of 19,95µg/mL scavenging DPPH and IC_{50} of 17,53µg/mL inhibiting lipid peroxidation. In relation to the *in vivo* antioxidant activity, a solution containing 0,5% of the extract prevented the GSH depletion in 15%, while a solution containing 1% of the extract increased the GSH depletion in 27%, showing a pro-oxidant activity.**Conclusions:** These results suggest that the topical use of extracts containing flavonoids may be a strategy preventing skin damages caused by UV radiation, since they are used in the suitable concentration.

Supervisor:Maria José Fonseca

CQ022-DETERMINATION OF OXYTETRACYCLINE BY DIFFERENTIAL PULSE VOLTAMMETRY

LUÍS FERNANDO DE FARIA SANTOS(IC)[(1)]; ÉRMESON LINCON DE OLIVEIRA TEIXEIRA(IC)[(1)]; LUÍS ANTÔNIO DA SILVA(PQ)[(1)]; ALEXANDRE ROSSI(PQ)[(1)]; VALÉRIA ALMEIDA ALVES(PQ)[(1)]

[(1)]Departamento de Farmácia-Bioquímica – Faculdades Federais Integradas de Diamantina, FAFEID / MG

Oxytetracycline hydrochloride (OTC) presents antibacterian action, being commonly used in veterinary drugs and animal nutrition. Pharmacopeia recommends its determination by HPLC. We intend to investigate if electroanalytical methods can present application for this, since they present high selectivity and low cost. The purposes of the present work are to study the electrochemical behavior of OTC in phosphate buffer (pH 6,82) and to construct a calibration curve for OTC determination. Glassy carbon and a platinum wire were the working and the auxiliary electrodes. The potential ranged from +0.5 V to +1.5 V vs. Ag/AgCl. It was observed a main peak in the differential pulse voltamogramms, at ~ +0.8 V, which was attributed OTC oxidation. Analysis of peak height furnished current values, which decreased after the first scan, possibly due to OTC adsorption on electrode surface. It was obtained a linear relationship between current and concentration, in the range from 1 to 5 mM, which worked out for OTC dosage in Terramicina®. As conclusion, OTC determination is viable using an electroanalytical method.

Financial Support: FAFEID, CNPq
Supervisor: Valéria Almeida Alves

CQ023-DETERMINATION OF CARVEDILOL IN PHARMACEUTICAL FORMULATIONS BY LIQUID CHROMATOGRAPHY

CARINE VIANA SILVA IEGGLI (PG)[1], SIMONE GONÇALVES CARDOSO (PQ)[1], SILVIA HELENA MIOLLO BORGMANN (PG)[1]

[1] Universidade Federal de Santa Maria

*Introduction***:** Carvedilol (CAR) is an anti-hypertensive agent available in tablets and compounded capsules. The official method for the assay of this drug in the bulk form is non-aqueous titration. Only one fluorimetric method has been reported to determine CAR in tablets. *Objective:* to develop a liquid chromatographic method for CAR determination in pharmaceutical formulations. *Methodology:* The quantitation was performed on a reversed-phase C_{18} column using a binary mobile phase composed of acetonitrile - phosphoric acid 0,1% pH 3 (50:50 v/v) and detection at 241 nm. Two commercially available tablets (A and B) and one batch of compounded capsules were evaluated by the proposed methods. The method was validated according to USP 28 and ICH. *Results:* The calibration curve for CAR was linear from 5 – 20 μg mL^{-1} range ($r > 0.9999$). The intra and inter-day precision showed good results (RSD < 2%). The mean concentration of CAR determined in tablets A, tablets B and capsules were 97.9% ±1.6; 102.8% ±0.8 and 100.1% ±1.8; respectively. The percentage recoveries ranged from 98.7 to 101.8. *Conclusion:* The method demonstrated to be of easy execution and viable for application in routines of quality control laboratories.

Supervisor: Simone Gonçalves Cardoso

CQ024-VALITATION OF QUERCETIN´S QUANTIFICATION METHODOLOGY

FABIANA T. M. CARVALHO (PG)[1]; MARIA JOSÉ V. FONSECA (PQ)[1]; M. VITÓRIA L. B. BENTLEY (PQ)[1].

[1]Department of Pharmaceutical Science FCFRP-USP.

Introduction: Topical administration of antioxidants as quercetin provides an efficient way to protect the skin against oxidative damage. A reliable analytical method is necessary to quantify the drug in the stability, delivery and permeation *in vitro* studies. Objective: The present study was designed to validate the HPLC assay which will be used to analyze the drug content of quercetin. Methodology: HPLC analysis was performed on a C18 Hypersyl column, methanol: acetic acid 2% (60:40) as mobile phase at a flow-rate of 1mL/min and the detection set at 254nm. Validation of chromatographic method included the analytical parameters: linearity, precision and accuracy (intra and inter-day), detection and quantification limits. Results: Good linearity of the method was established between 0.1-200 μg/mL, intra and inter-day precision and accuracy were 1.74% (n=5), 3.27% (n=9); 2.91 (n=5), 4.5% (n=9), respectively. Detection and quantification limits were 0.011 and 0.03 μg/mL respectively and the variation coefficient of the last one was 8.33% (n=5). Conclusion: All the results indicate that the method described above is adequate to quantify quercetin in delivery/permeation studies.

Financial Support: FAPESP and CAPES
Advisor: Maria José V. Fonseca

CQ025-STABILITY STUDIES OF TABLETS AND GRANULES OF CAPTOPRIL COATED WITH ETHYL CELLULOSE, ETHYL CELLULOSE / METHYLCELLULOSE AND POLYVINYLPIRROLYDONE.

HELLEN KARINE STULZER; ALINE CLAUDIA DE MELLO PG[1]; TALIZE FOPPA PG[1]

[1] Universidade Federal de Santa Catarina-UFSC

Introduction: The stability studies were employed in development of medicine with the aim to avoid future problems. These studies are considerate one of the most important phase in the development of new medicine. For pharmaceutical products, the stability can be esteemed like a period that above-mentioned product in your specific package continue yours physic, chemical, microbiological, therapeutic and toxicological properties in determinates limits, assured your quality.
Objectives: In this work, studies were carried out to available and comparison the stability and different mechanisms involved in degradation process of all formulation produced.
Methodology: All formulations were exposed in 50 ^{0}C and 40 ^{0}C of temperature, 90 % of humidity and UV light.
Results: The tablets and the granules coated with ethyl cellulose, ethyl cellulose/methylcellulose showed lesser degradation in relation the formulations coated with polyvinylpirrolydone. The tablets had a better stability than granules.
Conclusion: The polymers ethyl cellulose and methylcellulose demonstrated effectiveness to increase the stability of captopril tablets and granules.

Financial support: CAPES
Supervisor: Marcos Antônio Segatto Silva

CQ026-DEVELOPMENT OF AN ELECTROANALYTICAL METHOD FOR IRON DETERMINATION

FERNANDO ROBERTO FIGUEIRÊDO LEITE(IC)[1]; LUÍS ANTÔNIO DA SILVA(PQ)[1]; ALEXANDRE ROSSI(PQ)[1]; VALÉRIA ALMEIDA ALVES(PQ)[1]

[1]Departamento de Farmárica-Bioquímica – Faculdades Federais Integradas de Diamantina, FAFEID / Diamantina – MG, Brasil

It is known that quantitative iron determination in pharmaceutical formulations is based on spectrophotometry. However, electroanalytical methods can present application for this, presenting high selectivity and low cost. So, the purposes of the present work are to study the electrochemical behavior of iron and to construct a calibration curve using solutions of $FeSO_4$. The solutions were diluted from a stock (0,7000 M $FeSO_4$ + 0,50 KNO_3 + 0,30 mL H_2SO_4 conc.), whose measured pH values were around 2. Glassy carbon and a platinum wire were the working and the auxiliary electrodes, respectively. The potential ranged from -0.75 V to +0.75 V vs. Ag/AgCl. It was observed a main peak in the differential pulse voltamograms, at ~ +0.4 V, which was attributed to iron oxidation (Fe^{2+} to Fe^{3+}). Analysis of peak height furnished anodic current values. It was obtained a linear relationship between current and concentration, in the range from 20 to 100 mM. It was concluded that it is possible to construct a calibration curve for iron determination using electroanalytical method.

Financial Support: FAPESP / FAFEID
Supervisor: Valéria Almeida Alves

CQ027-STABILITY STUDY OF ATENOLOL SYRUP FOR PEDIATRICS USE.

TALIZE FOPPA PG[1]; ALINE CLÁUDIA DE MELLO PG[1]; HELLEN KARINE STULZER PG[1]; MARCOS ANTONIO SEGATTO SILVA PQ[1]

1.Universidade Federal de Santa Catarina

Introduction: Many pediatrics drugs are not available in the appropriate dosages. Few institutions of research give to bear to the development of liquid forms for pediatric use. Extemporaneous formulations are going to be prepared, being the study of stability in appropriate vehicles a critic point. Objective: It was carried out the stability study using atenolol in the form of syrup. Methodology: The behavior of the drug has evaluated by HPLC in 3 differents temperatures (4, 25 and 45ºC), in ambar and clear bottle. Results: The concentration of atenolol in the syrup on the 7th day had decrease. Therefore, the conclusion is that the drug has decrease due by an increase of the temperature and more future stability studies for liquid preparations for pediatric use is necessary.

Supervisor: Prof Dr Marcos Antonio Segatto Silva

CQ028-DEVELOPMENT AND VALIDATION OF A REVERSE-PHASE HPLC METHOD FOR ANALYSIS OF EFEVAVIRENZ

OSNIR SÁ VIANA (PQ)[1]**;** SIMONE JUVENAL SIMÕES (PQ) [1] **;**JOSÉ BENIGNO JÚNIOR (IC)[1]; FLÁVIA.P.M. MEDEIROS (PQ)[2] ; S. GRANGEIRO JÚNIOR (PQ)[1]; M. M. DE ALBUQUERQUE (PQ)[1]; P. J. ROLIM NETO (PQ)[1,2]

[1 -]Laboratório de tecnologia de Medicamentos – LTM – UFPE;[2-] Laboratório Farmacêutico do Estado de Pernambuco - LAFEPE

Efavirenz is a nonnucleoside reverse transcriptase inhibitor for the treatment of the HIV infection. A simple, high-performance liquid chromatographic method has been developed and validated for the quantitative determination of efavirenz. The development of the methodology was accomplished considering the physics and physic-chemical characteristics of this drug. The method was validated per USP 28 and ANVISA guidelines. The analysis was way UV detection at 252 nm, using a reversed-phase c_{18} column (250mm x 3,9 mm, 10 µm) and isocratic mobile phase consisting of ACN: water: ortho-phosphoric acid 85%. Statistical treatment was used in all the stages of the process of validation. The method assisted to the parameters of linearity, robustness, precision and accuracy, with limits of detection and quantification of 0,1652 and 0,5509 µg/mL, respectively. The results reached they showed that the method is an alternative for quantification of efavirenz, turning viable your use in industrial routine and in analytic laboratories.

Support financial: CAPES/CNPq
Supervisor: Pedro Rolim

CQ029-CHAGAS´S DISEASE : ANALYTICAL METHODOLOGY FOR TABLET OF BENZONIDAZOL

JOSÉ LAMARTINE SOARES(IC)[1];MÔNICA FELTS DE LA ROCA[1](PQ);ANA LUÍZA MAURER DA SILVA(PG)[1];ROSALI FERREIRA DA SILVA(PQ)[1,2];FLÁVIA MORAIS DE MEDEIROS(PQ)[1,2];PEDRO JOSÉ ROLIM NETO(PQ)[1,2]

[1]LTM-UFPE,[2]Lab. Farm. do Estado de Pernambuco

Chromatography is used at analysis laboratories for the qualitative/quantitative determination of drugs. It was aimed at to develop and to validate the methodology for benzonidazol tablets by HPLC. In the development it was evaluated: the mobile phase and proportions, the temperature and the column type. The validation followed the RE 899,ANVISA, with samples to 100 ppm and 316 nm. It was evaluated the following parameters: Robustness agitation type, proportion of Acetonotrile:Water and flow variation; Linearity concentrations (40 to 160ppm); LD and LQ starting from the equation of the straight line; Repetibility in six replicates; Intermediate precision in days and different analysts; Accuracy her 50, 100 and 150%. The validated Method was Acetonitrile: Water Pure Ultra (1:1), C18, 5 µm, to 25ºC, to 1 ml/min and tr of 3,6 min. The linearity was treated by ANOVA, with R^2 of 0,9985. The method was necessary among days and among analysts for test t. The detection limit was 0,987 µg/ml and the one of quantification 1,496 µg/ml. The method was exact among averages obtained value and expected, guaranteeing the good laboratory practices.

Financial Support: LAFEPE/CNPq
Supervisor: Pedro Rolim

CQ030-SPECTROPHOTOMETRIC METHODS FOR CARVEDILOL DETERMINATION IN PHARMACEUTICAL DOSAGE FORMS

EMANOELLE RAQUEL DORIGONI (IC)[(1)], CARINE VIANA SILVA IEGGLI (PG)[(1)], SIMONE GONÇALVES CARDOSO (PQ)[(1)]

[(1)] Universidade Federal de Santa Maria

*Introduction***:** Carvedilol (CAR) is an anti-hypertensive agent available as tablets and compounded capsules. The official method for the assay of the drug in the bulk form is non-aqueous titration. Only one fluorimetric method has been reported to determine CAR in tablets. *Objective:* To develop and to validate spectrophotometric methods for CAR determination in pharmaceutical formulations. *Methodology:* The methods were based on the reaction of this drug with the s-acceptor iodine or through ion-pair complex formation between the drug and bromotimol blue (BTB) and bromocresol green (BCG). The obtained complexes were measured at 363 nm, 411 nm and 414 nm, respectively for iodine, BTB and BCG. Two commercially available tablets (A and B) and one batch of compounded capsules were evaluated by the proposed methods. *Results:* Linear correlations were obtained between the absorbances and CAR concentration with good correlation coefficients ($r > 0.9999$) for both methods. The mean concentration of CAR obtained through the methods ranged from 95 to 105% of stated amount, with RSD < 2% ($n = 6$). *Conclusion:* The proposed methods can be used for determination of CAR in oral formulations with precision, accuracy and specificity.

Supervisor: Simone Gonçalves Cardoso

CQ031-DISSOLUTION PROFILE EVALUATION OF CETIRIZINE IN SOLID DOSAGE FORMS

LISIANE BAJERSKI (PG)[1]; SIMONE GONÇALVES CARDOSO (PQ) [1]; MARCELO MALESUIK (PG)[1], BIANCA DORFEY (IC)[1]

[1] Universidade Federal de Santa Maria (UFSM)

*Introduction***:** Cetirizine (CTZ) is a second generation of antihistamines used in allergic diseases. It is available as bulk material, tablets, oral solution and compounded capsules. There are no official methods for determination of dissolution rate of CTZ in solid oral dosage forms. *Objective*: To develop a dissolution test conditions for CTZ tablets and compounded capsules. *Methodology*: Three-dissolution medium (0.1M HCl, 0.01M HCl and pH 6.8 phosphate buffer, 900 ml) and USP Apparatus 1 and 2 (Nova Ética) were tested at speeds of 50 and 75 rpm. In all experiments, 5 ml sample aliquots were withdrawn at 5; 10; 15; 20; 30 and 60 minutes and replaced with an equal volume of the fresh medium. The drug concentrations in dissolution medium were determined by liquid chromatography and spectrophotometric methods previously validated. *Results:* The release rates from tablets were much faster than from compounded capsules in all tested conditions. Capsules had a more discriminative profile than tablets under the same conditions. *Conclusion:* The use of 900 ml of 0.1 M HCl acid, paddle as apparatus at the stirring speed of 50 rpm and 30 minutes of test provided satisfactory results for tablets and capsules.

Financial support: CAPES
Supervisor: Simone Gonçalves Cardoso

CQ032-PHYSICAL CHEMICAL QUALITY PARAMETERS OF COMERCIAL PARACETAMOL TABLETS

CIBELE BUBA (IC)[I]; SILVIO MIRÓ FRANCHI (PQ)[1]; CINTIA RIBAS(PQ)[I]; AUREANNA NEGRÃO(IC)[I]; THAIS BARBOZA (IC)[I].

[1]UNICENP

The implantation of gerneric medicine politic in Brazil was a government iniciative to provide a quality medice to Brazilian population. It guarantees the terapeutic efficiency, with an accessible prince, and support a true medicines national politic. This investigation has in view the comparison of qualiy parameters of referency paracetamol tablets (Tylenol®) with the generic one (Medley®), from Brazilian indurtry. The samples were analised according to Brazilian Pharmacopeia IV. It has been analised the desintegration time, the dissolution profile, the hardness and friability, and the variation of weight, using Nova Etica equipements. The results for referency paracetamol tablets were 2min 58s in desintegration time, average mass dissolved in 30min of 705,8mg, average hardnes higher than 16kgf, 0,0018% of friability and average weigth of 0,8139mg. The results for paracetamol generic tablets were 4min 8s in desintegration time, average mass dissolved in 30min of 705,3 mg, average hardnes higher than 16kgf, 0,0011% of friability, and average weight of 0,8760mg. It was confirmed that both simples met the requirements of quality tablets, according Brazilian Pharmacopeia IV. Referency and generic paracetamol tablets are quality similar.

Financial Support: UNICENP
Supervisor: Silvio Franchi

CQ033-VALIDATION OF CLEANIG GLASS APPARATUS METHODS USING B12 VITAMIN ASSAY.

AUREANNA NEGRÃO(IC)[(I)]; CINTIA RIBAS(PQ)[(I)]; SILVIO MIRÓ FRANCHI (PQ)[(1)]; CIBELE BUBA (IC)[(I)]; THAIS BARBOZA (IC)[(I)].

[(1)]UNICENP

This investigation has in view the validation of cleaning process of glass Laboratory, using B12 vitamin as cleaning marker. The cleaning agents were a 2% detergent, alcoholic potash, 50% sulphuric acid and Sulfuric Acid PA. The cleaning process has been tested in a 10 mL volumétric flask, in a 250 and 50 mL beker and in a 5 mL pipetta volumetric. Each flask were filled up with B12 vitamin solution at 1 to 20 µg/mL, and kept up for 30 minutes, them it was emptied. Each flask was added of two drops 2% detergent, with water, and it was brushed when it was possible. The flask were rinsed with tap water (7x) and with distilled water (2x), and dried using airgun. The cleaning procedures with 50% sulfuric acid, 98% sulfuric acid and alcoholic potash were carried out by filling up the flasks with these solutions for 30 min, then following the rinsage as described for 2% detergent process. The process efficiency was evaluated by UV spectrofotometry of the B12 viamin residue at 279 nm after cleaning. The results showed that 2% detergent procedure was able to clean only the bekers. Volumetric pipettes and bekers were successfully cleanned with alcoholic potash and 50% sulfuric acid. The volumetric flask only cleanned after using 98% sulfuric acid.

Financial Support: UNICENP

The authors did not follow the Scientific Committee's suggestion for an English language review

CQ034-THIN LAYER CROMATOGRAPHIC DETECTION OF L-DOPA

ALESSANDRA S. CUSTÓDIO (IC); DÉBORA M. R. CARVALHO (IC); EDNILSON M. GOMES (IC); ELIZABETE L. COSTA (PQ); ANTONIO JOSÉ C. SOUZA (PQ)*

Faculdade de Farmácia e Bioquímica -Universidade Católica de Santos – Av. Conselheiro Nébias, 300, Santos, São Paulo, Brasil - *letigabi@uol.com.br

L-dopa is an extensively used drug for Parkinson's disease treatment; this non protein amino acid has few structural differences with tyrosine and phenylalanine. Some methods for determination of L-dopa are reported in the literature such as liquid chromatography and capillary electrophoresis. However, most of these methods require expensive and sophisticated instruments. In this work, a simple, fast, and sensitive method for determination of L-dopa in pure form or from blood samples is proposed. After protein precipitation of 500µL plasma sample aliquots with trichloroacetic acid (TCA), the analytes were separated by thin layer cromatography (TCL), in plates covered with silica gel G (10 x 20cm), and activated before use, during 30 minutes. The developing solution was Butanol, acetone and water (40:40:5). After runs, the plates were dried and sprayed with ninhydrin reagent and heated at 90°C for 10 minutes to produce colored products. L-dopa, tyrosine, and phenylalanine were used as standard. This method was efficient to separate all amino acids without interference, with the advantageous possibility of the several analyses simultaneously.

Financial support:
Advisor: Antonio José Calixto de Souza

CQ035-PARTICULATE DISSOLUTION OF HYDROCHLOROTHIAZIDE (HCTZ) AND ITS RELATION WITH DISSOLUTION OF THIS DRUG FROM TABLETS

Tatiana Cupello Colonesi da Rosa (PG) [(1)]; Nádia Maria volpato (PQ) [(1)]

[(1)] UFRJ

Introduction: Drug dissolution knowledge is useful to show chemical equivalence between drugs to prevent differences in absorption and effectiveness. Objective: Evaluate particulate dissolution of HCTZ and correlate this with the dissolution from tablets. Methodology: Two kinds of HCTZ were selected, one with bigger (R) and other with smaller (A) particle size. Tables with these two HCTZ were manufactured. To evaluate both drug and product dissolution was used 900 mL of water and paddle at 50 rpm. To particulate dissolution evaluation, 50,0mg of drug in powder were added directly into dissolution media. Results: Particulate dissolution rates were calculated by linear regression (R = 1,16 and A = 2,75 mg/min). In relation to tablets dissolution, the product formulated with HCTZ-R released less than 50% of its labeled content in one hour, while the product manufactured with HCTZ-A released more than 90% in the same time. Mean dissolution time (MDT) was calculated (product manufactured with R = 37,25 and with A = 10,69 minutes. Conclusions: Particulate dissolution is an efficient methodology to forecast formulation problems. Drugs with small dissolution rate, generate products with bigger MDT, which can compromise the dissolution kinetic them.

Supervisor: Prof[a]. Dra.Nádia Maria Volpato

CQ036-ANTIOXIDANT ACTIVITY OF THE SOYBEAN OILS (SOS) OBTAINED USING DIFFERENT EXTRACTION PROCEDURES

SANDRA R. GEORGETTI (PG)[(1)], RÚBIA CASAGRANDE (PQ)[(1,2)], CARLA Y. YOKOYAMA (IC)[(1)], CLÁUDIA R.F. SOUZA(PG)[(1)], WANDERLEY P. OLIVEIRA (PQ)[(1)], MARIA J.-V. FONSECA(PQ)[(1)]

[1]Department of Pharmaceutical Science, FCFRP-USP
[2]Department of Food and Drugs Technology, CCA-UEL

Introduction: Soybeans present high lipid content including phenolic compounds with potential antioxidant activity. Objective: The aims of this study were to investigate the influence of the extraction procedures in the total phenol content and antioxidant activity of the SOs obtained. Methodology: The SOs were extracted using hexane, isopropanol or hexane/isopropanol mixture with magnetic agitation or ultrasonification. Total phenolic content was determined using the Folin Cioucateu reagent, and the antioxidant activity by the $DPPH^{\cdot}$ assay. Results: There was no significant statistical difference in the total phenol concentration of the SOs extracted. All the SOs obtained presented antioxidant activity, and the isopropanol/magnetic agitation extract presented the highest activity (63%). Only the different SOs obtained by magnetic agitation presented statistical significant differences. Conclusion: These results suggest the SOs as a promising source of antioxidants and that the method of extraction influences its activity.

Financial support: FAPESP
Advisor: Maria J.V. Fonseca

CQ037-PHARMACEUTICAL MANAGEMENT MODEL ON A NEW DRUG PRODUCT ANALYTICAL DEVELOPMENT

ÉRICO DAEMON DE OLIVEIRA(PG)[1]; GLAUCIA B. C. A. SLANA(PQ)[1]; LUCIANA P. B. GONÇALVES(PQ)[1]; NUBIA BOECHAT(PQ)[1]; ADELAIDE S. ANTUNES(PQ)[2]

[1] Farmanguinhos/Fiocruz; [2] Escola de Química/UFRJ

Introduction: Globalization has increased the revenue stream of pharmaceutical companies, which these companies contend expands their ability to undertake significant research and development programs. It is necessary a strategy plan for all of the critical steps during the analytical development of a new drug, to achieve national and international requirements for registration. **Objective:** The aim of this work is to apply a model of management based on competitive advantages of technological and professionals capacities available in Farmanguinhos (a public pharmaceutical organization of Ministry of Health), for the analytical development. **Methodology:** The strategy used involves a logical action sequence of procedures, decisions trees, protocols and staff training. **Results:** Development and validation protocols are being established. The stability protocol designed involves the evaluation and control of compatibility and related substances. **Conclusions:** An important improvement was obtained considering reports and rastreability. This model allows an easy and quick feedback for other departments involved on the drug development process.

Financial Support: Farmanguinhos /Fiocruz
Supervisor: Adelaide S. Antunes

CQ038-EVALUATION OF ESTROGENIC POTENCY OF SOY EXTRACT

MANUELA L. T. VIEIRA (PG)[1]; RODRIGO F. DUARTE (IC)[1];LÍGIA M. M. CAMPOS (PQ)[1]; ELZÍRIA A NUNAN (PQ)[1]

[1] Universidade Federal de Minas Gerais

There has been great interest in that soy isoflavones may be an alternative to postmenopausal hormone therapy. Many women avoid using the traditional hormone replacement due to concerns about side effects. There is a plenty of isoflavones supplements on the market, with little regulation regarding their manufacture and efficacy. The raw material, soy dry extract, revealed qualitative and quantitative differences in the isoflavones content. Many of the therapeutics indications that drive the supplements sales are based on clinical and nutritional data from soy foods,, rather than from soy dry extract. The objective of the study was evaluated the estrogenic potency of soy extract. A classic in vivo bioassay for estrogenicity was performed on one of the supplements with predominance of isoflavone genistein. Soy extract was suspended in arachis oil and administered by oral gavage to immature female rats for three consecutive days in a dose-dependent manner (125-4150mg/kg/day). There was an increase in uterine weight consistent with a significant estrogenicity. The ratio of the maximum mean uterine weight of the treated groups to the control was 3.0.

Financial support: FAPEMIG
Supervisor: Elzíria de Aguiar Nunan

CQ039-ANALYSIS OF THE "SENNE" (CASSIA ANGUSTIFOLIA) OBTAINED BY HERB SELLERS OPERATING IN THE CENTRAL AREA OF CAMPO GRANDE, MATO GROSSO DO SUL, BRAZIL.

DANILO ROBERTO DA SILVA (IC)[1];ANDRÉ LUIZ SOARES PANIAGO(IC) [1]; DALMAR ROCHA GODOY(IC) [1].

[1]Faculdade Estácio de Sá de Campo Grande-MS

INTRODUCTION: Medicines are produced of medicinal plants like that stem, leaves and roots. Those medicines, when used in a correct way, they can bring a lot of benefits for the health, mainly because they don't cause side effects in the same proportion that the conventional medicines. OBJECTIVE: to verify the quality of the medicinal plant "senne", one of the 20 medicinal plants requested from and/or indicated by herb sellers operating in the central area of Campo Grande, Mato Grosso do Sul, Brazil, bought in herb sellers operating in the same area. METHODS: degree of purity, in agreement with IV Farmacopéia brasileira. RESULT: in the analysis of 04 (four) samples were obtained the following values: Sample A - 9,18% of sludges and tenor of ashes 4,44%, sample B - 33% of sludges and tenor of ashes 4,73%; sample C - 19,66% of sludges and tenor of ashes 5,14%, sample D - 26,67% of sludges and tenor of ashes 4,53%. CONCLUSION: it can be observed that regarding the tests accomplished for determination of sludges, all of the samples were out of the patterns described second to IV Farmacopéia brasileira. When analyzed the tenor of total ashes, it was verified that all of the samples were inside of the patterns described second to IV Farmacopéia brasileira.

Financial Support: Proper resources
Supervisor: Rafaela Grassi

CQ040-DISSOLUTION OF GLIBENCLAMIDE TABLETS WITH TWO FORMULATIONS NO BIOEQUIVALENTS

EDILENE BOLUTARI BAPTISTA(PG)[1]; NÁDIA MARIA VOLPATO(PQ) [1]

[1] Faculdade de Farmácia, Universidade Federal do Rio de Janeiro

Introduction: Correlation between bioavailability and dissolution data of drug products can provide essential information of the best conditions choice of the dissolution test to the formulations. **Purpose:** Development of a dissolution method for glibenclamide 5 mg tablets and correlation between in vitro release and in vivo absorption rate. **Methods:** USP apparatus 2 (paddle), at 75 rpm, was used employing 900 ml of different dissolution media, namely: simulated intestinal fluid (SIF) pH 6.8, buffer pH 4.5 and buffer pH 5.5, pure and with addiction of surfactants. Polysorbatum 80 (Poly 80) and sodium lauryl sulfate (SLS), both 0.1% and 1% (w/v) concentration, were used. For employing multiple level C in vivo/in vitro correlation (IVIVC), partial areas under the plasma glibenclamide concentration-time curve were calculated in different time periods. **Results:** All media tested presented dissolution profiles distinct between the formulations. The highest amounts dissolved were obtained in media with elevated pH, on the other hand, the surfactants influence on dissolution was more evident in pH 4.5 and 5.5. **Conclusion:** The IVIVC study indicated that SIF plus Poly 80 1% and SIF plus SLS 0.1% are better able to discriminate between glibenclamide tablets.

Supervisor: Profª Nádia M. Volpato

CQ041-VALIDATION STUDY OF ANALYTICAL METHOD FOR CAPTOPRIL TABLETS BY HPLC

VIVIANE THEODORA MUNIZ[1](IC); ROBSON RONEY BERNARDO[2](PQ)

[1,2]Faculdade de Farmácia - Universidade Estácio de Sá Av. Prefeito Dulcídio Cardoso, 2900 - 22631-021 - Rio de Janeiro

Introduction. The first step for attainment reliable analytical results is in validation of chosen analytical method. Objective. The aim of this paper was to study the validation of analytical methodology in hplc and to analyzed captopril tablets from 4 different laboratories (A-D), comparing the weight uniformity and active principle drift. Methodology. LC analysis were performed using Shimadzu System connected with a UV detector (254 nm),with 20µl loop and the column used was a RP-18 (Merck). The samples were eluted with movel phase metanol:water :phosporic acid (55:45:0,5 v/v/v). The flow rate was 1.0ml/min.We used primary standards of captopril and dissulfite. Results The analytical method validation was realized by ICH method. Samples from 4 different laboratories had been analyzed by considered method. Conclusion In relation to the average weight one concludes that it had variation between the average weights of acquired tablets of different laboratories and only A lab present a unit out of variations limits. In relation to the drift of captopril in the samples, the lab A was the only presented proximity of value minimum drift established by USP Pharmacopeia. However, lab C, was that presented a more fearful result, in that exceeded in great rations the superior limit of tolerance of dissulfite captopril.

Supervisor: Robson Roney Bernardo

CQ042-DETERMINATION OF OXYTETRACYCLINE BY SPECTROPHOTOMETRY

ÉRMESON LINCON DE OLIVEIRA TEIXEIRA(IC)[1]; LUÍS FERNANDO DE FARIA SANTOS(IC)[1]; LUÍS ANTÔNIO DA SILVA(PQ)[1]; ALEXANDRE ROSSI(PQ)[1]; VALÉRIA ALMEIDA ALVES(PQ)[1]

(1)DEPARTAMENTO DE FARMÁCIA-BIOQUÍMICA – Faculdades Federais Integradas de Diamantina, FAFEID, Diamantina – MG, Brasil

Oxytetracycline hydrochloride (OTC) presents antibiotic action and is mainly used in veterinary drugs. It is recommended by Pharmacopeia that its determination be done by HPLC. In this work we intend to investigate the use of spectrophotometry for OTC determination. So, the purposes of the present work are to study the stability of OTC in phosphate buffer (pH 6,82) and to construct a calibration curve for OTC determination in dosage forms. It was used a UV-vis spectrophotometer from Micronal® and quartz cubets. The real sample (Terramicina®) was dissolved using small volume of HCl 6 M, being the final solution buffered at the same conditions of the calibration curve solutions. The maximum wavelength, $\lambda_{máx}$, observed in the absorption spectrum was in 360 nm. The absorbance values remained stable for 24 h at this $\lambda_{máx}$. It was observed a linear relationship between absorbance and concentration (R=0.99), in the range from $2{,}00 \times 10^{-5}$ M to $2{,}00 \times 10^{-4}$ M, which worked out for OTC dosage in Terramicina®. As conclusion, OTC determination is viable using the spectrophotometric method.

Financial Support: FAFEID, CNPq
Supervisor: Valéria Almeida Alves

CQ043-QUALITY EVALUATION OF FUROSEMIDE CAPSULES AND SCORED TABLETS

LUCIANE LAPORTA (PQ)[1]; CELSO BITTENCOURT (PQ)[2]; ALINE PIENIS (IC)[1] ; FLÁBIO PONS (IC)[1]; ANA LAURA ESCARRONE(PQ)[1]

[(1)] UNIFRA; [(2)] UFSM

Arterial hypertension is a chronic degenerative disease that affects 20% of the adult population and 65% of the elderly. Medicines used in its control have been widely consumed. It is known that adjusting its dose is of the utmost importance in the treatment of this disease. Breaking or compounding are the most used among the usual forms dosage adjustment The objective is to evaluate commercial brands of whole and broken tablets of furosemide 40 mg and compounded concentrations of 10 mg, 20 mg e 40 mg. The medicines were analyzed according to the monograph of the 4th edition of the Brazilian Pharmacopoeia. All of the commercial medicines analyzed were approved in tests of hardness, friability, weight variation, disintegration, dissolution, content uniformity and assay. However, when broken, they presented a standard deviation % above the permitted level. Some compounded medicines failed the test of content uniformity and dosage. Breaking the tablets did not prove to be a safe practice and could put the patient's treatment at risk, as great variations in the dosage administered occurred. We observed, as well, that the quality of the compounded medicines varied from pharmacy to pharmacy, making it difficult to assure the safety of its administration.

Advisor: Luciane Laporta

CQ044-MICROBIOLOGICAL ASSAY FOR CEFEPIME DETERMINATION IN INJECTABLE PREPARATIONS

MARINÊS SOUZA(PG)[12]; CLEBER SCHMIDT(PQ)[1]; ANA BERGOLD(PQ)[2]; ROSECLER KULMANN(IC)[1]; LUCÉLIA SILVA(IC)[1]; DANIELE NOGUEIRA(IC)[1]; ESTEVAN ZIMMERMANN(IC)[1]; GUSTAVO PARAGINSKY(IC)[1]

[(1)]Dept. of Industrial Pharmacy, UFSM, Santa Maria, RS-Brazil.[(2)]Postgraduate Program in Pharmaceutical Science and Technology, UFRGS, Porto Alegre, RS–Brazil

Introduction: Cefepime is a parenteral 4th-generation cephalosporin with broad spectrum activity. The literature describes HPLC methods for it determination in pharmaceutical formulations; however a bioassay has not been reported yet.
Aims: Develop and validate an agar diffusion bioassay for cefepime determination in injectable formulations.
Method: The cylinder-plate method was carried out using a strain of *Micrococcus luteus* ATCC 10240 inoculated on antibiotic medium 1 at 35ºC. Diluted cultures suspensions of 25% turbidity were obtained at 580 nm. The method was validated by determination of linearity, precision and accuracy.
Results: The methodology was linear (r^2=0.9999) in the concentration range of 8-32 µg/mL. The method showed good precision; and the accuracy ranged from 100.59% (RSD=1.53%) to 100.39% (RSD=0.39%), intra-day and inter-day, respectively.
Conclusion: The results demonstrated the validity of the bioassay that is useful methodology for the routine quality control of cefepime in pharmaceutical products.

Financial Support: FATEC
Advisor: Ana Bergold

CQ045-PRELIMINARY STUDIES FOR THE MOLECULAR DIAGNOSIS OF *ESCHERICHIA COLI* DRUG-CONTAMINANTS

MATEUS S. TERCETI (IC)[1]; DANIELA C. M. VIEIRA (PG) [1]; LUCIENE T. LIMA (IC) [1]; PAULO M. F. SILVA (PQ) [1]; MARÍLIA C. FRANCO (PQ) [1]

(1) Efoa/Ceufe, Alfenas-MG;

Text – Introduction: The importance of microbiological control of drugs resides in the fact that many times they are used by weakened patients. The disadvantage of conventional methods for the detection of microbial contaminants is the slowness in the evaluation and issue with the experts' report. Objective: Establishing a molecular method for the detection of E. coli as a drug contaminant. Methodology: The concentration of the inoculum was determined by the colony counting in agar LB plates. The phenol/chloroform and glass beads were the extraction methods tested to the pure culture. In the Polymerase Chain Reaction (PCR) tests, the variables were the annealing temperature and concentration of primers. Results: The concentration of the inoculum set up for the deliberate contamination of the drug was $3.15.10^{-3}$ CFU/mL. Both methods of extraction were efficient. The conditions for the extraction of DNA and PCR were standardized. The primer concentration in the reaction were 10 pmol. Conclusion: The inoculum concentration was established and the conditions were standardized for the extraction of DNA and PCR for the detection of *E. coli* drug-contaminants.

Financial Support: FINEP, FAPEMIG, Efoa/Ceufe
Supervisor: Dra Marília Caixeta Franco

CQ046-MICELLAR MEDIA IN EFFICACY OF THE ASSOCIATION BENZALKONIUM CHLORIDE AND CHLORHEXIDINE GLUCONATE IN ANTISEPTICS ACTION

SILVA, T. R. (PQ)[1], ARRUDA, E. J1., SILVA, C. M. (IC)[2], VICTORINO, C. A. (IC)[2], FIORINI, J. E. (PQ)[2]

[1]Pharmacy, MSMT – UCDB, Campo Grande, MS
[2]Laboratory of Biology and Physiology of Microorganisms, UNIFENAS

Introduction: The micellar properties of chlorhexidine(GC) and benzalkonium(CB) and mixture solutions were examined using surface tension technique and the evaluation of the antiseptic efficacy was conducted. GC and CB. They are effective against Gram-(-) and Gram-(+) bacteria, fungi. **Objective:** Evaluate the possible synergic action of such compounds *in vitro* and the micellar media and surface properties with activity in aqueous solution. **Methods:** The efficacy of the antiseptics was tested using different concentrations. The surface tension of the solutions were obtained by capillary technique and correlated with antiseptics efficacy. **Results:** GC solutions exhibited more efficacy than CB ones. The increase in concentration did not improve the efficacy of antiseptics. The mixture of antiseptics displayed lesser efficacy than GC solutions alone. **Conclusion:** The association of the antiseptics did not present a synergic action. Higher concentrations of CB reduced the efficacy of GC. The experimental data suggested that microbicide action of CB and GC are related to micellar media and molecular interactions that conditioned the antiseptic efficacy.

Financial Support: PIBIC/PROBIC
Supervisor: SILVA, T. R.

CQ047-MICROBIOLOGICAL AND PHYSICAL-CHEMICAL ANALYSIS OF THE LARANJA DOCE BROOK, DOURADOS, MS, BRAZIL.

JÚLIO CÉZAR ARAÚJO DO ESPÍRITO SANTO (IC)[1]; WILLIAM ROBERTO SCHLUCHTING (IC)[1]; JULIANA DA SILVA AGOSTINI (PQ)[1]; ÉRIKA VILHENA DA SILVA PEREIRA (PQ)[1].

[1]UNIGRAN

Introduction: The Laranja Doce brook is an important source of water to several small farms and homes in the city of Dourados. Its riverbed crosses over the city, supporting its pollution. Objective: This work aimed to know the quality of the water based on physical-chemical and microbiological patterns. Methods: In April 2005, two replicates of water samples were taken from four strategic brook sites: river-head and beginning, middle, and ending of the urban perimeter. The quantities of ammonia, Ph, bromine, free and total chlorine, iron, cyanuric acid and iodine, and presence of nitrates, salts of calcium and sulphates as well as the organoleptic characteristics were analyzed. Microbiological quality was based on total and fecal coliform. Results: Counting for total and fecal coliforms from all samples overreached 1,100 NMP/100cc indicating high degree of fecal contamination of the brook, and ph and iron values were out of the reference values. Contaminated samples from river-head indicate that the whole water table, which supplies several wells of the city, could be contaminated. Conclusion: The Laranja Doce brook is inappropriate for both human consume and leisure.

Financial Support: UNIGRAN
Advisor: Juliana da Silva Agostini

CQ048-SIMPLE AND RELIABLE HPLC METHOD FOR THE DISSOLUTION STUDIES OF FEXOFENADINE DETERMINATION IN PHARMACEUTICAL DOSAGE FORMS

DANIELE CARVALHO DE OLIVEIRA (PG)[1]; CLARICE MADALENA BUENO ROLIM (PQ)[1]

[(1)]Department of Industrial Pharmacy, Federal University of Santa Maria, RS-Brazil

Introduction: Fexofenadine hydrochloride is the metabolite active of terfenadine with does not present your cardiotoxic potential, is antihistamine drug which does not cross the blood-brain barrier.
Objetive: This work describes a new, fully validated, simple, rapid, selective, and sensitive HPLC method with UV detection for the determination fexofenadine dissolution studies in pharmaceutical dosage forms.
Methods and results: The HPLC system was operated isocratically using C18 Phenomenex (150 mm x 4.6 mm I.D, 5 µm particle size) column. The mobile phase employed was triethylamine phosphate 1%, pH 3.2 adjusted with phosphoric acid 85% : acetonitrile : methanol (50:30:20 v/v/v), with detection of 210 nm. The assay was linear in the concentration range 0.080-180 µg mL^{-1} (r^2> 0,999), data validation shows that the method is accurate (RSD<2%) demonstrating good precision (RSD<2%), specific and robust, with retention time (4.1 min).
Conclusion: The method has been successfully used for the quantification of fexofenadine for monitoring its concentration for in vitro dissolution studies of pharmaceutical dosage forms.

Advisor: Clarice Madalena Bueno Rolim

CQ049-VALIDATION OF 5-ASA IN RAW MATERIAL BY DPPH· METHOD.

JANICE APARACIDA RAFAEL (PG)[1]; FABIANA TESTA MOURA DE CARVALHO(PG)[1]; MARIA JOSÉ VIEIRA FONSECA (PQ)[1]

(1)Departamento de Ciências Farmacêuticas, FCFRP-Universidade de São Paulo, Avenida Zeferino Vaz S/N, 14040-903, Ribeirão Preto, SP, Brazil

Introduction: 5-ASAis a drug used in inflammatory bowel disease's treatment. The mechanism of action of this drug is not totally understood, however, its capability in scavenging reactive oxigen species have na important relationship with its pharmacological action. The 1.1-diphenyl-2-picrylhydrazyl radicals (DPPH·)is a method widely used to determine the antioxidant activity of phenolic compounds such as 5-ASA. Objective: The present work is intended to validate the DPPH· method in raw material and determine the stability of its at 40ºC during 6 months. Methodology: The DPPH· method was performed at 517 nm using 100 mmol/L acetate buffer, pH 5.5, ethanol and 250 µmol/L ethanolic solution of DPPH· .Results: The results indicate satisfactory intra and inter-day variability (1.50% and 2.60%R.D.S) respectively for 2 µg/mL concentration. The data obtained in stability test showed that the samples were stable having less than 10% degraded. Conclusion: The method have the advantage of using a feasible analytical procedure which needs only a simple samples. Furthermore, the stability test of 5-ASA showed that did not occur any spontaneous degradationin the antioxidant activity during the 6 months of evaluation at 40ºC.

Financial Support: CNPq
Supervisor: Maria José Vieira Fonseca

CQ050-CHROMATOGRAPHIC DETERMINTATION OF DIPYRONE IN PHARCEUTICAL PREPARATIONS

NÁDIA REZENDE BARBOSA (PQ)[1], IZABELA DE CASTRO POLISSENI (IC)[1], FERNANDA LEITE HUGHES DE CARVALHO (IC)[1] , MARIANA PRATES DE SOUSA (IC)[1]

(1) NIQUA - Departamento de Alimentos e Toxicologia, Faculdade de Farmácia e Bioquímica da Universidade Federal de Juiz de Fora, Brazil.

INTRODUCTION: High-performance liquid chromatographic (HPLC) method was developed for dipyrone (DIP) quality control. Although an effective analgesic and antipyretic, dipyrone may cause severe side-effects, including agranulocytosis. OBJECTIVE: To validate a method to DIP analysis in pharmaceutical preparations by HPLC. METHOD: DIP and an internal standard (caffeine) were prepared using organic solvent. Chromatographic separation was achieved on a Waters silica column. The mobile phase was potassium phosphate acetate buffer, acetonitrile, methanol (70: 20: 10, v/v/v), with ultraviolet detection at 230 nm. RESULTS: The method was linear in the range 1.95-700 µg/mL, with a mean coefficient of correlation (r)≥0.9926. The limits of detection and quantification were 1.95 and 3.9 µg/mL, respectively. Within and between-run precision studies demonstrated C.V.<4% at all tested concentrations. CONCLUSION: The method showed to be appropriate for DIP in liquid pharmaceutical preparations.

Financial support: FAPEMIG e PROPESQ/UFJF
Supervisor: Nádia Rezende Barbosa

CQ051-DEVELOPMENT AND VALIDATION OF A HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC METHOD FOR DETERMINATION OF PANTOPRAZOLE

ADRIANA NASCIMENTO DE SOUSA(PQ)[1]; SÉRGIO FERNANDO DE OLIVEIRA GOMES(PQ)[1]; JACQUELINE MEGRE DRUMOND NOGUEIRA(PQ)[1]; MÁRCIO LUIZ FROIS(IC)[1]

[1]Centro Universitário Newton Paiva, FACIBIS, Brazil

Introduction: Pantoprazole is a proton pump inhibitor, that inhibits specifically H+,K+-ATPase, the enzyme which is responsible for gastric acid secretion in the parietal cells of the stomach. There is no described analytical methodology in official compendiums to this drug. Objective: In this study, the development and validation of an analytical method for the determination of pantoprazole using high-performance liquid chromatography (HPLC) was reported. Methodology: The assay was performed isocratically using phosphate buffer and acetonitrile (500:450), as a solvent system, a octadecyl-bonded silica column and a diode-array UV detection at 289 nm. Results and Conclusion: The validation of the method showed it was linear from 0.008 to 0.012 mg/mL with a correlation coefficient of 0.998. The values obtained for the intra-assay and inter-assay accuracy were between 98.4 and 100,1%, and the relative standard deviation (%RSD) values for intra and interday precision studies are < 0.70%. The limit of detection and limit of quantification are 68 µg/mL and 206 µg/mL with a 0.49%RSD, respectively. This sensitive and fast method has proved to be suitable for the quality control analysis.

CQ052-DETERMINATION PEROXIDE RATE' OILS USED IN A MAGISTRAL PHARMACY

RENATA FALIVENE ANDRIGO(IC)[1]; BRUNO RICARDO M. DE OLIVEIRA(IC)[1]; HELLEN P. ZAPPAROLI DE LOSSO(IC)[1]; GISLAINE R. LEONARDI(PQ)[1]

(1) Universidade Metodista de Piracicaba

Introduction: The oils have been often added to the great magistrais bases because they can improve the quality of spreading of the formulation and in addition it can also improve the sensorial and even present some good effect to the skin. That is so, because there are several lipids which are important for the suitable physiological conditions. That fact also favours the use of these oils and their derivatives for formulation in dermatology. Among the several oils commonly used in formulation for skin use, there are examples such as almond, grape seed and rosa mosqueta oils.
Objective: The aim of this work was to evaluate the quality of these oils used in the formulations.
Method: by determining the peroxide rate (P.R.), following the Brazilian Pharmacopoeia method.
Results: The Rosa Mosqueta oil followed by the Grape Seed oil showed their peroxide rate (P.R.) as high as 5,99% and 7,39%; this represents a good condition for the use in formulations. However, the Almond oil reached a peroxide rate (P.R.) at 38,23%; showing us that it ought not be used in the formulation.
Conclusion: The tests of peroxide rate (P.R.) are very important and it should be evaluated to qualify the oils used in the formulations.

Supervisor: Gislaine R. Leonardi

CQ053-THE SUPPLIERS' QUALIFICATION PROCESS IN A PHARMACEUTICAL INDUSTRY

MARCIO ADRIANO FERNANDES (IC)[1]; ALEXANDRE BRONHARO FIORATTI (IC)[1]; VINÍCIUS MANTOVANI VICENTINI (IC)[1]

(1) Universidade Estadual de Maringá

Introduction: The suppliers' qualification is a requirement of the GMP, being its accomplishment not just compulsory, but a market necessity. The raw materials and the packaging materials profile has a direct influence in the final product quality, so being the suppliers qualification a fundamental tool to a company compromised with the high quality medicines production. Objective: To elaborate a way to accomplish the process for the creation of a list of qualified suppliers. Methodology: Methodologies can be used to the legislations accomplishment or complying with the ISO 9001 request. In the first case a periodical external auditory of GMP is enough, however to comply the ISO 9001 requests, there is a detailed evaluation, checking the whole quality really assets by the supplier. Results: Checking the delivery quality level, the receiving quality, quality system and the whole quality practiced possible to indicate if the supplier can be included in the qualifiers suppliers list. Conclusion: The qualified suppliers roll upkeep, bring a lot of odds to the company, such as the manufacture routine improving and avoid unconformities, being an important step to affirm the final product quality.

Advisor: Selma Lucy Franco

CQ054-CLEANING VALIDATION SCRIPT FOR PHARMACEUTICAL LABORATORIES

MOISÉS ROBERTO DA SILVA (IC)[1]; ALEXANDRE BRONHARO FIORATTI (IC)[1]; MÁRCIO ADRIANO FERNANDES (IC)[1]; VINÍCIUS MANTOVANI VICENTINI (IC)[1]; ELZA KIMURA (PQ)[1].

(1) Universidade Estadual de Maringá

Introduction: The cleaning validation is a documented evidence that the current cleaning procedures remove residues to pre-established and acceptable levels. The lack of information about the steps of validation may induce to failed procedures, resulting in sanitary risk and financial loss. Objective: to propose a script of cleaning validation for pharmaceutical laboratories. Methods: national and international regulations and scientific articles were used as references. Results: the script included the validation cleaning protocol, establishment of the target residues, sampling technique, validation of the analytical methodology with quantification and detection limits, setting the acceptance criteria and measurement of total residues in the samples, recovery factor, efficacy evidence of the cleaning procedure and re-validation. Conclusion: the present script is useful for all laboratories.

Financial support: LEPEMC - UEM
Advisor: Elza Kimura

CQ055 - ANALYTICAL METHOD VALIDATION FOR TWEEN 80 IN PENICILLIN G BENZATIN

ELIZABETH C. OLIVEIRA(PG)[(1)], MARGARIDA T. KATO(PQ)[(2)], TEREZINHA J. A. PINTO(PQ)[(1),(3)]

[(1)]Fund. Inst. de Pesq. Farmacêuticas – FIPFARMA; [(2)]Fund. para o Remédio Popular – FURP; [(3)]Fac. de Ciências Farmacêuticas da Univ. de São Paulo – FCF/USP

Introduction: Penicillin in suspension form contain added substances that promote the particles wettability improving the suspension formation and the administration. The Tween 80 is used to this purpose, but its control must be made with severity due to its possible toxic effect. Objective: The aim of this work was to validate the analytical methodology to the determination of Tween 80 in Penicillin G Benzatin. Methodology: It was employed TLC after previous extraction with toluene. The detection limit was made by semi-quantitative assays until the less detectable concentration. The specificity was tested by the comparison with standards, evaluating the method capacity in extract and to semi quantifies the compound. Robustness evaluation was made by parameters like shaking time sample. Results: The detection limit determined was 3 μg. The specificity was obtained so the extraction and semi-quantification were efficient. The robustness results showed the time of shaking and the number of extractions weren't decisive for results. Conclusions: The parameters evaluated permited to consider the method adequate to proposition.

Financial Support: FIPFARMA
Supervisor: Margarida T. Kato

CQ056-STANDARDIZATION OF PARAMETERS FOR VALIDATION OF FLEROXACIN BY MICROBIOLOGICAL ASSAY

MARIA BEATRIZ BASTOS LUCCHESI(IC)[1]; SANJAY GARG(PQ)[2]; HÉRIDA REGINA NUNES SALGADO(PQ)[12]

[(1)]PPG–FCF-UNESP
[(2)] FMHS, University of Auckland, New Zealand

Introduction: Fleroxacin is a 3rd generation fluoroquinolone that exhibits strong bactericidal activity against a wide range of Gram-negative and Gram-positive bacteria. Objectives: The aim was to establish the parameters to validate a microbiological assay of fleroxacin. Methodology: We carried out preliminary tests to check the best conditions, using *B. subtilis, E. coli* and *P. aeruginosa*, culture media, diluent solution as phosphate buffer pH 6.0 and 8.0, inocula concentration (1% and 2%) and drug concentration (1.0, 2.0, and 4.0; 2.0, 4.0, and 8.0; and 8.0, 16.0, and 32.0 μg/mL). Results: After overnight incubation at 35ºC ± 1ºC, the zone diameters of the growth inhibition were carefully measured using a caliper. Conclusions: In this work experimental 3 x 3 design followed the procedure described in Brazilian Pharmacopoeia. The standardization of parameters of microbiological assay indicated the *B. subtilis* ATCC 9372 as the test organism, drug at concentrations ranging from 4.0 to 16.0 mg/mL. The method was linear ($r = 0.9969$). We conclude that the used parameters for microbiological assay are satisfactory for quantification of fleroxacin in capsules.

Financial support: CNPq, CAPES, PADC-FCF
Supervisor: Hérida R. N. Salgado

CQ057-DETERMINATION OF MINOXIDIL IN CAPSULE BY UV SPECTROMETRIC AND DERIVATIVE UV SPECTROMETRIC METHODS

VALERIA PEREIRA DE SOUSA[1] (PQ); SHEILA GARCIA[1] (PQ);CARLA HOLANDINO QUARESMA[1] (PQ); NÁDIA MARIA VOLPATO[1] (PQ)

[(1)]UFRJ, Dep. de Medicamentos

Minoxidil is a potent vasodilator, used in the treatment of grave hypertension, that could not be treated with others drugs. In this study, was validated an UV spectrometric, first and second order derivative spectrometric method to assay minoxidil in a solid dosage form, to simplify and turn the analyses less costly. To quantify capsule with 5mg of minoxidil it was utilized a Shimadzu PC2401 spectrophotometer. The method was validated using the parameters praised by ANVISA. To evaluate the precision of the method was carried out analysis in 6 units of 3 lots. The recovery was tested in the same way of precision adding 5 and 10µg of standard. The drug was determined with accuracy in the presence of the excipients. It was obtained a linearity range of 1–50 µg/mL, the correlation coefficient was over of 0,999 in all the cases. All the parameters were tested for the first and second-derivative of the spectrum, showing that the proposed method can be also utilized to quantify minoxidil in pharmaceutical formulations where some excipiente absorb in the same wave length of linearity of the method. The proposed methods are precise, accurate, specific and sensitive and can be directly and easily applied for the assay of minoxidil in the solid dosage form.

CQ058-DEVELOPMENT AND VALIDATION OF A NEW HPLC ANALYTICAL METHOD FOR THE DISSOLUTION TEST IN TABLETS CONTAINING DEFLAZACORT.

FABÍOLA SILVA GARCIA; EDUARDO TOZATTO ; MARIA VITÓRIA LOPES BADRA BENTLEY; JULIANA MALDONADO MARCHETTI

Faculdade de Ciências Farmacêutica de Ribeirão Preto, Universidade de São Paulo, Brasil

A new simple high-performance liquid chromatography (HPLC) analytical method was developed and validated to quantify deflazacort in tablets as pharmaceutical formulation after their dissolution test. Determination of deflazacort was carried out by a LiChrospher® RP-Select B (250mm×2.1 mm, 5µm particle size) column and a mobile phase using Methanol - Water (60:40, v/v), a flow rate of 1 ml/min. The UV detector was set at 242 nm. The new analytical method showed the fundamental criteria for validation: selectivity, linearity, precision, accuracy and sensitivity. The method was applied all day for the quality control of commercial deflazacort tablets in order to quantify the drug and to check the content of the uniformity test. The retention time of deflazacort was 4.5 minutes. The calibration curve was linear over the concentration range 2.0 - 500 µg/mL ($r > 0,999$) and limit of quantification and detection was 0.5 and 0.04 µg/mL respectively. No interference was observed. The simple, sensitive and reproducible high-performance liquid chromatography assay method was suitable for the determination of deflazacort for the aimed purpose.

Supervisor: Profa. Dra. Juliana M. Marchetti

CQ059-DETERMINATION OF MEGESTROL ACETATE IN HUMAN PLASMA BY A SENSITIVE AND SELECTIVE LC-MS-MS METHOD

ISMAEL LEITE MARTINS(PG)[1], JANAINA PINHO TAVARES(PG)[1], ADRIANO NUNES CUNHA(PQ)[1], FERNANDO ANTÔNIO FROTA BEZERRA(PQ)[1], MANOEL ODORICO DE MORAES(PQ)[1], MARIA ELISABETE AMARAL DE MORAES(PQ)[1]

[(1)]Clinical Pharmacology Unity, UFC

Introduction: LC-MS-MS is one of the most common techniques employed for the quantification of drugs in biological matrices. Objective: To develop a sensitive and selective LC-MS-MS method to determine megestrol acetate (MA) in human plasma from 30 healthy volunteers. Methodology: The analyte and internal standard were extracted from plasma by hexane/ethyl acetate (1:1 v/v), and chromatographed on a C_{18} column. The mobile phase consisted of acetonitrila-water (80:20 v/v) including formic acid 0.1%. Detection was performed on a mass spectrometer. Results: The linear calibration curves were obtained in the concentration range 2–150ng/mL (r^2>0.998). The intra-batch precisions were 3.16, 4.65, and 2.68%; and the intra-batch accuracy was 6.77, 6.23, and 5.73% for 6, 60 and 120ng/mL, respectively. The inter-batch precision was 7.76, 6.23, and 6.37%, and the inter-batch accuracy was 0.08, 1.55, and 2.11% for the same concentrations. Conclusions: This validated method was successfully applied for the determination of pharmacokinetic profiles of MA tablets administered to volunteers.

Financial Support: CNPq, FUNCAP, InCB
Supervisor: Maria Elisabete A. de Moraes

CQ060-DETERMINATION OF DIACEREIN IN CAPSULES BY SPECTROPHOPTOMETRY

SÍLVIA HELENA MIOLLO BORGMANN (PG)[1]; SIMONE GONÇALVES CARDOSO (PQ)[1]; LUTIANE MOZZAQUATRO PARCIANELLO (IC)[1]; CARINE VIANNA SILVA IEGGLI (PG)[1]; LISIANE BAJERSKI (PG)[1] TANIA BOER (PG)[1]

[(1)] Universidade Federal de Santa Maria

*Introduction***:** Diacerein is a new anti-osteoarthritis agent available in capsules. At the present time there are no official pharmacopoeial monographs for this drug in raw material and capsules and no analytical procedures have been reported in the literature for quantitation of this drug. *Objective:* to develop and to validate simple spectrophotometric methods for diacerein determination in capsules. *Methodology:* The samples were dissolved in 0.1N sodium hydroxide and the absorbances were measured at 277 nm (UV) and 502 nm (VIS). *Results:* The absorbances were linearly correlated with concentration in the 6.0 – 24 μg mL^{-1} range (r = 0.9999) for UV and 10 – 34 mg mL^{-1} range (r = 0.9998) for VIS method. The mean concentrations of diacerein determined in capsules were 99.6% ± 0.43 (UV) and 98.2% ± 0.43 (VIS). The intra (n = 6) and inter-day (n = 3) precision showed good results (RSD < 2%). The recovery studies showed satisfactory results (> 95%). Statistical analysis by ANOVA showed no significant differences between the results obtained by two methods. *Conclusion:* The methods are precise and accurate and are potentially useful for a routine analysis.

Supervisor: Simone Gonçalves Cardoso

CQ061-MID-INFRARED SPECTROSCOPY APPLIED TO QUANTIFICATION OF AMOXICILLIN IN PHARMACEUTICAL FORMULATIONS

GRACIELE PARISOTTO[1] (IC); MARCO FLÔRES FERRÃO[2] (PQ); JOÃO CARLOS FURTADO[2] (PQ); ROLF FREDI MOLZ[2] (PQ)

[(1)]Curso de Farmácia, UNISC – RS; [(2)]Mestrado em Sistemas e Processos Industriais, UNISC – RS

The methodology currently used in the quantification of the active ingredients in drugs is based on chromatographic methods, which have numerous disadvantages, such as longer time of analysis; overlapping of peaks; and destruction of the sample. In this work the quantification of pharmaceutical formulations content amoxicillin, was studied, using spectra of diffuse reflectance infrared Fourier transform spectroscopy (DRIFTS), in association with partial least squares (PLS) regression. The spectra of samples of the 24 different samples (17 for calibration set and 7 for validation set), contained 76,7-94,3 % of amoxicillin in starch, had been collected in Nicolet Magna 550 spectrophotometer. For the PLS, the spectral information had been processed in software Pirouette® 2.7. The PLS models had been constructed with the autoscaled data, and multiplicative scatter correction (MSC). The best model presented R^2=0.9863, RMSEC=0.647 and RMSEV=0.786. The analytical method proposed is non invasive and the cost and time of analysis are very much reduced, making possible the fast and direct determination of the amoxicillin content.

Financial Support: PIBIC-CNPq
Supervisor: Marco F. Ferrão

CQ062-IN VITRO EVALUATION OF TABLETS CONTAINING GATIFLOXACIN

SIMONE GONÇALVES CARDOSO (PQ)[1]; KARIN GOEBEL (IC)[1]; GIANE CORREA (PQ)[1]; JOÃO RONALDO FERREIRA (PG)[1]; SILVIA HELEN MIOLLO BORGMANN (PQ)[1]; CRISTIANI C.G. OLIVEIRA LOPES (PG)[2]; HERIDA REGINA NUNES SALGADO (PQ)[2]

[(1)] Universidade Federal de Santa Maria (UFSM); [(2)] Unesp/Araraquara

*Introduction***:** Gatifloxacin (GTF) is an antibiotic of the class of fluorquinolones with a broad spectrum of action, as much for Gram-Negative, Gram-Positive. It is available as bulk material, and tablets. This drug, until the present, does not possess officially established monograph. *Objective*: To develop dissolution test conditions for GTF film coated tablets. *Methodology*: Three-dissolution medium (0.1*M* HCl, water and pH 4.0 phosphate buffer, 900 ml) and USP Apparatus 1 and 2 (Nova Ética) were tested at speed of 50 rpm. In all experiments, 5 ml sample aliquots were withdrawn at 5; 10, 15, 30, 40 and 60 min and replaced with an equal volume of the fresh medium. The drug concentrations in dissolution medium were determined by spectrophotometric method. Two different batches of GTF tablets were tested. *Results:* All active substance was dissolved in 30 min. in the whole tablets and conditions tested. *Conclusion:* The use of 900 ml of water, paddle as apparatus at the stirring speed of 50 rpm and 30 minutes of test provided satisfactory results for GTF tablets.

Financial support: CNPq
Supervisores: Simone Gonçalves Cardoso, Hérida Regina Nunes Salgado

CQ063-IN VITRO EVALUATION OF TABLETS CONTAINING LOMEFLOXACIN

SIMONE GONÇALVES CARDOSO (PQ)[1]; JOÃO RONALDO FERREIRA (PG)[1]; GIANE CORREA (PQ)[1]; SILVIA BORGMANN (PQ)[1]; GREICI CRISTIANI GOMES TOZO (PG)[2]; HERIDA R. N. SALGADO (PQ)[2]

[(1)] Universidade Federal de Santa Maria (UFSM); [(2)] Unesp/ Araraquara

*Introduction***:** Lomefloxacin (LMF), an antimicrobial of the class of fluoroquinolones of 3rd generation, is highly efficient in the treatment of the urinary and respiratory infections. It is available as bulk material, and tablets. At the present time there are no official pharmacopoeial monographs for this drug in raw material and tablets. *Objective*: To develop dissolution test condition for LMF tablets. *Methodology*: For the development of dissolution methods, three-dissolution medium (0.1*M* HCl, water and pH 4.0 phosphate buffer, 900 ml) have been tested at 37°C ± 0.5°C, at speed of 50 rpm, using USP Apparatus 1 and 2 (Nova Ética). Solutions were collected at 5; 10, 15, 30, 40 and 60 min. and the measurements were achieved by UV spectrophotometry. Two different batches of LMF tablets were tested. *Results:* The two products had percent of amount dissolved not less than 80% of the labeled amount of LMF within 30 min, in all tested conditions. *Conclusion:* The use of 900 ml of water, paddle as apparatus at the stirring speed of 50 rpm and 30 minutes of test provided satisfactory results for LMF tablets.

Financial support: CAPES, CNPq
Supervisoras: Simone G. Cardoso, Hérida R. N. Salgado

CQ064-DETERMINATION OF EBASTINE IN TABLETS BY SPECTROPHOPTOMETRY

SIMONE GONÇALVES CARDOSO (PQ)[1]; PATRÍCIA POZZATTI (PG)[1]; ADIENE GONÇALVES (PG)[1]; ANELISE WEICH (PG)[1]; CAIO OLIVEIRA(PG)[1]; EVERTON BOFF(PG)[1]; GIANE CORREA(PG)[1]; ISABEL DIEFENBACH; (PG)[1]; JOÃO FERREIRA(PG)[1]; JULIANA VALENTINI(PG)[1]; MARCIELE PILAU(PG)[1]; SÍLVIA BORGMANN(PG)[1]

[(1)] Universidade Federal de Santa Maria

*Introduction***:** Ebastine is a new generation of antihistamines available in tablets and oral solution. The official method for the assay of this drug in the bulk form is non-aqueous titration. No analytical procedures have been reported in the literature for quantitation of this drug in pharmaceutical formulation. *Objective:* to develop and to validate simple spectrophotometric method for ebastine quantitation in tablets. *Methodology:* The samples were dissolved in methanol and the absorbances were measured at 253 nm. The method was validated according to USP 28 and ICH guideline. *Results:* The absorbances were linearly correlated with concentration in the 5.0 – 20 μg mL^{-1} range ($r > 0.999$). The mean concentration of ebastine determined in tablets was 97.7% % ± 0.79 %. The RSD of intra ($n = 6$) and inter-day ($n = 3$) precision were < 2%. The recovery studies showed satisfactory results (> 95%). No interference from excipients was observed. *Conclusion:* Due to its simplicity, the method can be used for routine quality control analysis of ebastine in tablets.

Supervisor: Simone Gonçalves Cardoso

CQ065-QUANTIFICATION OF CHLOROGENIC ACID AND ß-SITOSTEROL IN THE BARK AND LEAVES OF *TRICHILIA CATIGUA* A. JUSS.

JESSÉ BOQUETT LAGOS(PG)[1]; OBDÚLIO GOMES MIGUEL(PQ)[1]

[(1)]Federal University of Paraná - Brazil

Trichila catigua A. Juss., MELIACEAE is a native tree widely distributed in Brazil commonly known as "catuaba". Its bark has been used in popular medicine as physical and mental tonic and as a sexual stimulant. Despite of its increasing use by the pharmaceutical and food industries there is a lack of publications concerning the chemical composition of its bark and none about the leaves. The objective of this study is to quantify the content of chlorogenic acid and ß-sitosterol in the bark and leaves of *T. catigua*. The dried bark and leaves were ethanol extracted in a Soxhlet apparatus for 4 hours. The analysis of chlorogenic acid was performed by HPLC using a RP-18 column and a gradient elution system of 0,2% phosphoric acid-acetonitrile with diode array detection set at 326nm. The content of ß-sitosterol was determined by gas chromatography with a wide bore ZB-1 column and flame ionization detection. The quantification of chlorogenic acid yelded 914µg/g in the bark and 1066µg/g in the leaves and the content of ß-sitosterol was of 249µg/g in the bark and 554µg/g in the leaves. The content of the analyzed compounds is higher in the leaves and these analytical methodologies can be used in the quality control of the plant material.

Supervisor: Obdúlio G. Miguel

CQ066-IN VITRO RELEASE TEST FOR MICONAZOLE NITRATE FROM SEMISOLIDS FORMULATONS

CAROLINA S. BEMVINDO[1] (PG); NADIA M. VOLPATO[1] (PQ)

[1]Faculdade de Farmácia, Universidade Federal do Rio de Janeiro

Introduction: The in vitro release test in Franz's diffusion cells is recommended by the FDA for quality control and to assure batch-to-batch uniformity of topical formulations. This method is also useful in formulation development. Objective: To evaluate in vitro release of three batches of two formulations of 2% miconazole nitrate lotions and to compare the use of polysulfone (PS) and cellulose acetate (CA) as synthetic membranes. Methodology: Each batch was applied in the donor chamber of the diffusion cells and samples of the receptor fluid (EtOH 10% v/v) were taken up to 180 minutes and analyzed by HPLC. Results: The slope of the curve of drug amount released per area vs time represents the flux and was calculated by linear regression of the last 5 points. The fluxes of the batches of Product A through PS membrane were: 0.481; 0.445 and 0.411 µg/cm^2/mim; and through CA membrane were 0.468; 0.433 and 0.440 µg/cm^2/mim. The fluxes obtained for Product B were 0.399; 0.397 and 0.464 µg/cm^2/mim for PS and 0.347; 0.329 and 0.332 µg/cm^2/mim for CA. Conclusion: The conditions employed demonstrated uniformity between the batches of both formulations tested. There was no difference between the results obtained with the two membranes ($P > 0.05$ for both products), at level of 5%.

Financial support: CAPES
Supervisor: Profa. Nadia Volpato

CQ067-ON-LINE SOLID PHASE EXTRACTION COUPLED WITH HPLC AND TANDEM MASS SPECTROMETRY (SPE-HPLC-MS-MS) FOR BROMAZEPAM (BRZ) BIOEQUIVALENCE STUDY IN HUMANS

JOSÉ EDUARDO GONÇALVES[1](PQ); TÂNIA MONTEIRO[1](PQ); CLÁUDIA NEVES [1](PG); KARLA GRAM[1](PG); NADIA VOLPATO[1](PQ); VIVIAN SILVA[1](PG); RICARDO CAMINHA [2](PQ); MARIA GONÇALVES [3](PQ); FÁBIO SANTOS4(PG); GABRIEL SILVEIRA4(PG); FRANÇOIS NOËL4(PQ)

[1]Faculdade de Farmácia; [2]Serviço Clínica Médica e [3]Laboratório Monitorização de Fármacos, HUCFF; [4]Departamento de Farmacologia Básica e Clínica – UFRJ.

Introduction: Automated methods for drug quantification in human plasma are desirable. Objective: To validate an on-line SPE coupled with HPLC-MS-MS for BRZ analysis for bioequivalence study. Methods: The method involved a dilution of plasma with internal standard solution (carbamazepine, CBZ), vortexing, centrifugation and injection of the supernatant. The analytes were ionized using positive electrospray MS then detected by MRM. The *m/z* transitions 316→182 (BRZ) and 237→194 (CBZ) were used for quantification. Results: The calibration curve was linear from 1 to 200 ng/mL. The retention times of BRZ and CBZ were 2.6 and 3.2 min. The intra and inter-day precision and accuracy were 3.4-15.4%; 5.2-17% and 94-103.9%, respectively. Conclusion: This new automated method has been successfully applied in the study and the tablet formulations of 6 mg BRZ were bioequivalent. Furthermore, the comparison of dissolution profiles with bioavailability data led to rational experimental conditions for this *in vitro* test.

Financial support: FINEP, Biosintética.

CQ068-MICROBIOLOGICAL AND PHYSICAL-CHEMICAL ANALYSES OF EMULSIONS PRODUCED BY MAGISTRAL PHARMACIES OF THE CASCAVEL CITY, PR

ALEXANDRE MALLER (IC); ALINE C. ARGENTA (IC); AMANDA C. IARK (IC); ANDRÉ R.L. DAMÁSIO (IC); ANY E.S.S. GONÇALVES (IC); CLÁUDIA R. IDE (IC); ÉRIKA S. KONOPATIZK (IC); HELENA T. TAKAHASHI (PQ); IONETE L.M. BARZOTTO (PQ); LARISSA M. TONDIN (IC); PRISCILA I. SIMPLICIO (IC); SILVIE R. BALZAN (IC); WILLIAN J. ANDRIOLLI (IC)

Unioeste

Emulsions are heterogeneous systems, consisting of an immiscible liquid dispersed in another one in the drops´s form, being a watery phase and another oily one. The objective of the present study was to analyze according microbiological and physical-chemical parameters samples of emulsions produced by different magistral pharmacies of the Cascavel city. The microbiological and physical-chemical analyses were evaluated according Brazilian Pharmacopoeia (1988) and Health Ministry (Brazil, 2004). Between of total of 12 samples, 11 (91,7%) were proper for total viable aerobic count and all the 12 samples (100%) were proper for yeasts and moulds count besides absence of total and fecal coliforms and pathogenic microorganisms. All the samples (100%) presented acceptable results for pH, viscosity, stability to the UV light and to the high temperatures, tests for high-speed stability and organoleptic characteristics. Eleven (91,7%) and 12 (100%) of samples were appropriated according microbiological and physical-chemical parameters.

Supervisoras: Prof. Helena T. Takahashi e Prof. Ionete L. M. Barzotto

CQ069 - LAMOTRIGINE ANALYSIS IN PHARMACEUTICAL PREPARATIONS BY HPLC

NÁDIA REZENDE BARBOSA (PQ)[1]; FERNANDA LEITE HUGHES DE CARVALHO (IC)[1]; YARA PELUSO CID (IC)[1]; IZABELA DE CASTRO POLISSENI (IC)[1]; ROGÉRIA FERNANDES DE MELO (IC)[1].

[1] NIQUA - Departamento de Alimentos e Toxicologia, Faculdade de Farmácia e Bioquímica da Universidade Federal de Juiz de Fora, Brazil.

Introduction: A sensitive and accurate high-performance liquid chromatographic (HPLC) procedure for lamotrigine (LTG) was developed and validated. Objective: To validate a method to LTG analysis in pharmaceutical preparations by HPLC. Method: LTG and an internal standard (AW725C) were use for validated this study. An isocratic normal-phase HPLC system with a cyanopropyl silica column was used with ultraviolet detection at 254 nm and elution with a mixture of potassium phosphate buffer : acetonitrile : methanol (70 : 20 : 10, v/v/v) as mobile phase. Results: The method was linear in the range 0.003 - 500 µg/ml, with a mean coefficient of correlation (r)³0.9986. The limit of detection (LOD) and limit of quantification (LOQ) were 3.9 and 7.8 µg/ml, respectively. Within- and between-run precision studies demonstrated C.V.<3% at all tested concentrations. Antiepileptic drugs tested did not interfere with the assay. Conclusion: The method showed to be appropriate for determination of LTG in pharmacutical preparations.

Financial support: FAPEMIG e PROPESQ/UFJF
Supervisor: Nádia Rezende Barbosa

CQ070-DETERMINATION OF ETORICOXIB IN PHARMACEUTICAL PRODUCTS BY LC/MS/MS

LIBERATO BRUM JUNIOR(PG)[1]; CLARICE MADALENA BUENO ROLIM(PQ)[1]; DANIELI CENI(IC)[1]; PAULO OLIVEIRA(PG)[1]; THIAGO BARTH(PG)[1]; SÉRGIO LUIZ DALMORA(PQ)[1]

[1]Department of Industrial Pharmacy, Postgraduate Program in Pharmaceutical Sciences, Federal University of Santa Maria, Santa Maria-RS, Brazil.

INTRODUCTION: Etoricoxib represents a second-generation of cyclooxygenase-2 inhibitors and it is used for the treatment of many inflammatory diseases.
AIMS: Develop and validate an LC/MS/MS method for the determination of etoricoxib in pharmaceutical dosage forms.
METHODS: The analysis were carried out using a reversed phase column Luna C_{18} (50mm x 4.6mm), maintained at 35ºC, with a mobile phase of acetic acid 0.1%/acetonitrile (10:90, v/v) run at a flow rate of 1.0 mL/min (split 1:5). The mass spectrometer equipped with an electrospray source in positive mode, was set up in multiple reaction monitoring, selecting the transition of 359.3>280.
RESULTS: The data validation show that the method is specific, fast, accurate and possesses excellent linearity (r^2>0.99) and precision characteristics without any interference from the excipients, and is suitable for the routine quality control of etoricoxib, giving potencies between 100.55 and 101.42%.
CONCLUSION: The validated method was successfully applied for the analysis of the pharmaceutical products.

Financial Support: Merck Laboratories and FIPE-UFSM.
Advisor: Sérgio Luiz Dalmora

CQ071-PURITY DETERMINATION OF CEFTAZIDIME IN PHARMACEUTICAL PREPARATIONS USING DSC

[1]ANDRÉIA DE HARO MORENO (PG); 1HÉRIDA REGINA NUNES SALGADO (PQ)

[1]PPG em Ciências Farmacêuticas, Faculdade de Ciências Farmacêuticas, UNESP, Araraquara (SP), Brazil

Ceftazidime is a new b-lactamase-stable third generation cephalosporin with a broad spectrum of antimicrobial activity. The objective of this work consists of the determination of the presence of CTZ in medicine using DSC-TGA techniques. Ceftazidime present in preparations for injection conyaining known quantities of drug was analized by DSC and DTA/TGA using aluminum saucepan with heating flow of 10 ºC for minute and nitrogen flow. The results of samples were compared with those presented by the reference substance. All the results were quite consistent with the manufacturer's stated contents of ceftazidime with testifies to the applicability for the proposed method to real samples. No interferences were observed in the presence of common excipients of the preparations for injection. The usefulness of the proposed method in pharmaceutical formulations was demonstrated suggesting its use as a reliable and advantageous alternative for routine analysis of ceftazidime.

Financial support: PADC-FCF-UNESP, CNPq-Brazil. CCLGO was funded by CAPES-Brazil. Ariston Farmacêutica.
Supervisor: Hérida Regina Nunes Salgado

CQ072-VALIDATION OF METHOD FOR ATENOLOL DETERMINATION IN SYRUPS SPECTROPHOTOMETER – UV

ALINE CLAUDIA DE MELLO PG[1]; TALIZE FOPPA PG [1];HELLEN KARINE STULZER PG; MARCOS ANTONIO SEGATTO SILVA PQ[1].

[1]Universidade Federal de Santa Catarina

Health professionals are often come across with doses modification for the pediatric. Then, in the absence of this preparation, the hospital pharmaceuticals need of extemporaneous formulations for to serve this demand. This practice happens in international scope, however the information for safe and effective use for the children is insufficient. In order to test the applicability of a new strategy for the bioanalitycal methods, an automated method was developed for the determination of atenolol in syrups (UV spectrophotometer). The concentration used was 10mg/mL, dissolved in methanol. The fixed wavelength was at 275nm. Analyzed parameters of linearity, accuracy and precision (repeatability and intermediate precision) as well as accuracy using quality control samples at different concentration levels over the range investigated. The results showed the linearity (r^2 0,99906), in range at 8 – 12 ug/mL. Accuracy was satisfactory (recover percentage was 98,9 – 101%). The repeatability and intermediate precision was coherent and doesn't show differences both. The results were analyzed for statistical test *t student,* without significant differences.

Supervisor: Professor Doutor: Marcos Antonio Segatto Silva

CQ073-COMPARISON BETWEEN ALCALIMETRIC TITRATION AND HPLC METHOD FOR THE DETERMINATION OF ALENDRONATE SODIUM

ANA FERREIRA RIBEIRO (PG)1; NÁDIA MARIA VOLPATO (PQ)1

[1] Faculdade de Farmácia – Universidade Federal do Rio de Janeiro.

Introduction: Alendronate sodium is a compound used in the inhibition of osteoclastic resorption. Titrimetry is a simple procedure, compared to HPLC with previous derivatization of the drug, but frequently shows poor specificity to the quantitation of alendronate. Objective: Compare the HPLC method with derivatization and the titrimetric analysis of alendronate in the bulk material. Methods: Three batches of alendronate and a reference substance were derivatized with 9-fluorenylmethylchloroformate (FMOC) and analyzed by reversed phase HPLC with UV detection. Potentiometric titration with NaOH 0.1 mol/L was also used for analysis of all materials. Results: The results are summarized below:

Table 1 – Values of the assay obtained by the two methods studied.

SAMPLE	Potentiometric titration		HPLC with FMOC	
	Assay (%)	RSD (%)	Assay (%)	RSD (%)
ALD-SR	100.41	0.33	99.60*	-
ALD-1	97.78	0.92	91.08	0.73
ALD-2	102.91	0.62	95.58	1.99
ALD-3	109.13	0.21	98.68	1.43

n = 6
* Labeled purity for reference substance (ALD-SR).

Conclusions: The methods presented different results for the materials analyzed. For two samples, HPLC analysis led to very low values for the assay. The lack of specificity of the volumetric method suggests the presence of acid impurities titrated by NaOH.

Financial support: CAPES.
Supervisor: Profª Nadia M. Volpato.

CQ074-EVALUATION MICROBIOLOGICAL, PHYSICAL AND CHEMICAL PARAMETERS IN WATER CONSUMED BY THE POPULATION OF WEST PARANÁ STATE

JANETE A. EVARINI (IC); DENILSON L. SILVA (IC); MÁRCIA L. SOUZA; AJADIR FAZOLO (PQ); FABIANA A. FALCONI (PQ); HELENA T. TAKAHASHI (PQ); SIMONE D. GOMES (PQ)

Unioeste

The potable water concept involves microbiological, physical and chemical parameters, which respect the potability standard and that do not offer health risks (Health Ministry -Brazil, 2004). The present work had the objective of monitoring, in respect to the microbiological and physical-chemical control of the water consumed by the population. Sixty-six samples from February to April 2005 had been analyzed. Total and fecal coliforms were analyzed using Colilert® Technique in cellophane. The methodologies for analysis of Chlorine, Fluoride and Turbidity are described in the Standard Methods For Examination of Water and Wastewater. The results revealed that Total coliforms and *E.coli* were detected in 62% and 21% of the samples respectively. For the physical and chemical parameters, the results revealed that most non-treated samples did not present readings. Some treated samples were above 0,2mg/L, Fluoride above 0,7mg/L and turbidity bellow 1,0NTU. According of microbiological parameters most of samples were in discordance with Brazilian drinking water standards. In relation to the physical and chemical parameters, most samples were in accordance to the Brazilian potability standards.

Financial support: Secretaria de Saúde do Paraná
Supervisores: Ajadir Fazolo; Fabiana André Falconi; Helena Teru Takahashi ; Simone Damasceno Gomes

CQ075-GASTROINTESTINAL TRACT EFFECTS IN MICE USING *BUMELIA SARTORUM* MART. (SAPOTACEAE)

FAUSTO CARNEVALE NETO (IC) HÉRIDA REGINA NUNES SALGADO (PQ)

FCF-UNESP-Araraquara

Bumelia sartorum Mart. (Sapotaceae), known as 'quixaba', is used in folk medicine for the treatment of gastritis, ulcer, and hyperglycemia. The present deals with the characterization of motility intestinal activity in mice of *B. sartorum* bark extract. The ground plant material was extracted by exhaustive percolation with ethanol 70. The supernatants were filtered and evaporated to dryness. The bark extract was reconstituted with sterile water to get 1000 and 2000 mg/mL. After food deprivation (3h) each experimental group was administered orally with different extracts and the control groups received water or loperamide (5mg/kg) by gavage. The distance traveled by the charcoal plug from the pylorus to the ceccum was determined.: The charcoal distance of control, loperamide and 1000 mg/mL and 2000 mg/mL treated groups were 47.79, 31.25, 48.86 and 33.90 cm, respectively. The weights of intestines were 2.42, 2.37, 2.73 and 3.05 g, respectively. The extract did not show significant activity the propulsive movement of intestinal contents in mice ($P < 0.05$). However, it shows increase of intestine weight in treated animals (2000mg/mL) as compared to control mice group. This effect supports the local traditional use of the *B. sartorum* against intestinal disorders.

Financial Support: CNPq, PADC-FCF
Supervisor: Hérida R.N. Salgado

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Cosmetologia / *Cosmetology* (CO)

CO001-STUDY OF THE INFLUENCE OF NACL ON THE SUN PROTECTION FACTOR (SPF) OF AN EMULSION CONTAINING A BLEND OF SUNSCREENS

[1] TATIANI DELICATO(PG); [2] ORLANDO D H SANTOS(PG); [2] PEDRO A ROCHA FILHO(PQ)

[1] FFCLRP-USP;[2] FCFRP-USP

Sun light is composed by radiation with many wavelengths. The ultraviolet radiations (UV) types A and B may cause a lot of harmful effects to the skin, (e.g. erythems, skin cancer). Use of sunscreens became indispensable to reduce these damages. Some environmental factor as seawater or sweat body could interact with the product decreasing its efficiency against radiation, so we must consider the kind of sun protection factor provided. The aim of this work was to evaluate the influence of NaCl addition on the SPF of an emulsion containing UV-A(benzophenone-3) and UV-B(octyl-methoxycinnamate) sunscreens. An in vitro method was used to quantify the SPF based on spectrophotometric readings in the UV-visible region. The obtained results showed a decrease of the emulsion's SPF when the NaCl was added, comparing to the emulsion without NaCl, as expected, when compared with a real situation, where the product is applied and submitted to the influence of seawater or sweat. This is probably due to interaction between ions of NaCl and the screens, changing its solvation. It was concluded that under these conditions the SPF is reduced, decreasing the protection against UV light.

Financial Support: CAPES
Supervisor: Pedro A Rocha Filho

CO002-ANDIROBA OIL/ PHOSPHORIC ESTER INTERACTION: LAMELLAR PHASES FORMATION

FERNANDA FROTA DE ANDRADE (PG)[1]; ORLANDO DAVID HENRIQUE DOS SANTOS (PG)[2]; DANIELA DOS SANTOS MASSON (PG)[2]; PEDRO ALVES DA ROCHA FILHO (PQ)[2]

[1]UNIMEP; [2]FCFRP–USP

In the cosmetic field, studies of ternary systems have been mainly used for two reasons: to achieve cosmetic formulations by using a unique water-surfactant-oil system and to understand physical chemistry aspects. In these systems, the results are graphically represented by a ternary diagram, becoming a useful tool to achieve complex dispersed systems, like emulsions with liquid crystals (LC). These structures can favor the stability and also prolong the release period. The aim of this work was to develop cosmetic formulations employing the phase diagram method, using water, andiroba oil and a self-emulsifying base (SEB), which is composed by cetearyl alcohol, dicetyl phosphate and ceteth-10 phosphate. Stable emulsions with liquid crystals, identified as lamellar, were obtained in specific regions of the ternary diagram. Such emulsions presented high viscosity owing to the nature of the SEB. In another region, dispersions were formed with a wax appearance, presenting several LC structures. Results showed that this ternary system was efficient to attain stable emulsions with lamellar liquid-crystalline phases, which could be used as cosmetic and pharmaceutical vehicle.
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Financial support: CAPES
Supervisor: Pedro A. Rocha Fo.

CO003-USE OF CUTANEOUS BIOENGINEERING TECHNIQUES TO ASSESS THE EFFECTS OF THE *TRITICUM VULGARE* EXTRACT ON SKIN PROPERTIES

MIRELA DONATO GIANETI[1] (IC), PATRÍCIA M. B. G. MAIA CAMPOS[1] (PQ)

(1)Faculdade de Ciências Farmacêuticas de Ribeirão Preto – Universidade de São Paulo

The *Triticum vulgare* extract, which contains high molecular weight proteins with filmogen properties, can be responsible for a skin tightening and instant anti-wrinkle effect and also for a moisture properties that is dependent from vehicle. Thus, the objective of the present study was to evaluate the effects of cosmetic formulations, containing or not *Triticum vulgare* extract, in the water content of the stratum corneum and the transepidermal water loss (TEWL). Two formulations, one emulsion and one gel, were elaborated and supplemented or not with 5% of the studied extract. The methodology consisted of the application of these formulations to the volar forearm of 20 female subjects followed by analysis of water content of the stratum corneum and the TEWL, before and after a single application (1 and 2 hours after the application). The results obtained in this experiment showed that all formulations enhanced skin moisture and reduced TEWL when compared to baseline values. In this experimental conditions, the formulation containing the *Triticum vulgare* extract did not alter significantly the skin moisture and TEWL when compared to the formulation without active substance (vehicle).

Financial support: CNPq
Supervisora: Dra. Patrícia Maria Berardo Gonçalves Maia Campos

CO004-EVALUATION OF DIETHYL AMMONIUM DICLOPHENAC IN GENERIC AND REFERENCE TOPICAL MEDICINES.

PEDRO ALVES DA ROCHA FILHO(PQ) [1],CINTHIA F. ZANATTA(PG)[1]

[1]Departamento de Ciências Farmacêuticas – Faculdade de Ciências Farmacêuticas de Ribeirão Preto – Universidade de São Paulo.

Fluid and semisolid emulsions structured by surfactant mixtures are widely used in pharmacy as vehicles to deliver drugs to the skin. However, this vehicle can influence the bioavailability of a drug in many ways, such as an interaction between the drug and the vehicle, where the latter can alter the former solubility or even its diffusion through the vehicle. The aim of this study was to evaluate the solubility of diethyl ammonium diclophenac in generic and reference emulgel. Emulsions were acquired in drugstores in Ribeirão Preto. Polarized light microscopy was realized before and after solubility tests, which were performed in glycerine, sorbitol and propylenoglycol at proportion of 1:9 (w/w) and in water/alcohol at 100:0; 75:25; 50:50; 25:75 and 0:100 (w/w), pH values were also measured. Solid crystals of diethyl ammonium diclophenac were found in all 3 generic samples. Solid crystals were only absent in ethyl alcohol 100%, but it remained present in all the others solvents. Significant differences were also found in pH values means. In conclusion, differences observed between generic and reference emulsions could affect delivery, absorption and bioavailability.

Supervisor: Pedro A. Rocha Filho

The authors did not follow the modifications suggested by the Scientific Committee

CO005-DETERMINATION OF THE CRITICAL HLB FROM BURITI OIL (*MAURITIA FLEXUOSA*).

CINTHIA F. ZANATTA(PG)[(1)] , PEDRO ALVES DA ROCHA FILHO(PQ) [(1)]

[(1)]Departamento de Ciências Farmacêuticas – Faculdade de Ciências Farmacêuticas de Ribeirão Preto – Universidade de São Paulo.

The Amazon rain forest is very rich in oily plants, representing great economic perspective for the region. High levels of micronutrients, especially antioxidants are commonly found in many of these plants, such as in buriti (*Mauritia flexuosa),* which oil has been frequently applied in cosmetics production. Owing to this properties, emulsions containing buriti oil are not simply a vehicle but also a product that possess a therapeutic or cosmetic activity. The aim of this study was to determinate the critical HLB of buriti oil. Emulsions were prepared by phase inversion temperature method (PIT) using distillated water, buriti oil and a mixture of Span 80 (HBL=4.3) and Tween 80 (HBL= 15.0) as surfactant system. Oil-surfactant mixes were prepared using 10% (%w/w) of oil and varying the concentrations of surfactant. Values of HLB from 5.0 to 14.5 were tested and preliminary stability tests were performed in centrifuge at 1500, 2500 and 3500 rpm per 15 min. Stable emulsions were obtained and remained unaltered after preliminary stability test in centrifuge at HBL value = 7.25.

Supervisor: Pedro Alves da Rocha Filho.

CO006-DEVELOPMENT AND EVALUATION OF LIQUID SOAPS WITH HERBAL EXTRACTS

DANIEL FASOLO (IC)[1]; CRISTIANE KRATZ (PQ)[1]

[1] Universidade Regional Integrada do Alto Uruguai e Missões

Introduction: The use of herbal extracts in the development of cosmetic and personal care formulations have resulted in excellent quality products. The soaps are classified as products of risk degree 1 - minimal risk to the health. However, they stay in direct contact with the skin. So, it is important the evaluation of the stability and security of these products. Objective: To develop liquid soaps formulations – a creamy and a gel base – using herbal extracts with different properties. Methodology: The formulations were submitted to the following stability tests: appearance/color/scent, physical-chemical tests (pH/ice-thaw cycle/vibrational test/final test in centrifuge), foam index, viscosity, skin irritation and the consumer's test. Main results: Both products presented satisfactory results in relation to the accomplished tests. It was observed in the end of studies a small variation in the appearance of the creamy soap (control) and the creamy soap with herbal extract maintained in stove, that did not invalidate the formulations' stability. None of products evoked skin irritation. Conclusions: The products of this work displayed technologically feasible, maintaining the original characteristics. So they showed stable and security for use.

Financial Support: URI/Santo Ângelo
Supervisora: CRISTIANE KRATZ

CO007-EFFECTS OF DIMETHYLAMINOETHANOL (DMAE) ON HAIRLESS MOUSE SKIN

KASSANDRA AZEVEDO TADINI (PG)[1]; LORENA R. GASPAR (PG)[1]; SUSI E. DAL'BELO (PG)[1]; PATRÍCIA M. B. G. MAIA CAMPOS (PQ)[1]

[1]Faculdade de Ciências Farmacêuticas de Ribeirão Preto – Universidade de São Paulo

Dimethylaminoethanol (DMAE) has been often used in topical anti-aging formulations, however there are few scientific studies about its efficacy. So, it is important to conduct scientific studies to assess the benefits of DMAE to the skin and understand its mechanism of action. The aim of the present study was to evaluate the effects of DMAE on hairless mouse skin by histopathological and histometric techniques. For this, formulations containing DMAE or not (vehicle) were applied to the hairless mice dorsum, once a day for seven days and histopathological and histometric evaluations were done. The results showed that the studied formulations enhanced viable epidermis thickness; this effect could be seen when treated regions were compared to the untreated ones (control). However, only the DMAE-supplemented formulation caused an increase on dermal thickness. Furthermore, histopathological evaluation showed that DMAE-containing formulation also induced a significant increase in collagen fibers thickness when compared to the vehicle formulation. Finally, since DMAE provoked changes in dermis, it can be suggested that the DMAE mechanism of action is related to its effects on this skin layer.

Financial Support: CAPES

CO008-A STABILITY EVALUATION OF CREAM WITH GLYCOLIC EXTRACT OF CAJÁ-MANGA (*SPONDIAS LUTEA*).

KAMILA Q. MIGLIOLI(IC)[1]; RAQUEL R. D. MOREIRA(PQ)[1]; HERIDA R. N. SALGADO(PQ)[1]; TATIANA M. SOUZA(PG))[1]; ROSEMEIRE C. L. R. PIETRO(PQ)[1,2]; VERA L. B. I. RANGEL(PQ)[1]

[1]Universidade Estadual Paulista–UNESP; [2]Universidade de Ribeirão Preto–UNAERP

Skin is responsible for our external appearance and its aging stimulates the search for a new cosmetic with antirust activity that retards or improves some acquired characteristics as wrinkles, loss of elasticity and hidratation. The objective of the present work was evaluate the stability of a non-ionic emulsion O/A with glycolic extract of *Spondias lutea* (cajá-manga). This extract obtained by percolation in propyleneglycol was incorporated in the cream and evaluated according to the Guide of Stability (ANVISA). Samples had been submitted to thermal stress and analyzed to its organoleptics and physical-chemistry characteristics in 0, 1, 7, 15, 30, 60 and 90 days. The cream maintained its homogeneity in the Test of Centrifugation, and in the Test of Accelerated Stability it was possible to verify maintenance of pH, viscosity, density and organoleptics characteristics in all samples. However, the concentration of active showed a gradual decrease in elevated temperatures that was higher than in low temperatures. The results showed that the cream was stable and can be used as a antirust cosmetic.

Support: PADC - FCF UNESP CNPq/PIBIC

CO009-EVALUATION OF SKIN HYDRATION OF COSMETICS CONTAINING DIFERENTS OILS OF BRAZILIAN BIODIVERSITY

FLÁVIO BUENO DE CAMARGO JR.[1] (PG); MARIA LAURA COSTANTINI GOMES[1] (PG); GLASIELA LEMOS ANCONI[1] (IC); LORENA R. GASPAR [1] (PG); PATRÍCIA M. B. G. MAIA CAMPOS[1] (PQ)

(1)Faculdade de Ciências Farmacêuticas de Ribeirão Preto – Universidade de São Paulo

Extracts and oils derived of Brazilian Biodiversity have been often applied in research and development of cosmetic products due to their composition and emollient proprieties, which can lead to an enhancement of skin moisture. Thus, the objective of the present study was to evaluate the effects of cosmetic formulations, containing or not 5% of *Mauritia flexuosa* oil or *Bertholletia excelsa* oil or *Passiflora* oil in the water content of the stratum corneum and in the transepidermal water loss (TEWL). The methodology consisted of the application of these formulations on 20 volunteers forearm skin followed by analysis of the moisture content of the epidermis and the TEWL, before and after a single application (1 and 2 hours after the application). The results obtained in this experiment showed that all formulations enhanced skin moisture when compared to baseline values. However, the formulation containing the oils under study did not alter significantly the skin moisture and when compared to the formulation without active substance (vehicle). TEWL were not altered with the application of the formulations under study.

Supervisor: Profa. Dra. Patrícia Maria Berardo Gonçalves Maia Campos

CO010 - EVALUATION OF ELETROSTATIC STABILITY OF VEGETABLE OIL EMULSIONS WITH LIQUID CRYSTAL

ORLANDO DAVID HENRIQUE DOS SANTOS (PG), PRISCILA DORIGÃO YUVAMOTO(IC), PEDRO ALVES DA ROCHA FILHO(PQ)

Departamento de Ciências Farmacêuticas – FCFRP-USP

The Latin-American biodiversity provides a great source of raw materials to pharmaceutical and cosmetic industry. A good choice is to use oils extracted from them, which are composed by different kinds of ethers of fatty acids and glycerol and some actives carried out by the oil. Emulsion as a vehicle has some advantages as decrease the oily feel and the option of add different actives on both phases. Liquid crystals provide an increased stability through of the formation of a physical barrier into the external phase, but it has a small influence on the electrostatic mechanism. In this work we evaluated the influence of changing the oil phase on the zeta potential of O/W emulsions. They were prepared with oils of Andiroba, Avocado, Apricot, Brazil Nut, Buriti, Cupuaçu, Marigold, Passion Fruit, Pequi and mineral. Results shown that for all emulsions values of zeta potential were on the region of intermediate stability with only small variations among the samples. This demonstrates that the liquid crystal formation was the main responsible for the stability of these emulsions, being very useful to the development of products with these oils.

Financial Support: Capes
Supervisor: Pedro Alves da Rocha Filho

CO011-CHEMICAL STABILITY OF COMMERCIAL EXTRACT OF EXOTIC BRAZILIAN PLANTS IN TOPICAL FORMULATION

CAROLINA PENTEADO MORAES MACIEL[1](IC); ANDRÉ ROLIM BABY[1](PG); VIVIAN ZAGUE[1](PG); TÂNIA OISHI[1](IC); DEBORAH NISHIKAWA[1](IC); DIEGO DE ALMEIDA SILVA[1](IC); CLAUDINÉIA SALES DE OLIVEIRA PINTO[1](PQ); VERA LUCIA BORGES ISAAC RANGEL[2](PQ); TELMA MARY KANEKO[1](PQ); MARIA VALÉRIA ROBLES VELASCO[1](PQ)

[1]School of Pharmaceutical Sciences, University of São Paulo
[2]School of Pharmaceutical Sciences, UNESP, Araraquara

Introduction: Flavonoids are potent antioxidants and, when incorporated in formulations, those substances must present adequate stability. Objective: This research evaluated the chemical stability of *Trichilia catigua* (and) *Ptychopetalum olacoides* extract as raw material and added into a topical formulation by accelerated stability test. Methods: Extract and topical formulation containing it at 5% w/w were stored at different temperatures during 30 days. Chemical stability was assessed with flavonoids quantification by spectrophotometry. Results: Flavonoids from extract and from topical formulation have reduced more intensively at 40.0 ºC (17.6%) and the storage at low temperatures has provided reduction of flavonoids lesser than 8.9%. Conclusions: The chemical stability of the commercial extract has not been altered by the topical formulation at the storage conditions employed.

Financial support: CNPq, PIBIC
Supervisora: Dr.ª Maria Valéria Robles Velasco

The authors did not follow the modifications suggested by the Scientific Committee

CO012-DEVELOPMENT OF O/W EMULSION WITH CUPUAÇU BUTTER CONTAINING LÍQUID CRYSTAL BY THE HLB SYSTEM.

(1)KAUÊ P. BOOCK (PG); (1)JACQUELINE M. DE MORAIS (PG); (1)DANIELA S. MASSON (PG); (1)ORLANDO D. H. SANTOS (PG); (1)PEDRO A. ROCHA FILHO (PQ)

(1) DCF– FCFRP / USP

O/W emulsion with liquid crystals (LC) is a complex system for delivery of actives into/across the skin since LC modulate this delivery, increase stability and solubility of slightly soluble substances in oily or aqueous phase and also support the skin moinsturization by decreasing the Transepidermal Water Loss (TEWL). The development of emulsions with vegetable oils is growing each day more considering that, natural raw materials are more compatible with the human organism and there are lots of unexplored materials provided by the Rain Forest. In this work, emulsions were developed with Cupuaçu (*Theobroma grandiflorum*) butter as the oily phase. The choice for the HLB system was made for the selection of the emulsifying agents in order to determine the best ratio in the total amount for a perfectly stable emulsion. The required HLB value for the Cupuaçu butter was established using Span 80 and Tween 80. In a second step, other surfactants were mixed to investigate the presence of Liquid Crystals. It was concluded that the HLB required by the Cupuaçu butter equals 7.6 and all surfactants associations containing ceteth-2, steareth-2, ceteareth-5, ceteth-10 and ceteareth-20, presented LC.

Supervisor: Dr. Pedro A. Rocha Filho.

CO013-CLINICAL EVALUATION OF COSMETIC FORMULATIONS CONTAINING A COMBINATION OF BIOFLAVONOIDS AND VITAMINS A, C AND E

MARINA MILENA DA SILVA (1) (IC); PATRÍCIA M. B. G. MAIA CAMPOS (1) (PQ)

(1) FCFRP – USP

Some vitamins and botanical extracts have antioxidant and moisturizing properties and consequently can protect the skin from oxidative stress and water loss (TEWL) provoked by environment factors. A new tendency in cosmetic products has been the association of active substances, i.e. vegetal extracts and vitamins, to improve skin conditions. The aim of this study was the clinical evaluation of cosmetic formulations containing a combination of bioflavonoids and vitamins A, C and E in human skin. For this purpose, formulations containing or not 5 % of associated of bioflavonoids, vitamins A (retinyl palmitate), E (tocopheryl acetate) and C (ascorbyl tetraisopalmitate) were applied to the volar forearm of twenty two female subjects. Skin conditions in terms of water content of the stratum corneum and of TEWL were analysed before and after 1 and 2 hours of a single application. The results showed that the formulations studied acted on skin decreasing the TEWL and enhancing the water content of the stratum corneum significantly when compared to the control. Therefore, both formulations studied improved skin moisture but this effect was more evident with the formulation containing a combination of active substances studied.

Financial support: CNPq
Supervisora: Patrícia M. B. G. Maia Campos

CO014-INFLUENCE OF PROCESSING CONDITIONS IN THE ADDITION OF KOJIC ACID IN O/W EMULSIONS CONTAINING NON-IONIC SELF-EMULSIFYING BASE

DANIELA S MASSON (PG)[1]; ORLANDO D H SANTOS (PG) [1]; ROCHA-FILHO, PA (PQ) [1]

[1]DCF - FCFRP/USP

Kojic Acid (KA) has been commonly used as a skin-depigmenting agent and according to many authors can easily be added in gels, cream-gels and emulsions due to its water solubility. However, in the development of nonionic emulsions containing self-emulsifying base we noted that manufacturing conditions can influence in its physical stability.
The aim of this work was to evaluate the influence of processing conditions in addition of KA in O/W emulsions. Three primary emulsions (without acid) were developed, each one with a different humectant, and the influence of resting time was analyzed. Resting time of 24, 48, 72 hours and 7 days were analyzed. After each period KA was added in emulsions and afterwards centrifuged, polarized light microscopy and pH values.
Results showed that physically stable emulsions were attained by adding KA after 48 hours of resting time from primary emulsions preparation. The addition of humectants presented no influence in physical characteristics and all formulations showed lamellar liquid crystalline phase formation and adequate pH values.
In conclusion, this kind of system must be probably structured before KA addition and in this way, the stability of final product can be improved.

Financial Support: CAPES
Supervisor: Pedro A Rocha Filho

CO015 - SYNTHESIS OF DERIVATIVE MOLECULES OF RUTIN AS A POTENTIAL FOR SUN PROTECTION FACTOR (SFP)

LEANDRA DE CÁSSIA BERNUSSO (PG); CARLA APARECIDA PEDRIALI (PG); KARINE GARGIONI (PG); KARINA HONDA ADATI (PG); LAURA TEIXEIRA ALVES AFFONSO (IC); BRONISLAW POLAKIEWICZ (PQ).

Universidade de São Paulo - Faculdade de Ciências Farmacêuticas - Departamento de Tecnologia Bioquímico-Farmacêutica

Background: Acute as well as chronic sun exposure induce biologically damaging effects on skin, including photo ageing and cancer. Ultraviolet UVA and UVB radiation are involved in this process. Sunscreens preparations generally contain organic ultraviolet filters and they are substances composed by complexes molecules, like derivatives of rutin. Therefore, these molecules provide efficient and stable protection against UVA and UVB radiation. Objectives: This study aims the synthesis of derivative molecules of rutin with sun protection factor (SFP) for applications in cosmetics sun care products. Methods: The methods proposed in this work were based on the synthesis of derivative of esters of rutin. Assays of solubility, capillary electrophoresis, infrared (IR), Nuclear Magnetic Resonance (NMR) and spectral transmittance at UV range from 200nm to 400nm of the samples were done. Results: The derivatives of rutin showed spectrum of protection in the 260-360nm range. Conclusion: The results of the derivatives solubility showed promising dates related to UVA and UVB absorption radiation. Considering the results, derivatives of rutin offer an alternative to sunscreens products and cosmetics sun care products.

Financial Support: CAPES
Main lider: Bronislaw Polakiewicz

CO016 - COSMETIC HOMEMADE FORMULAS IN POPULAR MAGAZINES

ADRIANO FRANZONI WAGNER (IC) [(1)]; LUCIANA LEHMKUHL VALENTE (PG) [(1)]; CÉLIA MARIA TEIXEIRA CAMPOS (PQ) [(1)]

[(1)] Federal University of Santa Catarina

Introduction. Cosmetics are developed products to guarantee a good appearance and the welfare of the skin. Currently, there are different cosmetics forms and technological innovations to satisfy the necessities of the consumer. Even tough there are beauty hints for skin and hair cares based on natural ingredients that are easily found in magazines that manipulate homemade cosmetics. Objective. By virtue of the frequent absence of benefits and side effects caused by the inadequate use of these ¨natural cosmetics´, this work had as an aim to evaluate homemade prescriptions widespread in popular magazines. Methodology. There have been analyzed 15 magazines with different editions in the period of February to April/2005. Results. From 135 found prescriptions 82% contained fruit, 9% vegetables, 5% daily products, 13% others. Just 21% alerted for cares in the application and the responsible professionals not informed 62%. Conclusions. Although the use of homemade cosmetics is easier and cheaper, the gotten result can not be reached, beyond inconveniences such as: burnings, spots, injuries and allergy. These types of cosmetics do not offer any clinical security and guarantee effectiveness.

Supervisor: Célia Maria Teixeira Campos

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EV001-MEDICATION ERRORS IN A PUBLIC AND A PRIVATE HOSPITAL

LINDEMBERG A. COSTA (PG)[1]; SEBASTIÃO LOUREIRO (PQ)[2]; MÁRCIO G G DE OLIVEIRA (PG) [3]

[1] Faculdade de Farmácia / Ufba [2] ISC/Ufba [3] HUPES/Ufba

INTRODUCTION: in the last decade we have seen a growth in the interest about health system safety, especially about medication safety. The medication errors comprises: prescription, dispensing and administration errors. OBJECTIVE: to assess the medication error in a public and in a private hospital. METHODS: Cross-sectional 638 doses were assessed to opportunities for errors (doses + unordered doses) in a public and in a private hospital in Salvador, Bahia, Brazil in January, 2005.The error rate was calculated by the following equation: number of doses/error opportunities. The errors were classified according to the categories: omission, unordered dose, extra-dose, wrong dose, wrong route, wrong form, wrong time, wrong technique. RESULTS: Out of 638 error opportunities, 209 (32,9%) were in error, and 430 (67,4%) correct. When "wrong time error" was excluded this rate diminished to 156 (25%). Unordered doses (13,2% vs 6,2%; $p< 0,004$) and wrong time (5,8% vs 11,7%) error rates differed, for public and private hospitals, respectively. CONCLUSIONS: the public hospital showed a double-fold unordered dose error rate as compared to the private hospital. Inversely, the private hospital showed a double-fold wrong time error rate than the public hospital.

Supervisor: Sebastião Loureiro

EV002-MEDICINES ADVERTISING MATERIAL ANALYSIS ABOUT LEGISLATION AND ETHICAL PRINCIPLES

BRUNA CAROLINA PIMENTEL(IC)[1]; FRANCISCO DE PAULA GARCIA CARAVANTE JR(PQ)[1]

[1]Fundação Hermínio Ometto "Uniararas".

The concern with the possibility of medicines causes damage to the pacients is quite old. The most complete describe about adverse reaction was made by Withering in 1785,when he related the digitalic intoxication. Advertising may influence physicians practices, particularly about prescribing. In agreement with WHO the ethical criteria related with the advertising drug, include the respect about sanitary legislation, true and up date information, the information absence that take to misleading interpretations, over the clear necessity it garanty total legible add. In Brazil the Agency National of Vigilance Sanitary, published in 2000 RDC n° 102, the drugs publicity´s regulations. In that sence, was collected advertising material between 2003 and 2004, especially to drugstore and public no expert with intention to access the agreement to legislation and respect about the ethical principles addressed by WHO. In the total of 58 advertising only 3,5% respect the legislation, while 59,0% presented among 1 and 3 divergence, and 62,0% presented some ethical conflict under the point of view to induce drugs consumption. The analyses suggest that there is instant ethical and legal desrespect, in the aspects linked by clearly and legibility about information, and absent information, about companies addresses, and it induce self medication.

Supervisor: Francisco de Paula Garcia Caravante Jr.

EV003-USE OF GLYCOPEPTIDES BY INPATIENTS OF A PUBLIC HOSPITAL

MARIA INÊS DE TOLEDO(PQ)[1,2]; LÍVIA LUIZE MARENGO(IC)[2]; JAQUELINE ALVES SEBASTIÃO(IC)[2]; CELSO NAKAGAWA(PQ)[1]; EDUARDO LEITE CROCO(PQ)[1]

[1]Conjunto Hospitalar de Sorocaba (CHS); [2]Universidade de Sorocaba (UNISO)

Introduction: Given the increased rates of antimicrobial resistance of Gram-positive cocci, and the increase in glycopeptide consumption, surveillance of this group of drugs has been recommended. Objective: The purpose of this study was to review the use of glycopeptides in a public hospital. Methodology: The investigation was conducted at CHS, a public hospital in Sorocaba, SP, Brazil. Data on antimicrobial order forms issued from March 2004 to February 2005 were supplied as an Excel spreadsheet by the hospital's Service for Nosocomial Infection Control (SNIC). Results: Of the drug orders analyzed, 401 were requests for vancomycin for 363 patients, that 33% had renal insufficiency and 24 were for teicoplanin for 22 patients, that 41% had renal insufficiency. The hospital's SNIC inform that roughly 40% of the infectious agents isolated were staphylococci, with *Sthaphylococcus aureus* accounting 60% of this group. Conclusion: Characterization of the sensitivity profiles of these bacteria and identification of occurrences of oxacillin-resistan, *S. aureus* strains expected an important contribution to the rational use of antimicrobials in this hospital.

Financial Support: UNISO
Supervisora: Maria Inês de Toledo

EV004-TOXOCOMONITORING IN THE TOXOCOLOGY LABORATORY OF STATE UNIVERSITY OF MARINGÁ (UEM), 2004

JULIANA GALDEANO DIAS(IC)[1]; MARCIO ADRIANO FERNANDES(IC)[1] ; MIGUEL MACHINSKI JUNIOR(PG)[1]

[1]UEM

Introduction: The Toxicology Laboratory (LAT) through the education project " the contribution of Laboratory of Toxicological Analyses in the poisoning notification carries out a toxicological monitoring service joined to Maringá Controlling Center of Poisoning (CCI-Maringá), when notifying the poisoning suspicious in Maringá and region. Objective: This work aims to characteriza the patients whose resulted examinations have been suspected of poisoning. At the beginning a survey of probable cases of poisoning through the Lat examination controlling files were carried out. Methodology: The patients were obtained through phone calls in exemplification of the cases. After being contacted, Toxicological Occurrence Filing had been obtained and those have been duly directed to CCI. Results: LAT observed 685 patients in this period, 256 (37,4%) has been shown poisoning suspicious. Male has been stood out with 67.2%. The most attacked age group has been from 30 to 39 years old with 20,3% of the cases. The examination the most caused poisoning suspicious has been the cyclosporin therapeutical monitoring (35,5%). Conclusions: The result shows the notification importance of poisoning probable cases observed at LAT in order to provide epidemiological subsides.

Supervisor: Miguel Machinski Junior

The authors did not follow the Scientific Committee's suggestion for an English language review

EV005-A COMPARATIVE STUDY OF USES OF 17 MEDICINAL PLANTS ACCORDING TO THE SCIENTIFIC LITERATURE

DANIEL M IFTODA(IC)[1];POLLYANNA TAMASCIA(IC)[1];ANELISE BRAGGION(IC)[1];HENRIQUE K UTSUNOMIYA(IC)[1];MARIANGELA MORIYA(IC)[1];FABIANA K OLIVEIRA(IC)[1] MARIA A UETUKI(IC)[1];ROSIVALDO ROCHA(IC)[1];DIEDY GAZOTTO(IC)[1];RENATA A FALIVENE(IC)[1];MARIANA GAVA(IC)[1].

[1]Universidade Metodista de Piracicaba

[Introduction]The use of medicinal plants in medicines has steadly increased over the years, but in many cases their uses and indications are still done on an emphirical basis, without proper and controlled clinical studies. [Objectives]The aim of this study is to select some of the most used phytotherapic products and compare the manufacturer´s claims against data from clinical studies.[Methods]Survey on scientific databases to find out clinical and pre-clinical studies about the effects of the plants used in those products.[Results]A total of 117 products have been analyzed. It has been found that 80% of those 17 plants who compounds those products have no more than 3 published studies each. Furthermore, 35 of those products are not even registered with ANVISA.[Conclusion] The old legislation allows that many products have been commercialized without controlled clinical studies. However, a new resolution (RDC48/04) states that those products must comply with the new legislation within a 10 year period. That must include controlled clinical studies in order to be registered.

Supervisor: Prof.Dr.Luciane Cruz Lopes

EV006-EVALUATION OF TWO ANTI-RETROVIRAL DISPENSER SERVICE PROFILE OF RIBEIRÃO PRETO, SP

REGINA C.G. ANDRADE[1,2]; MÍRIAM A. MORAIS[1]; LÚCIA H.T. R. PEREIRA[1]

Municipal Health Service of Ribeirão Preto[1]; Faculty of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo[2]

The availability and accessibility of antiretroviral (ARV) treatment for HIV is a pledge took on Brazil Ministry of Health that can improve the quality of life of people that live with HIV/AIDS. The objective of this work was to evaluate the ARV consume, the predominant therapeutic scheme and to determine the user sex and age in two adults dispenser services in Ribeirão Preto, Testing and Counseling Center Alexander Fleming (S1) and Basic Health Unit Sumarezinho (S2). The dates were obtained from the informatized system of medicine delivery of Ribeirão Preto health services, in 2005 march. The results showed that the predominant therapeutic scheme in two services include 2 nucleoside analogs and 1 non-nucleoside, 69% in S1 and 53% in S2, a recommended by WHO regimen. The average consume is 5 tablet/day/person, cost of R$ 296,00/month/person in S1 and 6,6 tablet/day/person, cost of R$ 486,00/month/person in S2. The men are predominant in both services, 61% in S1 and 56% in S2, and the majority has among 31 and 40 years old, 48% in S1 and 56% in S2. We wait that our results may to aid the Ribeirão Preto HIV/AIDS program in the planning, monitoring and evaluation and counseling for prevention and adherence.

EV007-ADVERSE REACTIONS BY THE USE OF LOPINAVIR/RITONAVIR AT INSTITUTO ESTADUAL DE INFECTOLOGIA SÃO SEBASTIÃO : A PRELIMINARY STUDY

FABIANE R. FERREIRA (PQ) (1) ;TERESINHA GOULART(PG)(1);GABRIELA MOSEGUI (PG)(1)

(1) Faculdade de Farmácia – Universidade Estácio de Sá

Introduction: The development of new drugs must be followed by proceedings in order to guarantee the safety profile by the use of these medicines. That is the main purpose of pharmaco surveillance. Objective: Detect the most common adverse reactions by the use of Lopinavir/Ritonavir, a protease inhibitor of HIV, used on AIDS treatment. Methodology: An interview conducted with 30 patients listed under the IEISS and their handbooks. Results: Diarrheas (88%), headaches (75%) and the dyslipidemias (42%) that were separated in lipodistrophy (71%) and increase of glucose levels (23%). Conclusion: Although diarrheas and headaches would have been caused by another agents, the high prevalency detected suggest the straight relation with the medicine. Dyslipidemias were linked with the treatment trough the observation of glucose levels and triglyceride taxes before and after the begin of therapy. Lipodistrophy could compromise adhesion on treatment, increase risk of myocardial infarction and induce diabetes type 2. Pharmaco surveillance arise to guarantee the rational use of medicine and assure an efficient pharmaceutical assistance.

Financial Support: Secretaria de Saúde do Estado do Rio de Janeiro
Supervisora: Teresinha Goulart

The authors did not follow the Scientific Committee's suggestion for an English language review

EV008-ANAPHILAXIS DECURRENT OF THE USE OF METAMIZOLE.

KÉSIA GEMIMA PAMA RIGO[1] (PQ); LÍGIA NAVES GODOI DE CASTRO[1] (PQ); CRISTIANE EMI SUGIURA[1] (PQ); MICHELLE CAROLINE ESTEVAN[3] (PQ); WALDEREZ PENTEADO GAETTI FRANCO (PQ)[1]; PAULA NISHIYAMA[1] (PQ).

[1] State University of Maringá – Paraná.

INTRODUTION: The metamizole is a painkiller and antipyretic derivative of pyrazolone very used in Brazil. Its safety has been questioned, mainly for relating to serious adverse drug events. OBJECTIVE: This report describes the occurrence of an anaphylaxis in one puerpera that was medicated with metamizole. CASE REPORT: A.D. 20-year-old, had to have a caesarean and three hours later, she reported pain in abdominal region and was medicated with metamizole. After the medication, she developed redness in the left superior member, pruritus, no palpable pulse, hypotension, piloerection, formigation and glottis edema. She was medicated with ephedrine, hydrocortisone, dexametasone; oxygen and physiological serum were administered. The medicine was substituted by paracetamol and the patient improved. CONCLUSION: The anaphylaxis is a feared complication due to its fast onset and unexpected nature, with a high morbidity and mortality rates. This report demonstrates the importance of a good anamnesis before using any medicine, to prevent adverse drug reaction.

Supervisor: Paula Nishiyama

EV009-A TREATMENT AND EPIDEMIOLOGICAL STUDY OF BACTERIAL ENTERITIS IN PRIMATES OF THE CALLITHRIX GENDER CAUSED BY THE INGESTION OF POLLUTED WATER

WELLIGTON DE MATTOS SANTUSSI (PG)[(1)]

[(1)]Unip – São Paulo University campus Araçatuba

This study deals with an occasional bacterial infection in primates of the Callithrix gender caused by the ingestion of polluted water. A hundred ten (110) animals were involved in this research. Our main aim is to describe and compare the clinical effectiveness among different antibiotics for the treatment of this enteritis. The infected animals were divided in groups that received orally different kinds of antibiotics [sulfametoxazol 40mg/Kg/day + trimetropin 8mg/Kg/day (SMZ+TM), ciprofloxacin 15mg/Kg/day (CFX) and nalidixic acid 55mg/Kg/day (ANX)] during 7 days. We have observed that this protocol has resulted in 80% of deaths in the group treated with CFX, 30% of deaths in the group treated with SMZ+TM, 18% of deaths in the group treated with ANX. It is important to observe that the animals that have received CFX regurgitated the medicine soon after the ingestion probably due to the unpleasant flavor. The obtained results suggest that the ANX was the one that presented the largest acceptance among the animals and the best cost/benefit relationship. The dose adjustment was made based on the pediatric reference.

Financial support: UNIP - São Paulo University
Supervisora: Profa. Dra. Roseli A.C. Biondo

EV010-IMPLEMENTATION OF THE FARMACO-VIGILANCE PROJECT'S IN THE MATERNIDADE ESCOLA JANUÁRIO CICCO, UFRN.

TAYNE ANDERSON CORTEZ DANTAS-PG[1]; ELAINE CRISTINA ALVES-PG[1]; TATIANA XAVIER DA COSTA-PG[1]; GIOVANNA RODRIGUES DE ARAÚJO-IC[2]; IDYLLA SILVA TAVARES-IC[2]

[1]Pharmacist MEJC - UFRN; [2]Trainee MEJC - UFRN

Introduction: The ANVISA defines the "Farmaco-vigilance" as being a science relating to a detection, evaluation, comprehension and prevention of the adverse reactions or any problems related to medicines. The notification of RAM could be made by users of the medicines and/or through the active search of RAM, made by the qualified healthy professional. Therefore the actual sub-notification of RAM shows the importance of the Farmaco-vigilance in the accompanying of the use of medicines by the patients of the MEJC, becoming a determinant notification in the corrections of errors or even in the remotion from the market of products and bad services (bad care). Methodology: It has been done a week of sensitiveness of the clinic body and the nursing, showing the importance of the voluntary notification. Results and Conclusions: It has been done, a explanation and a conscientious campaign to the MEJC target people, which became more vigilant relating to the RAM detection and the promotion of a continued study over the standardization of the medicines in this institution and the support to the "Hospitais Sentinelas" Project (ANVISA).

Supervisor: Tayne Anderson Cortez Dantas

The authors did not follow the Scientific Committee's suggestion for an English language review

EV011-EVALUATION OF ELDERLY DRUGS PRESCRIPTIONS IN A NURSING HOME IN FORTALEZA-CE

WIVIANY THAISE L. MENDES(PG); MILIAN D. SOARES(IC); PAULO SÉRGIO D. ARRAIS(PQ)

Mestrado em Ciências Farmacêuticas/UFC

INTRODUCTION: The elderly are particularly vulnerable to diseases and use of multiple drugs, consequently, they are more exposed to problems involving drugs. OBJECTIVE: To evaluate the quality of drug use among elderly living in a nursing home in Fortaleza. METHODS: with a standardized and tested formulary, were obtained the sex and age of the elderly, the drugs prescribed and their dosing information. The prescriptions were evaluated considering combination in a fixed amount, essentiality, potential pharmacological interaction and pharmacotherapy redundancy. RESULTS AND CONCLUSION: 138 elderly were inquired, presenting a mean age of 73.37 years old. 50.3% were females. 57.3% of the elderly used 3 or more drugs (μ=2.8), 40.6% presented potential drug interactions and 2.2% presented pharmacotherapy redundancy. 387 pharmaceutical specialties were detected; 5.7% of those specialties were in fixed amounts and 70% were essential. Thus, a correct prescription evaluation presents itself as an important strategy in promoting the Pharmaceutical Assistance to the elderly in that nursing home.

Financial support: CAPES, PIBIC/CNPQ
Supervisor: Paulo Sérgio Dourado Arrais

EV012-TREATMENT OF CHAGAS DISEASE (DC) PATIENTS WITH BENZONIDAZOL (BZ) AND ADVERSE EVENTS(AE): A FOLLOW-UP STUDY IN AMBULATORIAL CARE IN FORTALEZA-BRAZIL

VÂNIA MARIA PONTES (PG)[1]; MARCONDES TAVARES CRUZ (PQ)[2]; HELENA LUTÉSCIA COELHO (PQ)[1]; LUCIANA COSTA MENEZES (IC)[1]; IVO CASTELO BRANCO COELHO (PQ)[3]; MARIA DE FÁTIMA OLIVEIRA [1]

[1]Mestrado de Ciências Farmacêuticas -UFC; [2]HC-UFC; [3]NMT-UFC

Introduction: BZ is the only drug being used in Brazil for CD disease treatment. AE are a limiting factor to the complete treatment. Objective: To study prospectively the incidence of AE in CD patients treated with BZ to identify points for pharmaceutical care interventions. Methodology: Ten patients with indeterminate form of human chronic CD were followed up until the end of the 60 days of BZ treatment. Clinical examination and laboratorial tests were performed and AE were registered by the patients on a specific formulary at home. Patients were interviewed by the pharmacist at least 3 times during the study. Main Results: Patients were 30-40 years old, 62,5 %males and rural origin 100%. BZ treatment was stopped in two cases because serious AE. In one case transitory anemia, leucopenia and trombocitopenia was observed. Cutaneous reactions, muscular weakness, articular pain and numbness on the extremities were frequent. Conclusion: AE are frequent in patients treated with BZ. Pharmaceutical care can help patients to deal with these problems contributing for better clinical results.

Supervisora: Maria de Fátima Oliveira

The authors did not follow the Scientific Committee's suggestion for an English language review

EV013-THE ADHERENCE OF MENTALLY ILL PERSONS TO PSYCHOPHARMACOLOGICAL TREATMENT.

LUCILENECARDOSO(PG) [(1)]; SUELI APARECIDA FRARI GALERA (PQ) [(1)].

(1) University of São Paulo at Ribeirão Preto College of Nursing.

Introduction: Adherence to pharmacological treatment is a determinant factor in the aggravation of chronic illnesses and is closely related to relapses. Objective: In this literature review, we aimed to identify the main contents related to mental patients' adherence to psychopharmacological treatment. Method: A bibliographical review in Medline and Pubmed with adherence, schizophrenia and anti-psychotic medication as key words. Results: 52 papers were selected. Most of them (73 %) aimed to identify the factors that could influence the adherence to the treatments. The remaining 27% of the selected papers tried to assess professional interventions' influence on adherence.Conclusion: The main adherence-related factors referred to patients, medication type and social factors. With respect to interventions, we observed that combinations of educational and behavioral strategies are more efficient.

Financial Support: CAPES
Supervisora: Prof ª. Dr ª. Sueli Aparecida Frari Galera.

EV014-INTENSIVE MONITORING OF ADVERSE REACTION TO OXACILLIN IN PATIENTS HOSPITALIZED IN FORTALEZA/CE.

MARIANA O. BRIZENO DE SOUZA(PQ)[1]; HANNAH IORIO DIAS(IC)[2]; MARTA CUNHA C. PINHEIRO(PG)[1]; MARTA DE FRANÇA FONTELES(PQ)[1]; HELENA LUTÉSCIA COELHO(PQ)[1]

[1]Post Graduation in Pharmaceutical Science/Federal University of Ceará(UFC);
[2]Pharmacy Course/UFC

Introduction:The large use of oxacillin in Brazil and the high frequency or adverse reactions observed justifies this investigation. Objective: To know the incidence of adverse reactions to oxacilin (ARO) and to identify risk factors associated. Methodology: Follow up of hospitalized patients in use of oxacillin in a public hospital, register of suspected adverse reactions, analisys regarding the imputability, severity and type of reaction. Results: 76 patients with an avarage age of 35; 56,6 %male, were folowed up (2463 patient-days). The accumulated incidence of ARO was 31.6%, the most frequent reactions were: increase of transaminases (22,1%), fever (17,0%) and rash (13,6%). In terms of imputability the reactions were considered Probable (44,1%) and Moderate (66,1%); the major part was type B reactions (86,4%) probably hipersensibility. ARO was more frequent among patients up to 14 years (P=0,0159/RR=2,22) and adverse reaction to other drugs also were more frequent between patients with ARO (P=0,0036 R = 2,66). Conclusion:The cautious administration of oxacillin is recommended in children and in patients with hipersensibility to other drugs.

Supervisor**:** Profa Dra Marta Maria de França Fonteles

EV015-LACK OF PRESCRIBING INFORMATION TO RATIONAL DRUG USE AT A BRAZILIAN TEACHING HOSPITAL.

JOICE MARA CRUCIOL-SOUZA (PQ)[1]; MARLI CARLETTO (PG) [1]; DOUGLAS GODOY CATISTI (IC)[1]; GUSTAVO HENRIQUE ANTONIETTI (IC)[1]

[1]Universidade Estadual de Londrina – UEL; Depto Tecnologia de Alimentos e Medicamentos – TAM/CCA

Introduction: Prescription order is the origin of drug utilization practices. Rational Drug Use means complete prescription order to the right patient. Objectives: This work intended to identify prescription order quality of information at a Brazilian teaching hospital. Methods: Random sampling of 1785 prescription orders from adult wards (1027; 60% male) during 4 months period in 2004. EpiInfo statistics. Study approved by Ethic Committee. Results: Patient identification was incomplete in 210 (12%) prescriptions. Prescriber information were not presented in 205 (12%) prescriptions. Drug information and instructions to use were not clear in 941 (55,2%). Dosage unit was missing in 353 (21%) orders. Time between doses were not specified in 159 (9,3%) prescriptions. At least one medicine prescribed "as need" was found in 1551 (91%) orders. Discussion and Conclusions: Lack of prescribing information may lead to wrong drug use. It may delay actions and pharmacy services. Systems for safety use of drugs there must be implemented, as well as pharmaceutical care does. This study promotes rational drug use through knowledge of drug problems.

Supervisor**:** Joice Mara Cruciol-Souza

EV016-BACTERIAL CULTURES AND THERAPEUTIC PROFILE OF ACUTE BACTERIAL MENINGITIS: CONTRIBUTION OF VIGILANCE PHARMACEUTICAL IN SERVICES.

AURIGENA FERREIRA (PG)[12]; KARLA QUEIROZ (PG)[3]; KERGINALDO TORRES (PG)[1]; GERLANE COELHO BERNARDO GUERRA (PG)[1]; MARIA ALVES (PG)[4]

[1]Departamento de Biofísica e Farmacologia da UFRN
[2]Supervisor: Aurigena Antunes de Araújo
[3]Doutoranda pelo Programa de Pós-graduação em Biologia Celular e Molecular pela USP
[4]Programa de Pós-graduação em Ciências da Saúde

Objective: The goal of this study is to identify the bacteria species and antibiotics used in Acute Bacterial Meningitis. Metodology: Treatment in patients treated at the Giselda Trigueiro Hospital in Natal, RN, Brazil. The hospital records indicated that 243 in-patients were underwent to treatment during the period from 2000 to 2002 . The data is analyzed by percent frequency and for the associations between the most utilized antibiotics, Chi-squared Test is applied with a significance level of 5%. Results: A reduction in the prevalence of Haemophilus influenzae is observed among individuals aged equal or less than 5 years. In the 6 to 14, 15 to 25 and over 26 year age groups Neisseria meningitidis is prevalent. The individuals up to 1 years old use of ceftriaxone, isolated or associated with oxacillin or ampicillin. The individuals from 2 to 5 years use ampicillin with ceftriaxone or cloranfenicol. The individuals from 15 to 25 years and over 26 years ampicillin predominated. The individuals from 6 to 14 age group the association of ampicillin with rifampycin prevailed. Conclusion: The study calls attention for the large quantity of undetermined bacterial cultures which suggests the necessity for more accurate methods of diagnosis.

Supervisor: Aurigena Antunes de Araújo Ferreira

EV017-FACTORS ASSOCIATED TO PAINFUL SYMPTOMATOLOGY IN PATIENTS WITH CHRONIC PAIN TREATED AT A PAIN UNIT – A STUDY ON DRUG PRESCRIBING

GERLANE COELHO BERNARDO GUERRA [(1)] (PQ); AURIGENA ANTUNES DE ARAUJO FERREIRA (PQ) [(1)]; NEÍSA ARAUJO DE MOURA (IC); WADKLÉIA ALVES SARAIVA (IC).

[1]Universidade do Rio Grande do Norte

INTRODUCTION: The effectiveness of treatment and follow-up depend on the assessment and measurement of pain in a reliable and competent manner. OBJECTIVES: Investigate the factors related to painful symptomatology and assess drug prescribing in patients with chronic pain at a pain unit. METHODS: The study was an analytic and transversal type with a sample consisting of patients with chronic pain, treated at a pain unit. Data were collected regarding socio-demographic variables and drug prescribing. The individuals were assessed using McGill Pain Questionnaire and Wisconsin Brief Pain Questionnaire. RESULTS: 40% of the patients reported unbearable pain, 60% described the pain as severe and 10% felt moderate pain. The majority patients that to frequented the unity pain to possessed variety types of cancer. Through Pearson's correlation test, the association of pain intensity and daily activities was verified, showing that there is a correlation for mood, walking and work. CONCLUSION: For pain of oncologic origin, the most prescribed drug was morphine while for non-oncologic pain gabapentin and amitriptilyne predominated.

Advisor: Gerlane Coelho Bernardo Guerra

EV018-STUDIES OF DRUG UTILIZATION IN DOWN'S SYNDROME PATIENTS

THAIS ADRIANA DO CARMO(PQ)[(1)]; JOSÉ EDUARDO DA FONSECA(PQ)[(1)]; RAQUEL C.D.R. GRECCHI(PQ)[(1)]; ALESSANDRA C. DE CAMPOS(IC)[(1)]; LÍVIA M.E. SANTO(IC)[(1)], PRISCILA M. BUCK(IC)[(1)]

[1]Universidade Metodista de Piracicaba–UNIMEP

Introduction: Down Syndrome (DS) or trisomy 21 is an accidental chromossomic alteration that provokes a general delay in the neuropsychomotor development and cardiovascular, digestive, visual and auditive disturbances. In addiction, the pacients present harm congenital formations and metabolic alterations that modify the efficacy and the toxicity of drugs. Therefore, these pacients are classified as risk population. Studies of Drug Use identify how the drugs are utilized by the patients and the potential problems. Methodology: The Associação dos Pais e Portadores de Síndrome de Down users were accompanhised and observed twice a month, in the period from february untill june, 2003. Results: 94,7% of patients utilized some drugs (mean: 5,2 drugs/user), 36,8% , used drugs chronically, 17,0% of drugs were used to threat infections. Conclusion: Prolongated drug utilization can produce different disturbances to users. It suggests the importance of the correct orientation to families and to health profissionals. One konws that drugs of drawn out use can cause problems to the carriers, promoving the rational use of drugs and na a improvement of the life quality.

Financial support: FAE-UNIMEP
Supervisor: Thais A. Carmo

The authors did not follow the Scientific Committee's suggestion for an English language review

EV019-ANALYSIS OF A MEDICATION ERROR OCCURRING AT A UNIVERSITY HOSPITAL: ROOT CAUSE ANALYSIS

THALYTA CARDOSO A. TEIXEIRA (PG) [1]; SILVIA H. B. CASSIANI (PQ)[1]; SIMONE P. OPTIZ (PG)[1]; PAULO C. P. TELLES FILHO (PG)[1]

(1) EERP – USP

Medication errors may occur in any of the phases of the medication system.This study aimed at analyzing a medication error occurring at a university hospital.The root cause analysis model was used in order to analyze the error and observed by an undergraduate nursing student.The error was defined as
"Prescribed insulin administration which should not have administered to the patient on the day preceding surgical procedures". The medical order included information concerning insulin which had not been entered the standardized area of the medical form, and the direction for "not administering insulin in the immediate pre-operatory period" had been added to the area designed for care instructions and not to that concerning medication, which could confuse the nursing team at the moment of medication administration. During the monitoring phase, the undergraduate student was informed that the medication should not have been administered. A communication failure occurred between the physician and the nursing team for if the insulin was not to be administered to the patient, it should not have been prescribed on that day. It was observed that a potential medication error occurred, which resulted from an incorrect medical order.

Supervisor: Silvia H. de Bortoli Cassiani

EV020-PATIENT SAFETY: THINKING ECOLOGICALLY ABOUT MEDICATION ADMINISTRATION

SILVIA H B CASSIANI (PQ)[1];CRIS R GROU (PG)[2]; DANIELA O DA SILVA (IC)[1]; ADRIANA I MIASSO (PG)[1];PATRICIA MARCK (PQ)[3]

[1]EERP – USP. [2]HCFMRP-USP. [3]University of Alberta.

Thinking ecologically about complex health systems encourages us to examine the structures, processes, and relations that support the delivery of safe care. This study aimed at determining and analyzing the types of questions auxiliaries and technicians ask nurses about medications and the sources and accuracy of nurses' answers to staff questions. Researchers asked clinic nurses to record all questions about medication safety which they received from auxiliaries and technicians. Of 255 questions recorded, 139(54.5%) were presented by auxiliary nurses. The categories of questions were: dilution of the medications(40.4%), mode of administration (15.7%), drug interactions(11%); infusion(7.5%); preparation(7.5%); indications for use(5.5%); mode of action (4.3%); dosage calculations(4.3%); drug name(2.0%) and interpretation of prescriptions(1.6%). Only 9% of answers were provided by pharmacists. The majority of nurses' answers(39.2%) were obtained from written sources. When checked against up-to-date medication information, 64.5% of nurses' answers were correct. Increased clinic access to pharmacists for accurate, up-to-date medication information is needed to strengthen nurses' knowledge and ability to safely supervise medication administration.

Financial Support: FAPESP

EV021-MEDICATION ORDERS: ASPECTS OF MEDICATION ERRORS

ADRIANA INOCENTI MIASSO(PG)[(1)]; REGINA C. OLIVEIRA(PG)[(1)]; ANA ELISA B. C. SILVA(PG)[(1)]; SÍLVIA H. B. CASSIANI(PQ)[(1)]

[(1)] University of São Paulo at Ribeirão Preto College of Nursing

Introduction: Medication errors represent a sad reality in hospital organizations, entailing serious consequences for patients. Objetive: To evaluate aspects of medication prescription that may contribute to medication errors, starting from how the medical prescriptions are written. Methods: The study was carried out at medical clinic units of 04 hospitals of the Sentinela network. The sample consisted of 864 medical prescriptions. Data were collected through a structured script. Results: Only one Hospital had implemented the electronic medical prescription and used the generic medication name in the prescriptions. At the other hospitals, prescriptions were elaborated manually and both generic and brand names were used. Only electronically printed prescriptions were practically 100% readable. All hospitals allowed for the use of abbreviations in the prescriptions. At all study hospitals, times circled with the observation "not available" were the most frequent justifications for not administering the prescribed medication. Conclusion: This study disclosed a range of weak points in the medication process at the study hospitals. Improving the system is essential with a view to greater quality and safety in patient care.

Financial Support: FAPESP

EV022-ANALYSIS OF MEDICATION ERROR TYPES IN A HOSPITAL

FRANCISCA EDIVONE FREITAS DE MORAES (IC)[1]; VANESSA MAROLLA BERNARDES ANTONIO (IC)[1]; ROSANE GNOATTO HALLAL (IC)[1]; PAULO CELSO PRADO TELLES FILHO (PG)[1-2]; SIMONE PERUFO OPITZ (PG)[2]; THALYTA CARDOSO ALUX TEIXEIRA (PG)[2]

[1] University of Branco Castelo Camilo (UNICASTELO) Campus VIII; [2] University of São Paulo at Ribeirão Preto College of Nursing

One of the attributions of the nursing practice which deserves reflection is the administration of medication involving the legal and ethical aspects of professional action. This study aimed at analyzing the types of medication errors occurring at a hospital in São Paulo state based on the account of a nursing supervisor working for the aforementioned institution. A case study was used in which the nursing supervisor was interviewed and reported medication errors. As a result, the reported errors were: dosage errors, errors concerning lack of communication, errors due to work overload, errors due to lack of knowledge and/or information. It is concluded that guidance and education regarding the preparation and administration of medication are required as strategies for error reduction. Training and updating the nursing team must be a constant procedure, and permanent education development becomes essential, thus promoting safer care for patients and professionals.

Supervisor: Paulo Celso Prado Telles Filho

EV023-OPPORTUNITIES OF ERRORS IN PRESCRIPTIONS WITH HIGH-ALERT MEDICATIONS AT A BRAZILIAN HOSPITAL

MÁRIO BORGES ROSA (PQ)[1]; EDSON PERINI (PQ)[1]; TÂNIA AZEVEDO ANACLETO (PQ)[1]; HESSEM M. NEIVA (PQ)[1]

(1) Group of Studies of Safety in Drug Use, Minas Gerais - Universidade Federal de Minas Gerais

Introduction: Medication errors are an important problem in Public Health nowadays. Objective: To evaluate opportunities of errors in prescriptions with high-alert medications Methodology: Cross-sectional study performed at a hospital in Minas Gerais including all prescriptions with one or more high-alert medications, during 30 days, in 2001. Results and Conclusions: 7148 high-alert medications were assessed in 4026 prescriptions considering legibility, pharmaceutical form, concentration, administration route, interval and infusion rate, and 3177 discrepancies were found. The most prevalent problems were absence of concentration (49,6%) and pharmaceutical form (25,4%), poorly legible (8,8%) and doubtful concentration (5,6%). Discrepancies concentrated on heparin (33,7%), fentanyl (21%), midazolam (11,4%), nalbufine (9,6%) and pancuronium (4,5%). Intensive Care Units and Neurology showed higher number of discrepancies per prescription contrasting with Acute and Chronic Burnt Units. Intensive Care Units and Neurology don´t have protocols of high-alert medications use in opposite to burnt units. Data encountered help to provide measurements which can improve safety in the process of drug utilization**.**

EV024-DISPENSING ERRORS IN A BRAZILIAN HOSPITAL PHARMACY

TÂNIA AZEVEDO ANACLETO (PQ)[1]; EDSON PERINI (PQ)[1]; MÁRIO BORGES ROSA (PQ)[1]

(1) Group of Studies of Safety in Drug Use, Minas Gerais – Universidade Federal de Minas Gerais

Introduction: Dispensing failures break one of the last links in safety of drug use and can cause damage to patients once they create opportunities to medication errors. Objective: To analyse occurrence of dispensing errors in a hospital, reference in emergency in Minas Gerais, during 21 days, in 2002. Methodology: Errors were detected by a check on the medication separated for dispensation with the prescription. Results and Conclusions: At least one dispensing error was registered in 81,8% of the prescriptions (2143 dispensed medications). Some type of error was found in 33,6% of medications dispensed. Higher chance of error was observed in pre-typed prescriptions with nine or more medications and with injectable drugs. The most frequent type of error was dose omission (57,3%). Among 431 injectable drugs dispensed with errors, 31% were high-alert medications. It was concluded that drug dispensing system at the studied hospital has few defences, many latent failures and several conditions which predispose to occurrence of errors. Implantation of a safe system is fundamental to ensure dispensation where opportunities of medication errors are minimized in the hospital.

EV025-CLINICAL EFFECTIVENESS AND POSSIBLE SIDE EFFECTS OF FLUOXETINE IN THE TREATMENT OF OBESITY.

CAMILA GUIMARÃES(PG)[(1)]; LEONARDO RÉGIS LEIRA PEREIRA(PQ)[(1)]; MARIA DE LOURDES PIRES BIANCHI(PQ)[(1)]; JOSÉ EVANDRO CESARINO(PQ)[(1)]; CARLOS ALBERTO NOGUEIRA DE ALMEIDA(PQ)[(2)].

[(1)] FCFRP – USP.
[(2)] Universidade de Ribeirão Preto (UNAERP).

Introduction: Obesity is a chronic condition that has been reaching epidemic proportions worldwide. It is a risk factor for numerous medical disorders and excessive mortality. Long-term treatment, including pharmacotherapy, may be necessary for many obese patients. Objectives: This study aimed to assess the effects of Fluoxetine, as an adjunct therapy to a 1.500 Kcal/day diet, on weight reduction. Methods: Fluoxetine (F) 60 mg/day, was compared to placebo (P) in 19 obese females in a 90-day trial. Results: F therapy (n=9) resulted in a statistically significant greater mean reduction in BMI (-3.64 vs -0.45 Kg/m²), % fatty-tissue (-4.67 vs +0,07) and waist circumference (-12.3 vs -2.9 cm), than P group (n=10). There was also an elevation of HDL-cholesterol (25.8%) and mean triglycerides levels was reduced in F group (-28.3%). The drug was generally well tolerated and side effects most commonly reported by the patients were insomnia and somnolence. Conclusions: We concluded that Fluoxetine may provide an effective and well tolerated possibility for the treatment of obesity.

Financial Support: CAPES
Supervisor: Regina Helena Costa Queiroz

EV026-THE KNOWLEDGE OF PHARMACOLOGY AND ITS IMPLICATION TO THE PATIENT'S SAFETY IN DRUG ADMINISTRATION

ADRIANNE R. C. M. B. F. DE SANTANA(PG)[1]; SÍLVIA HELENA DE BORTOLI CASSIANI(PQ)[2]

[1,2] Ribeirão Preto Nursing School from the University of São Paulo

Introduction: drug administration involves the multidisciplinary health team, where the nurse has a fundamental role in ensuring the safety of the assistance, being mandatory the knowledge of the pharmacology related to the administration, action, means of administration, doses, toxicity and side effects. Objective: analyze how this problem has been studied in Brazil and worldwide. Methodology: literature review accessing the Medline and Lilacs databases within the last ten years using the nursing, knowledge and pharmacology descriptors. Results: twenty articles were found, three national and seventeen international. The themes described were the nurses' educational needs to administer the drugs; the nurses' perception of pharmacology teaching; strategy for evaluating the knowledge in pharmacology in graduation courses; use of pedagogic strategies for teaching pharmacology and drug administration. Conclusion: it is necessary to broaden the knowledge on the subject to ensure the quality of the assistance and safety in the cares with the patient.

Supervisor: Prof.ª Dr.ª Sílvia Helena de Bortoli Cassiani

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FF001-CHRONIC ETHANOL INTAKE ALTERS CARDIOVASCULAR FUNCTIONS IN CONCIOUS RATS

CARLOS R. TIRAPELLI(PQ)[(1)], LEONARDO B. M. RESSTEL(PG)[(1)], VERA L. LANCHOTE(PQ)[(2)], SÉRGIOA. UYEMURA(PQ)[(2)], FERNANDO M. A. CORRÊA(PQ)[(1)], ANA M. DE OLIVEIRA (PQ)[(3)]

[(1)]FMRP – USP, [(2)]FCFRP – USP

Introduction and Objectives: We investigated the effect of chronic ethanol consumption on arterial blood pressure (BP), heart rate (HR) and homodynamic responses to vasoactive agents in conscious rats. Methods: Male Wistar rats were divided into 3 groups: Control (C; received water), Ethanol (E; received a solution of ethanol 20%) and Isocaloric (I; received isocaloric amounts of sucrose instead ethanol). Results: Ethanol ingestion for 2, 6 or 10 weeks enhanced systolic, diastolic and mean arterial BP. No changes were observed in HR after long-term ethanol intake. The pressor response for phenylephrine (PHE) were enhanced after 2 weeks but not altered after 6-weeks of ethanol feeding. At week 10 there was a reduction in BP reactivity to PHE in the ethanol-treated rats. The hypotensive response induced by sodium nitroprusside (SNP) was enhanced in comparison to C and I groups after the three different periods of treatment. Conclusion: The enhanced mean arterial BP observed after ethanol intake is a consequence of enhanced systolic and diastolic BP. The lack of hypertensive effect of PHE on 6 and 10-weeks treated rats indicates that tolerance had developed.

Financial Support: FAPESP
Supervisora: Ana M. De Oliveira

FF002-ADAPTATION OF RATS OF DIFFERENT AGES TO INTESTINAL RESECTION: INGESTION AND WON OF WEIGHT

LUCIANE GONSALES(PQ)[1];MARCELO RODRIGUES(PQ)[1];BEATRIZ TRAZZI (PQ)[1];MARCELO MORGUETI(PQ)[1];MARCOS PAGANI JR(IC)[1]; PATRICIA SHIMABUKU(IC)[1]

UNIMAR – Universidade de Marilia – Sao Paulo

INTRODUCTION: Short Bowel Syndrome is responsible for metabolic alterations that commit the patient's state nutrition. The intestinal adaptation wakes up interest, because the intestine is absorption road for countless medications. **OBJECTIVE:** It was studied the ingestion and the weight gain after partial resection of the intestine small of rats of different ages. **METHODS:** Rats Wistar, males, they were divided in two groups of 24 animals, recently-weaned with 21 days (R) and adult with 3 months of ages (A and R), both groups suffered resection of 50% of the intestine small forming 3 experimental groups: P (A and R) - resection proximal, D (A and R) - resection distal and C (A and R)-controls, with transaction. The result was evaluated in three different periods: PI: 1-4 days; PII: 5-8 days, PIII: 9- 12 days, powder-resection. **RESULTS:** The animals with resection presented smaller ingestion and weight gain, only increasing after the first 4 days. After this period the ingested amount was stabilized for all the groups. **CONCLUSIONS:** The weight gain and the ingestion are influenced by the place of the resection. In the animals control the weight gain was larger after the second period.

Supervisor: Luciane Gonsales

FF003-CENTRAL EFFECTS OF HYDROXICARVONE IN MICE

FERNANDO DE S. OLIVEIRA (PG); DAMIÃO PERGENTINO DE SOUSA (PQ); FRANKLIN FERREIRA DE FARIAS NÓBREGA (IC); MARCELO DANTAS DE MOURA (PG); REINALDO NÓBREGA DE ALMEIDA (PQ)

Laboratório de Tecnologia Farmacêutica / Universidade Federal da Paraíba

The essential oils are natural products with different applications, especially in the medicine area. The aim of the present work concerned with the field of evaluation the psychopharmacological effects of hydroxicarvone (HC) a monoterpene obtained in synthesis. Swiss male mice (25-35 g) (N=10) were treated intraperitoneally. The LD_{50} values were 800.2 (724.6 – 883.6) mg/kg. HC at a dose of 200 mg/kg produced ptosis, sedation, reduction of answer of the touch and discrete analgesia. In the pentobarbital-induced sleep time test HC produced a significant increased in the time of sleep (100 mg/kg: 87.5 ± 19.8; 200 mg/kg: 76.5 ± 7.8; $p<0.05$) in comparison with those from the control group (38.5 +3.8). In addition, HC 400 mg/kg in the test of convulsion induced by pentylenetetrazol test significantly increased the latency (365.1 ± 107.5), compared to control group (143.1 ± 19.4) ($p<0.05$). These data indicative that HC have an effects in the CNS of mice, at route and doses tested.

Financial Support: CNPq
Supervisor: Reinaldo N. de Almeida

FF004-5-HT RECEPTORS OF BASOLATERAL AMYGDALA IN THE MODULATION OF THE TONIC IMMOBILITY.

ANA LUISA B. TERZIAN(IC)[1]; ALINE A. FERRARESE(IC)[1]; LEDA MENESCAL-DE-OLIVEIRA(PQ)[2]; CHRISTIE R.A. LEITE-PANISSI (PQ)[1].

[1]MEF – FORP – USP, [2]FISIOL. – FMRP – USP.

Introduction: The tonic immobility (TI) response occurs in situation of intense fear. In addition, it is known that the level extracellular of serotonin in the basolateral amygdala (BLA) is increased during the fear.
Objective: This study investigated the effect of the activation of 5-HT receptors of the BLA, in the TI behavior and in the open field test in guinea pigs.
Methods: A guide cannula was implanted into the BLA and the animals were submitted to five maneuvers of TI induction before and after the treatment. The TI induction consisted of the restraint and postural inversion, and the duration of the episodes was recorded in sec. In group 1 and 2, the animals received into the BLA 8-OH-DPAT ($5\text{-}HT_{1A}$ agonist) or a-metil 5-HT ($5\text{-}HT_2$ agonist), at the doses 0.01 and 0.1µg/0.2µl in two consecutives days. The locomotive activity (LA) was evaluated per 5 min, after saline or the drugs in study.
Results: The results showed that both treatments in the higher doses promote IT reduction and increase of the LA.
Conclusion: Our data suggest that the activation of $5\text{-}HT_{1A}$ or $5\text{-}HT_2$ receptors of the BLA reduce the fear, and consequently decrease the TI response and increase of the LA.

Financial Support: FAPESP
Supervisor: Christie R. A. Leite-Panissi.

FF005-VASOPRESSIN AND OXYTOCIN SECRETION IN SEPSIS INDUCED BY CECAL LIGATION AND PUNCTURE

GABRIELA RAVANELLI DE OLIVEIRA(PG)[1]; MARIA JOSÉ ALVES DA ROCHA(PQ)[2]

[1]FCFRP – USP; [2] FORP – USP .

Introduction: Sepsis is the systemic response to severe infection showing several physiological alterations. Our aim was to study the time course of vasopressin (AVP) and oxytocin (OT) neurosecretion following cecal ligation and puncture (CLP), an experimental animal model that most resembles human sepsis. Methods: Male Wistar rats (200-250g) submitted to CLP (20 punctures - 16G needle) or to sham operation were decapitated at 0, 0.5, 2, 4, 6 or 24h after surgery. AVP and OT measurements were made by RIA in the plasma, neurohypophysis (NH) and hypothalamic nuclei. Results: Plasma AVP levels in the CLP group showed two peaks, a larger one immediately after the surgery (107.6±18.0pg/mL,$P<0.05$) and another one smaller at 6h later (10.9±2.2pg/mL,$P<0.05$). Plasma OT levels were also high but their temporal profile differed from that of AVP. In CLP group the increase in hypothalamic AVP and OT content was delayed, while in the NH an increase in hormone content was observed only for OT. Conclusion: These results demonstrate that the hypothalamic neurosecretory system is altered in sepsis induced by CLP, being unable to answer to the physiological stimuli with AVP and OT secretion increase, in spite of the increased hypothalamic content.

Financial Support: FAPESP
Advisor's name: Profa. Dra. Maria José Alves da Rocha

FF006-FEVER TO CINC-1 IN RATS: EFFECT OF ANTIPYRETICS AND FUCOIDAN.

DENIS M SOARES(PG) [(1)]; RENES R MACHADO(PG) [(1)]; GLÓRIA. E P SOUZA(PQ) [(1)]

[(1)]Laboratório Farmacologia-Depto Física e Química – FCFRP – USP

Introduction: Cytokine-induced neutrophil chemoattractant (CINC)-1 acts as cell activator and chemoattractant however, there are no evidence regarding its pyrogenicity.
Aim: To investigate: if CINC-1 injected in the 3rd ventricle (i.c.v.) or hypothalamus (i.h) causes fever; the effect of ibuprofen (IBU), indomethacin (INDO), dexamethasone (DEXA) and fucoidan (FUCO) on this response.
Methods: Male Wistar rats (200g) received CINC-1 i.c.v. (3µl) or i.h. (0.5µl). Values are mean±s.e.m. of 4-8 rats. Rectal (rT) and skin tail (sT) temperatures were measured by telemetry during 6 h.
Results: CINC-1 i.c.v. raised rT of rats (3ªh,°C, 1ng: 0.12±0.1; 5ng:0.8±0.3; 25ng: 1.0±0.2; 50ng: 1.3±0,2). INDO (2mg/kg, i.p.) and IBU (10mg/kg, i.p) reduced 63% and 75%, respectively, the fever to CINC-1 (25ng i.c.v.). CINC-1 i.h. raised rT of rats (3ªh, °C, 5pg: 1.1±0.5; 12.5pg: 1±0.2; 25pg: 1.8±0.4; 50pg: 0.8±0.5; 200pg: 0.8±0.3) and reduced sT of rats (2ªh, °C, tail skin: -0.63±0.1). DEXA (0.5mg/kg, s.c.) reduced 45% the fever to CINC-1 i.h. FUCO did not alter this response.
Conclusion: Centrally injected CINC-1 increases rT and decreases sT of rats indicating a fever response. This fever depends on PGs synthesis and other pyrogenic mediators but not on selectin expression.

Support: CAPES
Supervisor: Glória E.P. Souza

FF007-PROSTAGLANDINS, BUT NOT IL-1, ARE INVOLVED IN RANTES-INDUCED FEVER IN RATS

RENES R. MACHADO(PG)[1], DENIS M. SOARES(PG)[1], AMANDA PROUDFOOT(PQ)[2] AND GLÓRIA E.P. SOUZA(PQ)[1].

[1] Lab. Pharmacology, Faculdade de Ciências Farmacêuticas de Ribeirão Preto – Universidade de São Paulo, São Paulo, Brazil;[2] Serono Pharm. Res. Institute, Geneva, Switzerland.

Introduction- Injection of RANTES (Regulated on activation, normal T cells expressed and secreted), a CC chemokine, into the anterior hypothalamus preoptic area (AH/POA) promotes fever in rats.
Objective- To investigate the involvement of prostaglandins and IL-1 on fever induced by RANTES.
Methodology- RANTES (25pg/rat) was injected into the AH/POA in male Wistar rats (200g). Control animals received vehicle only. Changes in body temperature were measured for up to 6 h by radio-telemetry. INDO (2 and 8mg/kg, i.p.) and CELEC (5mg/kg, v.o.) were administered 30 min before and DEXA (0.5mg/kg, s.c.) 1 hour before RANTES. IL-1ra (20µg/rat, i.h.) was administered 15 min before RANTES or IL-1b (300pg/rat, i.h.).
Results- Fever to RANTES was modified by 2 and 8 mg/kg of INDO (62% and 86%, respectively), DEXA (65%) and CELEC (96%). IL-1ra reduced (60%) the fever induced by IL-1β but did not change that induced by RANTES.
Conclusions- Fever induced by RANTES depends on prostaglandins, probably via COX-2, but not on IL-1β. However, the involvement of other mediators can not be discarded.

Support: FAPESP
Supervisor: Glória E.P. Souza

FF008-EFFECT OF LOSARTAN INJECTION ON PROLACTIN RESPONSE TO STRESS IN FEMALE WISTAR RATS ON DIESTRUS

MARCELA PASSOLONGO DA SILVA(IC)[1]; EVERSON FERREIRA MENEZES(IC)[1]; KARINA MIURA DA COSTA(IC)[1]

[1] Universidade Estadual do Oeste do Paraná

Angiotensin II (Ang II) is a peptide that exerts an excitatory effect upon pituitary prolactin (PRL) release through direct stimulation on lactotrophs. Since Ang II and PRL are know to be affected by stress, the main objective of this work was to evaluate the possible participation of Ang II in stress-induced response of PRL in female on diestrus. The right jugular vein of adult Wistar females rats were cannulated and in the following afternoon, microinjection of saline 0,9% or losartan i.v. (30mg/kg, n=8 or 10mg/Kg or n=6 or 2mg/kg, n=6); 15 min after animals were submitted to ether which was applied 5min before blood sample were collected. The PRL plasma levels were determined by radioimmunoassay. Animals injected with losartan presented reduced PRL level in the 3 concentrations (10.91 ± 1.67); (11.98 ± 1.42); (16.43 ± 3.46) respectively, when compared to animals submitted to saline injection (20.49 ± 5.6), however, the concentration 2mg/kg was not statistically significant, $p < 0.05$. Our results show that stress-induced PRL increase in females in diestrus is mediated by Ang II AT_1 receptor in lactotrophs and this modulation depends on the concentration applied.

Financial Support: UNIOESTE
Supervisor: Sara Cristina Sagae

FF009-COMBINED ACTION OF GLUCOCORTICOID AND BENZODIAZEPINE ON WATER CONTENT IN TARGET ORGANS OF RATS

VIKTOR IVANOVITCH GOUDOCHNIKOV (PQ)[(1)]; CAROLINA WEBER (IC)[(2)]

[(1)]Departamento de Ciências da Saúde; [(2)]Curso de Biologia, UNIJUÍ, Ijuí – RS, Brasil

(Introduction and Objective) Previously we have shown that dexamethasone acetate (DMA) inhibited body and organ growth in rats, whereas diazepam interacted with this influence. Recently we have employed this experimental model to explore drug-induced changes in water content. (Methodology) Young and mature adult, male and female rats received four IP injections of DMA (1-2 mg/kg BW) and/or diazepam (1.5-8 mg/kg in different experiments), with 2-3 day intervals between injection dates. 24 hours after the last injection, target organs were isolated and weighted, before and after drying for 48-72 hours at 50°C, in order to calculate aqueous fraction of the organ weight. (Main Results) DMA caused differential and statistically significant water loss in thymus, spleen, adrenals and pituitary gland of young and adult rats, males and females, both in the absence and presence of diazepam. When used alone, benzodiazepine exerted complex influence on water content in target organs. (Conclusions) It is suggested that water loss under the influence of DMA may explain partially both glucocorticoid-induced growth inhibition and age-dependent, maturational decrease in body water content.

Financial Support: UNIJUÍ
Supervisor: Viktor I. Goudochnikov

FF010-EVALUATION OF ANTINOCICEPTIVE EFFECT OF QUERCETIN ON INFLAMMATION INDUCED NOCICEPTION

DANIEL A.R. VALERIO(IC)[1]; WALDICEU A. VERRI JR.(PG)[1]; THIAGO M. CUNHA(PG)[1]; SANDRA R. GEORGETTI(PG)[2]; MARIA J.V. FONSECA(PQ)[2]; RÚBIA CASAGRANDE(PQ)[3]; FERNADO Q. CUNHA(PQ)[1]; SÉRGIO H. FERREIRA(PQ)[1].

[1]Dept of Pharmacology FMRP-USP; [2]Dept of Pharmaceutical Sciences FCFRP – USP; [3]Dept of Food and Drug Technology – UEL.

INTRODUCTION: Quercetin, a bioflavanoid, attenuates neurophatic thermal nociception in diabetic rats, and inhibits carrageenan (Cg)-induced release of TNF-a and chemokines in the air pouche. OBJECTIVE: Therefore this study investigated the antinociceptive effect of quercetin on inflammatory hypernociception. METHODOLOGY: Male swiss mice(25g) received an intraperitoneal injection of vehicle or quercetin 30min before intraplantar stimulus with Cg(100μg), TNF-α(300pg), IL-1β(2ng), KC(20ng), dopamine(10μg) or PGE_2(100ng). The hypernociceptive responses were evaluated by the electronic pressure meter paw test. RESULTS: Quercetin (30-100mg/Kg) inhibited Cg effect in a dose-dependent manner (40% and 52%respectively). Furthermore, quercetin (100mg/Kg) inhibited TNF-α (43%), KC (38%) and IL-1β (45%) hypernociception, although did not affect the effects of the final mediators dopamine and PGE_2. CONCLUSIONS: These results suggest that quercetin acts preventing rather than directly antagonizing the nociceptor sensitization.

Financial Support: FAPESP e CNPq
Supervisor: Sergio Henrique Ferreira

FF011-INTRATHECAL (I.T.) ADMINISTRATION OF A NOVEL PYRAZOLYL-THIAZOLE DERIVATIVE INDUCES ANTINOCICEPTION IN MICE.

ALESSANDRA HÜBNER SOUZA(PG)[1]; CARINE CRISTIANE DREWES(IC)[1]; VALÉRIA SINHORIN(PG)[1]; PATRICIA SAUZEM(PG)[1]; GABRIELA SANT'ANNA(IC)[1]; GERUSA DALMOLIN(PG)[1]; MARIBEL ANTONELLO RUBIN(PQ)[1]

[1]Universidade Federal de Santa Maria

Introduction: Since pain is the most common complaints in clinical practice, we have been investigating the antinociceptive effects of new pyrazolyl-thiazole derivatives.
Objective: We investigated whether the i.t. injection of the novel pyrazolyl-thiazole derivative 2-[5-trichloromethyl-5-hidroxy-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]-4-(4-bromophenyl)-5-methylthiazole (B50) cause antinociception in mice, using the hot plate test.
Methodology: Male albine mice received B50 (200 nmol/5 µl), morphine (6.5 nmol/5 µl), suspended in 2.5% Tween 80 in saline (vehicle) or vehicle, 90, 120 or 150 minutes before hot-plate test. In this test, the animal was placed on a metal plate maintained at 50 ± 0.1°C. The latency to show nociceptive responses, such as hindpaw licking or jumping was measured. A cut-off time of 90 sec was established.
Results and Conclusions: B50 caused antinociception 90 minutes after its administration. It had no effect on spontaneous locomotion, indicating that the currently reported antinociceptive effect of B50 is not related to unspecific motor effects.

Financial Support:CNPq/ UFSM/CAPES.
Supervisor: Maribel Antonelo Rubin

FF012-MECHANIMS OF BRADYKININ (BK)-INDUCED MECHANICAL HYPERNOCICEPTION IN MICE

THIAGO M CUNHA (PG), WALDICEU A VERRI JR (PG), ANA TG GUERRERO (PG), TÂNIA S GARÇON (PG), CARLOS A PARADA (PQ), SERGIO H FERREIRA (PQ) & FERNANDO Q. CUNHA (PQ).

Depto. Of Phamacology, FMRP-USP.

Introduction Controversies related to the mechanism of bradykinin (BK) induces hypernociception remains. Objective In the present study, it was investigated the mechanisms by which BK induces hypernociception in mice. Methods Hypernociception was quantified with the electronic pressure meter test for mice. Cytokines in the paw of mice was measured by ELISA. Results BK but not B1 receptor agonist (DALK) induced hypernociception in naïve mice. BK effect was inhibited by indomethacin or guanethidine, but not by IL-1ra, antibody against KC or in TNFR1 knockout mice. BK did not stimulate cytokines release in naive mice paw. On the other hand, in LPS-primed paw mice DALK induced hypernociception. DALK effect was inhibited by indomethacin, guanethidine, antiserum against TNFα and IL-1ra. Reinforcing, DALK induced TNFα and IL-1β release in paw primed mice. Conclusion These results suggest that in naïve mice BK directly induces the release prostanoids and sympathetic amines acting on B2 receptor-induced hypernociception. However, after priming the BK acting on B1 induces TNFα, IL-1β, prostanoids and sympathetic amines release mediating hypernociceptive effects.

Financial Support: FAPESP, FAEPA
Supervisor: Sergio H Ferreira

FF013-EFFECTS OF b-CARBOLINE ALKALOIDS ON NOVEL OBJECT RECOGNITION MEMORY IN MICE

CAMILE RORIG (IC)[1]; DAIANE LOSS VIEIRA (IC)[1]; DINARA JAQUELINE MOURA(PG)[2]; JOÃO ANTONIO PÊGAS HENRIQUES (PQ)[2]; JANE MARLEI BOEIRA (PQ)[1]

[(1)]Depto. de Ciências da Saúde, URI, Campus Erechim/ RS; (2) Pós-Graduação em Biologia Molecular e Celular, Universidade Federal do Rio Grande do Sul, Rio Grande do Sul

The β-carboline alkaloids harman, harmine, harmaline and harmol are present in plants and have been of interest due to their psichotropic effects. They exhibit potent inhibition toward monoamine-oxidases and modulate the levels of various neurotransmitters. The aim of these study was to evaluate the effects of the systemic administration of these alkaloids on novel object recognition memory in mice. Adult male mice were given an i. p. injection of alkaloids (1.0; 2.5 or 5.0 mg/kg) or saline 30 min before training in an object recognition task. Both alkaloids did not effect the total time exploring both objects. All alkaloids increase the time exploring to novel object in short and long-term memory. Therefore, the date suggested that these alkaloids induced facilitation of novel object recognition test. Probably, these effects were due to the interactions of these alkaloids with receptors involving in memory, like dopamine, serotonine and gama-aminebutiric acid and their inhibition on enzyme monoamines-oxidase-A.

Financial support: FAPERGS; PROBIC/URI
Supervisor: Jane Marlei Boeira

FF014-ROLE FOR IL-18, TNF (VIA TNFRI) AND LEUKOTRIENES IN IL-15-INDUCED NEUTROPHIL MIGRATION

WALDICEU A VERRI, JR(PG)[(1)]; THIAGO M CUNHA(PG)[(1)]; FOO Y LIEW(PQ)[(2)]; SÉRGIO H FERREIRA(PQ)[(1)] & FERNANDO Q CUNHA(PQ)[(1)]

[(1)]Dept. Pharmacology, Universidade de Sao Paulo - Ribeirão Preto, Brazil; [(2)]Division of Immunology, University of Glasgow, UK

INTRODUCTION IL-15 is a pro-inflammatory cytokine, and despite of its *in vitro* chemotatic activity, there is no demonstration of such effect *in vivo* AIM Therefore, we evaluated the IL-15-induced neutrophil migration and the mediators involved in this effect METHODS Wild type or deficient mice (-/-) received IL-15 or PBS intraperitoneal injection. Cells from the peritoneal cavity were harvested with 2ml PBS/EDTA. Total cell counts were determined using diluting fluid in a Neubauer chamber and differential counts performed using Rosenfeld-stained cytospin preparations. RESULTS IL-15 induced dose-(6.7-60ng) and time-(0.5-48h) dependent neutrophil migration. The treatment with dexamethasone (corticosteroid,2mg/Kg,sc,1h;55%) or MK886 (FLAP inhibitor,3mg/Kg,po,1h;56%) inhibited IL-15-(20ng/cav)induced neutrophil migration, which was diminished in TNFRI (-/-;96%), 5-lipoxigenase (-/-;67%) and IL-18 (-/-;46%) mice. CONCLUSIONS These results suggest that IL-18, TNF(TNFRI) and/or leukotrienes targeting therapies could represent a useful tool to control IL-15-induced neutrophil migration dependent diseases.

Financial Support: FAPESP, FAEPA, CAPES and CNPq
Advisor: Fernando Q Cunha

FF015-THE EFFECT OF IBUPROFEN IN THE CHANGE IN BODY TEMPERATURE INDUCED BY CECAL LIGATION AND PUNCTURE (CLP) IN RATS

MARIA JOSÉ FIGUEIREDO (PG)[1]; DIEGO TORRES-DUEÑAS (PG)[2]; FERNANDO DE Q. CUNHA (PQ)[2]; GLÓRIA E.P. SOUZA (PQ)[1]

Pharmacology, [1]FCFRP-USP and [2]FMRP-USP

Introduction: Sepsis is the systemic response to severe infection in which the fever is the most frequent manifestation.
Aim: To investigate changes in body temperature and survival after CLP-sepsis induction and the effect of ibuprofen on these events.
Method: Body temperature (bT) was measured by biotelemetry in male Wistar rats (200-250 g), each 30 min, by 48 h, after surgical procedure (sham or CLP) and the survival was monitored by 7 days.
Results: After puncture of antimesenteric cecal surface (four punctures, 16-gauge needle) the body temperature increased from 37.5±0.08 to 39.0±0.3 ºC, 6th h, $P< 0.001$). The rate of survival was 42% (48h). Ibuprofen (10 mg/kg) given 1 h thereafter, but not 30 min or 1h before, reduced the increase in body temperature to CLP (38.6±0.43 to 37.7±0.06 ºC, 6th h, $P< 0.001$). In addition, only given 1h prior ibuprofen reduced to 20% (20h) the survival when compared to Sal- CLP group.
Conclusion. CLP constitute a model to study fever to infection and is sensible to pos-treatment with ibuprofen, a non-selective COX-1 and COX-2 inhibitor. The advantage or disadvantage of fever blockage in this experimental model (CLP) needs to better investigate.

Support: CAPES
Supervisor: Glória E. P. Souza

FF016-HEMODYNAMIC AND HORMONAL ALTERATIONS IN EXPERIMENTAL SEPSIS

JOÃO ALEXANDRE TRÉS PANCOTO(PG)[1]; MARIA JOSÉ ALVES DA ROCHA(PQ)[2]

[1]FCFRP – USP, [2]FORP – USP.

Introduction: A systemic inflammatory response to infection characterizes sepsis that, when associated with hypotension turns into severe sepsis. The aim of this study was to evaluate hydroeletrolytic, hormonal and cardiovascular alterations after sepsis induced by cecal ligation and puncture (CLP) in rats. Methods: Male Wistar rats (200-250g) submitted to CLP (10 puncture, 16G needle) or to sham operation were decapitated at 0, 2, 4, 6 and 8h after surgery. The blood was collected for hematocrit and osmolality determination. Plasma vasopressin (AVP) level was measured by RIA. The mean blood pressure (PAM) and heart rate (HR) were registered during 5h after surgery. Results: The hematocrit increased from 2h to 8h after CLP. The osmolality did not show any alteration compared to sham group. The PAM of the CLP group decreased progressively from 1h (88.5mmHg vs 111.6mmHg, $P<0.05$) until 5h after the injury (68.5mmHg vs 111.6mmHg, $P<0.05$). The reduced PAM was accompanied by an increase in the HR. The AVP plasma level showed a peak at 4h (6.0±1.1pg/ml vs 1.1±0.2pg/ml, $P<0.05$), returning to basal levels at 8h after CLP (2.3±0.5pg/ml vs 1.9±0.2pg/ml,). Conclusions: The hypovolemia and hypotension may stimulate AVP plasma increase at 4h after CLP, however this increase does not seem to be able to restore the PAM. The increased HR in response to PAM decrease suggests that the baroreflex function is normal in these rats.

Financial Support: FAPESP
Supervisor: Profa. Dra. Maria José Alves da Rocha

FF017-DIACEREIN PREVENTS FEVER AND REDUCES LEUKOCITARY MIGRATION INDUCED BY BAKER YEAST

ANA PAULA DE OLIVEIRA FERREIRA(IC) [1]; JULIANA SAIBIT PASIN(PG) [1]; ROSÁLIA ANDRIGHETTO(IC) [1]; VIVIANE RATZLAFF(PG) [1]; ANDRÉ SARAIVA(IC) [1]; CARLOS FERNANDO MELLO(PQ) [1].

[1]Physiology Department of Federal University of Santa Maria.

Introduction: Diacerein is an anti-inflammatory and analgesic drug, whose mechanism of action seems to involve interleukin -1β (IL-1β) and tumor necrosis factor-a (TNFa) synthesis inhibition. Both cytokines are involved in the febrile process, but no study has addressed the antipyretic role of diacerein.
Objective: Investigate the effect of diacerein on baker yeast-induced fever in young rats (25-28 days).
Methodology: Immediately after measuring the basal temperature (8:00 a.m.), the rats (male, 70-90 g) were injected with baker yeast (0.135 g/kg, i.p.) or apyrogenic saline (10 ml/kg). One hour later, they received diacerein (5 mg/kg, s.c.) or vehicle (5% Tween 80, 5 ml/kg) and had their rectal temperature (Tr) measured every hour up to 3 p.m. The same protocol was used to measure leukocyte migration, except that Tr was measured up to 1 p.m., when peritoneal washing was performed for leukocyte counting.
Results: Diacerein prevented fever [$F(8,20)=13.63$; $p<0.001$]and reduced the leukocyte migration [$F(1,9)=8.33$; $p<0.05$].
Conclusion: Diacerein prevents baker yeast-induced fever and concomitantly reduces leukocyte migration into the peritoneal cavity.

Financial support: CNPq.
Supervisor: Carlos Fernando Mello.

FF018-COMPLEX OF ALBENDAZOLE BETA-CYCLODEXTRIN INCREASES THE BIOAVAILABILITY OF ALBENDAZOLE SULPHOXIDE IN RAT PLASMA.

CRISTINA NISHI (IC)[(1)]; MARIANNA MICHAELA CORREA (IC)[(1)]; LUCIANA PEDRIÇA MARQUES (IC)[(1)]; GRACIETTE MATIOLI (PG)[(1)] ; ELZA KIMURA (PQ)[(1)]

[(1)] UEM

Albendazole (ABZ) is a low-soluble anthelmintic benzimidazole carbamate drug. To improve its solubility a complex of albendazole with beta-cyclodextrin (CD) was prepared and a bioavailability study was carried out. The complex of ABZ-CD was prepared 1:8, stoichiometry. ABZ was suspended in 0,5% CMC and ABZ-CD was dissolved in saline and a dose equivalent to 100 mg/Kg of ABZ was administered, *per os*, to the rats. Blood samples were collected at 15, 30, 45, 60, 180 and 360 minutes after the dose. Plasma concentrations of ABZ and albendazole sulphoxide (ABZ-SO) were assayed by HPLC. ABZ-CD presented higher values of Cmax (ABZ=1,86 ± 0.51μg/ml and ABZ-CD=2.78 ± 0.45μg/ml, $p<0.05$) for ABZ and slightly shorter Tmax (ABZ=0.8 ± 0.11μg/ml and ABZ-CD=0.67 ± 0.2μg/ml, $p<0.1$) compared to ABZ in CMC. The AUC0-∞ of ABZ was not different for either formulation (ABZ=3.11 ± 0.79 μg/ml and ABZ-CD=3.65 ± 1.53mg/ml), but for ABZ-SO a significant increase (ABZ=72.3 ± 22.4 μg/ml and ABZ-CD=138.4 ± 29.4 μg/ml, $p<0.05$) was observed after ABZ-CD dose. The complex of ABZ-CD increased the bioavailability of ABZ-SO and improved the rate of absorption of ABZ.

Financial support: PPG – UEM
Advisor: ELZA KIMURA

FF019-STUDY OF PATIENTS' PHARMACOLOGICAL PROFILE FROM THE UNIVERSITY HOSPITAL INTENSIVE CARE UNIT IN MARILIA CITY: IDENTIFICATION, ANALYSIS AND CLASSIFICATION OF DRUG INTERACTIONS.

PATRÍCIA DE SOUZA ROSSIGNOLI(IC)[(1)]; CRISTIANE FÁTIMA GUARIDO(PQ)[(1)]; IVANICE MARIA CESTARI(PQ)[(1)]

[(1)]UNIMAR - Marilia University, Pharmacy Course

Because of acute and serious illnesses, many patients need intensive care. In order to treat these diseases, the patients often require a multiple pharmacotherapy which make them predisposed to drug interactions (DI). Therefore, drug pharmacological effects may be altered, contributing to the appearing of drug adverse reactions. The objective of this paper was to identify, analyze and classify DI, according to their clinical meaning, as therapeutical (T) and non-therapeutical (NT) and, according to their action mechanism, through medical prescription, as pharmacokinetic, pharmacodinamic ou physicochemical. 103 prescriptions from 45 patients (25 females), 62.82±4.72 (average±SD) years old, from March to May, 2005 were analyzed. Drug interactions have been observed in 67% prescriptions presenting 10.72±4.72 (average±SD) drugs per prescriptions. It could be concluded that the DI study is a major tool for therapeutical design optimization, and may contribute, among others, to the safety, efficiency and quality search for the drug therapy.

Adviser: Prof. Dr. Ivanice Maria Cestari

FF020-ELECTROCHEMICAL STUDY OF DOPAMINE ON GLASSY CARBON ELECTRODE

PAULO CÉSAR SOUZA DE OLIVEIRA(IC); LUÍS ANTÔNIO DA SILVA(PQ); VALÉRIA ALMEIDA ALVES(PQ); ALEXANDRE ROSSI(PQ)

Faculdades Federais Integradas de Diamantina

Introduction: The electrochemical analysis of dopamine is of fundamental importance for further application concerning the monitoring of this neurotransmitter *in vivo*. Objective: In this work we intend to do an electrochemical characterization of dopamine using a glassy carbon electrode. Methodology: It was used differential pulse voltammetry, DPV, and ultraviolet-visible spectrophotometry to characterize dopamine. The DPV was done using a Potenciostate/Galvanostate from Autolab interfaced with a computer, monitored by a GPES program. The absorption studies were done using a Spectrophotometer from Micronal. Results: The dopamine solution showed to be stable in acid and neutral pH values. In alcaline pH, according to DPV and absorption measurements, the neurotransmitter is unstable, due to degradation of the molecule. In the other pH values it was observed a decrease of the current with the potential scans, possibly associated to adsorption of dopamine on the electrode surface. The number of electrons and protons involved in the oxidation mechanism was two. The detection limit of dopamine using glassy carbon was of 10 μM. Conclusion: It was possible to study the electrochemical oxidation of dopamine.

Financial Support: FAPEMIG
Supervisor: Luís Antônio da Silva

FF021-ROLE OF ENDOGENOUS IL-18 ON PHENYLBENZOQUINONE-INDUCED WRITHINGS

WALDICEU A VERRI JR (PG); ANDRESSA C DOMINGUES (IC); THIAGO M CUNHA (PG); DANIEL A R VALÉRIO (IC); CARLOS A PARADA (PQ); SÉRGIO H FERREIRA (PQ); FERNANDO Q CUNHA (PQ).

Department of Pharmacology - FMRP-USP

INTRODUCTION There are evidences that endothelin (ET) induces nociception. Recently, we demonstrated that IL-18 induces hypernociception via endothelin **OBJECTIVE** In the present study we evaluated the role of endogenous IL-18 in a nociceptive test in which endogenous ET participates **METHODOLOGY** Wild type Balb/c and IL-18 deficient (-/-) mice received an intraperitoneal stimulus with phenylbenzoquinone (PBQ; 630ug/Kg) or acetic acid (AcAc; 0,6%; 10mL/Kg). Another group was treated with bosentan before stimulus (mixed ET_A/ET_B ET receptor antagonist, 100mg/Kg, po). The number of abdominal writhings was recorded over 20 min **RESULTS:** The nociceptive response induced by PBQ was significantly diminished in IL-18 -/- mice (8.4 ± 2.6 n=5) compared to wild type mice (24.5 ± 2.9 n=6). However, there was no modification on AcAc-induced writhings. Corroborating, bosentan inhibited the PBQ-induced writhing (44%), while not affecting AcAc-induced writhings **CONCLUSIONS:** These results suggest the role of endogenous IL-18 in the PBQ-induced writhings, and that PBQ and AcAc trigger different nociceptive mechanism to induce writhings.

Financial Support: FAPESP, CNPq
Advisor: Carlos A Parada

FF022-ISOFLAVONE ACTIVITIES (DRY EXTRACT) IN PRE-PUBERTY RATS

VALÉRIA ROMERO[1,2](PG);CYNTYA DELA CRUZ[1](IC); EFIGÊNIA QUEIROZ DE SANTANA[1](PQ)

(1) Universidade do Sagrado Coração-Bauru-SP; (2) Universidade Estadual Paulista-Botucatu-SP

INTRODUCTION: The Isoflavone presents similar structure to estradiol and has received attention as an alternative for the menopause and osteoporosis prevention. OBJECTIVE: Perform a "screening" to test the activity and estrogenic power of the isoflavone dry extract using the uterotrofic test. METHODS: Five groups of Wistar albinic rats (n=5), considering 2 negative and positive controls (NC and PC); three researched ones (OG) at 21-22 days old received isoflavone extract, (EI) 17βEstradiol (E) or dimethyl sulfoxide (DMSO)+Propylene glycol (PG) by gavage for three subsequent days. The samples were prepared NC (DMSO+PG v/v); PC(E) (0,4 mg/Kg/day) and OG (IE) 10,0; 33,3; and 100 mg/Kg/day. RESULTS AND CONCLUSION:The OG uterus mass average rate with 10,0 mg/Kg (343,77 mg±21,63) IE was higher to the other dosage, including the PC (243,28mg±27,91). The analyzed dosages comparison suggests the 10mg/kg LOAEL dosage. Lower dosage studies should be done in the attempt to explain this answer. The possible increase in the active components in the higher dosages would affect the IE answer in the estrogenic receptors at this age.

Financial Support: USC e UNESP.
Advisor: Dr.Oduvaldo Camara Marques Pereira.

The authors did not follow the modifications suggested by the Scientific Committee

FF023-THE HORMONAL THERAPY EFFECTS OF THE TIBOLONE ON THE REACTIVITY TO THE NOREPINEPHRINE IN CASTRATED FEMALE RATS

GARCIA Jr,R.P(PG)[(1)] ; LAMAS,A.Z(IC)[(1)]; BRAVIM,F.T(IC)[(1)]; GUIDONI,C.M(IC)[(1)];); BISSOLI,N.S(PQ)[(1)]

(1) Physiological Science Department Federal University of Espírito Santo – Vitória ES

Introduction: The Tibolone (T) is a synthetic hormone used in the hormonal therapy, because it has few effects on the breast and endometrium (sites of cancer risk), where estrogen, generally, has action. It also prevents the osteoporosis and it reduces the risk of cardiovascular diseases.
Objective: To evaluate the effect of the T on the norepinephrine (N) reactivity in mesenteric bed vascular of female rats.
Methods: Wistar female rats with free access to food and water; divided in 4 groups: control (C); castrated (CA); castrated and treated with T 1,5 (CT1) and 3,0 µg/Kg/day (CT2). It was done a curve dose-response with N.
Results: It has been demonstrated that the castration increases the results of the N, and the T modified the vascular reactivity.

N (µg/0,1ml)					
	0,39	1,56	6,25	25	100
C	13±3	36±10	81±16	114±9	135±8
CA	24±7	51±17	139±19**	165±18**	156±12*
CT1	7±2	22±8	56±11	92±12	97±9**
CT2	6±1	14±4	46±10	96±11	98±8**

Values mean ± SD *p<0.05 e **p<0.001 when compared to C. Number of animals: 5
Conclusion: The oophorectomy increases the N reactivity, taking off the modulating effect of estrogen; but the T decreased the maximum response.

Financial support: PIBIC-UFES, CAPES
Supervisora: Nazaré Souza Bissoli

FF024-ATORVASTATIN REDUCES PULMONARY ARTERIAL HYPERTENSION INDUCED BY ACUTE PULMONARY EMBOLISM (APE) IN RATS

MARIA CAROLINA SEMPRINI(IC)[1]; DÉBORA CRISTINE SOUZA-COSTA(PG)[1]; JOSÉ EDUARDO TANUS-SANTOS(PQ)[1]

[1]Pharmacology, FMRP-USP

Introduction: APE is a highly lethal medical emergency. Atorvastatin increases endothelial nitric oxide synthase expression in the cardiovascular system, thus increasing nitric oxide (NO) production which is a powerful endogenous vasodilatador. Objective: Prove that atorvastatin attenuate APE-induced pulmonary hypertension. Methods: Wistar rats were treated with atorvastatin 30mg/kg/day (or water) by gastric gavage for 14 days when they were studied in an isolated lung perfusion set up. APE was induced through the injection (solution of polidextrane microspheres-9.0mg/kg) into the pulmonary artery. Mean pulmonary arterial pressure (MPAP) was measured. Control group: n=4 rats water/not embolism; Emb group: n=10 rats water/embolism; Atorv group: n=4 rats atorvastatin/not embolism; Atorv+Emb group: n=10 rats atorvastatin/embolism. Two-way ANOVA analyzed the data with P<0.05 statistically significant. Results: No increases in MPAP was observed in Control group and in Atorv Group and lower increases in MPAP were seen in Atorv+Emb group compared with Emb group (26.9±1.6mmHg Atorv+Emb group X 30±1.8mmHg Emb group; P<0.05). Conclusion: Atorvastatin attenuated APE-induced pulmonary hypertension.

Financial support: FAPESP-CAPES-CNPq
Supervisor: José Eduardo Tanus-Santos

FF025-NEURONAL ACTIVATION IN AUTONOMIC CENTERS DURING POLYMICROBIAL SEPSIS

FERNANDO H. P. BRUHN (IC)[1]; POLLYANNA B.F.CORRÊA (PG)[2]; MARIA JOSÉ A. ROCHA (PQ)[3]

[1, 2]FCFRP–USP,[2]FORP–USP.

Introduction: Sepsis is associated with profound cardiovascular and hydroelectrolytic abnormalities, such as hypotension, and altered vascular permeability, and changes in neuroendocrine function, resulting in alterations in vasopressin secretion. The Aim of this study was to verify the neuronal activation in area postrema (AP), nucleus tractus solitari (NTS), ventrolateral medulla (VLM), locus coeruleus (LC) and parabrachial nucleus (PB) after Cecal Ligation and Perforation (CLP) using c-fos expression as marker. Methods: Male rats were perfused 0, 6 and 24h after CLP or sham operation (n=6); the brains were removed and processed for Fos imunocytochemistry (ABC peroxidase method). Results: We observed an increase in c-fos expression 6h after CLP in all nuclei studied ($p<0,001$), followed by a reduction after 24h in AP and NTS ($p<0,05$) and a decrease to basal levels in VLM, LC and PB. In control animals, c-fos expression was minimal or absent. Conclusion: autonomic centers are activated during the early phase of sepsis, but this activity is reduced or abolished during the late phase.

Financial Support: FAPESP.
Supervisor: Profa. Dra. Maria José A. Rocha.

FF026-IMPAIRMENT OF LPS-INDUCED MECHANICAL HYPERNOCICEPTION IN TLR-4 SIGNALING DEFICIENT MICE

IGOR L CALIL(IC)(1); WALDICEU A VERRI, Jr(PG)(1); THIAGO M CUNHA(PG)(1); CARLOS A PA RADA(PQ)(1), FERNANDO Q CUNHA(PQ)(1) & SÉRGIO H FERREIRA(PQ)(1)

[1]Dept of Pharmacology - FMRP-USP

INTRODUCTION There are consistent evidences that the LPS-induced inflammation depends on the activation of TRL-(toll like receptor) 4. OBJECTIVE Thus, we evaluate the role of TRL-4 in the LPS-induced mechanical hypernociception. METHODS The nociceptive responses were evaluated using the Dynamic Plantar Aesthesiometer (Ugo Basile) before and after inflammatory stimulus on intraplantar (ipl) injection in C3/HePas (wild type;WT) and C3H/HeJ (TLR-4 signaling deficient mice;TLR-4-/-). RESULTS LPS ipl injection induced dose- (30-300ng/paw) and time- (1-24h) dependent hypernociception in WT, but not in TLR-4-/- mice. The nociceptive effect of LPS is mediated by prostanoids (indomethacin,COX inhibitor,5mg/Kg,40min;47.84%), sympathetic amines (guanethidine,30mg/Kg,1h;64.40%), KC(antibody anti-KC,500ng/paw,15min;29.19%) and IL-1β(IL-1ra, 500ng/paw,5min;44.37%). Corroborating, the hypernociceptive responses induced by prostaglandin, dopamine, KC, IL-1β or even zymosan are not altered in TLR-4-/- mice. CONCLUSIONS These data suggest that LPS triggers a sequential cytokine cascade in mice via TLR-4, which might be a target for novel analgesic therapies

Financial Support: FAPESP and CNPq
Advisor: Sérgio H Ferreira

FF027-INFLUENCE OF THE INHIBITION OF METALLOPROTEINASES WITH DOXYCYCLINE ON THE PRESSURE EFFECTS OF NICOTINE IN RATS

ANNA L B J FERREIRA(IC)[1]; MÁRCIO L L MARTINEZ(PG)[1]; ANA C T PALEI(IC)[1]; RAQUEL F GERLACH(PQ)[2]; JOSÉ E TANUS-SANTOS(PQ)[1]

[1] Farmacologia – FMRP, USP; [2] Morfologia, Estomatologia e Fisiologia – FORP, USP

Introduction: Nicotine plays a role in the cardiovascular alterations of smokers, and may activate and increase the expression of matrix metalloproteinases (MMPs). It has been shown that MMP-2 regulates the vascular reactivity, at least in part, by releasing endothelin 1-32. Objective: Examine whether a non-specific MMPs inhibition with doxycycline affects the hemodynamic responses to nicotine. Methodology: Wistar rats anesthetized and mechanically ventilated, had their MAP artery-monitored throughout the experiments. Doxycycline (30mg/kg) or saline was injected (iv) 15 minutes before the injection of nicotine (2µMol/kg) or saline (iv) (N=6-10/group). Results: MAP increased by 42±18 mmHg after injection of nicotine in rats pre-treated with saline. A trend towards lower increases in MAP were observed when rats were pretreated with doxycycline (28±16mmHg; P=0.08). Conclusion: Our preliminary results suggest that doxycycline may attenuate the increase in MAP induced by acute administration of nicotine in rats and that MMPs have a role in the hemodynamic changes associated with nicotine administration.

Financial Support: CNPq, FAPESP, CAPES
Advisor: José Eduardo Tanus dos Santos

FF028-DOPAMINE-ACETYLCHOLINE INTERACTION ON LOCOMOTOR ACTIVITY IN RATS

EMMANUELLE COELHO NORONHA(PG)[(1)]; MIRELLA LEITE PEREIRA(IC)[(1)]; PATRICIA BEZERRA GOMES(PG)[(1)]; FRANCISCA CLÉA FLORENÇO DE SOUSA(PQ)[(1)]

[(1)]Federal University of Ceará, Brazil

Introduction: Neurochemical and behavioral studies have elucidated interactions between dopaminergic and cholinergic systems in brain areas associated with movement. Objective: Study the effects of cholinergic and dopaminergic drugs on open-field test. Methodology: Female Wistar rats (180-200g) received saline (10mL/kg), pilocarpine (pilo), pirenzepine(pz), 1, 5, 10mg/kg, i.p. or p.o., and mazindol(maz) 5, 10, 20mg/kg, p.o., alone and associated with pilocarpine(pilo) 80mg/kg, i.p. or pimozide(pim) 20mg/kg, p.o.. The open-field test was performed 30min or 1h after drug treatment. Results: Values represent mean±SEM, number of animals in parenthesis. Pim[0.0±0.0(09)] blocked totally the motor response induced by pilo[1=13.9±1.89(8); 5=9.8±1.75(8); 10=7.3±1.13(9)] and pz[1=11.0±1.44(8); 5=14.8±2.31(8); 10=13.7±1.78(9)], as compared to control[9.9±0.81(49)]. High doses of maz[10=9.4±0.82(8); 20=8.5±2.19(8)] inhibited the effect induced by pilo 80[10=10.9±1.40(7); 20=9.33±2.67(6)], but lower dose did not. Conclusion: The results suggest a relationships between M1 and D1 receptors and M2 and D2 receptors.

Financial Support: CNPq
Supervisora: Dra. Francisca Cléa F. de Sousa

The authors did not follow the modifications suggested by the Scientific Committee

FF029 - ANTICONVULSANT PROPERTIES OF RIPARIN I (RIP I) AND RIPARIN III (RIP III) FROM *ANIBA RIPARIA* (NEES) MEZ (LAURACEAE) IN MICE

ANDREISA PAIVA MONTEIRO(IC)[1]; CARLA THICIANE V. MELO(PG)[1]; CAROLINE P. LEITE(IC)[1]; FRANCISCO EVANDO RODRIGUES FILHO(IC)[1]; STANLEY GUTIERREZ(PG)[2]; JOSÉ MARIA BARBOSA FILHO(PQ)[2]; FRANCISCA CLÉA F. SOUSA(PQ)[1]

[(1)]Federal University of Ceara; [(2)]Federal University of Paraiba, Brazil

Introduction: Rip I (methyl ethers of N-benzoyl tyramine) and Rip III (N-(2,6-dihydroxybenzoyl) tyramine) have been isolated from *Aniba riparia*. Objective: Study the effects of rip I and III on pentilenetetrazole (PTZ)-induced convulsions and rotarod test in mice. Methodology: Male Swiss mice (20-30g) were treated with rip I and III, 25 and 50 mg/kg, i.p.. Controls received saline. Results: Values represent mean±SEM number of animals in parenthesis. Rip I (25 and 50mg/kg, i.p.) increased the latency to 1st convulsion [25=121.6±17.4(s)(8); 50=120.4±14.9(s)(8); c.=73.6±6.8(s)(10)], mortality time [25=567.5±119.3(s)(4); 50=706.0±97.1(s)(7); c.=418.0±45.3(s)(8) and survival [25=55.6%; 50=22.2%; c.=0%] as related to controls. Rip III increased lethal time [25=338.2 ± 27.6(s)(10); 50=304.5 ± 30.0(s)(10)] as related to control [220.5±18.3(s)(23)]. Diazepam, positive control increased all parameters observed. Rotarod test was unaltered. Conclusion: Rip I and III presents a protective effect in seizure and are devoid of myorelaxant effect (rotarod).

Financial support: CNPq
Supervisor: Francisca Cléa F. Sousa

FF030-CELLULAR MECHANISMS UNDERLYING INCREASED PHE-INDUCED CONTRACTION IN CONTRALATERAL CAROTID AFTER BALLOON CATHETER

VANIA CLAUDIA OLIVON(PG)[1];CLAUDIA DE ANDRADE CR(PG)[2];LEANDRA RAMALHO(PQ)[2]; ANA MARIA DE OLIVEIRA(PQ)[1]

[1]FCFRP–USP; [2]FMRP–USP

Introduction: Balloon catheter induces an increased in contralateral (CL) carotid reactivity to Phe-induced contraction.
Aim: Investigate the participation of Ca^{++} and Rho-Kinase (RK) on increased reactivity in the CL to Phe compared to control (CO).
Methods: Arteries from control adult rats and animals that underwent unilateral balloon catheter injury during 4 days. To study vascular reactivity carotids were removed and placed in an organ chamber.
Results: Phe Emax was increased after balloon injury in CL (0.59±0.06 g) when compared to CO artery (0.43±0.02g). In the absence of endothelium, Emax was 0.58±0.02g in CO, while in CL was 0.40±0.03g. Y27632 (RK inhibitor) inhibited concentration dependents way the Phe-induced contractions, maximal inhibitory effect (100%) was produced by 10^{-7} M in CO artery. In CL Y27632-maximal effect was reduced to 22.23%. Extracellular Ca^{++} mobilization induced by Phe was reduced in CL artery when compared to CO (0.24±0.03 *vs* 0.44±0.07, respectively), while intracellular Ca^{++} mobilization was similar in both groups.
Conclusions: The increase on Phe-induced contraction in CL carotid after balloon injury the participation of RK and calcium was significantly reduced.

Supported by: FAPESP
Supervisor: Ana Maria de Oliveira

FF031-NICOTINE ACCUTELY INCREASES PLASMA MMP-9 ACTIVITY

ANA C T PALEI (IC)[1]; RAQUEL F GERLACH (PQ)[2]; JOSÉ E TANUS-SANTOS (PQ)[1]

[1]Farmacologia-FMRP/USP; [2]Morfologia, Estomatologia e Fisiologia-FORP/USP

Introduction:Matrix metalloproteinases (MMPs) break down the extracellular matrix and affect the cardiopulmonary system. Nicotine is a component of smoke and is involved in the alterations of the cardiopulmonary system in smokers. Objective:We examined if nicotine acutely increases plasma MMP-2 and -9 activities. Method: Blood samples were drawn into citrate tubes from eight healthy volunteers. Whole blood samples were incubated (25ºC, 30min) with nicotine 0nM (vehicle), 50nM, or 150nM, and were centrifuged (1000g, 15min). Gelatin zymography of MMP-2 and -9 from plasma samples were performed under nonreducing conditions on 7% polyacrylamide copolymerized with gelatin 1%. Gels were washed Triton X100, incubated in Tris–$CaCl_2$ buffer (37°C, 16h) and stained with Coomassie Blue. Enzyme activity was assayed by densitometry. All results were normalized by the results obtained with vehicle. Results: Nicotine 50nM did not significantly change MMP-9 activity. Nicotine 150nM increased MMP-9 activity by 166±86% (N=8; $P<0.05$). No significant changes were seen in MMP-2 activity. Conclusion:Results show that nicotine increased plasma MMP-9 activity, thus suggesting a mechanism by which nicotine may cause injury to the cardiopulmonary system in smokers.

Apoio Financeiro: CNPq
Supervisor: José E Tanus-Santos

FF032-BETA-CARBOLINES INDUCE ANXIOLYTIC EFFECTS IN MICE

KÁTIA SZTORMOWSKI (IC)[1]; JANE MARLEI BOEIRA(PQ)[1,2]

(1) Depto. Ciências da Saúde, URI , Erechim, RS

Beta-carboline alkaloids harmaline, harmine, harman and harmol were originally identified in *Peganum harmala* and are found too in others medicinal plants. Various pharmacological effects of these compounds are related with their action on cardiovascular, muscular and central nervous systems. These study investigated the potential anxiolytic effect of these alkaloids using the elevated plus maze in mice. The apparatus was made of wood and consisted of two opposite open arms and two opposite arms of equal size enclosed by 40 cm high walls. The arms were connected by a central 5 cm x 5 cm square and the maze formed a plus shape, and was elevated 45 cm from the floor. Thirty minutes before the test, mice received different doses of alkaloids. To compare the effects were given diazepan. Animals were separated in groups of 10, and each one after injection substance were placed in the center of the maze facing a closed arm and allowed 5 min of free exploration. The time to explorer open and closed arms were evaluated and differences between groups were analyzed by ANOVA. The results showed that harmine did not induce ansiolytic effect. However, harmaline, harman and harmol induced effect like diazepan. Probably these results were due to interactions of these alkaloids with benzodiazepines receptors.

Supported by FAPERGS; URI
(2)Supervisor

FF033-CANCER AND THE TREATMENT WITH ANTINEOPLASTIC CHEMOTHERAPEUTIC AGENTS: AN ORAL ADMINISTRATION ANALYSIS

ALEXANDRE BRONHARO FIORATTI (IC)[1]

[1]Universidade Estadual de Maringá

Introduction: Cancer is a genetic disease when excessive mutations in genetic material of cells results in generation of neoplastic cell. Neoplastic cell can multiply and generate a malignance mass. Surgical procedures, radiotherapy and/or pharmacological treatment are responsible for cure of about 50% of patients with cancer. Objective: To accomplish an oral administration analysis of antineoplastic chemotherapeutic drugs. Methodology: A systematic review of cancer chemotherapy. We used electronic databases and searches of published references at scientific sites. Results: The analysis of articles showed that the chemotherapeutic agents in great part are administered by intravenous route in oncologic offices what requesti a series of cares on manipulating and administrating. However, current studies are aimed in the development of oral chemotherapeutic agents for the cancer treatment. Oral chemotherapeutic agents present several advantages compared to the intravenous route. Conclusions: The main barrier for the largest adoption of oral administration route consists in non-compliance by the patient. Health professionals must be aware in developing tools, such as informative panflets in orderto make cancer chemotherapy more effective.

Financial Support: Sesu/MEC
Supervisora: Carolina Justus Buhrer Ferreira Neto

FF034-EFFECTS OF INDUCIBLE NITRIC OXIDE SYNTHASE (INOS) INHIBITION ON VASOPRESSIN (AVP) SECRETION AND NEURONAL ACTIVATON IN POLIMICROBIAL SEPSIS

POLLYANNA B.F.CORRÊA(PG) [1]; MARIA JOSÉ A. ROCHA(PQ)[2]

[1]FCFRP–USP, [2]FORP–USP.

Introduction: Sepsis causes nitric oxide (NO) release and alterations in AVP secretion. The aim of this study was to evaluate the role of iNOS in organum vasculosum of lamina terminalis (OVLT), paraventricular (PVN) and supraoptic (SON) nuclei activation and AVP secretion of rats submitted to sepsis by cecal ligation and puncture (CLP). Methods: Male rats submitted to CLP or sham operation were treated with aminoguanidine (AG) or vehicle i.p. A group of animals was decapitated 0, 2, 6 and 24h after the surgery. Blood was collected for AVP measurements by RIA. In another group, rats were perfused at 0, 6 and 24h after surgery and brains were processed for Fos imunocitochemistry. Results: There was an increase in the number of Fos-like immunorreactive (FLI) cells 6h after CLP in OVLT, PVN and SON, but values returned to basal levels at 24h. AG i.p. reduced the number of FLI cells in all nuclei 6h after CLP, but after 24h this decrease persisted only in SON and OVLT after 24h. AVP plasma levels increased at 6h in CLP-AG and CLP-vehicle groups, but AG reduced this increase. In both groups, AVP levels were basal 24h after CLP. Conclusion: NO produced in the early period of sepsis does not prevent neuronal activation and AVP secretion yet it does so in the late phase.

Financial Support: FAPESP
Supervisor: Profa. Dra. Maria José A. Rocha

FF035-THE LATEX NATURAL BIOMEMBRANE INHIBITORY EFECT ON THE IN VITRO BACTERIAL GROWTH

DANIEL ZUCCHI LIBANORE(PG)[1]; THIAGO ANDRADE(PG)[1]; FERNANDO DE QUEIROZ CUNHA(PQ)[2]; MARCO ANDREY CIPRIANI FRADE(PQ)[1]

[1]Internal Medicine and [2]Pharmacology Departments of Medicine School Ribeirão Preto-USP

Introduction: Cutaneous ulcers reach superficial dermis and can compromise other deep tissues. An important complication for the closing of those ulcers is the bacterial colonization. The biomembrane of natural latex from *Hevea brasiliensis* (BLN) has been showing effective in the desbridament of chronic ulcers. The study compared the BLN inhibitory effect on the in vitro bacterial growth with antibiotics and with cruel latex. Methods:The specimes *S. aureus* and *S. tiphymurium* were sowed in Petri´s plate in Agar Muler-Hinton. Different groups were constituted according the disks (Group I=Ciprofloxacin,II=Gentamicin,III=BLN and IV=glove). Each group was constituted of 9 disks (n=9),incubated to 37ºC for 24h and after the inhibition halos were measured. Results: There was inhibition in both bacterial types, statistically significant ($p < 0,001$) for the Bonferroni´s test, when compared the results of the groups I, II and III with the group IV. Conclusions: The results show that BLN presents inhibitory activity of the bacterial growth bigger than the glove, important property to in the cutaneous ulcers treatment.

Financial Support:FAEPA-FMRP-USP
Supervisor:Marco Andrey Cipriani Frade

FF036-KININ SYSTEM (KS) IN PATIENTS WITH SYSTEMIC LUPUS ERITHEMATOSUS (SLE) AND DIABETES MELLITUS (DM) AFTER ADMINISTRATION OF FENOPROFEN (FEN)

DOUGLAS COSTA MORAIS(IC)[1]; GIULIANO RODRIGO BARISSA(PG)[1]; JOSIANE CRISTÓFANI POGGI(PG)[1]; MARINA LEMOS DOS REIS(PQ)[1]; VERA LÚCIA LANCHOTE(PQ)[1]

[1]FCFRP – USP

Introduction: Studies showed FEN has its enantioselective metabolism altered by diseases as SLE and *DM*. Studies in diabetic rats showed increase in unidirectional inversion of (-)R to (+)S-FEN, enantiomer with antiinflammatory activity. The KS besides to be important inflammatory mediator also stimulates the production of prostaglandin, nitric oxide and cytokines.
Objective: Evaluation of KS in patients presenting SLE and DM, before and after FEN administration.
Methods: We studied 15 SLE patients, 8 diabetic and 10 healthy volunteers. They received single dose of racemic FEN and blood samples were collected. The Kininogen (Kg) were evaluated by ELISA, kallikreins (Kal) and Kininase II (Kn II) by enzymatic activity on selective substrates. The Mann-Whitney test was used for statistical analysis.
Results and Conclusion: Kn II activity had a high increase in DM and SLE patients. The results also showed that 4h after FEN administration in patients, Kg levels and plasmatic Kal activity decreased significantly. These results indicate the interference of SLE and DM or FEN enantioselective metabolism on the KS.

Financial Support: CNPq
Supervisora: Profª. Dr.ª Marina Lemos dos Reis

FF037-ANTYPIRETIC EFFECT OF ACETAMINOPHEN

BRUNO L. P. BATISTA[1](IC), GLÓRIA E.P. SOUZA[1](PQ)

[(1)]Lab. of Pharmacology, FCFRP-USP, SP, Brazil

Introduction The mechanisms by which acetaminophen (ACET) exert antipyretic effect are not clearly understood.
AIM To investigate the effect of ACET given by different routes of administration on the LPS induced fever in rats.
Methodology Fever was induced in Male Wistar rats (≅200 g) by i.p. (intraperitoneally) or i.v. (intravenously) injected LPS (50 µg/kg). ACET (diluted in ethanol 10% + 2 drops of Tween 80) was given i.p (50, 75,150 mg/kg) or per os (p.o., 50, 75, 150, 300 and 450 mg/kg) 30 min before LPS Changes in rectal temperature were measured until 6h by telethermometry
Results. ACET 450 mg/kg p.o. abolished fever to i.v. LPS (2.5h, n=6) while at 150 mg/kg it was ineffective. ACET 150mg/kg i.p. reduced 77 % (2.5 h, n=6) the fever to LPS i.p. while promoted a brief and strong antipyresis (100 % from 2 to 2.5h) on fever to i.v. LPS (2.5 h, n=8)
Conclusion Given i.p. ACET was more effective on fever to LPS i.p. than to i.v. Fever to LPS i.p. depends on vagus nerve and *nucleus tractus solitarium* (NTS) to signal the hypothalamus to trigger fever. Increased glutamate release in the NTS was observed on fever to i.p. but not to i.v. LPS and ACET given i.p. inhibits glutamate release. So, the antipyretic effect of ACET given i.p. could be related to the inhibition of glutamate release

Support FAPESP
Supervisor Glória E. P. Souza

FF038-PHENYLEPHRINE INDUCES OSCILLATORY ACTIVITY IN AORTA FROM SINOAORTIC-DENERVATED RATS.

MATHEUS LAVORENTI ROCHA (PG)[(1)]; LUSIANE MARIA BENDHACK (PQ)[(2)]

[(1)] FMRP–USP; [(2)] FCFRP–USP.

Introduction: The sinoaortic-denervation (SAD) is a model of blood pressure lability without sustained hypertension. Aim: Since these rats present arterial lability, the aim of this study was to investigate the possible oscillatory activity (OA) on the contractile response to phenylephrine (PHE) in aortic rings from SAD rats and sham-operated rats (SO). **Methods:** The arterial pressure was recorded 3 days after the surgeries. Concentration-effect curves for PHE (10^{-9} to 10^{-5} M) were constructed in intact endothelium (E+) or denuded arteries (E-) from SAD and SO rats. **Results:** Only the SAD rats presented arterial pressure lability. The contraction to PHE was similar in SAD (Emax: 1.43±0.13g, pD_2: 8.04±0.35, n=5) and SO (Emax: 1.12±0.08g, pD_2: 8.0±0.20, n=6) E+ rat aortas. The contraction induced by PHE elicited OA in the range from 10^{-8} to 10^{-7}M in isolated aortic rings from both groups in E+ and E-. In E+, 4/5 aortas of SAD and 3/6 SO and in E- 6/7 SAD and 3/7 SO presented OA. The OA appeared in the low concentrations of PHE, which disappeared when its concentration was increased. **Conclusions:** The SAD rats presented arterial lability and most of the aortas from these rats presented OA. No changes in vascular reactivity of SAD and SO rats was observed to PHE.

Financial support: FAPESP and CNPq.
Supervisor: Lusiane Bendhack

FF039-*IN VIVO* EFFECT OF DIMINAZENE DIACETURATE (USED IN THE TREATMENT OF LEISHMANIASIS) ON MACROPHAGES PHAGOCYTOSIS

POLLYANA SOUTO(IC)[1]; ISABELA FURTADO(IC)[1]; OSVALDO NUNES BARBOSA(PQ)[1]; ANDRÉ KLEIN(PQ)[1]

[1] Universidade Federal de Mato Grosso do Sul, Brazil

Introduction- The species of *Leishmania sp* infect cells of the phagocytic system, where obtain to escape of humoral response inhabiting in phagolysosome and determining a response mediated by cells.
Objective- To examine the effect by treatment *in vivo* with Diminazene diacerutate (Dd) on macrophages phagocytosis in response to zymosan.
Methodology- Swiss mice were pre-treated with Dd, being the peritoneal exudate cells pre-stimulated with LPS and stimulated with zymosan. The Phagocytic Index was evaluated in presence or absence of this drug.
Results- In cellular culture, the treatment with Dd (300 and 420 μg/animal) presented strong inhibition of the macrophages Phagocytosis Index, as well as reduced the number of cells that phagocyted zymosan particles.
Conclusions. The treatment with Dd was capable to inhibit Phagocytosis Index in way dose-dependent, suggest that, part of observed effects antileishmania can reduce macrophages phagocytosis, decreasing the entrance by parasite in the cell.

Financial support: CNPq
Advisor: André Klein

FF040-ANTITUMORAL EFFECTS OF DICHLORINE-BIS-PYRAZOLE PALADIUM II IN MICE INOCULATED WITH ASCITES EHRLICH TUMOR

GUSTAVO ROSSANEZI (IC) [1]; TARSILA G. BONATELLI (IC) [1]; DEJAIR C. DO NASCIMENTO (PQ) [1]; ANTÔNIO E. MAURO (PQ) [2]; DULCE H. J. CONSTANTINO (PQ) [1]; VICENTE A. L. NETTO (PQ) [1]

[1] Universidade do Sagrado Coração; [2] Instituto de Química, UNESP - Araraquara

INTRODUCTION: Cancer is the second leading cause of death nowadays. Even though many researches have been developed, there are basically three treatments against cancer, such as: radiotherapy, immunotherapy and chemotherapy. OBJECTIVE: Evaluate the effect of dichlorine-bis-pyrazole palladium II over ascites ehrlich tumor cells in mice. METHODOLOGY: Four groups of Swiss mice, males, with 30-45 days, received $3,0.10^3$ tumor cells and, after 2 days, their treatment started. The control group received DMSO 0,5%/day and the other groups, 1μg, 2μg and 4μg /day of the compound. After the treatment (8 days), peritoneal cells, obtained from peritoneal lavage, were counted. RESULTS: The group who received 4μg /day had a decrease of 73,4% of tumor cells in comparison to the control group. The other groups showed an interest decrease as well: 1μg/day = 27,3%, and 2μg = 59,4%. CONCLUSION: According to this research, the dichlorine-bis-pyrazole palladium II may have decrease effects on ascites ehrlich tumor cells in mice.

Financial support: PIBIC-CNPq
Supervisor: Dejair C. do Nascimento

FF041-ANTINOCICECEPTIVE EFFECTS OF NOVEL PYRAZOLES IN THERMAL MODEL OF PAIN IN MICE

JULIE MILANO(PG)[(1)]; SARA MARCHESAN DE OLIVEIRA (IC)[(1)]; MATEUS ROSSATO(IC)[(1)]; PATRICIA SAUZEM(PG)[(1)]; LEONARDO MARTINI(IC)[(1)]; MARIBEL ANTONELLO RUBIN(PQ)[(1)]; CARLOS FERNANDO MELLO(PQ) [(1)].

[(1)]Universidade Federal de Santa Maria

Introduction: The discovery of novel drugs that have high efficacy as well as low side effects represents one of the main subject in current pain research.
Objective: We evaluated the antinociceptive effect of four novel pyrazoles: 3-methyl-5-trifluoromethyl-5-hydroxy-4,5-dihydro-1*H*-pyrazole-1-carboxymehtyl(MPF3),4-methyl-5-trifluoromethyl-5-hydroxy-4,5-dihydro-1*H*-pyrazole-1-carboxymehtyl (MPF4),3-phenyl (4-methoxi)-5-trifluoromethyl-5-hydroxy-4,5-dihydro-1*H*-pyrazole-1-carboxymehtyl(PPF1) and 3-phenyl(4-fluor)-5-trifluoromethyl-5-hydroxy-4,5-dihydro-1*H*-pyrazole-1-carboxymehtyl (PPF2), using hot-plate test.
Methodology: Male mice received intraperitoneally vehicle (rice oil or 5% Tween 80), or pyrazoles (0.1-1.0mmol/kg), or dipyrone (1.5mmol/kg) and subjected to the hot-plate test (50±0.1°C) 15, 30 and 60 min thereafter. The latency to show nociceptive responses, such as licking their hindpaws or jumping was measured.
Results and Conclusions: MPF3, MPF4, PPF1 and PPF2, caused antinociception in the hot-plate test after drug administration.

Financial Support: CNPq/UFSM
Supervisor: Maribel Antonello Rubin

FF042-ANTINEOPLASIC ACTIVITY OF THE C*AESALPINA ECHINATA* LAM. IN SARCOMA OF YOSHIDA

ELISANGELA CHRISTHIANNE BARBOSA OF SILVA (PG)[1]; ALDO CÉSAR PASSILONGO DA SILVA (PG)[1]; KAREN PENA DE SOUZA CAVALCANTI (PQ)[2]; IGOR ARTUR DA FARIAS (PQ)[1]; IVONE ANTÔNIA DE SOUZA (PQ)[1]

[1]UFPE Pharmacy Department, Recife, Brazil; [2] UFPE Hospital of the Clinics, Recife, Brazil.

INTRODUCTION: The cancer incidence in Brazil is increasing every year. The treatment discoveries don't accompany that incidence increase. The *Caesalpinia echinata* Lam., of the family Leguminosae - Caesalpinoideae, is a typical arboreal species of tropical forests. Among your medicinal properties, it is told that the log is astringent, corroborant and drying, odontalgic and tonic. OBJECTIVE: To evaluate the antineoplasic action of the rude ethanolic extract (EEB) of *C. echinata* in comparison to Yoshida's solid Tumor. METHODOLOGY: The study of the antineoplasic activity was accomplished according to Stock (1955). The treatment was begun after 48 hours of the it implants with a daily dose for eight days, orally. RESULTS: The tumor inhibition of Yoshida's sarcoma when agreement with EEB *of C. echinata* was of 64%. CONCLUSION: The rude ethanolic extract of the log of *C. echinata* possesses noticeable inhibitory action in comparison to the tested tumor.

Supervisor: Ivone Antônia de Souza

The authors did not follow the Scientific Committee's suggestion for an English language review

FF043-*IN VITRO* EFFECT OF AMPHOTERICIN B ON THE PHAGOCYTIC ACTIVITY OF MACROPHAGES

ISABELA FURTADO (IC)[1]; POLLYANA SOUTO (IC)[1]; OSVALDO N. BARBOSA (PQ)[1]; ANDRÉ KLEIN (PQ)[1]

[1]Universidade Federal de Mato Grosso do Sul; Brazil

Introduction-The parasites that infect macrophages survive at the humoral answer of hospitable using structures of cell membrane of macrophages involved in the process of phagocytosis. Thus, is possible that a major phagocytosis carries to a major infectivity.
Objective-To evaluate the importance of Amphotericin B, a drug used in the treatment of parasitic diseases, to the action in the phagocytosis, answering to the Zymozan.
Methodology-The murine macrophages were pre-stimulated with LPS, incubated with Amphotericin B (1-10 µg/ml/well) and stimulated with Zymosan. Afterward, the Phagocytosis Index from this cells was evaluated in presence or absence of the drug.
Results-The pre-incubation of macrophages with Amphotericin B decreased approximately 40% the number of cells that phagocyted, farther to decrease the number of phagocyted particles, decreasing the Phagocytosis Index.
Conclusion-In all the experiments, the administration of Amphotericin B inhibited the Phagocytosis Index suggesting that this reduction could contribute to the organism against the parasite.

Financial Support: CNPq
Advisor: André Klein

FF044-CHARACTERIZATION OF HEPATOTOXICTY OF CROTALIC VENOM.

GUSTAVO TEIXEIRA (PG)[1]; RAFAELA FRANÇA (PG)[1]; RODOLFO VIEIRA (PG)[1]; ANTÔNIO C. PRIANTI (PG)[1]; RODRIGO MARTINS (PQ)[1]; JOSÉ C. COGO (PQ)[1]; WELLINGTON RIBEIRO (PQ)[1]

[1]Department of Pharmacology, IPD, UNIVAP, S. J. dos Campos, São Paulo, Brazil. lab_farmacologia@yahoo.com.br

Crotalic snakebite results in systemic disorders and hepatic alterations were observed in few cases. The aim of this study was investigate the protective action of Ca^{2+} channel blocker, verapamil, against hepatotoxic envenoming caused by South American rattlesnake (C.d.t.) venom in rats liver. Male Wistar rats (n=24) were divided into four groups (n=6): group 1 – control (saline), group 2 – C.d.t. venom (200 µg/Kg, i.m.), group 3 – verapamil (25 mg/Kg, i.p.) and group 4 – pre-treatment with verapamil + venom. Each of these groups are divided at times of 1,2,3 and 12 hours after intervention, they were sacrificed. Blood were collected for enzymatic measurement of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and liver samples were collected and processed for histological analysis by light microscope. Enzymatic levels and histological changes were observed. Cases of steatohepatitis have been reported in association of calcium channels blockers including verapamil. Possibly the hepatic regeneration, are induced by release of cytokins mediated by crotalic crude venom, by drugs in acute inflammatory response or both.

The authors did not follow the modifications suggested by the Scientific Committee

FF045-LUNG ORGANOGENESE AND SPINE GANGLIONS IN FETUS AND NEWBORN OF CHRONIC ALCOHOLISM SUBMITTED FEMALE RATS STUDY

GUILHERME AUGUSTO BERTOLINO (IC)[1]

[1]Centro Universitário Barão de Mauá

Introduction: Chronic Alcoholism determines many different organic abnormalities, which should be evaluated to make possible the relation to Biomedical and Pharmaceutical behavior.
Objective: The objective is to explain congenital alterations due to chronic alcoholism fetus. Method: Eight adult female rats from Wistar lineage were used and they were divided in two groups: In the control group, female rats didn't ingest alcohol. In the experimental group, they got sugar cane alcoholic liquor dissolved at 30º as the only liquid food, having as solid one balanced ration. The female rats were sacrificed in the conventional way, without suffering, seven, fourteen and nineteen days after coupling. Fetus and newborn were microscopic examinated with histologic slices and also macroscopic evaluated. Results: The experimental group rat newborn lungs were analyzed microscopically and showed thicken septum and dilated alveolar lumen as well as intra alveolar edema. A decrease of the number of neurons and citoplasmatic vacuolization in the spine ganglions were found in the experimental group.
Conclusion: Our findings may alert to the necessity in healthy professionals to adequate therapeutics treatments when taking care of chronic alcoholic individuals.

Advisor: Maria Helena Simões Jorge
Co – advisor: Ana Rosa Crisci

FF046 - ROLE OF ENDOGENOUS NITRIC OXIDE IN MODELS OF SPONTANEOUSLY HYPERTENSIVE AND NORMOTENSIVE RAT PLEURISY

CIOMAR A BERSANI-AMADO[1], ADRIANO A FERREIRA[1], TIELES CO DELANI[1], MARIA ANGÉLICA RCP SILVA[1], ROBERTO KN CUMAN[1], SILVANA M CAPARROZ-ASSEF[1], FÁBIO H KWASNIEWSKI [2].

[1] Lab. of Inflammation-University of Maringá-PR, [2] UMC, University of Mogi das Cruzes, Brazil.

AIM:To investigates the role of NO during the acute inflammatory response induced in the pleura of spontaneously hypertensive rats (SH) and normotensive rats (NT). METHODS:Carrageenan (200µg/cav) and ovalbumin were used (OVA 1g/cav, in sensitized animals (OVA-10µg/rat) 14d before). 30min and 4h after the induction of pleurisy, inflammatory exudates were collected. L-NAME (30mg kg^{-1}) was injected into the animals iv 30min before the pleurisy. RESULTS:a) The response to carrageenan develops similarly in SH and NT (exudate vol.:SH=0,69±0,03, NT=0,76±0,02mL; migrated leukocytes:SH=61020±959;NT=63640±952). L-NAME reduced response intensity in both groups. b) Plasma exudation induced by active anaphylaxis was less in SH than in NT rats at 30min; but similar 4h after stimulation (SH=0.5±.02, 1.0±.08; NT=0.9±.03; 0.9±.06, mL). The number of neutrophils increased in the 4thh in both rat lineages (SHR=42890±2039;NTR=32031±1671), unaffected by L-NAME treatment. CONCLUSION:Inflammatory response in SH differs from that in NT rats, depending on the nature of the inflammatory stimulus. Endogenous NO plays clear role in carrageenan-induced inflammation, but not in immuno-mediated inflammation.

Supervisor: Ciomar A. Bersani-Amado

FF047-CENTRAL EFFECTS FROM *PETIVERIA ALLIACEA* L. (TIPI) IN MICE

PATRICIA BEZERRA GOMES(PG)[(1)]; NATÁLIA N. SARAIVA(IC)[1]; EMMANUELLE COELHO NORONHA(PG)[(1)]; JOSÉ NOBERTO BEZERRA(PG)[(1)]; MANOEL ANDRADE NETO(PQ)[(1)]; FRANCISCA CLÉA FLORENÇO DE SOUSA(PQ)[(1)]

[(1)]Federal University of Ceara, Brazil

Introduction: *Petiveria alliacea* L., a bush distributed in South America including Brazil, is known as tipi, pipi, erva-pipi, anamu. Previous data cited antiinflammatory, antimicrobial, anticancer and stimulant effects, among others. Tipi was used in religious ceremony by slaves, who called the herb "to tame the master" a reference to its toxic and sedative properties. Objective: Study the central effects of the hexanic fraction (FH) isolated from the root of tipi on animals models. Methodology: The open-field, barbiturate-induced sleeping time and forced swimming tests were used. Female mice were treated with FH 100 and 200 mg/kg, i.p.. Results: Values represent mean±SEM, number of animals in parenthesis. FH reduced the locomotor activity[100=44.4±3.99(13); 200=36.8±3.17(17); control=66.0±2.28(30)] on open-field test. There was a prolongation of the pentobarbital-induced sleeping time[100=69.0±7.6(7); 200=81.7±12.46(6); control=40.6±2.20(29)]. In the forced swimming test, FH increased the immobility time[100=105.4±12.48(9); 200=104.7±5.89(9); control=62.4±4.43(20)]. Conclusion: Tipi presents depressant-like and sedative-like effects.

Financial Support: CNPq
Supervisora: Dra. Francisca Cléa F. de Sousa

The authors did not follow the modifications suggested by the Scientific Committee

FF048 - K_{ATP} CHANNELS ACTIVATION IS INVOLVED ON RAT AORTA RELAXATION STIMULATED WITH CIS-$[RU(BPY)_2(PY)(NO)](PF_6)_3$.

MOLIN, J.C.; SAUAIA, M.G.; DA SILVA, R.S.; BENDHACK, L.M. DEPTO DE FÍSICA E QUÍMICA,

FCFRP-USP.

Introdution: It has been reported that NO donors induce vascular smooth muscle relaxation. One of the mechanisms proposed to explain the relaxation is K^+ channels activation. Aim: To investigate the contribution of K^+ channels to the relaxation induced by cis-$[Ru(bpy)_2(py)(NO)](PF_6)_3$. Methods: Denuded rat aortic rings pre-contracted with phenylephrine (Phe) were stimulated with increasing concentrations of the complex, in the absence (control) and in the presence of the selective K^+ channel blockers. One group of arteries was pre-contracted with 60 mM KCl. The parameters analyzed were the maximum relaxant effect (Emax) and the potency (pD_2). Results: In KCl-contracted arteries (Emax: 50.8±1.8%, pD_2: 4.63±0.04, n=6) and in Phe-contracted arteries in presence of glibenclamide (K_{ATP} blocker) (Emax: 85.3±4.9%, pD_2: 4.44±0.46, n=6) the relaxation was reduced as compare to control (Emax: 105.2±1.7%, pD_2: 5.69±0.08, n=5). The other K^+ channel blockers (iberotoxin (K_{Ca}), tetraethylammonium (non selective), 4-aminopyridine (K_V) and apamine (K_{Ca}) failed to have effect. Conclusion: Our results indicate that the relaxation induced by cis-$[Ru(bpy)_2(py)(NO)](PF_6)_3$ involves the activation of K_{ATP} channels. Financial Support: FAPESP, CNPq.

Supervisor: Lusiane Maria Bendhack

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Genética e Terapia Gênica / *Genétics and Gene Therapy* (GE)

GE001-ANTIMUTAGENIC EFFECT OF URSOLIC ACID IN BONE MARROW OF BALB/C MICE

FLÁVIA APARECIDA RESENDE(IC)[1]; CLAUDETE APARECIDA M. A. BARCALA(PG)[1]; MÁRCIA CRISTINA DA SILVA FARIA(IG)[1]; FABIANA HIBARY KATO(IC)[1]; WILSON ROBERTO CUNHA(PQ)[1] AND DENISE CRISPIM TAVARES(PQ)[1]

[1]Universidade de Franca. São Paulo, Brazil

INTRODUCTION: The ursolic acid (AU) is a triterpenoid component found in food, medicinal herbs and various other plants, in form of free acid or aglucones for triterpenoid saponins. It is known for its activities: antimicrobial, hepatoprotective, anti-inflammatory, antiallergic, antiviral and cytotoxic. The goal of this study was to evaluate the antimutagenic activity of AU using the analysis of micronucleated polychromatic erythrocytes in mice bone marrow. METHODS: The animals, weighing nearly 25 g, were divided into five treatment groups: treated with AU (80 mg/kg body weight, b.w.); antineoplastic agent doxorubicin (DXR, 90 mg/kg b.w.); AU e DXR, and negative and solvent controls. The frequency of micronuclei was analyzed in 2000 polychromatic erythrocytes. RESULTS: The animals treated with AU e DXR showed a reduction in the micronuclei frequency when compared to those treated with only DXR. CONCLUSION: This way, the AU demonstrated antimutagenic activity in the experimental conditions used on the study.

Financial Support: FAPESP & Universidade de Franca
Advisor: Denise Crispim Tavares

GE002-THE USE OF CYTOGENETICS TO ESTABLISH THE RISK OF CERVICAL CANCER

LÍZIA MARIA FRANCO DOS REIS E CAMPOS(PG)[1]; FRANCISCA DA LUZ DIAS(PQ)[2] ; EDDIE FERNANDO CÂNDIDO MURTA(PQ)[3].

[1][2]Genetics – FMTM; [3]Gynecology – FMTM

Introduction: The oncogenic factors can induce cytogenetic alteration in the exfoliative cells of the uterine cervix, which can be detected by means of the Micronucleus Technique (MN), which is being used as a marker of carcinogenic agents. Purposes: Evaluate the frequency of MN in cervical cells, correlating the increase of MN with the factors that predispose to cervical cancer (CC). Methods: Samples collected from the cervix were submitted to analysis, by means of the MN Technique, with 4% Giemsa coloration. 2,000 exfoliated cells per patient were counted. Results and conclusions: In a total of 30 patients analyzed, 43.3% showed the presence of MN above the reference value (VR: 0-4 MN/1000 cells). The MN frequency was distributed by risk factors, in which 66.7% of the HPV/infections, 57.1% of the NICs, 57.9% of the smokers and 58.6% that are on the oral pill, showed higher values than VR. The results were in agreement with the technique used for the cytogenetic findings, in which the presence of the MNs was caused by factors that led to the increase of nuclear atypies, and failures in the cell differentiation. The MN frequency in cervical cells can be an additional criterion in establishing the CC risk.

Tutor: Dra. Francisca da Luz Dias.

GE003-ASSESSMENT OF GENOTOXIC POTENTIAL OF *PHYSALIS ANGULATA* IN HUMAN LYMPHOCYTES

CRISTIANE PONTES ANDRADE(IC)[1]; ROMMEL RODRIGUES BURBANO(PQ)[2]; FRANCISCA DA LUZ DIAS(PQ)[1]; LUSÂNIA MARIA GREGGI ANTUNES(PQ)[1]

[1]Faculdade de Medicina do Triângulo Mineiro; [2]Universidade Federal do Pará.

Introduction: *Physalis angulata* (*Pan*) is used in the popular medicine in the treatment of inflammations, malaria and reumathism. The diverse medicinal properties attributed to *Pan* stimulated us to investigate its genotoxic activity, in accordance with recommendation for the validation of phytoterapics. Objective: The aim of this study was to evaluate the genotoxicity of *Pan* on the micronucleus (MN) induced *in vitro*. Methodology: The MN assay was used in the peripheral blood lymphocyte culture taken from 4 healthy volunteers. The cells were treated with the extract of *Pan* in the following concentrations: 0.1, 0.5, 1.0, 2.0, 3.0 and 6.0 µg/ml, and 8,000 binucleated cells were scored from each concentration. Results: The results indicate that *Pan* did not affect either the proliferative index or frequency of MN significantly different to the untreated control. Conclusion: *Pan* was not genotoxic in the experimental conditions of this study. The tests of assessment of the genotoxicity of plants with medicinal properties are important and are required for the register of the phytoterapics.

Financial support: FAPEMIG
Supervisora: Lusânia Maria Greggi Antunes

GE004-EFFECTS OF CURCUMIN ON BLEOMYCIN-INDUCED MICRONUCLEUS *IN VITRO*

CLÁUDIO FIDALGO(PG)[1]; MARLY APARECIDA SPADOTTO BALARIN(PQ)[1]; LUSÂNIA MARIA GREGGI ANTUNES(PQ)[1]; PÂMELA AVEIRO RESENDE(PG)[1].

[1]Depto. Ciências Biológicas – Faculdade de Medicina do Triângulo Mineiro.

Introduction: The use of dietary antioxidants to prevent antitumor agent-induced chromosomal damage in nontumor cell is currently eliciting considerable interest. Curcumin (CMN) a dietary antioxidant has been reported to protect macromolecules. Objective: The present study was undertaken to examine the possible protective effect of CMN on the micronucleus (MN) induced by the mutagenic agent bleomycin (BLM), commonly used as a chemotherapeutic drug. Methods: The MN assay was used in the peripheral blood lymphocyte culture taken from 6 individuals. Each sample was exposed to 9 treatments (control, DMSO, BLM, CMN 2.5; 5.0 and 10 µg/ml alone or combined with BLM) and 2000 binucleate cells were scored from each treatment/individual. Results: The concentrations of CMN did not increase the frequency of MN significantly different to the negative control. Nevertheless, the MN frequency after BLM or BLM plus CMN treatments was significantly increased when compared to the negative control. Conclusion: Cultures simultaneously treated with CMN and BLM showed a statistically significant concentration-dependent increase in the frequency of MN induced by BLM.

Financial Support: FUNEPU
Supervisora: Marly Aparecida Spadotto Balarin.

GE005-PROTECTIVE EFFECT OF OLEANOIC ACID EXTRACTED OF *MICONIA RUBIGINOSA* IN THE BONE MARROW MICRONUCLEUS TEST

CLAUDETE APARECIDA MATTOS ANDRADE BARCALA(PG)[1]; MARCIA CRISTINA DA SILVA FARIA(IC)[1]; FLÁVIA APARECIDA RESENDE(IC)[1]; FABIANA HIBARY KATO(IC)[1]; WILSON ROBERTO CUNHA(PQ)[1] AND DENISE CRISPIM TAVARES(PQ)[1].

[1]Universidade de Franca, São Paulo, Brazil

INTRODUCTION: Oleanoic acid (OA) is a triterpenoid compound that exists in natural plants in free acid form or aglycones in triterpenoid saponins, used in meals, cosmetics and drugs. This work evaluated the antimutagenic potential of the OA extracted from *Miconia rubiginosa* (melastomatacea) using micronucleus (MNs) frequency analysis in balb/C mice bone marrow. METHODS: To evaluate the anti-mutagenic effect of the OA, the animals received the treatment with OA (80 mg/kg body corporal weight, b.w.) associated with antineoplastic agent doxorubicin (DXR, 90 mg/kg b.w.). The treatment groups were also carried out with OA or DXR, and negative and solvent controls. The smears of the bone marrow were accomplished 24 hours after the treatment. The MNs analysis was accomplished from the counting of 2000 bone marrow anucleous polycromatic erytrocyte by animal. RESULTS: The treated animals with OA and DXR showed a decrease in the MNs frequency when compared to the group treated only with DXR. CONCLUSION: The OA showed an anti-mutagenic effect, under the conditions used in this work.

Financial support: FAPESP & UNIFRAN
Adviser: Denise Crispim Tavares

GE006-SILENCING OF PKR GENE BY RNA INTERFERENCE IN MELANOMA B16-F10 CELLS

NAYARA DELGADO ANDRÉ (PG) [(1)]; FERNANDO L. DE LUCCA (PQ) [(1)]

[(1)]Department of Biochemistry and Imunology, School of Medicine University of Sao Paulo, Ribeirão Preto, S.P., Brazil.

INTRODUCTION. RNA interference (RNAi) has become a powerful tool to investigate the function of mammalian genes by degrading a specific mRNA target. The mediators of sequence-specific mRNA degradation are double-stranded small interfering RNAs (siRNAs). Recent studies have implicated PKR in the regulation of cell proliferation, suggesting that this protein kinase has a tumor suppressor function which is still controversial. OBJECTIVE. Here, we examine the possibility of RNAi to inhibit the expression of PKR gene in melanoma B16-F10 cells. METHODS. The transfection of B16-F10 cells with the anti-PKR siRNA expression vector (psiSTRIKE) was by calcium phosphate method and the PKR gene silencing was monitored by Western blotting. RESULTS AND CONCLUSION. Our results indicate that specific siRNA was effective in PKR gene silencing in B16-F10 melanoma cells. This clone has been used as a model of experimental metastasis since the B16-F10 cells are able to colonize lungs of animals after intravenous injection. Thus, the injection of these B16-F10 cells transfected with siRNA may contribute to determine whether PKR has a tumor suppressor function in this model of experimental metastasis.

Financial Support: CAPES
Supervisor: Fernando L. De Lucca

GE007-CANCER GENE THERAPY EMPLOYING MULTIGENIC ADENOVIRUS

JULIANA COLOZZO GREGÓRIO(PG)[1]; RENATA GONÇALVES DE MORAIS(PG)[1]; PAULA FRATINI (PG)[2]; LIA KARINA MUSCHELLACK(PG)[1]; BRYAN ERIC STRAUSS(PQ)[2]; EUGENIA COSTANZI-STRAUSS(PQ)[1]

[1] Department of Cell Biology, Lab.Gene Transfer, ICB/USP; [2]Sector Viral Vectors, InCor/USP

Gene therapy is a strategic area in the gene-drug discovery field. Almost all human cancers have mutations in p16 and p53 tumor suppressor genes and their pathways, suggesting that gene therapy strategies would require the simultaneous co-expression of various genes in order to obtain a complete effect. Multicistronic viruses are a sophisticated and practical solution to improve the efficiency of cancer gene therapy. For this reason, we have constructed and produced the bicistronic adenovirus Adp16IRESp53. Characterization and functional assays of Ad16IRESp53 have confirmed transduction of both cistrons and showed an inhibitory effect in cellular proliferation. In vivo validation of this multigenic therapeutic approach has been initiated using a lung cancer model to study the dose, temporal-spatial expression and biodistribution of the viral agent in the treated animals after in situ administration of the AdeGFP and AdLacZ reporter viruses. We propose that the multigenic replacement of p16 and p53 will have an enhanced effect beyond single tumor suppressor gene treatment.

Financial Support: FAPESP; CAPES
Advisor: Eugenia Costanzi-Strauss

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Brazilian Journal of Pharmaceutical Sciences

Hematologia e Citologia / *Hematology and Cytology* (HC)

HC001 - EFFECTS OF ULEINE ON LEUKOCYTE CHEMOTAXIS

WESLEY MAURICIO DE SOUZA(PG)[(1)]; CID AIMBIRÉ DE MORAES SANTOS(PQ)[(1)]; ALMERIANE MARIA WEFFORT-SANTOS(PQ) [(1)]

[(1)]Programa de Pós-graduação em Ciências Farmacêuticas–UFPR–Curitiba,Brazil

INTRODUCTION/OBJECTIVE:The effects of uleine isolated from *Himatanthus lancifolius* (Muell. Arg.) Woodson barks in leukocyte chemotaxis induced by casein was investigated using the Boyden chamber. METHOD:Peripheral blood leukocytes harvested from volunteers were treated with uleine (10^{-9}–10^{2}µg/ml) for 30min at 37°C, and induced to migrate towards casein gradient. Dexamethasone (10^{-5}M) was used as a negative control. RESULTS:Uleine inhibited significantly the casein-induced migration of leukocytes in a dose-dependent fashion. The highest effect was at 10^{-6} µg/ml, with only 50.1±5.8% (n=7; $p<0.05$) of the treated-cells recovered from the lower chamber; for dexa-treated cells, the values were 68.6±11.8% (n=8). These effects were not resultant of uleine toxicity as cell viability estimated by the trypan blue test was always >94%. Also, uleine showed no chemoattractant activity itself. Of particular interest were the results observed after pre-treating the cells with morphine (10^{-6}M) and naloxone (10^{-6}M) before migration, in which such effect could be blocked. CONCLUSIONS:These data suggest that the uleine effects may be mediated through opioid receptors, and supports the anti-inflammatory effects of *H. lancifolius*.

Financial support: CNPq
Supervisor: Cid A.Santos

HC002-FAS AND FASL EXPRESSION ON CHRONIC MYELOGENOUS LEUKEMIA: A BETTER UNDERSTANDING TO DISEASE PROGRESS

BERGANTINI, ANA PAULA (PG) [1]; VOLTARELLI, J.C.[2] (PQ), PALMA, P.V.B.[3] (PQ), MORAIS, F.R.[3] (PQ), CASTRO, F.A.[4] (PQ) & FETT-CONTE, A. C.[1] (PQ)

[1]FAMERP-UNESP; [2]FMRP–USP, [3]FUNDHERP & [4]FCFRP–USP.

Introduction: Chronic myeloid leukemia (CML) is a three-phase myeloproliferative disorder, caused by the Bcr-Abl oncoprotein, product of the t(9;22) chromosomal translocation. Bcr-Abl is a constitutively activated tyrosine kinase responsible for cell malignant transformation, such as resistance to apoptosis. CML cells are highly resistant to apoptosis induced by chemotherapeutic drugs and recently some patients showed also resistance to imatinib mesylate. Alterations in the apoptotic process and escape of leukemic cells from the antitumoral immune response explain, in part, the selective advantage of these cells. Objective: To measure the Fas receptor and Fas Ligand (FasL) expression on CML patients. Method: The Fas and FasL expression were evaluated in 21 CML patients peripheral blood mononuclear cells in different phases of disease by flow cytometry. Results and conclusion: Results showed a reduction of Fas and FasL expression in natural killer cells and T $CD8^{+}$ lymphocytes in CML-blastic phase patients. Taken together these results suggest that apoptosis resistance found in CML-BP is caused by at least by reduction of Fas and FasL expression.

Financial support: FAMERP &FUNDHERP
Supervisor: Agnes C. Fett-Conte

HC003-A COMPARATIVE STUDY OF THE RED SERIE ON HEALTHY PEOPLE AND BEARERS OF ACUTE LYMPHOCYTIC LEUKEMIA

FERNANDA CAROLINA FREGONESI (IC)[(1)]; MARCO AURÉLIO SICCHIROLI LAVRADOR (PQ)[(2)]; FÁTIMA MARIA HELENA SIMÕES PEREIRA DA SILVA (PQ)[(2)]; ANTONIO CARLOS DA SILVA FILHO (PQ)[(3)]; ANDRÉ LUIS PEREIRA MANTOANI (PQ)[(2)]

[(1)]Centro Universitário Barão de Mauá; [(2)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto da Universidade de São Paulo; [(3)]Universidade de Ribeirão Preto

The variables that compose the red series in the blood count are of special importance in the leukemic processes because they are responsible for the final symptoms of the pathology, such as lack of air and fatigue.
So, we seek to establish a characterization of the properties of the distribution of these variables in healthy children and leukemia bearers, residents in the city of Ribeirão Preto, Brazil.
For this purpose we used a dataset of 23 healthy children and 23 bearers of acute lymphocytic leukemia, obtained respectively from the LAC/FCFRP-USP and from the Fundação SOBECCan - Ribeirão Preto. The children's age varied from 1 to 13 years old. We only used the hematocrit (HT), hemoglobin (HG) and erythrocyte (ET), once the other variables of the red series can be obtained in function of these.
For the healthy children we obtained: mean(sd): HT: 36.8(4.3), HG:11.8(1.6) and ET: 4.9(0.4). For the leukemic children we obtained: HT: 23.9(6.5), HG: 7.5(2.1) and ET: 2.8(0.8).

Supervisor: Marco Aurélio Sicchiroli Lavrador

The authors did not follow the modifications suggested by the Scientific Committee

HC004-DEVELOPMENT OF A CHEMILUMINESCENT ASSAY AS A SUBSTITUTE FOR CYTOCHEMISTRY DETERMINATION OF NEUTROPHIL ALKALINE PHOSPHATASE

MARÍLIA PYLES PATTO KANEGAE[1](PG); VALDECIR FARIAS XIMENES[1](PQ); IGUATEMY LOURENÇO BRUNETTI[1](PQ); ROBERTO PASSETO FALCÃO[2](PQ); LUIZ MARCOS DA FONSECA[1](PQ)

[1]Depto de Análises Clínicas, FCF-UNESP
[2]Depto de Clínica Médica, FMRP-USP

INTRODUCTION:The determination of neutrophil alkaline phosphatase (NAP) is useful in the differential diagnosis between chronic myeloid leukaemia (CML) and neutrophilic leukaemoid reactions (NLR). In NLR the NAP content is increased and in CML it is reduced. OBJECTIVE:Developing a non-subjective and sensitive chemiluminescent assay to substitute the classic cytochemistry assay for NAP determination that is subjective. MÉTHODS:Blood samples from 32 healthy patients were studied. The cytochemistry assay was performed using the kit Leucognost Alpa®. The chemiluminescent assay was carried out using the commercial substrate IMMULITE®. The assays were triggered by adding the leukocytes and the reaction was monitored for 15 minutes. RESULTS AND CONCLUSION:A strong correlation ($R=0.96$ $p<0.0001$) was obtained when the light emission per cell (mean±SD (2.85±2.10) 10^{-5}mV.s/cell; range (0.61-8.49)10^{-5}mV.s/cell) was compared with the cytochemistry score (mean±SD (58±40); range (11-158)). This technique is potentially useful as a substitute for the subjective cytochemistry assay for CML and NLR discrimination.

Financial support: CAPES
Supervisor: Prof. Dr. Luiz Marcos da Fonseca

HC005-EFFECT OF THE PHYSICAL EXERCISE IN THE IMMUNOLOGICAL SYSTEM

FREITAS, C.F.(PG)[1]; JABUR, M.N.(PG)[1]; TRISTÃO, L.C.(IC)[1]; RIBEIRO, I.P.(IC)[1]

[1]University of Ribeirão Preto

The physical exercise can cause alterations of some sanguineous cells, being able to intervene with the human immunological system. The immunological reply it can be: immune innate or immune adaptative. The objective of this work was to observe alterations in the number of leukocytes by means of physical effort (aerobic)de moderate and high intensity. For this 14 pupils of the course of Physical Education of the University of Ribeirão Preto had been evaluated, with average age of 22 years. The first sample was collected in rest, second immediately after physical effort e, the 90 minutes after the physical exercise. In the one after physical exercise of moderate intensity it observed na increase of leukocytes (neutrophils) and reduction of lymphocytes, persisting until the third hemograma. In the one after physical exercise of high intensity it observed an increase of leukocytes (lymphocytes) and reduction of neutrophilis. After the 90 minutes it observed a reduction of the lymphocites and increase of neutrophilis. The physical exercise of moderate and high intensities provokes alterations in the concentration of the cells of the innate system and of the adaptative, being able to be decurrent of the increase of the hormones and mechanical factors that modulate the immune reply front to the physical activity.

Supervisor: Cristiane de Freitas Tavares

The authors did not follow the Scientific Committee's suggestion for an English language review

HC006-EFFECT OF THE OIL OF COPAIBA IN MACROPHAGES

KARIN CRISTINA DUARTE SAIF(IC)[(1)];CLAUDIA CONSUELO DO CARMO OTA(PQ)[(1)]; ROSELI CORREA SILVA(IC)[(1)]; KARLA AZUMA(IC)[(1)]; JOSIANE BUENO(IC)[(1)]

[(1)]Universidade Tuiuti do Paraná. Curitiba, Brazil

INTRODUCTION: Copaiba oil, has been used for indigenous medicine and by people as an anti-inflammatory. sectioned in the abdomen. The phagocytosis was activated with solution of colored zimosan, and interrupted with a setting solution, then the cells were centrifuged Some studies were made with the oil for treatment of ulcer, healing, anti-tumoral. OBJECTIVE: The objective of this study is to elucidate the effect of the administration of copaíba oil on phagocytosis of macrophages. METHOD: In this work 80 rats of Wistar, lineage were chronichaly treated with the oil in doses of 450, 700 and 900 mg per body weight in a period of 28 days. To obtain the macrophages, the animals were decaptated and subsequently and lised with an extration solution. The phagocytic activity was analyzed in a spectrophotometer. RESULTS: The control group presented 240±12 Abs, the treated groups with 450, 700 and 900 mg per body weight presented 260±16; 310±22 e 280±13 respectively. CONCLUSION: The results show that the treated groups with doses of 450 and 900, did not presente increase in phagocytosis when compared with the control group, being treated with 700 disclosed increase in phagocytosis.

Supervisor: Claudia C. C. Ota.

HC007-PROLIFERATION LYMPHOCYTES IN RATS DEALT WITH OIL OF *COPAIFERA LANGSDORFFII*

ROSELI CORREA SILVA(IC)[1];CLAUDIA CONSUELO DO CARMO OTA(PQ)[1]; JOSIANE BUENO(IC)[1]; KARIN CRISTINA DUARTE SAIF(IC)[1]; KARLA AZUMA(IC)[1]

[1]Universidade Tuiuti do Paraná.Curitiba,Brazil.

INTRODUTION: The oil of copaíba, obtained from several species of Copaifera sort, is often used in popular medicine, mainly in Amazon region., having a anti inflammatory action. OBJECTIVE: This work aimed the T lymphocytes proliferation, wich were cultived from mesenterius linphonod of rats, treated with copaiba oil and stimulated with phitohemaglutinin. METHOD: It was taken rats Wistar, weiching around 180 grams. They were distributed in four groups: control, 450, 700 and 900mg/kg. After 28 days of treatment, these animals were decapiteted and had their linphonod dramn in cirurgic process. The viability was tested before the cultive, using the blue trypan test, where only the cells refringents were considered viable. The cultive was done during 12, 24 and 48 hours. RESULTS: Obtaining the following results in relation to the control group, the animals wich took the 450mg/kg range at 12, 24 and hours didn't have significative change, whili the 700mg/kg group had a cellular proliferation decrease, in 58,5% in 12 hours, 61,7% in 24 hours and 85,6% in 48 hours.CONCLUSION: what reveals that in high concentration, the oil presents imunosupressed characteristic.

Supervisor: Claudia C. C. Ota.

The authors did not follow the Scientific Committee's suggestion for an English language review

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Modelagem Molecular / *Molecular Modeling* (MM)

MM001-VALIDATION OF SEMI-EMPIRICAL METHODOLOGY FOR GEOMETRY OPTIMIZATION OF HIV-IN INHIBITORS.

EDUARDO B. DE MELO (PG)[(1)]; ALINE T. BRUNI(PQ)[(2)]; MÁRCIA M. C. FERREIRA(PQ)[(3)]

[(1)]UNIOESTE; [(2)]IBILCE/UNESP; [(3)]IQ/UNICAMP.

The integrase (IN) is indispensable for the replication of HIV. The only HIV-IN/inhibitor complex is the PDB 1QS4 (5CITEP/IN). When not much crystallographic informations are avaliable, the best starter point for a theoretical study are the most stable calculated geometries. In this trial were selected the best semi-empirical theory (AM1 or PM3) for the optimization of this compounds. The comparison criteria utilized were: the bond lengths of 5CITEP PDB; properties of the optimized geometries; and literature data. The 5CITEP, a keto-enol, were optimized for these two theories. The bond lenghts of the obtained geometries were similar to the 5CITEP PDB. Overlap between AM1 and PM3 geometries showed that they were identical. HOMO, LUMO and dipole moment (D) values are also similar. However, the heats of formation values (ΔH_f) presented great difference (Δ = 43 Kcal/mol). The same was observed for the partial charges of the atoms. In the literature, the AM1 theory is described as capable to compute most exacts values for D, HOMO and partial charges that the PM3. Furthermore, is indicate for the study of keto-enols. Therefore, AM1 is the semi-empirical theory indicated for a molecular modeling study of keto-enols inhibitors of HIV-IN.

Supervisor: Márcia M. C. Ferreira.

MM002-TRYPANOTHIONE-REDUCTASE: DOCKING STUDIES OF PEPTIDE ANALOG INHIBITORS

SAMUEL SILVA DA ROCHA PITA (PG)[1]; MAGALY GIRÃO ALBUQUERQUE (PQ)[1]; JOSÉ JAIR VIANNA CIRINO (PQ)[1]; RICARDO BICCA DE ALENCASTRO (PQ)[1]; CARLOS RANGEL RODRIGUES (PQ)[1]; HELENA CARLA CASTRO (PQ)[2]

[1] Instituto de Química – UFRJ [2] Instituto de Biologia – UFF

Trypanothione-reductase (TR) is an enzyme of *T. cruzi*, the etiological agent of Chagas' Disease (CD), and a promising target to drug design. McKie *et al*. [Amino Acids 2001 20:145] showed that 21 peptide analogs block TR in a reversible and selective manner. This work aims to study the binding mode of these analogues at the TR active site by a docking method. Calculations were carried out using FlexX/Sybyl. The complex TR-trypanothione structure was taken from Protein Data Bank (1BZL) as a reference. The ligands were docked after hydrogen atoms addition, charges assignment, and minimization. All docked complexes contained the inhibitor and the active site residues included in a 12Å radius of each inhibitor atoms, and the best binding modes were evaluated based on an energy score. Comparing with the experimental results, the most potent inhibitors were not necessarily the best scored by FlexX, but the least ones, were the worst scored. In addition, some of the achieved binding modes revealed new insights to propose new peptide analogues as potential inhibitors of TR on the development of drugs against CD.

Support: CAPES – CNPq – FAPERJ – FUJB
Advisors: MGA, CRR

MM003-AM1 SEMI-EMPIRICAL STUDY IN THE OPTIMIZATION OF PRODRUGS WITH POTENTIAL ANTICHAGASIC ACTIVITY

GUSTAVO H. G. TROSSINI (PG); ELIZABETH I. FERREIRA (PQ); CARLA M. S. MENEZES (PQ)

LAPEN, Faculty of Pharmaceutical Sciences, University of Sao Paulo, Brazil

Introduction: Cruzain is the major cysteine protease of *Trypanosoma cruzi*, the causative parasite of Chagas' disease. This enzyme hydrolyzes peptide compounds specially those containing either arginine (Arg) or other hydrophobic amino acid residues such as phenylalanine (Phe). Objective: To evaluate stereoelectronic features of double and mutual nitrofurazone (NF) and primaquine (PQ) potential antichagasic prodrugs containing dipeptides as spacer groups (PheAla, AlaPhe. LysArg, PheArg) concerning to cruzain cleavage. Methodology: Molecular modeling study of the NF double prodrugs and mutual NF-PQ prodrugs was performed using the AM1 semi-empirical method (Spartan O2 for Linux/Unix v.119). Results: Space filling model and MEPs of minimal energy conformers indicate the aminoacid nature and dipeptide sequence as determinant to nucleophilic attack of cruzain, although similar electrostatic charges have been observed. Hydrogen bonds and, hydrophobic and dipole-dipole interactions may be responsible for the lower volumes of NF double prodrugs, also the lowest lipophilics. Conclusion: LysArg and mutual NF-PQ prodrugs seem to be the best substrates for cruzain cleavage.

Financial Support: FAPESP, CAPES and CNPq
Supervisor: E. I. Ferreira

MM004-QSAR STUDY OF PIPERINE AND THEIR ANALOGUES WITH THE AID OF CHEMOMETRIC TOOLS

HELLEN M. OLIVEIRA (IC); PRISCYLA R. MENDANHA (IC); GILBERTO L. B. AQUINO (PQ); MARCELO M. SENA (PQ).

UnUCet-UEG

Piperine is a major alkaloid of piper species and has been reported to inhibit several cytochrome P450 activities. In this work, 6 physicochemical properties, logP, polarizability (Po), molar refractivity (mR), molar volume (mV), superficial area (SA) and hidratation energy (HE), were estimated for piperine and 22 analogues through chemical computational calculations by using HyperChem® software. These analogues has been previously synthesized by Koul *et al.*[a] and had their inhibition activities studied with relation to two cytochrome dependent enzymes. Principal Component Analysis (PCA) was applied to this 23 x 6 data set and provided a model that, with 3 components, accounted for 96.6 % of the total variance, and allowed to discriminate, from the whole set of molecules, two groups with a particular behavior. The first one was characterized by higher values of HE, showing lower activity and presenting a 2,2-dimethyl-3,4-dihydrobenzopyran ring. The second one was characterized by higher values of Po, mR, mV and SA, showing higher activity and presenting a 2-methoxy-4-benzyloxyphenyl ring. Another chemometric method, Hierarchical Cluster Analysis, corroborated these results, clustering the molecules in a way similar to the one provided by PCA.
[a] Koul *et al.*, *Bioorg. Med. Chem.* 8 (2000), 251

Financial Support: UEG – Universidade Estadual de Goiás
Supervisor: Gilberto Lucio Benedito de Aquino

MM005-DIBENZOYLMETHANES: HANSCH ANALYSIS FOR THE INIBITION OF MCF7 CELL LINES.

QUIRINO A. DE LIMA NETO(IC)[1]; RALPHO R. DOS REIS(PQ)[1]; MARISA A. NOGUEIRA(PQ)[1]; EDUARDO B. DE MELO(PQ)[1].

[1] – UNIOESTE - Curso de Farmácia - Universidade Estadual do Oeste do Paraná (UNIOESTE)[1]

The breast cancer constitute the first cause of women's death in Brazil. The dibenzoylmethanes are a rare group of flavonoyds which presents anticancer activities *in vitro*. This trial on carrying out a Hansch Analysis of a set of nine compounds sintetized and ensaied for Nogueira *et al* for the inibition of MCF7 breast cancer cell lines. The structures were optimized at AM1 level in the Hyperchem. Fourty five descriptors (30 electronics, 12 sterics and 3 hydrophobics) were evaluate. The Log %TI (percentage of total inhibition) was the dependent variable. The QSAR was performed in the BuildQSAR. The best models with a single descriptor were: (I) -0.1850 LogP + 2.8803 (r=0.912; s=0.083; q^2=0.701) e (II) -0.0119 MR +3.1360 (r=0.858; s=0.103; q^2=0.565). Values of *r* and q^2 were best for (I), however, the *r* for external validation with a set of three compounds (-0.70 and -0.67, respectively) showed that the equations presents practically the same capacity of prediction. These models demonstrate that hydrophobics and sterics factors are important for the described activity, with bigger prominence for the first one, what already it was observed in anothers works.

Financial Support: FUNDEP UNIOESTE.
Supervisor: Eduardo B. de Melo.

MM006- CONSTRUCTING PROTEIN PRUNING MODELS TO PERFORM RECEPTOR-DEPENDENT (*RD*) 4D-QSAR ANALYSIS OF A SET OF DIAZABORINE DERIVATIVES

KERLY FERNANDA MESQUITA PASQUALOTO[1] (PQ); MÁRCIA MIGUEL CASTRO FERREIRA[1] (PQ); OSVALDO ANDRADE SANTOS-FILHO[2] (PQ) ; ANTON J. HOPFINGER[2] (PQ)

[1] UNICAMP
[2] UIC

Introduction: Receptor pruning is an approach for achieving reasonable conformational ensemble profile and performing practical *RD* 4D-QSAR analysis in terms of time and computational resources. Purpose: Reduce the size of a model structure of enoyl-acp reductase (ENR) from *E. coli*, FabI, to allow ligand-receptor molecular dynamic simulations (MDSs) to be computationally economical yet still provide meaningful binding thermodynamic data. Methodology: Three reduced-size models of FabI were created by pruning away all residues greater than 12, 10 and 8 Å radius. The largest ligand was docked in the active site to define the largest required receptor model. Energy minimization and MDSs were carried out using the MOLSIM 3.2 program. The lowest energy structure for each of receptor models from MDSs was compared by root mean square (RMS) fit to the equivalent portion of the crystal structure of FabI. Results: A scale-down 12 Å receptor model of the enzyme FabI maintains the structural integrity of the composite parent crystal structure. Perspectives: Structure-based design of new antituberculosis agents regarding the similarity in the active site of two ENRs, FabI and InhA (*M. tuberculosis*).

Financial Support: CNPq
Supervisor: Márcia Miguel Castro Ferreira

MM007- A HCA STUDY FOR ANTIMUTAGENIC ACTIVITY OF DIBENZOYLMETHANES IN *SALMONELLA TYPHYMURIUM.*

MARCELO C. FRIOZI(IC); QUIRINO A. DA LIMA NETO(IC); RALPHO R. DOS REIS(PQ); MARISA A. NOGUEIRA(PQ); EDUARDO B. DE MELO(PQ).

Curso de Farmácia – Universidade Estadual do Oeste do Paraná

The dibenzoylmethanes, a seldom group of flavanoids, have been studied as agents in cancer chemoprevention. Chosi et al. (Chem. Pharm. Bull. 40, 1047) synthesized and studied the antimutagenic effect in *S. typhymurium* with twenty ring-substituted derivatives of this class. This study accomplished a Hierarchical Cluster Analysis (HCA) with these derivatives regarding to qualitative standards for the cancer chemoprevention. Twenty derivatives structures (twelve actives and eight inactives) were optimizated with AM1 theory. Twenty-nine descriptors (24 eletronics, 4 esterics and LogP) were utilized, in special the partial charges of the basic-structure atoms. The analysis of the compounds-centred dendogram showed a tendency to cluster the inactives with the most electron attractor effect over the rings. The variable-centred showed high correlation between the charges of some carbon atoms in this rings. In conclusion, an increase of antimutagenic activity of this compounds can be related to an increase of electronic density of the rings, with substitutions in the adequate positions.

Financial support: FUNDEP UNIOESTE.
Supervisor: Eduardo B. de Melo.

MM008-AZASUGARS: A CORRELATION STUDY BETWEEN α-GLUCOSIDASE INHIBITION VS ELECTRONIC DESCRIPTORS

RICARDO LORENZONI (IC); EDUARDO B. DE MELO (PQ).

Curso de Farmácia – Universidade Estadual do Oeste do Paraná.

α-Glucosidases inhibitors have great potential for the development of drugs to diseases like diabetes and AIDS. This work aim to realize a basic study QSAR for azasugars with biologic activity (BA) against rice ±-glucosidase. A set of twelve structures of natural azasugars are optimized with the AM1 theory in the software Hyperchem 7.1. Considering the interactions between these substances and α-glucosidases, six electronic descriptors [HOMO, LUMO, Gap (or $\Delta_{LUMO-HOMO}$), Dipole Moment, and the charges of nitrogen (Q_N) and anomeric carbon (Q_C)] were selected. The correlation (r) between descriptors and BA was individually measured. The correlations between the descriptors were measured too. In the first case, r values were bad (r > 0.7). The $r_{AB\ vs\ HOMO}$ and $r_{AB\ vs\ LUMO}$ were the greater (0.61 and 0.64, respectively). High correlations between some descriptors ($r_{LUMO\ vs\ HOMO}$ = 0.82; $r_{Gap\ vs\ HOMO}$ = -0.74; $r_{QC\ vs\ HOMO}$ = -0.76; $r_{QC\ vs\ Gap}$ = 0.81) were observed. In conclusion, observing the high correlations between HOMO, Gap (an expression of compound reactivity) e Q_C, is possible the existence of an electron-donator effect, important for the interaction of this compounds with the active-site of the ±-glucosidase, in the anomeric carbon of the azasugars.

Supervisor: Eduardo B. de Melo.

MM009- APPLICATION OF UNSUPERVISED CHEMOMETRICS METHODS TO A SET OF INHIBITORS OF *ESCHERICHIA COLI* ENOYL-ACP REDUCTASE, FABI

FLÁVIA DA SILVA PEREIRA[1] (PG); WALKÍRIA RÉGIS DE MEDEIROS[1] (PG); KERLY FERNANDA MESQUITA PASQUALOTO[1] (PQ); MÁRCIA MIGUEL CASTRO FERREIRA[1] (PQ)

[1] UNICAMP

Introduction: The important structural element of diazaborines is a heterocyclic 1,2-diazine ring containing a boron as a third hetero atom. Purpose: Selection of the descriptors calculated from a set of fifty-one diazaborines based on their relationship with the biological activity data. Methodology: Three-dimensional models of diazaborines in their neutral forms were built using two crystallographic structures as geometry reference. Partial atomic charges were computed employing the AM1 semipempirical method. Energy minimization and molecular dynamic simulations (MDSs) were carried out (MOLSIM 3.2). The lowest energy conformer for each of ligand from MDSs was used to obtain the descriptors. Principal component analysis (PCA) and hierarchical cluster analysis (HCA) were used to treat the calculated descriptors. Results: Three sample groups are shown in the HCA. According the PCA, the partial atomic charges of the 1,2-diazine ring are seemingly important contributions to the biological activity. Perspectives: Apply the receptor-independent (*RI*) 4D-QSAR formalism to this set of diazaborines for predicting the interaction pharmacophoric elements (IPEs) as well as the alignment in the FabI active site.

Financial Support: CNPq
Supervisor: Márcia Miguel Castro Ferreira

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Parasitologia, Microbiologia e Imunologia /
Parasitology Microbiology and Immunology (MI)

MI001-BIOCIDES IN THE DISINFECTION OF DENTAL UNIT WATERLINE: MICROBIOLOGICAL AND SEM EVALUATION

EVANDRO WATANABE (PG)[1]; WILSON MATSUMOTO (PQ)[2]; IZABEL YOKO ITO (PQ)[1]; ALESSANDRA MARÇAL AGOSTINHO(PQ)[2]

[(1)]FCFRP-USP; [(2)]FORP-USP

The contamination of dental unit water, due to biofilm formation in the waterline, can represent risk of infection to the dental team and patients. In this research analyzed three chemical agents: castor oil-based detergent, Amonex TA and Ster-4-spray, in dental units of the Disabled Patients Clinic at FORP-USP, having a control group submitted only to flushing water. The aim was to assess the reduction of CFU/mL in the effluent water, using the Petrifilm™System (3M) and the effect on waterline biofilm by scanning electron microscopy (SEM). Before treatment, the dental unit water presented contamination higher than the recommended by ADA for dental treatment (<200UFC/mL), reaching $3.94x10^7$CFU/mL. After treatment, contamination level in most of dental unit water was less than 200UFC/mL. The SEM revealed the presence of a well established biofilm in the waterlines in all the groups. However, the recontamination occurred in few weeks. In conclusion, the chemicals analyzed improved the microbial quality of dental unit water.

Financial Support: CAPES
Advisor´s Name: Izabel Yoko Ito

The authors did not follow the Scientific Committee's suggestion for an English language review

MI002-EXOENZYME SECRETION BY CANDIDA ALBICANS AND CANDIDA TROPICALIS ISOLATES FROM WHOLE SALIVA OF ORAL LESION PATIENTS.

KAREN REGINA CARIM DA COSTA (PG)[1];JOSEANE CRISTINA FERREIRA(PQ)[1];MARILENA CHINALI KOMESU (PQ)[2]; REGINA CELIA CANDIDO (PQ)[1]

[(1)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto –USP;[(2)]Faculdade de Odontologia de Ribeirão Preto-USP.

The supplementary microbiota role played by yeasts found in oral cavity is an important fact, since in certain situations they can trigger oral or systemic diseases. The genus Candida is the most frequently observed. These organisms can secrete enzymes phospholipase and proteinase which have important role during infections. The aim was to evaluate exoenzyme activity of strains isolates on unstimulated saliva from patients with clinical signs of oral candidosis and compare it with health subjects. The evaluation of phospholipase was carried out based on PRICE et al (1982) and proteinase on RUCHEL et al (1982). Among C. albicans strains of 40 patients with candidosis, phospholipase were detected in 95% and proteinase 100%, while the health subject strains produced both enzymes. C. tropicalis showed 27% proteinase activity in candidosis patients against one health subjects strain. In conclusion, based on our data was possible to observe that C. albicans presented high activity of exoenzyme in both groups. C. tropicalis produced only proteinase with high frequency in candidosis group.

Advisor´s Name: Profa. Dra. Regina Célia Candido

MI003-INTERFERON-ALPHA-2A INHIBITS BRAZILIAN ORTHOBUNYAVIRUS REPLICATION

MÁRCIA CRISTINA LIVONESI (PG)[1]; RICARDO LUIZ MORO DE SOUSA (PG)[2]

(1) Faculdade de Medicina de Ribeirão Preto, USP-Ribeirão Preto, SP, Brasil;
(2) Instituto de Ciências Biomédicas, USP-São Paulo, SP, Brasil.

Introduction: Oropouche, Caraparu, Guama, Guaroa and Tacaiuma are ssRNA viruses that belong to Orthobunyavirus genus. These viruses are transmitted by mosquitoes, and have been associated with febrile illness, as well as meningoencephalitis in humans.
Objective: To evaluate the susceptibility these Orthobunyaviruses to antiviral action of Interferon-alpha-2a (IFN-a-2a) in vitro.
Methodology: Plaque assay.
Results: IFN-α (100,000 IU/mL) presented expressive antiviral activity on all the viruses tested, as much of the treatment of the cells had been initiated before as after viral infection. Doses lower than 100,000 IU/mL showed antiviral effect on Caraparu, Guama, Guaroa and Tacaiuma viruses, but not on Oropouche. Moreover, IFN-α was able to inhibit the replication of Guaroa and Tacaiuma viruses when the treatment of cells was initiated 24 hours after infection.
Conclusion: These results suggest that Caraparu, Guama, Guaroa and Tacaiuma viruses, but not Oropouche, are susceptible to the IFN-α-2a, which could be used to treat diseases caused by these viruses.

Financial Support: CAPES and FAPESP
Advisor´s Name: Prof. Dr. Luiz Tadeu Moraes Figueiredo

MI004-EVALUATION OF GUINEA PIGS LUNG PARENCHYMA AFTER VACCINATION WITH DNA VACCINE HSP65 FOLLOWING *MYCOBACTERIUM TUBERCULOSIS* INFECTION

LÚCIA DE PAULA (PG)[1]; CAMILA MATIAS-PERES (PG)[1]; DANIELA CARLOS (PG)[1]; CARLOS ARTÉRIO SORGI (PG)[1]; [2]CÉLIO LOPES SILVA (PQ)[2]; EDSON SOARES GARCIA (PQ)[3] AND LÚCIA HELENA FACCIOLI (PQ)[1].

[1]DACTB, FCFRP/USP; [2]CPT, FMRP/USP; [3]DP, FMRP/USP, Ribeirão Preto, São Paulo, Brasil.

Introduction: A DNA vaccine codifying the HSP65 protein can prevent infection with *M. tuberculosis* reducing the number of bacteria in infected mice. Objectives: To assess prophylactic effects of DNA hsp65 vaccine in guinea pigs model of pulmonary tuberculosis. Methods: Guinea pigs were vaccined with DNA hsp65 or inoculated with empty plasmid. Subsequent challenge with 10^5 viable *M. tuberculosis* H37Rv strain was done fifteen days after the last vaccination by i.t. route. Thirty days after the challenge, the lungs were removed and fixed in 10% formalin and histological analysis was performed by HE staining. Results: In infected animals, was observed granuloma formation with caseous necrosis. Macrophage and lymphoid influx disarranged almost 50-80% of lung parenchyma and DNA hsp65 or empty plasmid did not reduce this inflammatory reaction. Conclusions: Similar pathological lesions were observed in infected animals vaccinated or not with DNA hsp65 or empty plasmid.

Financial Support: FAPESP, CNPq.
Supervisor: Prof. Dra. Lúcia Helena Faccioli.

MI005-ROLE OF LEUKOTRIENES ON THE SYSTEMIC CANDIDIASIS

ROSANE MARIA FALASCO BOLZONI (PG); ALEXANDRA IVO DE MEDEIROS (PQ); CAMILA MATIAS PERES (PG), CARLOS ARTÉRIO SORGI (PG), WALTER MIGUEL TURATO (PG); FABIANI GAI FRANTZ (PG); REGINA CÉLIA CÂNDIDO (PQ); LÚCIA HELENA FACCIOLI (PQ)

DACTB - FCFRP - USP

Introduction: *Candida* species are commensal fungal organisms as well as opportunistic pathogens of mucosal tissues. Leukotrienes are classical mediators of inflammatory response. However, new aspects of these mediators function have been recently described for their role as antimicrobial host defense mediators.
Objective: To investigate the role of the leukotriene in *Candida albicans* infection. Methods: Female 5-LO$^{-/-}$ or WT mice were infected with *Candida albicans* intravenously. On the 1st, 3rd, 7th and 14th days post infection (p.i) and the number of *C. albicans* CFU in the kidney was determined. Results: The recovery of yeast CFU from kidney of 5-LO $^{-/-}$ infected-mice decreased 1 $\log_{10}$ (3d), 0.8 $\log_{10}$ (7d) and 2.7 $\log_{10}$ (14d) p.i. in comparison to WT infected-mice. Conclusion: These results demonstrate opposing effects of leukotrienes such as antimicrobial host defense mediators. They suggest a possible therapeutic potential of leukotrienes antagonist or inhibitor in the treatment of systemic candidiasis.

Financial Support: FAPESP, CNPq.
Tutor: Lúcia Helena Faccioli

MI006-DEXAMETHASONE INHIBITS CELL RECRUITMENT DURING *STRONGYLOIDES VENEZUELENSIS* INFECTION.

DANIELA I. SOUZA (PG)[(1)]; ELEUZA R. MACHADO (PG)[(1)]; ERIKA SILVA (TC)[(1)]; CAROLINE FONTANARI (IC)[(1)] and LÚCIA H. FACCIOLI (PQ)[(1)]

[(1)]DACTB – FCFRP – USP

Introduction: Human strongyloidiasis is an infection characterized by an increase in the number of eosinophils. Objective: To investigate the effect of dexamethasone (dex) treatment on the increase of total leukocytes in blood, peritoneal cavity (PC) and bronchoalveolar space (BAL) in rats infected with *Strongyloides venezuelensis* (S.v.). Methods: Wistar rats were divided in three groups: Non-infected animals (NIA); infected (IA) with S.v. and infected and treated daily with dex (TIA). On the 1st, 3rd, 5th, 7th, 14th and 21st days after infection, the rats were killed and the numbers of cells were determined. Results: There was an increase in the number of total leukocytes, eosinophils and mononuclear cells in the blood, PC and BAL in the IA group when compared with NIA on all days analysed. In the TIA group, there was a significant inhibition of cells in the PC and BAL when compared with IA. However, the treatment induced an increase in the number of total leukocytes in the blood when compared with IA or NIA. Nevertheless, eosinophil numbers were completely inhibited in those compartments. Conclusion: Eosinophilia in the S.v. infection is mediated by a factor inhibited by dex treatment.

Financial Support: FAPESP.
Advisor´s Name: Lúcia H. Faccioli.

MI007 - IL-5 DOES NOT CONTRIBUTE TO LUNG EOSINOPHILIA IN LEUKOTRIENES DEFICIENT MICE

FERNANDA DE FREITAS ANIBAL (PG)[12] ALEXANDRE DE P. ROGÉRIO (PG)[2], ELEUZA R. MACHADO (PQ)[2] , ÉRIKA VITALIANO GARCIA DA SILVA (PQ)[2] AND LUCIA H. FACCIOLI (PQ)[2]

FMRP[1]AND FCFRP[2] – USP

INTRODUCTION: Leukotrienes (LTs) are lipid mediators that participate in inflammatory diseases; IL-5 is factor for eosinophils (EO) differention and recruitment. OBJECTIVE: In the present study we investigated the participation of IL-5 and LTs in the EO recruitment to lung of Toxocara canis (Tc)-infected mice. METHODOLOGY: The 5-LO KO and 129 mice were infected or not with 1000 Tc eggs. The treatments of Tc-infected mice were as follows: 5-LOKO mice were treated or not with TRFK-5 i.p. (anti-IL-5 Ab); 129 mice treated or not with TRFK-5 or MK-886 (leukotrienes inhibitor, p.o., daily, 1mg/Kg) or both. Mice were killed 18 days after infection and EO migration were evaluated in bronchoalveolar lavage. RESULTS: Tc-infected mice not treated developed lung eosinophilia. The EO migration to the lung was inhibited only in Tc-infected 129 mice treated with TRFK-5 and MK886. No significant alterations in EO migration to the lung were observed in Tc-infected 5-LO KO mice treated with TRFK-5. CONCLUSIONS: The lung eosinophilia in Tc-infected 129 mice dependent of IL-5 and LTs, while, in Tc-infected 5-LO KO infected mice appears to be IL-5 independent.

Supported by: CAPES, CNPq, FAEPA, and FAPESP
Advisor: Dra. Lucia H. Faccioli

MI008- *TOXOCARA CANIS* INFECTION DOES NOT INTERFERE ON THE TH1 IMMUNE RESPONSE IN THE EXPERIMENTAL TUBERCULOSIS.

[1,2]Fabiani G. Frantz (PG); [2]Rogério S. Rosada (PG); [1,2]Walter M. Turato (PG); [1,2]Camila M. Peres (PG); [1]Érika Silva (TC); [2]Célio L. Silva (PQ); [1]Lúcia H. Faccioli (PQ).

[1]DACTB/FCFRP/USP, and [2]CPT/FMRP/USP

Introduction: Th1 and Th2 are immune response patterns induced by Mycobacterium tuberculosis (Mtb) and helminthes infection, respectively. Objective: To demonstrate the impact of these opposite patterns on immune response development. Methods: Mice were primarily infected with T. canis (Tc) and inoculated i.t. with Mtb 18 days later. Cell recruitment in bronchoalveolar fluid (BALF), CFU number, nitric oxide (NO) production in the lungs and cell number in peripheral blood were evaluated 30 days after mycobacterial infection. Results: Coinfected mice lung cells secreted higher amounts of NO than mice with Tc only, producing similar NO levels than Mtb-mice. When compared with Mtb-mice, coinfected mice BALF neutrophil and mononuclear cell numbers decreased while eosinophils increased. Coinfected mice have similar neutrophil and eosinophil counts and smaller number of mononuclear cells in blood, compared to Mtb-mice's. Mtb clearance was not changed in coinfected animals. Conclusions: Th2 induced by Tc failed to alter Mtb-induced Th1 response. Our findings provide contribution on coinfection immune regulation.

Financial Support: FAPESP, CNPq
Mentor: Lúcia H. Faccioli

MI009-INCIDENCE OF AUTOIMMUNE HYPOTHYROIDISM IN PATIENTS WHO WERE UNDER TREATMENT IN TRES DE MAIO CITY, RS

TATHIANE HOFSTETTER & LETÍCIA BEATRIZ MATTER (PQ)

Universidade Regional Integrada do Alto Uruguai e das Missões, Av. Univ. das Missões 464, Santo Ângelo, RS

INTRODUCTION: Hashimoto's Thyroiditis (HT) is an autoimmune disease considered the main etiology of primary hypothyroidism. OBJECTIVES: analyzing the incidence and the profile of patients with autoimmune hypothyroidism. METHODOLOGY: the study was evaluated retrospectively, from March to December of 2003, using patients'cadastro of the São Vicente de Paula Clinic. RESULTS: 60 patients with hypothyroidism were analyzed, with 2 to 96 years old. Of these, 22 cases (36,7%) presented thyroid antibodies, being 18 female and 04 male, in a proportion of 5:1, located in the agricultural area (36,36%) and in the urban area (63,64%). The occurrence of congenital Hashimoto's thyroiditis was positive in 5 cases (22,72%). The hypersensitivity to medicines was observed in 2 cases. The study also demonstrated 7 patients with some historical exposition to toxic agents. CONCLUSIONS: considering the results one might conclude that the prevalence of cases with thyroid antibodies in thyroid disorders is significant. And the relation with the exposition to toxic agents should be more studied.
Key-words: Hashimoto's thyroiditis, hypothyroidism, thyroid antibodies.

Supervisor: Leticia B. Matter - lmatter@urisan.tche.br

MI010-*IN VIVO* TRYPANOCIDAL ACTIVITY OF TRITERPENES FROM *MICONIA ALBICANS*.

DANIELE DA SILVA FERREIRA(PG)[1]; SÉRGIO DE ALBUQUERQUE(PQ)[1]; WILSON ROBERTO CUNHA(PQ)[2].

[1]Universidade de São Paulo–Via do Café, s/n–Ribeirão Preto-SP CEP 14040-903
[2]Univeridade de Franca –Av. Dr. Armando Salles de Oliveira, 201–Franca-SP

Introduction.In our laboratory several extracts from *Miconia* species and their isolated compounds have demonstrated biological activities.
Objectives.The aim of the present work was to evaluate the *in vivo* trypanocidal activity of isolated triterpenes of the methylene chloride extract of *M. albicans*.
Methodology.The methylene chloride extract of *M. albicans* afforded a mixture of ursolic acid (UA) and oleanoic acid (OA). The mixture of these triterpenes was separated by HPLC. The mixture and the pure triterpenes as well as the salt derivative from UA were evaluated *in vivo* assay against *Trypanosoma cruzi*. The male Balb/c albino mice were treated (2mg/kg) daily for 10 days. The positive control was Benznidazol.
Results. The group treated with UA showed a significant reduction of parasites and after the parasitemic peak the number of parasites kept constant. The substances OA, mixture of UA and OA and the salt derivative had also showed a significant reduction of parasites and displacement of parasitemic peak in comparison with negative control group.
Conclusions. Overall, it can be that these triterpenes posseses significant activity *in vivo* against *T. cruzi* in the used model.

Financial support: FAPESP,CNPq
Supervisor: Sérgio de Albuquerque

The authors did not follow the Scientific Committee's suggestion for an English language review

MI011-BIOFILM: INFLUENCE OF A TRICLOSAN-CONTAINING DENTIFRICE ON TOOTHBRUSH CONTAMINATION

MARCELO VAN VLIET LIMA(IC)[1]; GISELE FARIA(PQ)[2]; MARAÍSA PALHÃO VERRI(PQ)[1]; EVANDRO WATANABE(PG)[1]; IZABEL YOKO ITO(PQ)[1]

[(1)]FCFRP-USP; [(2)]FORP-USP

The toothbrush is a dissemination/infection source of microorganisms from the oral cavity. The aim of this study was to evaluate the mutans group streptococci (MGS) biofilm formation on Científica® toothbrushes "spears" from 52 students at FCFRP-USP. The students were divided in 3 groups: At step I, they brushed their teeth without dentifrice, at step II with fluoride dentifrice (Sorriso®) and step III with a dentifrice containing triclosan (Colgate Total®). Only 30 (57.7%) of 52 students participated of all steps. The toothbrushes were seed in tubes with Sucrose Bacitracin Broth. After incubation at 37°C for 3 to 4 days, the toothbrushes were analyzed by a stereomicroscopy to assess the number of colony forming units of MGS. The biofilm were in 22 (73.3%) toothbrushes at step I, 4 (13.3%) at step II, and no biofilm/colonies at step III. The results were statistically analyzed. The toothbrushes became contaminated after a single brush of 2.0 minutes. In conclusion, the dentifrices reduced the biofilm formation on the toothbrushes "spears", and there was no significant statistical difference between them.

Financial Support: PIBIC/CNPq
Supervisor: Izabel Yoko Ito.

MI012-MELANIN PRODUCTION BY *CRYPTOCOCCUS* SPP ON DIFFERENT CULTURE MEDIUM

REGINALDO DOS SANTOS PEDROSO (PG)[1]; KAREN REGINA CARIM DA COSTA (PG)[1]; JOSEANE CRISTINA FERREIRA (PQ)[1]; REGINA CELIA CANDIDO (PQ)[1].

[(1)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto/USP

The ability to produce melanin-like pigments utilizing various phenolic compounds as substrates have been used for *Cryptococcus* neoformans identification, although other species of this genus are able to produce it. The aim was to study melanin production on different culture medium: potato-carrot, Niger seed, sunflower seed and L-dopa agar. The avaliation of melanin production was carried out based on colony pigmentation. Melanin production was observed in: 15 C. *neoformans* strains (80% on potato-carrot; 46% on Niger seed; 53% on sunflower seed; 86% L-dopa), 11 C. albidus strains (36% on potato-carrot; 9% on Niger seed; 36% on sunflower seed; 27% L-dopa), 10 C. *laurentii* strains (60% on potato-carrot; 60% on Niger seed; 50% on sunflower seed; 30% L-dopa). In conclusion, based on our data was possible to observe that potato-carrot agar detected melanin production in the majority. Sunflower seed agar showed clear and easy visualization of pigmentation compared with other mediums.

Supervisor: Prof. Dr. Regina Celia Candido.

MI013- PROFILE OF PROTEINASE AND PHOSPHOLIPASE ENZYMES OF *CANDIDA SPP* ISOLATED FROM DIFFERENT ANATOMICAL SITES OF THE SAME INDIVIDUAL

JAQUELINE OTERO SILVA(PQ)[1]; JOSEANE CRISTINA FERREIRA(PQ)[2]; REGINA CÉLIA CANDIDO(PQ)[2]

[(1)]Adolfo Lutz Institute-Ribeirão Preto; [(2)]Facultie of Pharmaceutical Sciences of Ribeirão Preto-USP

Yeasts of the genus *Candida* are saprophytes and opportunistc. Abilith of *Candida* spp to secrete extracellular enzymes has been suggested as factors of pathogenicity. The study evaluated the enzymatic profile of *Candida* spp isolated from different anatomical sites in the same individual. The total of 37 strains obtained from feces and/or oral, vaginal, anal mucosae of 17 patients were analyzed for the production of phospholipase (PRICE et al, 1986) and proteinase (RÜCHEL et al, 1982) enzymes. There was no production of phospholipase in 16% of the strains (Pz=1) while 58% and 27% of the yeasts presented median activity (0.63<Pz<1.0) and strong activity (Pz≤0.63), respectively. Regarding the proteinase, 62% of the yeasts presented strong activity (Pz≤0,63) and 38% median activity (0.63<Pz<1.0). The same enzymatic profile was observed in samples of 8 (21%) patients, when compared with each other. These data demonstrate the presence of this factor of pathogenicity of *Candida spp* isolated from human endogenous sources in different anatomical sites.

Financial support: Facultie of Pharmaceutical Sciences of Ribeirão Preto-USP
Supervisor: Regina Célia Candido

MI014-*IN VITRO* LEUKOCYTE LIPID BODY FORMATION INDUCED BY *HISTOPLASMA CAPSULATUM*

CARLOS ARTÉRIO SORGI (PQ)[1]; CAMILA MATIAS-PERES (PG)[1]; WALTER MIGUEL TURATO (PG)[1]; ROSANE MARIA FALASCO BOLZONI (PG)[1]; ALEXANDRA IVO DE MEDEIROS (PQ)[1]; PATRÍCIA TORRES BOZZA (PQ)[2] AND LÚCIA HELENA FACCIOLI (PQ)[1].

[1]DACTB, FCFRP/USP, Ribeirão Preto, SP; [2]FIOCRUZ, Rio de Janeiro, RJ; Brasil

Introduction: Lipid bodies (LBs) are rapidly inducible, lipid-rich cytoplasm domains and sites for eicosanoid-forming enzyme localization which may have specific roles in enhanced inflammatory mediator production during pathology. Objective: In this work, we analyzed the lipid body occurrence in either *H. capsultum* (Hc) or different fraction of its cell wall. Methods: Alveolar macrophages from BALF in C57/Bl6 mice, were incubated with Hc, dead fungus, alkali-insoluble fraction 1 (F1) which contains mainly ß-glucan from the cell wall of Hc and LPS for 0, 1, 4, 8, 16 and 24 hours. Control cells were incubated with medium (RPMI). LBs were assessed by osmium staining. Results: The Hc, dead fungus, F1 and LPS increased lipid body formation within 1 hour in cell culture, maximum within 8 hours and decrease thereafter. Conclusion: The infection by Hc induced time-dependent increase in the numbers of LBs in pulmonary leukocytes, like as the dead fungus. Therefore, ß-glucan appears to be the responsible compound for inducing LBs increase.

Financial support: FAPESP and CNPq.
Supervisor: Prof. Dra. Lúcia Helena Faccioli.

MI015-*IN VITRO* INVESTIGATION OF DMSO EFFECTS ON LYMPHOCYTES

*ANGELA FLORÃO (PG); JEANINE MARIE NARDIN (PG); **FABIANA HERRERA ROCHA (IC) ALMERIANE MARIA WEFFORT-SANTOS (PQ)

Programa de Pós-graduação em Ciências Farmacêuticas – UFPR – Curitiba, Brazil

INTRODUCTION/OBJECTIVE: DMSO is a solvent widely used for diluting compounds or mixtures for *in vitro* biological assays. In this work, the effects of DMSO on human lymphocytes proliferation were evaluated through cell viability with trypan blue, cell multiplication in a flow cytometer, morphological studies on stained smears, and AgNOR quantification. METHOD: Human peripheral blood mononuclear cells induced to proliferate by phytohemagglutinin were simultaneously treated with DMSO or ethanol (2–4ug/ml) for 5 days at 37°C, and 5% CO_2. RESULTS: DMSO, but not ethanol, inhibited significantly the lymphocyte proliferation in a dose-dependent manner. These effects were not resultant of DMSO toxicity as cell viability estimated by the trypan blue exclusion test was always >90%. Lymphocyte morphology instead blasts predominated on DMSO-treated cultures (>80%) while low numbers of AgNORs, which are DNA segments that transcribe ribosomal RNA, were found. CONCLUSIONS: The growth inhibitory effects observed suggest that DMSO acts at the activation step of lymphocyte proliferation, making it unsuitable as a solvent for incorporating substances into aqueous growth media.

Supervisor: A.M. Weffort-Santos
Financial support: *Capes; **Fundação Araucária

MI016- *EUPHORBIA TIRUCALLI* CRUDE LATEX DRIVES IMMUNOLOGICAL PROFILE OF PERIPHERAL BLOOD T CELLS TOWARD A TYPE-1 CYTOKINE POROFILE

FELIPE JOSÉ NOBRE LÉLIS (IC)[1]; VANESSA A. MENDONÇA (PG)[1]; RENATO SATLER (PG)[2]; OLINDO A. MARTINS-FILHO (PQ)[2]; GUSTAVO E. A. BRITO-MELO (PQ)[1]

[1] FAFEID; [2] FIOCRUZ/BH.

Natural products from *Euphorbiaceae* family provide pharmacologically relevant bioactive principles displaying antiviral and anti-tumor properties. Herein, we have performed an extensive investigation focusing the immunological properties of *Euphorbia tirucalli* crude latex (EUF) against innate and adaptive immune related cells. For this purposes, we have accessed, by flow cytometry, the intracytoplasmatic cytokine profile of peripheral blood leukocytes from 10 healthy individuals after short-term stimulation *in vitro*, using PMA and DMSO as control cultures. Our data demonstrated that EUF increases the frequency of IFN-γ+ T-cells, both CD4+ and CD8+ as well as CD4+TNF-α+ T-Lymphocytes in comparison to PMA/DMSO control cultures. Together, these findings pointed out that EUF is able to drive the adaptive immune response toward a type-1 cytokines pattern. We are currently investigating the impact of EUF on major innate leukocyte subpopulations. These studies counted for the discovery of new immunomodulatory bioactive principles. Further investigations are necessary to identify and isolate the major bioactive principles form EUF.

Financial support: FAFEID, FAPEMIG and FIOCRUZ.
Supervisor: Gustavo E. A. Brito-Melo.

MI017 - ASSESSMENT OF THE EFFECTS OF DISINFECTANTS AGAINST *STAPHYLOCOCCUS AUREUS* BIOFILM

TATIANE KAREN CABEÇA (PG)(1); ELISABETH LOSHCHAGIN PIZZOLITTO (PQ)(1).

(1)Faculdade de Ciências Farmacêuticas – Unesp/Araraquara.

Introduction and aims: The attachment of bacteria to steel surfaces used in food processing and the subsequent development of biofilm is a potential source of contamination that may lead to transmission of diseases. Considering that bacterial biofilm is more resistant to antimicrobial agents, in this study we evaluated the effects of disinfectants used in food industries against *Staphylococcus aureus* biofilm. Methods: Sterilized stainless steel coupons (1cm x 1cm) were placed separately in tubes containing 15 ml of Mueller-Hinton broth and 20ml of a suspension of *S. aureus* with about 10^8CFU/ml. The tubes were incubated at 37 ºC with shaking (100rpm) for 5 days. The coupons were removed from tubes, rinsed with sterile physiological saline, placed separately in Petri dishes containing 20µl of a tested disinfectant (iodine, biguanide, quartenary ammonium, peracetic acid and chlorine) for 10 minutes and immediately transferred to 2 ml of Letheen broth. They were then prepared for scanning electron microscopy (SEM) observations. Results: SEM showed cocci adhered on coupons after treatments with the disinfectants. Conclusion: The results reported here show that the tested disinfectants could not eliminate *S. aureus* biofilm.

Advisor: Dra. Elisabeth Loshchagin Pizzolitto

MI018- EVALUATION OF TOOTHBRUSHES CONTAMINATION IN FUNCTION OF ORAL ANTISEPTICS

ANDRESA PIACEZZI NASCIMENTO (PG)[(1)]; GISELE FARIA (PQ)[(2)]; MARCELO VAN VLIET LIMA (IC)[(1)]; EVANDRO WATANABE (PG)[(1)]; IZABEL YOKO ITO (PQ)[(1)]

[(1)] FCFRP-USP; [(2)] FORP-USP

Introduction: toothbrushes become contaminated by oral microorganisms, being able to function as microorganisms reintroduction vehicle. Objective: it was evaluated the effect of Periogard and Plax, in spray, on biofilm formation by mutans group streptococci (MGS) on the toothbrush bristles. Methodology: system in three steps involving 53 university students of FCFRP-USP. The research was carried out according to randomized study. After 2 minutes of toothbrushing without dentifrice, each solution was sprayed over the toothbrush bristles and maintained at room temperature for three hours. After toothbrushes were put in test tubes containing sacarose bacitracin broth and incubated at 37ºC for 3-4 days. The biofilm/colony on the bristles was counted by stereomicroscope with reflected light. Results: 41 subjects took part in all steps. In the control group (water), 38 (92.7%) toothbrushes presented biofilm by MGS. Periogard and Plax inhibited formation of biofilm in the bristles of 37 (97.4%) and 32 (84.2%) toothbrushes, respectively. Conclusion: antiseptics evaluated were able to inhibit the formation of biofilm by MGS on toothbrushes. (Ethics Committee: Process CEP/FCFRP # 33)

Financial Support: CAPES
Supervisor: Izabel Yoko Ito

MI019-MYCOBACTERIAL PHOSPHOLIPASE (PLC) INDUCES LEUKOCYTE RECRUITMENT IN THE *MYCOBACTERIUM TUBERCULOSIS* INFECTION

CAMILA MATIAS PERES (PG)[(1)]; SYLVIA CARDOSO LEÃO (PQ)[(2)]; CÉLIO LOPES SILVA (PQ)[(3)] AND LÚCIA HELENA FACCIOLI (PQ) [(1)].

[(1)]DACTB/FCFRP-USP, [(2)]UNIFESP, [(3)]CPT-FMRP-USP.

Introduction: PLC is involved in the virulence of *Mycobacterium tuberculosis* (Mtb). Objective: Evaluate the role of PLC in the cellular recruitment induced by Mtb. Methods: BALB/c mice were infected by i.t with either isolates 97-1505 (presence of *plc*A, *plc*B and *plc*C genes) or 97-1200 (no *plc* genes) of Mtb. On days 2, 7, 15 and 30 post infection (p.i.), the leukocytes counts were evaluated in the bronchoalveolar space (BALF). Results: The isolate 97-1505 induced significant neutrophil accumulation to the lungs in all days p.i. However, except on day 2, animals infected with 97-1200-Mtb presented reduced neutrophil counts in the BALF when compared with 97-1505 Mtb-infected animals. Both isolates induced mononuclear cells recruitment to the lungs in comparison to the control animals. Furthermore, from the day 15 p.i., mononuclear cell counts into the BALF as a response to isolate 97-1200 were smaller than those of 971505-infected animals. Conclusion: PLC participates in the leukocyte recruitment to the lungs during infection by Mtb. Further studies will be performed to understand the mechanisms involved in this effect.

Financial support: FAPESP, CNPq
Supervisor: Lúcia Helena Faccioli

MI020-A NEW EXCRETED/SECRETED PROTEIN FROM *LEISHMANIA INFANTUM* INDUCES A HUMORAL IMMUNE RESPONSE

JOANA MACIEL[1, 2]; MARTA SILVA[1, 2]; ANA TOMÁS[2,3]; ANABELA CORDEIRO-DA-SILVA [1, 2]

[1]Serviço de Bioquímica, Faculdade de Farmácia, [2]IBMC e [3]ICBAS da Universidade do Porto.

Leishmania is an intracellular pathogen that causes leishmaniasis, which continuous as an important medical problem in several countries. *Leishmania* live as either extracellular flagellated promastigotes in the digestive tracts of their sand fly vectors or as nonflagellated amastigotes on macrophages.
We are cloning and sequencing a new excreted/secreted protein from *L. infantum*, determined the parasite localization of this protein, analyzed the cell populations modified after *in vitro* and *in vivo* treatment and studied the expression of this protein in promastigote and amastigote forms of the parasite by immunofluorescence microscopy. Cell markers like CD4 (CD4 cell), CD8 (CD8 cell), μ (B cell) and CD69 (early activated marker) were studied in each cell population in spleen of Balb/c mice using flow cytofluorometric analysis. The functionality of the different cell populations will be shown by determination of interleukine levels and immunoglobuline production by ELISA assay.
The new protein was localized on organelle structures in the promastigote as in the amastigote phase of the parasite.
We have observed that the effect this protein *in vitro* and *in vivo* in spleen cell proliferation was dose dependent, active B and T cells and induce IgG immunoglobulin isotype production.
Our study shows that *Leishmania* can excrete a new protein with an important role in B cell activation and differentiation.

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Anabela Cordeiro-da-Silva

The authors did not follow the Scientific Committee's suggestion for an English language review

MI021-PROTEINS INVOLVED IN ERYTHROCYTE INVASION BY *BABESIA BOVIS*

ANA PATRÍCIA YATSUDA(PQ)[(1)]; FRITS FRANSSEN(TEC)[(2)]; HENK JAN HAM(PG)[(2)]; DANIELE LEE(PG)[(2)]; ERIK DEVRIES(PQ)[(2)]

[(1)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo; [(2)]Veterinary Faculty, Utrecht University, Netherlands

Introduction:*Babesia bovis* is a tick-transmitted apicomplexan parasite infecting bovine erythrocytes. Both pathogenesis of babesiosis as well as life cycle resemble malaria from *Plasmodium falciparum*, but little is known on *B. bovis.*
Objetive: Identification of novel proteins crucial for erythrocyte invasion by *B. bovis.*
Methods An EST database was searched for specific microneme motifs and an *in vitro* invasion assay with free merozoites invading new erythrocytes in a protein free environment was used.
Results:Proteins were searched with a transmembrane domain (TM) and a short cytoplasmic tail (with acidic residues and a tryptophane) and a TM with spitz motif properties (rhomboid protease substrate). A potential micronemal protein named BbMIC2 was cloned and sera against the recombinant protein inhibited 75% of invasion. Confocal microscopy pointed towards an apical localization for BbMIC2. Finally, 2D gel is being employed to identify proteins secreted during *in vitro* invasion as these constitute a set of molecules involved in the mechanism of invasion.
Conclusion: A novel *B. bovis* protein, BbMIC2, has a potential role in host cell invasion deserving further investigation.

Financial support: Intervet International BV
Supervisor: Erik deVries

MI022- PREVALENCE OF DRUG RESISTANCE AMONG TUBERCULOSIS PATIENTS IN RIBEIRAO PRETO CITY AND REGION

MARIA IZILDA TAVARES PINI(PQ)[1]; CACILDA ROSA CARDOSO SILVA(PQ)[1]; CRISTINA ABADE MARABINI(PQ)[1]; JOSÉ PEIXOTO HENARES(PQ)[1]; LEONARDO NEVES DE ANDRADE(PG)[1]; JUVENAL DE OLIVEIRA CAMPOS(PG)[1]; MARIA CLARICE ERRERA(PQ)[1]; NATALIA TAIS SARDELLA(PG)[1]; DAISY NAKAMURA SATO(PQ)[1]

[(1)] Instituto Adolfo Lutz (IAL)– Laboratório I de Ribeirão Preto

INTRODUCTION: The emergence of resistance to antituberculous drugs is an increasing public health problem worldwide. OBJECTIVE: The aim of this study was to evaluate the prevalence of drug resistant tuberculosis among patients in Ribeirao Preto and region. MATERIAL AND METHODS: Drug susceptibility testing (DST) was performed in 265 isolates of newly diagnosed cases and 262 relapses/treatment failures cases between 2001 and 2004, using the Proportion Method to the first line antituberculosis drugs. RESULTS: Among new cases and relapses/treatment failures cases the results were respectively, 81.9% and 68.3% were pan-susceptible; 6.8% and 10.3% were monoresistant; 5.6% and 8.8% were poliresistant; and 5.6% and 12.6% were MDR. CONCLUSION: Routine follow-up of drug resistance rates in re-treatment cases may be the easiest and fastest way to evaluate the impact of tuberculosis control programmes, besides being useful for clinical purposes.

Financial Support: IAL
Supervisor: Maria Izilda Tavares Pini

MI023-DIRECT DETECTION OF *Mycobacterium bovis* BY PCR ASSAY IN MILK SAMPLES.

CLESO MENDONÇA JORDÃO JUNIOR (PG)[1]; MARCOS ROGÉRIO ALVES PINTO (PQ)[2]; ELIANA ROXO(PQ)[3]; CLARICE QUEICO FUJIMURA LEITE (PQ)[1].

[1]Departamento de Ciências Biológicas FCF/UNESP; [2]Médico veterinário; [3]Instituto Biológico, São Paulo, Brasil.
INTRODUCTION. Bovine milk is an important source of protein and other nutrients but can be contaminated by pathogenic agents, especially *Mycobacterium bovis*. OBJECTIVE. In this study, we standardized an efficient PCR method for *M. bovis* identification from milk. METHODOLOGY. A known number of *M. bovis* AN5 were inoculated in the milk that was submitted to a serial dilution. Two different PCR protocols were done to evaluate the threshold of *M. bovis* detection. Two set of primers were used, one to detect *Mycobacterium* spp (INS1 e INS2) and other to detect *M. bovis* (JB21 e JB22). Dilutions were also submitted for culture using Stonebrink medium and incubated at 37°C/90 days, to determine the number of bacilli in milk. RESULTS AND CONCLUSION. The results of PCR showed that the protocol using primers INS1/ INS2 was positive until 10^{-3} dilution (800 CFU/mL). The protocol with primers JB21/JB22 was more sensitive and specific, detecting *M. bovis* until 10^{-4} dilution (80 CFU/ mL). This method can be applied for routine diagnosis of *M. bovis* in milk samples.

Financial Support: CAPES
Supervisor: Profª Drª Clarice Queico Fujimura Leite

MI024-SENSITIVITY PROFILE OF GENUS *STAPHYLOCOCCUS* ISOLATED FROM UNIVERSITY HOSPITAL OF SANTA MARIA (UHSM)

FABIANE DO AMARAL(IC)[1]; RODRIGO BUSKE(PQ)[1]; RITA WEISS(PQ)[1]; ROSANE FRIEDRICH(PQ)[1]; GUSTAVO NESI(PQ)[1]

[1]Universidade Federal de Santa Maria

INTRODUCTION: The increase of the bacterial resistance in hospitals is a problem for the Public Health. The genus *Staphylococcus* is an important agent in hospital infections. OBJECTIVE: The objective of this work was to verify the sensitivity profile of *Staphylococcus aureus* and *Staphylococcus epidermidis* samples isolated from the Surgery Unit (SU), Intensive Care Unit of Adults (ICU-Adult) and of Newborn (ICU-Newborn) and from the Bone Marrow Transplant Center (BMTC) of the UHSM. METHODOLOGY: The sensitivity profile was compared using the method of diffusion in Müller-Hinton agar. Antimicrobial drugs had been used according to NCCLS, 2004. RESULTS: The isolated bacteria from the ICUs had a lesser profile of sensitivity than the ones isolated from the SU and the BMTC. All the bacteria isolated were 100% sensitive to Vancomicina. In the SU, the microorganisms were 100% sensitive to Ampicilina + Sulbactam, while in the ICUs were found some samples resistant to this association. *S. epidermidis* had presented some sensitivity in all units, mainly in the SU. *S. aureus* and *S. epidermidis* multiresistant were isolated. CONCLUSIONS: The results obtained confirm the necessity of the controlled and conscientious use of the drugs.

Adviser: Rita Weiss

MI025-CONTAMINATION OF HEMODIALYSIS MACHINE WATER BY POTENTIALLY PATHOGENIC BACTERIA

LILIAN BUENO MONTANARI(IC); FLÁVIO GARCIA SARTORI(IC); REGINA HELENA PIRES-GONÇALVES(PQ); EVERTON GIOVANNI ALVES(PG); CARLOS HENRIQUE GOMES MARTINS(PQ)

Universidade de Franca, 14404-600, Franca, SP, Brazil.

INTRODUCTION: Hemodialysis patients are more susceptible to infection by microorganisms, both from endogenous and exogenous sources, than the general population. OBJECTIVE: Identify and assess the bacteria present in this water. METHODOLOGY: The samples were taken in the hemodialysis unit in São Paulo State, Brazil, in January and February 2005. In each month, 1L of water was taken from each of 17 dialysis machines, making 34 samples in all. Colony-forming bacteria were isolated by filtering the water through a membrane (0.22µm), which was cultured on enriched medium. Bacterial species were identified by traditional methods. RESULTS: 56 strains were recovered, 14.2% of which were *Staphylococcus epidermidis,* 1.8% *Bacillus cereus*, 26.8% *Escherichia coli*, 3.6% *Klebsiella pneumoniae* and 1.8% *K. oxytoca.* Non-fermenters isolated included *Pseudomonas stutzeri* (21.4%) and *Stenotrophomonas maltophilia* (1.8%). CONCLUSION: The water used in the hemodialysis machines in question carries some potentially pathogenic bacteria. Further studies are recommended, to discover whether these bacteria prejudice the health of patients after prolonged exposure.

Financial Support: PIBIC/UNIFRAN
Supervisor: Carlos HG Martins
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MI026-INHIBITION OF NITRIC OXIDE PRODUCTION BY *ALCHORNEA TRIPLINERVIA* METHANOLIC EXTRACT

FLÁVIA CRISTINE MASCIA LOPES(PG)[(1)]; TAMARA REGINA CALVO(PG)[(2)]; WAGNER VILEGAS(PQ)[(2)]; IRACILDA ZEPPONE CARLOS(PQ)[(1)]

[(1)] FCF/UNESP-Araraquara; [(2)] IQ/UNESP-Araraquara

Introduction. Since medicine exists, plants are useful. The importance of the immune system for human survival and the search for compounds derived from plants motivate the development of chemical and biological strategies to discover new active substances. Nitric oxide (NO) can have beneficial effects killing pathogens, but it is involved in several diseases and can promote tumor angiogenesis and metastasis. Objective. Study the inhibition of NO production by *A. triplinervia* methanolic extract in LPS-activated macrophages. Methodology. The viability of the cells was evaluated by MTT and NO was determined through Griess reaction. Phytochemical studies were performed. Results and Conclusion. Good viability levels were observed in the tested concentrations, higher than 77% in most of the samples. The methanolic extract inhibited NO production according to the concentration of samples (47% to 98%). The main classes of compounds observed were flavonoids and alkaloids. These results are important since inhibitory agents are potentially useful in the treatment of several diseases associated with NO overproduction, including neurodegenerative disorders and inflammation.

Financial Support: CAPES/FAPESP
Supervisor: Iracilda Z. Carlos

MI027-IN VITRO BIOFILM CONTINUOUS CULTURES

ELISSA G. O. SILVA (IC); ANA C. T. MARTINS (IC); GISLENE. G. F. NASCIMENTO (PQ); MARIA ONDINA PAGANELLI (PQ); MARIA L. POLACOW (PQ); MARIA H. S. C. TAVARES (PQ) (1).

(1) Methodist University of Piracicaba

Introduction: Bacterial biofilms are formed in a variety of surfaces and habitats and have been studied *in vitro* by non destructive methods. They form complex structures that represent a primitive model system to study microbial development, communication and interaction among cells.
Objective: *In vitro* experiments were conducted to standardize continuous flow system to study biofilms on glass slide surfaces and to control the process.
Methodology: The continuous system was an adaptation of Wolfaardt et al. (1994) methods. For the strains P. *aeruginosa* (standard) and the isolates 13, 1P and 9P the biofilm formation data were expressed by the growth surface area against time. Measurements were done by direct optic microscopy and image captures.
Results: The formations of biofilms could be followed up to 48h and depth field distortions were unavoidable in later phases of development.
Conclusions: Biofilms cultivation in the continuous flow system were achieved for the P. *aeruginosa* strains that made possible to measure mobility and growth on the surface area. This *in vitro* system opened up the possibility of further studies on the morphology, physiology and composition of biofilms.

Financial support: FAP-UNIMEP
Advisor: Maria Helena Santini Campos Tavares

MI028-HEMATOLOGICAL EVALUATION IN *MUS MUSCULUS* INFECTED WITH *L.(V.) BRAZILIENSIS* AND TREATED WITH DIFFERENT BIOTHERAPICS

KARINA PONTIN(PG)[1]; VALDELICE OLIVEIRA BURGOS(PQ)[2]; MIRIAN PAULA TOLDO(PQ)[3]; FERNANDA GOMES VELASQUE GAMA(PG)(4); FABRICIO VILLELA MAMEDE(PG)(4); SÉRGIO ALBUQUERQUE(PQ)[2]

[(1)]UNICAMP; [(2)]UNIGRAN; [(3)]FCFRP-USP; [(4)]UNESP

Introduction: The leishmaniosis have a world incidence of 600.000 people/year and a prevalence of 12 million of cases. The current drugs used for treating this disease displays serious side effects, besides the fact of inducing parasite resistance. Objectives: To evaluate the hemogram profile in mice infected and non-infected with *L.(V.)braziliensis* treated with different biotherapics. Methods: *Mus musculus,* were infected with promastigote forms of the parasite. The oral treatment took 60 days. Positive control (PC) was administered according to the therapeutic standards for this medicine. Treated control groups of 5 animals each were killed after the end of the treatment with biotherapics for hemathological evaluation. Results and Conclusions: Infected and treated animals displayed a slight drop in hemoglobin and erythrocyte levels with enhanced drop for PC group. We suppose that the biotherapics obtained from amastigote and promastigote forms could stimulate the immune response, which can be noted by enhanced number of lymphocytes when compared with PC and other treated groups.

Financial support: CAPES
Supervisor: Prof. Sérgio de Albuquerque

MI029-PROFILE OF OTHER MEMBRANE PROTEIN (OMP) IN SAMPLES OF *ACINETOBACTER BAUMANNII* RESISTANT TO CARBAPENENS.

FABRÍCIA RÉ (IC)[1]; ANA C. GALES (PQ²; LOURDES B. GARCIA (PQ)[1]; MARIA CRISTINA B. TOGNIM (PQ)[1].

[(1)]State University of Maringá; [(2)] Federal University of São Paulo

Introduction: In recent years, the number of hospital infections caused by carbapenens resistant to *Acinetobacter baumannii* (CRAb) has increased significantly. Beta-lactams antibiotics penetrate the outer membrane through porins and carbapenens resistance may arise due to the decrease, loss or hiper-expression of outer membrane proteins (OMPs). Objective: The study aimed at verifying OMPs patterns in samples of CRAb. Methods: OMPs profiles were observed on 12% SDS-PAGE of a total of 21 different clones of *A. baumannii* isolated between 1993-2001. The strain ATCC 19606 was used as the sensitive pattern. Results: Ten strains (47,6%) showed an alteration in the OMPs. In just one sample there was the loss of a protein of approximately 29 kDa, and in other three we verified a decrease in the expression of this porin. In the other six was verified a decrease or hiper-expression of OMPs between 30 and 50 kDa. Conclusions: The results demonstrate that the alterations in OMPs can contribute for *A. baumannii* resistance to antibiotics and make the treatment of infections caused by these microorganisms more difficult.

Financial Support: CAPES/ CNPq
Supervisor: Maria Cristina B. Tognim

MI030 - DETECTION OF AMPC β LACTAMASE AND EFFLUX PUMP IN ACINETOBACTER SPP. CLINICAL ISOLATES

DEBORAH P. GONZALES (IC)[1]; ANA C. GALES (PQ)²; LOURDES B. GARCIA (PQ)[1]; MARIA CRISTINA B. TOGNIM (PQ)[1].

[1]State University of Maringá;[2] Federal University of São Paulo

Introduction: The spread of multi-drug-resistant Acinetobacter spp. (MDRAc) clones constitutes a serious cause of nosocomial infections. Objective: This study verified the production of inducible AmpC ß-lactamase (AmpC) and the presence of efflux pump (EP) in 21 clinical isolates of Acinetobacter spp. with reduced susceptibility to the carbapenens. These samples were selected from previous studies, which belonged to different clones and were isolated from 1993 to 2001. Methods: the technique of agar dilution was used in agreement with NCCLS for the tests. The production of AmpC was determined by the MIC of meropenem, cefepime and ceftazidime in the presence and in the absence of the inhibitor Syn 2190 (4 mg/L), and the presence of EP was verified by MICs of the same antibiotics with and without the inhibitor reserpine (25mg/L). Results: A total of eleven strains (52,4%) were positive for the production of AmpC, while two samples (9,52%) presented active EP. Conclusions: The high percentage of AmpC in with or without the combination of EP can be an important mechanism of resistance to the ß-lactam antibiotics in MDRAc.

Financial Support: CAPES/ CNPq
Supervisor: Maria Cristina B. Tognim

MI031-SLIME PRODUCTION BY COAGULASE NEGATIVE *STAPHYLOCOCCUS*

ADILSON CÉSAR ABREU BERNARDI (PG)[1]; ELISABETH LOSHCHAGIN PIZZOLITTO (PQ)[1]; ANTONIO CARLOS PIZZOLITTO (PQ)[1]

[(1)]Universidade Estadual Paulista-UNESP Faculdade de Ciências Farmacêuticas- Araraquara.

Introduction: Coagulase-negative staphylococci are the most common cause of foreign-body-associated infection. The pathogenesis of such infections has been correlated with the ability of these strains to produce extracellular material termed slime. Objective: The aim of this study was to detect the production of slime by coagulase-negative staphylococci using qualitative and quantitative methods. Method: In this study, the presence of slime was searched for in a collection of 27 coagulase-negative *Staphylococcus* strains from catheter-associated infections. Slime-forming ability was phenotypically tested on Congo red agar plates and the attachment ability of these bacteria was tested using polystyrene microtiter plates. Results: Data obtained indicated that 59.26% of the strains produced slime, and 81.4% adhered to polystyrene. Conclusion: The detection of slime-producing coagulase-negative staphylococci may prevent catheter-related infections. The slime seems to be the most important factor by which these strains adheres and colonizes catheters.

Financial Support: CRD/NAC – FCF-UNESP
Supervisor: Antonio Carlos Pizzolitto

MI032-EVALUATION OF HUMORAL IMMUNE RESPONSE IN SUBJECTS PPD REACTANT OR NOT, SYMPTOMATIC AND ASYMPTOMATIC

LÍVIA COSTA SOUZA(IC)[1]; WARLY BARCELOS(PG)[1];VICENTE DE PAULO COELHO PEIXOTO DE TOLEDO(PQ)[1]; SILVANA SPINDOLA DE MIRANDA(PQ)[2]; JULIANA FULGÊNCIO HENRIQUES(IC)[2]; MARCIO HAMILTON PROUZTNER OLIVEIRA(PQ)[2]; TÂNIA MARA PINTO DABÉS GUIMARÃES(PQ)[1]

[1] Faculdade de Farmácia/UFMG, [2] Faculdade de Medicina/UFMG

Introduction–*Mycobacterium* antigens and host factors related to protection against tuberculosis(TB) are not clarified.
Objectives-To assess specific IgG and variables as BCG vaccinal scars(VS), PPD and contact backgroud(CB), in asymptomatic subjects(AS), HIV- and patients with active TB(sugestive chest X-ray, positive culture and baciloscopy)and after healing.
Methods–Screening by IgG ELISA, in 78 AS, reactant PPD(26)(≥10mm) non reactant PPD(52), TB patients (38)and healled(16).
Results-It was showed lower levels of IgG (cut off ≤ DO 0,214) in AS, reactant PPD(26) and non reactant(52). From PPD+, 17 were CB and 9 VS. From PPD-, 12 were CB and 15 VS, 9 were PPD conversion and 13 booster. Patient with TB(38) and healled showed higher levels of IgG (>cut off).
Conclusion–TB patients(non protected) showed higher IgG levels and TB patients(protected) lower IgG levels. VS and CB and PPD reactant do not affected the IgG production. This parameter could contribute to the disease's diagnosis and to the high risk's subjects follow-up (PPD reactant).

Supervisor: Tânia Mara Pinto Dabés Guimarães

MI033-ANTIMYCOBACTERIAL ACTIVITY OF GREEN PROPOLIS

CARLOS HENRIQUE GOMES MARTINS(PQ)[1]; DAISY NAKAMURA SATO(PQ)[2]; LEONARDO NEVES DE ANDRADE(PG)[2]; TATIANE CRUZ DE CARVALHO(IC)[1]; DENISE CRISPIM TAVARES(PQ)[1]; JAIRO KENUPP BASTOS(PQ)3; WILSON ROBERTO CUNHA(PQ)[1]

[(1)]Universidade de Franca; [(2)]Instituto Adolfo Lutz – Laboratório I de Ribeirão Preto; [(3)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto - USP

INTRODUCTION: Propolis is a hive product constituted in a series of substances as resinous, beeswax and plant-derived substances such as resin and volatile compounds. Among the identified chemical compositions of propolis it can be mentioned the cinnamic acid, flavonoid, mono and sesquiterpenes that probably contributing to the antimicrobial activity. Green propolis derives mainly from vegetative apices of *Baccharis dracunculifolia* (alecrim plants). OBJECTIVE: We investigated the antimycobacterial activity of green propolis. METHODOLOGY: The analytical method used was the Resazurin Microplate Assay (REMA) that determines the Minimal Inhibitory Concentration (MIC) of propolis that kills mycobacteria in vitro. RESULTS: The MIC of green propolis was respectively 500 µg/mL and 250 µg/mL against *M. avium* complex and *M. kansasii*. CONCLUSIONS: The MIC results indicated significant antimycobacterial activity of green propolis but further studies should identify the active compounds.

Financial Support: FAPESP/UNIFRAN
Supervisor: Carlos Henrique Gomes Martins

MI034-LEUKOTRIENE B_4 AND PLATELET-ACTIVATING FACTOR COOPERATES IN REGULATING POLYMORPHONUCLEAR NEUTROPHIL TRAFFICKING TO INFLAMED LUNGS

CAROLINE BÉLANGER(PG)[1]; PIERRE BORGEAT(PQ)[2]; SYLVIE MARLEAU(PQ)[1]

[(1)]Faculté de pharmacie, Université de Montréal ; [(2)]Centre de recherche en Rhumatologie et Immunologie, CHUL, Québec, Canada.

INTRODUCTION. LTB_4 and PAF play an important role in regulating PMN extravasation to inflammatory sites by regulating PMN adherence and vascular permeability. OBJECTIVE. To investigate the role of LTB_4 and PAF on PMNs trafficking to the lungs in a model of pulmonary inflammation. Selective BLT1 (CP-105,696) and PAF (SR-27417) receptor antagonists were used to delineate the role of the lipid mediators. METHODS. Rats were pretreated orally with SR-27417 (0.3 mg/kg) and/or with CP 105,696 (30 mg/kg) 2 and 16 hours before an i.v. injection of Sephadex beads (15 mg/kg). RESULT. Sephadex beads injection elicited an early pulmonary neutrophilia ($0,50 \pm 0,07 \times 10^6$ PMN/g lung tissue compared with $0,18 \pm 0,05 \times 10^6$ PMN/g in control rats 4 hours following injection. Pretreatment with the drugs alone did not significantly modulate PMN accumulation to the lungs whereas the concomitant administration of the drugs reduced lung neutrophilia by $52 \pm 5\%$ ($p < 0.05$). CONCLUSION. We conclude that PAF and LTB_4 exert a cooperative effect on PMN trafficking to the lungs elicited by Sephadex beads.

Financial support: Canadian Institutes of Health Research.
Advisor: Sylvie Marleau

MI035-PROZONE PHENOMENON AND SERUM-REACTIVITY TITERS IN VDRL TEST OF PATIENTS BEARING SYPHILIS

GERALDO CAVALCANTI JR(PQ); LUCIANA AZEVEDO(IC); PAULO FERNANDES (IC); DANY SILVA (PG); MILENA ARAÚJO (IC); SARAH MEDEIROS (IC); DIOGO LOPES (PG); VALÉRIA SALES (PQ)

* DACT, UFRN

Amongst the non-treponemic tests for syphilis the "Veneral Disease Research Laboratory" (VDRL) stands out, it uses cardiolipin as antigen. It is a very sensible screening test, although it is not specific for syphilis. A prozone phenomenon occurs due to the excess of antibodies and the reaction is seen as non-reactive or weakly reactive, however when the serum is diluted at 1:2, 1:4 or 1:8 the test shows to be reactive. This work aims to evaluate the serum-reactivity of individuals bearing syphilis through the VDRL test, as well as the presence of the prozone phenomenon. Serum samples of 40 individuals with positive serology for syphilis (through FTA-Abs test) had been analyzed. Of the 40 samples, 8 (20%) had presented the prozone phenomenon. Two of these cases had presented a not reactive standard in the not diluted samples and intense flocculation when diluted at 1:8. The other six sera had presented a borderline reaction when not diluted, also contrasting with the very strong reactive results when diluted at 1:8. Thus, we could demonstrate the difficult formation of antigen-antibody cross link which characterizes the prozone phenomenon and the necessity of the sera dilutions when we accomplish the VDRL test.

Supervisor: Prof. Dr. Geraldo Cavalcanti Jr

MI036-VIRULENCE POTENTIAL OF YEASTS ISOLATED FROM NEWBORNS

DANIELA S. VANDRESEN (IC); LUCINEIDE A. BONASSOLI (PG); THÂMARA A. BERTONINI (IC); CLEISON L. TAIRA (PG); ARTHUR E. SVIDZINSKI(IC); TEREZINHA I. E. SVIDZINSKI.

Universidade Estadual de Maringá – PR

Introduction: The incidence and frequency of hospital infections caused by yeast has increased and Candida species are considered now to be the fourth cause of systemic nosocomial infection. Objective: Determine the virulence potential and identify isolated yeast from newborns, without signs of infection, admitted to the UTI-Neonatal of University Hospital. Methods: Biological samples were collected from skin and cultured on CHROMágar Candida, incubated at 35ºC up to five days. Each colony was identified by classical method and the protease activity was evaluated by medium with added casein. Results: Nineteen yeasts were isolated, including 5 Candida species, among which 15.8% were positive, 73.7% strongly positive and 10.5% were negative. Conclusion: The newborns are colonized by many yeast species and most of then have virulence potential. These data suggest that there are high susceptibility of patients from UTI to systemic infection by yeast, in view of the colonization and expose to invasive methods.

Financial Support: Fundação Araucária
Supervisor: Drª. Terezinha I. E. Svidzinski

The authors did not follow the Scientific Committee's suggestion for an English language review

MI037-BRAZILIAN PROGRAM FOR TUBERCULOSIS DRUG DISCOVERY

FABIO CÍCERO DE SÁ GALETTI (PG)[1]; JOSÉ MARIO STABILE JUNIOR (IC)[1,2]; TATIANE ANDRADE LEMOS (IC)[1]; LUÍS ALBERTO MORAES (PQ)[2]; ANA OLÍVIA DE SOUZA (PQ)[3]; CÉLIO LOPES SILVA(PQ)[1].

(1)Centro de Pesquisas em Tuberculose – FMRP/USP – Ribeirão Preto-SP, Brazil; (2)FFCLRP/USP– Ribeirão Preto-SP, Brazil; (3) Biochemistry and Biophysics Laboratory/Instituto Butantan – São Paulo-SP, Brazil.

Introduction: Tuberculosis incidence is a health problem and a challenge for drug discovery.
Aim: To determine antimycobacterial activity of samples from natural and synthetic sources.
Methods: Antimycobacterial activity is performed by susceptibility assay on Mycobacterium tuberculosis H37Rv through Minimal Inhibitory Concentrations determination. Samples with MIC bellow 16-32 μg/mL (or $\mu MolL^{-1}$) are evaluated for cellular viability (IC_{50}) by MTT reduction assay and those with SI ($SI=MIC/IC_{50}$) higher than 10 are selected to intracellular antimycobacterial activity determination and latter to in vivo study. Purifications of crude extracts are guided by the bioassays and isolated compounds are tested in vitro and in vivo.
Results: In our study there are at least 20 promising samples with SI higher than 10, which are now being studied in in vivo tuberculosis models.
Conclusions: Results are indicative of the efficiency of the Brazilian drug discovery program for tuberculosis.

Financial Support: FAPESP, CNPq/MCT, REDE-TB.
Supervisor: Célio Lopes Silva

MI038-MIGRATION OF THE EOSINOPHIL AND MONONUCLEAR CELL NUMBERS TO BRONCHOALVEOLAR FLUID AND PERITONEAL CAVITY IN INTELEUKIN-12 KNOCKOUT AND C57BL/6 MICE INFECTED BY *Strongyloides* venezuelensis

ELEUZA RODRIGUES MACHADO(PG)[1]; DANIELA CARLOS (PG)[1]; ELAINE VICENTE LOURENÇO(PG)[2]; FERNANDA ANIBAL FREITAS(PG)[1]; CARLOS ARTÉRIO SORGI(PG)[1]; ÉRIKA VITALIANO GÁRCIA SILVA(PG)[1] AND LÚCIA HELENA FACCIOLI(PQ)[1]

1)FCFRP and (2)FMRP (USP-SP)

Eosinophilia is a characteristic of helminthiasis, but few studies are available concerning the induction of *S. venezuelensis* in IL-12 knockout (IL-12 KO) mice. Objective: The aim of this study was to investigate the migration of the eosinophil (EO) and mononuclear cell (MC) numbers to peritoneal cavity fluid (PCF) and bronchoalveolar fluid (BALF) in IL-12 KO and C57BL/6 mice infected by *S. venezuelensis*. Methodology: IL-12 KO and C57BL/6 mice were infected by *S. venezuelensis* infective larvae. No-infected mice were used as control. On the 7th and 14th day after infection, the animals were killed and the number of leucocytes PCF and BALF, larvae and worm parasites were quantified. Results: The EO and MC number significantly increased in C57BL/6 and IL-12 KO mice treated or not with MK886 when compared with control groups. The treatment significantly inhibited EO and MC in the PCF and BALF in C57BL/6 mice. Also, the number of larvae and recovered worm parasites were significant in the IL-12 KO and in both groups treated with MK886 on the 7th day. However, the infection was maintained up to the 14th day only in the groups treated. Conclusion: These data show that IL-12 is important in the immune response induced by *S. venezuelensis* and the persistence of parasitism in the host.

Supervisor: Profª. Drª. Lúcia Helena Faccioli.
Financial Support: FAPESP/CAPES/CNPq.

MI039-COMPARATIVE STUDY OF REFERENTIAL AND GENERIC VERSIONS OF CIPROFLOXACIN, CEFTRIAXONE AND AMPICILIN ANTIMICROBIAL ACTIVITY AGAINST *ESCHERICHIA COLI* ISOLATES FROM URINARY TRACT INFECTIONS.

ANGELMA GENARO(1); CARLOS ALBERTO DE M. LOPES [1].

[(1)]Instituto de Biociências, UNESP, Botucatu, SP

Introduction: *Escherichia coli* is one of the common agents of urinary infection whose antimicrobial multi-resistance has been subject of concern by public health authorities in recent years. Objective:The aim of this work was to compare the effectiveness ciprofloxacin, ceftriaxone and ampicilin in their generic and referential versions against *E. coli* isolates from urinary tract infections. Methodology: For this purpose, 80 *E. coli* isolates were submitted to minimal inhibitory concentration tests and beta-lactamases qualitative disc assay. Results: The activity showed by the generics was lower, if compared with that by the referentials. The agreement percentage was as follows: 96.3, 90.2, and 77.1, respectively for ciprofloxacin, ceftriaxone and ampicilin. Yet, only the difference for ampicilin proved to be statistically significant. Except for one strain, all the remaining were able to produce beta-lactamases. Conclusions: The results indicate that, for some antimicrobial classes, generic drugs may not be as effective as referentials.

Financial Support: Fundunesp.
Supervisor: Prof. Dr. Carlos Alberto de Magalhães Lopes

MI040-MICROBIOTA ANALYSIS OF HUMAN AND DOG GINGIVAL FLUID WITH CHECKERBOARD DNA–DNA HYBRIDIZATION

SANDRA SATO(PG)[1]; IZABEL YOKO ITO(PQ)[2]; VINÍCIUS PEDRAZZI(PQ)[1]

[(1)]FORP–USP; [(2)]FCFRP–USP

Checkerboard DNA-DNA hybridization is a molecular biology technique useful for the enumeration of bacterial species in microbiologically complex systems. The aim of this study was to compare the microorganisms present in the gingival crevicular fluid (GCF) of humans and dogs, both with periodontitis. Four samples of GCF were collected from humans and 6 from dogs using sterilized paper points. Theses points were put into eppendorfs with 1,0mL of saline and were vortexed for 1 min. The points were discarded and the eppendorfs were centrifuged for 15 min at 3000 rpm. The centrifuged sediment was suspended in 0,15mL of TE and 0,15mL of NaOH. The processed samples were sent to the Institute of Microbiology Prof. Paulo de Góes–UFRJ, where the microorganisms were identified using checkerboard DNA technique. From 29 DNA probes used, the most prevalent species in both humans and dogs were *T. forsythensis*, *C. rectus*, *P. intermedia*, *P. gingivalis* and *T. denticola*. These microorganisms are part of the microbial complexes related to periodontal diseases. Checkerboard DNA–DNA hybridization showed that microorganisms present in the GCF of humans and dogs with periodontitis were similar, validating this animal model to test new therapies for the treatment of periodontal diseases.

Supervisor: Vinícius Pedrazzi

MI041-INHIBITORY ACTIVITY OF VENOM FROM THE ANT *DINOPONERA AUSTRALIS* (*HYMEMOPTERA, PONERINAE*)

DANIELA BERALDO BARBOSA(IC)[1]; CAMILA TAKENO COLOGNA(IC)[1]; CYNARA DE MELO RODOVALHO(PG)[1]; LUCIANA DE OLIVEIRA ALMEIDA (PG)[1]; FLÁVIA ASSUMPÇÃO SANTANA(PG)[1].

(1) INGEB-UFU

Ponerinae is a primitive subfamily, distributed around the entire world. It is represented by several genus including *Dinoponera*, which consists of the largest ants, with just six species. There are no studies about the biological properties of those ants venom, therefore the inhibitory activity has been tested to determine the minimal inhibition concentration (MIC) of *D. australis* venom against two strains of *Escherichia coli* and two of *Staphylococcus aureus.* The activity was determined in microtitulation dishes with 100µL of different ants' venom concentration diluted in PBS buffer and 100µL of bacteria grown in BHI broth. Those dishes were warmed to 37°C and Optic Density was measured in 550 nm in the Diagnostics Pasteur spectrophotometer every 15 minutes. Those samples which had stabilized or diminished the bacterial growth were placed in agar Mueller Hinton dishes. The control consisted of buffer and buffer with bacteria. The results showed that MIC is 3µg/µL of ants' venom. This study suggests that venom may be used to protect the ants against internal pathogens arising from feeding.

CNPq; UFU
Malcon A. M. Brandeburgo

MI042-HISTOPLASMOSIS IN CD18^{LOW} MICE

WALTER M. TURATO (PG)[12]; FABIANI G. FRANTZ (PG)[12]; ALEXANDRA I. MEDEIROS(PQ) [1]; CÉLIO L. SILVA (PQ)[2]; LÚCIA H. FACCIOLI (PQ[1]

(1)DACTB- FCFRP-USP; (2)CPT-FMRP-USP

Introduction: *Histoplasma capsulatum* (*Hc*) is a pathogenic fungus, optional intracellular parasite. CD18 participates in cell migration and is used by *Hc* to penetrate in phagocytes. Objective: to evaluate the role of CD18 in cell recruitment to the broncoalveolar space fluid (BALF), for protection and systemic immunity against *Hc*. Methodology: CD18-deficient (CD18$^-$) and wild type (WT) C57Bl/6 mice were infected i.t. with *Hc* and on the 2nd, 7th and 14th post infection (p.i.), the animals were killed and lungs and spleen were analyzed. Results: *Hc*-infected CD18$^-$ mice have increased the neutrophil numbers in the BALF when compared to *Hc*-WT mice. On 2nd day: WT *Hc*= 0,47±0,07; CD18$^-$ *Hc*= 2,26±0,41; 7th: WT *Hc*= 0,28±0,39; CD18$^-$ *Hc*= 0,73±0,09; 14th: WT *Hc*= 1,01±0,16; CD18$^-$ *Hc*= 1,44±0,1x10^6/ml. The p.i. CFU number from lungs of CD18$^-$ was 1,4 $\log_{10}$ less than the WT until the 7th day and equivalent on the 14th day p.i. No differences were found when cytokines were quantified at spleen culture supernatant from WT and CD18$^-$ mice. Conclusion: Results show that the neutrophil recruitment in *Hc* infection is independent of CD18 and this molecule may be important to host protection but not to systemic immunity in histoplasmosis.

Financial support: CNPq, FAPESP, FAEPA
Supervisor: Lúcia H. Faccioli

MI043 - EFFECT OF HISTAMINE ON INNATE IMMUNE RESPONSE IN A MURINE MODEL OF PULMONARY TUBERCULOSIS

[1]CARLOS, D.,[1]MATIAS-PERES, C.,[1]PAULA, L.,[2]SORGI, C. A.,[2]SILVA, C.L., [1]FACCIOLI, L.H.

[1]Faculdade de Ciências Farmacêuticas de Ribeirão Preto, [2]Faculdade de Medicina de Ribeirão Preto, São Paulo, Brasil.

Introduction: Histamine is a biogenic amine synthesized from L-histidine by histidine descarboxylase and stored mainly within granules in mast cells. Objective: To investigate the role of histamine in the inflammatory response induced by *M. tuberculosis* infection. Methods: Balb-c mice were infected by intratracheal route with 1 x 10^5 viable *M. tuberculosis* or inoculated with PBS and treated by subcutaneous route with 20 mg/ml of pyrilamine (H1 antagonist) or cimetidine (H2 antagonist). Results: On the 15^{th} day of infection we observed intense inflammatory reaction with predominance of neutrophils and mononuclear cells when compared to the control group. Treatment of mice with pyrilamine reduced in 57% the number of neutrophils in the bronchoalveolar space and decreased the release of IL-1, TNF, KC and MCP-1 in lung homogenates. However, there was an increase of 78% in the number of neutrophils after treatment with cimetidine. Conclusion: These findings suggest that histamine plays a critical role in the immune response to *M. tuberculosis* infection.

Financial support: FAPESP, FAEPA and CNPq.
Advisor: Prof. Dra. Lúcia Helena Faccioli

MI044-CHLORIDRIC ACID AND BOVINE BILE TOLERANCE OF THIRTEEN STRAINS OF *ZYMOMONAS MOBILIS*

KAREN PENA DE SOUZA CAVALCANTI(PG)[1]; ALDO CESAR P. SILVA(PG)[2]; ELISANGELA C. B. SILVA(PG)[2]; IVONE ANTÔNIA DE SOUZA[1]; EULÁLIA C. P. A. XIMENES(PQ)[1]

[1] Antibiotic department of the Federal University of Pernambuco; [2]UFPE Pharmacy Department, Recife, Brazil

INTRODUCTION: Since its isolation for Linder in 1924, *Zymomonas mobilis* has been showing a grate probiotic potential. Among the characteristics for probiotic classification, including the acid and bile tolerance, that permit, the viability during its passage across the gastrointestinal tract. OBJECTIVE: Based on these criteria the objective was to characterize the acid bile tolerance of thirteen *Z. mobilis* strains isolated from alcoholic fermentation. METHODS: Acid or bile tolerant strains were selected, that evaluation was made for colony formation unit enumeration (CFU/mL), after a 4-hour contact in acidified SSDL culture media, at different levels of pH or at different bile concentrations. RESULTS: In culture media with pH equal or higher than 3, or with bile bovine concentration equal or lower than 0.5% all the studied strains have grown. CONCLUSIONS: In these conditions, all strains of *Zymomonas mobilis* have presented tolerance.

Eulália C. P. A. Ximenes

The authors did not follow the Scientific Committee's suggestion for an English language review

MI045-HEMOLYTIC ACTIVITY OF THE SERUM COMPLEMENT IN WOMEN USING ORAL CONTRACEPTIVES

JAMILE CAROLINA RAMOS BERETELLA (IC)[1]; KELIN CRISTINA CASARINI (IC)[1]; OTAVIANO MENDES MARTELLI (IC)[1]; ANA ELISA CALEIROS SEIXAS AZZOLINI (PQ)[2]; YARA MARIA LUCISANO-VALIM (PQ)[2]; CLENI MARA MARZOCCHI-MACHADO (PQ)[1,2].

[1]UNIARA; [2]FCFRP-USP

INTRODUCTION: It has been described that the use of estrogen, as oral contraceptive (OC) or hormone replacement therapy, is associated with the increase of the serum levels of factor XII, decrease of the S protein and a clinical manifestation similar that due to the deficiency of C1 inhibitor. Since the complement and coagulation are related physiological systems, there is an important interest in the investigation of the estrogen effects on these systems in the inflammatory processes. OBJECTIVE: To analyze the effect of the OC on the hemolytic activity of the complement. METHODS: The hemolytic activity of the complement was determined using a static assay. Sera from OC users (n=10) and a nonuser (n=10) were analyzed. Healthy volunteers, 18-30 year-old women, were included in both groups. RESULT: The hemolytic activity of the complement was higher in the group of OC users than in nonuser group (p=0.043, Mann-Whitney test). CONCLUSION: This result can be related to the decrease of the C1 inhibitor and/or S protein associated to the estrogen use and shows the importance in monitoring the effects of this hormone in women with inflammatory diseases.

Supervisor: C.M. Marzocchi-Machado

MI046-CYTOKINE, CHEMOKINE AND CELLULAR INFILTRATE IN GUT ALLERGIC INFLAMMATION

PAULINE ROSSETTI PROVINCIATTO (IC)1; CRISTINA RIBEIRO BARROS CARDOSO (PG)2; DANIELLE GODOI (PG)2; BEATRIZ ROSSETTI FERREIRA (PQ)2; CRISTIANE MILANEZI (PQ)2; GERLINDE TEIXEIRA (PQ)3; MARCOS ANTÔNIO ROSSI (PQ)2; FERNANDO QUEIROZ CUNHA (PQ)2; JOÃO SANTANA DA SILVA (PQ)2

[(1)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto,[(2)]Faculdade de Medicina de Ribeirão Preto/USP,[(4)]Universidade Federal Fluminense

Introduction:gut immune system responds to pathogens remaining unresponsive to food antigens. Disturbing such homeostasis leads to inflammation and allergy with leukocyte infiltrate, and cytokines/chemokines production that drives disease's outcome. Objective:study a model of intestinal allergic inflammation induced by peanut seed proteins (PSP). Methods:mice were immunized with PSP and challenged with peanut seeds for 30 days. Sera and gut sections were collected for subsequent analysis. Results:allergic mice showed increased $CD8^+$, NK, B cells, TNF-α, Mig, edema and alterations in gut architecture while diminished TGF-β and IFN-g mRNA, besides high titres of IgG1 and IgE and low IgG2a compared to controls.
Conclusions:experimental animals developed gut inflammation with specific cellular infiltrate, altered intestinal morphology, Th2 type antibodies and cytokine/chemokine expression resembling food-induced intestinal allergic inflammation.

Financial support: FAPESP/CNPq
Supervisor: Prof.Dr.João Santana da Silva

MI047-NEW POTENTIAL ROLE TO MK886®: IMMUNOSUPPRESSOR AND ANTI TUMOR ACTIVITY.

HARIANE CÔCO (IC)[(1)]; PATRICIA M. HAYASHIDA (IC)[(1)], FABIANI G. FRANTZ (PG)[(1,2)]; LÚCIA H. FACCIOLI (PQ)[(1)], AURO NOMIZO (PQ)[(1)] [(1)]DACTB- FCFRP-USP; [(2)]FMRP-USP.

Introduction: MK886® compound is a potent inhibitor of leukotriene biosynthesis which inhibits the 5-LO activating protein (FLAP). Also it is a non-selective inhibitor of PPARs and mPEG syntase. Objective: The aim of this work is to investigate the role of MK886 on T cell functional properties (proliferation by stimulation with antiCD3 mAb and full allogeneic cell stimulation-MLR) and also the cytotoxic activity against JURKAT and B16F10 tumor cell lines. Methodology: Mouse spleen cells or tumor cell lines were cultivated alone or with different concentrations of MK886 (10^{-4}-10^{-6}M) for 24-48h. Proliferation or cytotoxicity was evaluated by MTT colorimetric assay. Results: Results showed that MK886 strongly suppress T cell proliferation and MLR response. Besides, this compound presented high cytotoxic activity against all tumor cells tested. Conclusion: We conclude that MK886 have a new potential application, acting as a potent immunosuppressor and anti tumor drug.

Financial support: CNPq, FAPESP, FCFRP-USP
Supervisor: Auro Nomizo

MI048-RESISTANCE PROFILE OF *ESCHERICHIA COLI* ISOLATED FROM PATIENTS WITH URINARY TRACT INFECTION IN BRAZIL

WILSON A. CARVALHO JR[1]; WILSON A. CARVALHO[1,2]; VÂNIA RICCIO TEIXEIRA[2]; MÔNICA AMANO[2]

[1]UNIME Pharmacy School, [2]São Rafael Hospital, Salvador-Bahia-Brasil

Introduction: *Escherichia coli* is the most common pathogens isolated from urinary tract infection (UTI), whether from hospitalized patients or outpatients. An estimated 11 percent of all U.S. women aged 18 and older report at least one physician-diagnosed urinary tract infection per year. Objetive: At this study we aimed to determine the antimicrobial susceptibility profile of *Escherichia coli* isolated from urinary tract infection. Methods: In the proposal of isolating *Escherichia coli*, urine samples from adults hospitalized (n=160) and outpatients (n=145) presenting urinary tract infectious were collected in 2004. The susceptibility testing was performed using the VITEK (Biomerrieux) system. The results were interpreted using guidelines established through the NCCLS. Results: From outpatients, 65% were female, and 70% of hospitalized patients were female and 30% male. The main pathogens isolated from urine samples of hospitalized patients were the following: *Escherichia coli* (65%), *Klebsiella* (14%), *Proteus* (11,6%), *Pseudomonas* (4,6%) and *Enterobacter* (4,6%). In the outpatients group the following susceptibility patterns were observed: 15,4% of resistance to ciprofloxacin, 15,4% to gatifloxacin and 23,0% to TMP-SMX. For the hospitalized patients were observed a resistance of 25,0 % to ciprofloxacin, 21,0% to gatifloxacin, and 50,0% to TMP-SMX. Conclusion: These data suggest that fluroquinolones and TMP-SM resistance among strains of *Escherichia coli* causing urinary tract infectious is increasing, especially in strains from hospitalized patients.

MI049-ALTERATIONS IN THE URINE EXAM AND PRESENCE OF ANTI NATIVE DNA ANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

SARAH MEDEIROS (IC); MILENA ARAÚJO (IC); DYNÁ ATANÁSIO (IC); DIOGO LOPES (PG); GERALDO CAVALCANTI JR(PQ); VALÉRIA SALES (PQ)

DACT/UFRN

Systemic Lupus Erythematosus (SLE) is an inflammatory chronic autoimmune illness characterized by the direct action of auto-antibodies and tissue deposition of immune complexes. Anti native DNA antibodies occur almost exclusively in the SLE, they are pathognomonic of active renal disease. This work had as objective to correlate the presence of anti native DNA antibodies with the findings of the urine exam in patients bearing SLE. 13 patients with SLE had been studied, of which, 7 presented nephritis. The detection of the anti native DNA antibodies was accomplished by the technique of indirect imunefluorescence using as substrate the protozoan *Crithidia luciliae*. The urine samples had been evaluated for physical, chemical and sediment features. Amongst the studied samples, positivity for anti native DNA was observed in 10 patients (77%), of which 100% had presented alteration in the urine exam for presence of protein, red blood cells and cylinders, from these, 4 (40%) had presented 3 of these alterations; 4 (40%) 2 types of alterations and 2 (20%) only one type. It can be concluded that anti native DNA antibodies have correlation between the presence of antibody and the renal injury in patients with SLE.

Supervisor: Dra.Valéria Sales

MI050 - OPPORTUNISTIC PARASITES IN HIV-INFECTED PATIENTS IN RIBEIRÃO PRETO REGION, SP, BRAZIL

FERNANDO ROGÉRIO PAVAN(PG)[1]; MADALENA H. T. OKINO(PQ)[1]

[1]Ribeirão Preto Adolfo Lutz Institute

INTRODUCTION: The opportunistic parasites *Cryptosporidium* spp and *Isospora belli* are diarrhea etiologic agents in AIDS patients. OBJECTIVE: This study aims at evaluating the frequency of these parasites in HIV-infected patients, before and after the introduction of highly active anti-retroviral therapy (HAART), in 1996. METHODOLOGY: Between July 1990 and April 2005, faeces from 2878 patients (63% men and 47% women) were submitted to formol-ether and modified Ziehl-Neelsen stain techniques. RESULTS: We observed a prevalence of 5,4% of *Cryptosporidium* spp, 4,1% of *I. belli* and 0,4% of mixed infections. Comparing 1990-1996 and 1997-2005 periods, pre and post HAART, there was a significant reduction of the investigated patients, from 1716 to 1162. On parasite frequency it has been observed a decrease of *Cryptosporidium* spp, from 6,4% to 4,0%, and in mixed infections, from 0,6% to 0,2%. However, there was an increase in *I. belli* prevalence, from 3,7% to 4,6%. We observed on both sex, infection reduction by *Cryptosporidium* spp and mixed one. There was just on women an increase in infection by *I. belli*, from 1,8% to 5,1%. CONCLUSIONS: These results demonstrate the public health laboratory importance in monitoring these parasites in HIV-infected patients.

Financial Support: IAL
Supervisor: Divani M. Capuano

MI051-THE PROTECTIVE IMMUNITY ELICITED BY ANTIGENS FROM *P. BRASILIENSIS* FORMULATED IN MPL® ADJUVANT

JAQUELINE O. VANCIM(IC); KAREN A. CAVASSANI (PG); MOREIRA AP; CAMPANELLI AP; MILANEZI C AND JOÃO SANTANA DA SILVA (PQ)

Departament of Biochemistry and Immunology of School of Medicine of Ribeirão Preto-USP

Introduction and Objective:Paracoccioidomycosis, a chronic granulomatous disease caused by *Paracoccidioides brasiliensis*, is endemic in Latin America.The resistance to infection is mediated by a Th1 type response.Here, we investigated the potential of the use of MPL-SE as adjuvant to protect mice from the infection. Methods and Results:C57BL/6 mice were immunized by subcutaneous route with surface antigens of *P. brasiliensis* (sPbAg) formulated with MPL-SE.Two weeks after the boost, the animals were infected (iv) with viable yeasts of *P. brasiliensis*.The results showed high amount of fungus in the lungs and liver of animals previously inoculated with MPL or antigen alone (control groups).The histological evaluation of the organs of mice immunized with MPL-SE plus sPbAg (days 15, 30 and 60pi) reveled an absence of fungus-induced granulomas in sections analyzed, in contrast to control groups. Conclusion:The immunization was able to elicit protective immunity against *P. brasiliensis* infection and, therefore, is its use as adjuvant take us closer to the realization of affordable and safe vaccine against paracoccidioidomycosis.

Financial support:CNPq and FAPESP.
Advisor:Prof. Dr João Santana da Silva

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Produtos Naturais / *Natural Products* (PN)

PN001- ANTIDIABETIC POTENTIAL OF *LEANDRA LACUNOSA* EXTRACT IN RATS.

GLENDA MARQUETI ARANTES(PG); DANIELE DA SILVA FERREIRA(PQ); ALESSANDRA IARA OLIVIERA (PG); ANTONIO EDUARDO MILLER CROTTI(PQ); WILSON ROBERTO CUNHA(PQ).

Universidade de Franca Av. Dr. Armando Salles de Oliveira, 201 Franca SP CEP 14404-600

Introduction. Diabetes has long been treated orally with several medicinal plants or their extracts, based on folkloric claims. *Leandra lacunosa* (Melastomataceae) has been used in folkloric Brazilian medicine for the treatment of this disease. Objectives. The aim of the present work was to evaluate the antibiabetic activity of a hydroalcoholic extract of aerial parts of *L. lacunosa*. Methodology. Extracts of the plant were obtained by maceration with ethanol/water (8:2 v/v). Normal male Wistar rats (n=5) were treated with this extract at a 500mg/Kg (p.o.) dose and given oral glucose (10g/Kg). Blood glucose levels were measured at 0, 1, 2 and 3 h after glucose treatment. The control group received glucose only. Results. The group treated with the extract exhibited a delay in peak blood glucose levels when compared with the untreated rats. Statistical significance was analyzed using ANOVA. The extract was also tested for its hypoglycemic effect in normal rats and led to a reduction in the normal glucose concentration. Conclusions. The present study confirms the folkloric use of this species for the treatment of diabetes. Further pharmacological and biochemical investigations are underway to elucidate the mechanism of these hypoglycemic effects.

Financial support: FAPESP
Supervisor: Wilson Roberto Cunha

PN002-CHEMICAL STUDY AND BIOLOGICAL ACTIVITIES EVALUATION OF THE FUNGUS *PISOLITHUS TINCTORIUS*

MARIA LUCÍLIA MOTINHA ZAMUNER (PQ)[1]; DIÓGENES APARÍCIO GARCIA CORTEZ (PQ)[1]; EDSON RODRIGUES FILHO (PQ)[2]

[1]Universidade Estadual de Maringá; [2]Universidade Federal de São Carlos

Introduction: The fungus *Pisolithus tinctorius* is a member of the *Basidiomycetes* class of great interest in agriculture for its ability to produce ectomycorrhizas with several species of *Eucalyptus* and *Pinus*, resulting in countless benefits for the development of both. Objective and methodology: In this work, besides the fungus collected in the field ("Pista de Saúde" at UFSCar), two strains (185 and 1604) grown *in vitro* were used to isolate and identify secondary metabolites and establish its chemical profile through experiments of GC/MS. Antibacterial, antifungal and molluscicidal bioassays were carried out using extracts and fractions. Results and conclusions: The main secondary metabolites identified were the triterpenes lanosterol derivatives and the naphthalenoid pigments, but it was also detected fatty acids, hydrocarbons, diterpenes and steroids. The biological trials resulted in weak activity against bacteria, fungi and on the mollusk *Biomphalaria glabrata*. It was observed a decrease of the antibacterial activity with the fractionations procedures. Thus, the activity could be related to a synergistic interaction among the components.

Financial Support: CAPES/UFSCar/UEM
Advisor´s Name: Edson Rodrigues Filho

PN003-ANTI-INFLAMMATORY ACTIVITY OF *LAFOENSIA PACARI* EXTRACT IN MURINE ASTHMA

ALEXANDRE DE PAULA ROGERIO(PG)[(1)]; FERNANDA DE FREITAS ANIBAL(PG)[(1)]; CAROLINE FONTANARI(IC)[(1)]; LÚCIA HELENA FACCIOLI(PQ)[(1)]

[(1)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto – USP/SP

Introduction: In a previous study, we demonstrated a reduction in the eosinophils number in mice infected with *T. canis* and treated with *L. pacari* extract. Objective*:* To evaluate the anti-inflammatory activity of ethanolic extract of *L. pacari* in a chronic eosinophilic inflammation model (murine asthma). Methods: On weekly intervals, animals were immunized and boosted by an i.p. injection of 100 µg ovalbumin (Ova)/1 mg of aluminium hydroxide gel in 0.2 mL PBS followed by one intratracheal (i.t.) injection Ova challenge with 600 µg Ova/100 µL PBS on the 14th day. Sensitised mice were treated with water or *L. pacari* (200 mg/kg, p.o.) from day 12 to 16. On the 2th day after the i.t. challenge, the mice were killed. The neutrophils (NE), eosinophils (EO) and mononuclear cells (MO) number in the bronchoalveolar fluid (BALF) were determined. Results: We observed an increase of NE, EO and MO in BALF of mice treated with water after i.t. Ova challenge and a reduction in the number of these cells in mice treated with *L. pacari*. Conclusion: Our results demonstrate a potential therapeutic effect of *L. pacari* to treat allergic disease like as asthma.

Financial Support: CAPES and CNPq
Advisor´s Name: Dra. Lúcia H. Faccioli

PN004-MICROSCOPIC CHARACTERIZATION OF THE LEAF OF *CHAPTALIA NUTANS* (L.) POL., ASTERACEAE

CLÁUDIA BONISSONI EMPINOTTI (PG)[1]; MÁRCIA DO ROCIO DUARTE (PQ)[1]

[1]Programa de Pós-graduação em Ciências Farmacêuticas, Universidade Federal do Paraná

Introduction: *Chaptalia nutans* (L.) Pol., Asteraceae is a perennial herb employed in Brazilian folk medicine for treating bruises and wounds. Objective: This work has aimed to investigate the microscopic characterization of the leaf, in order to contribute for the species identification. Material and Methods: The botanical material was collected in Palotina-PR, in February 2005, and the voucher was identified. Mature leaves were fixed in FAA50, either freehand sectioned or embedded in glycol methacrylate and sectioned by microtome, and stained with astra blue and basic fuchsine. Scanning analysis was also carried out. Results: The blade has a uniseriate epidermis with sinuous anticlinal cell walls in surface view and coated with a thin and striate cuticle. It shows anomocytic stomata on both faces, located on the same level or slightly raised above the surrounding cells. Numerous non-glandular and glandular trichomes occur, predominantly on the lower side. The mesophyll is dorsiventral and does not comprise typical distinctive chlorenchymas. The midrib is biconvex and traversed by four to six collateral bundles in open arc, which may have collenchymatous cap and be encircled by a starch sheath.

PN005-EVALUATION OF ANTIOXIDANT ACTIVITY OF *VOCHYSIA DISCOLOR* (WARM.)

FERNANDO PETACCI(PQ)[1], RAFAELA RODRIGUES DA SILVA LEITE(IC)[1], ELIENAI DUARTE COLARES(IC)[1], EDIANY SILVA(IC)[1], GRÍNIA FERREIRA DE SOUZA(IC)[1], RINA EMANUELA LELIS DE OLIVEIRA(IC)[1], FLAVIANA COSTA(IC)[1], VINICIUS ARAÚJO ROCHA(IC)[1], NAJEH MAISSAR KHALIL(PQ)[1]

[1] DFB–FAFEID, Diamantina/MG

Introduction: In the investigation course of plants antioxidant properties from "campos rupestres" of Minas Gerais state, we performed assays using ABTS cation and hypochlorous acid (HOCl) scavenger of flower´s ethanolic extract of *Vochysia discolor*, known in the local folk medicine as "vinheira". Objective: Evaluate the antioxidant properties of the extract cited above. Methods: Flowers were collected in october, 2003, in Diamantina – MG, dried and extracted with ethanol (2 weeks). The dried extract was ressuspended and the antioxidant activity was determined by assays based on the decolorization of $ABTS^{\bullet+}$ and for HOCl (35 µM) scavenger. The assay without extract corresponds to the control. Results and Conclusion: ABTS assay: concentration of 5, 10 and 20 µg/ mL inhibiting 24,10 ± 3,17; 40,03 ± 2,37 and 65,67 ± 2,50. HOCl scavenger assay: concentration 2.5, 10 and 20 µg/ mL inhibiting 54,30 ± 1,46; 82,30 ± 0,70 and 92,70 ± 0,53 (both results expressed as % compared with control, respectively). We concluded that the extract tested is efficient as antioxidant.

Financial support: Fapemig
Supervisor: NAJEH MAISSAR KHALIL

PN006-CHEMICAL COMPOSITION AND ANTIBACTERIAL ACTIVITY OF THE ESSENTIAL OIL FROM *LIPPIA ALBA*

LUCIANA SAKUNO (IC)[1]; MARISA A. NOGUEIRA (PQ)[1]; GASPAR DIAZ (PQ)[2]; FABIANA A. FALCONI (PQ)[3]; MARIA HELENA SARRAGIOTTO[4]

Laboratórios de [1] Farmacognosia, [2] Química Orgânica, [3] Microbiologia-Unioeste, [4] Dpto. de Química-UEM

Lippia alba (Verbenaceae) is popularly known in Brazil as "erva cidreira" (lemon herb) and most used in the treatment of influenza, colds, digestive disorders and infectious deseases. The aim of the present work was to analyze the differences on oil chemical composition and biological activity obtained from two different regions of Brazil: Ji-Paraná (RO) and Cascavel (PR). The essential oil from leaves of *L. alba* was obtained by hydrodistillation using a Clevenger type apparatus. The yield of the oil has been about 0.5% (v/w). The oils were analyzed by GC-MS. The oil antibacterial activity was performed by bioautography methods against the following microorganisms: *Staphylococcus intermedius, Escherichia coli, Bacillus subtilis, Proteus mirabilis, Pseudomonas aeruginosa* and *Acinetobacter baumanii*. The results showed that oils from both regions were active against *Staphylococcus intermedius*, *Bacillus subtilis* and *Escherichia coli* bacteria and are in accordance to the folk use of this plant for infectious diseases. They showed an interesting antibacterial activity, against the Gram + and – bacterias. The analysis of the essential oils suggests that *L. alba* from south and north regions are carvone and citral chemotypes, respectively

Financial Support: Unioeste
Supervisor: Marisa Alves Nogueira

PN007-EVALUATION OF THE ANTIMICROBIAL ACTIVITY OF PROPOLIS FROM THREE DIFFERENT REGIONS OF BRAZIL

CRISTIANE MINAKO KOGA (IC)[1]; MARISA A. NOGUEIRA (PQ)[1]; GASPAR DIAZ (PQ)[2]; FABIANA A. FALCONI (PQ)[3]

Laboratórios de [1] Farmacognosia, [2] Química Orgânica, [3] Microbiologia-Unioeste.

Propolis, honey-glue, is a resinous beehive product that has been extensively used for many years in folk medicine principally as antimicrobial. The effects have been associated with the chemical profile of propolis that may very widely depend upon both the regions where it is produced and on the season it is collected. The aim of the present work was to analyze the differences on propolis antimicrobial activity obtained from three different regions of Brazil (Minas Gerais, Parana and São Paulo States). The antimicrobial activity of the ethanolic extracts of propolis was evaluated against *Streptococcus muttans* and *Lactobacillus casei* cariogenic microorganisms using the bioautography methods. The results showed that the propolis from Minas Gerais State was more actives than that from the other states evaluated. On the other hand, these results also show the different existing referent to amount of production and diversity of secondary metabolites from propolis associated with regions that was produced and the different season that was collected.

Financial Support: Unioeste
Advisor´s Name: Marisa Alves Nogueira

The authors did not follow the Scientific Committee's suggestion for an English language review

PN008-ROOT-DERIVED CALUS CULTURE OF *TABERNAEMONTANA FUSCHIAEFOLIA* (APOCYNACEAE)

ELISÂNGELA FUMAGALI (M)[1]; ARILDO JOSÉ BRAZ DE OLIVEIRA(PQ)[1]; MÁRIA DE FÁTIMA PIRES MACHADO (PQ) [2]; GENTIL VIDOTI(PQ)[3]

[1] Departamento de Farmácia e Farmacologia; [2] Depto. de Biologia Celular e Genética; [3] Depto. de Química – Universidade Estadual de Maringá – Maringá-PR

Tabernaemontana fuchsiaefolia is a lacticiferous tree that pharmacological studies showed antiplasmodial activity. The antiplasmodial alkaloids are in the roots that implicate in destructive harvesting. Plant biotechnology is an alternative for this problem. The work's objectives were to induce root-derived callus and to detect the alkaloids. The induction was tested from root of plantets on B5 medium with sucrose (3%), different concentrations of 2,4-dichloro-phenoxyacetic acid (2,4-D, 0; 2; 4; 8 mg/L) and kinetin (0; 1; 2 mg/L), coconut milk (10%), active charcoal (AC, 0,1%), casein hydrolyzed (CH, 0,1%) and agar (0,7%) that were cultured in the dark at 28 ºC by 4 weeks and subcultured each 4. Callus were induced on the B5 with 2,4-D (4 mg/L). Browing and necrosis occurred during subcultures that were reduced by successive passages to WPM medium with 2,4-D (4 mg/L), CH (0,1%) and AC (0,1%). Callus was extracted with ethanol and analyzed by TLC and GC/MS. This analysis evidenced the alkaloids. Callus of *T. fuchsiaefolia* will *be* used on further studies.

Financial Support: Fundação Araucária; CAPES
Advisor´s name: Arildo J. B. Oliveira

The authors did not follow the Scientific Committee's suggestion for an English language review

PN009-SCANNING ELECTRON ANALYSIS OF TWO SPECIES OF *BACCHARIS*, ASTERACEAE

JANE MANFRON BUDEL (PG); MÁRCIA DO ROCIO DUARTE (PQ)

Laboratório de Farmacognosia, Universidade Federal do Paraná

Introduction: The genus *Baccharis* has been studied, mostly due to its content in phytochemicals with potential pharmacological activities, in order to confirm the alleged stomachic, diuretic and anti-inflammatory actions in traditional medicine. Differing from the many investigated members of the taxon, *Baccharis coridifolia* DC. and *B. megapotamica* Spreng. present macrocyclic trichothecenes, which are considered toxic terpenoids responsible for cattle poisining. Objective: Aiming to contribute for the differentiation of these species from medicinal ones, this work has analysed the leaf and stem epidermal system of *B. coridifolia* and *B. megapotamica*. Material and Methods: Mature leaves and stem fragments were fixed, dehydrated in a graded ethanolic series and by the critical point procedure, coated with gold and analysed by a scanning electron microscope. Results: In both species, the blade has an epidermis coated with a striate cuticle, stomata even with the surrounding cells and numerous glandular trichomes. *B. coridifolia* also exhibits non-glandular ones. The stem epidermis has shown similar features. Conclusion: These anatomical characters are relevant contributing elements for their morpho-diagnosis.

PN010-ANTISNAKE ACTIVITY OF METHANOLIC FRACTION OF *CASEARIA SYLVESTRIS* SW

MARIANA C. FRANCISCHINELLI(IC)[(1)]; MARLI GERENUTTI(PQ)[(1)]; MAGALI G. SILVA(PQ) [(1)]; NEWTON ANDRÉO-FILHO(PQ) [(1)]; GILDO B. LEITE(PQ) [(2)]; ADÉLIA C.O. CINTRA(PQ) [(3)]; LEA RODRIGUES-SIMIONI(PQ) [(2)]; YOKO OSHIMA-FRANCO(PQ) [(1,2)]

[(1)]University of Sorocaba; [(2)]University of Campinas; [(3)]University of São Paulo

Introduction: Bothropstoxin-I, BthTX-I, a myotoxin from *Bothrops jararacussu* snake venom induces neuromuscular blockade. The serum therapy is efficient against the lethality but only partially against the local effect. Plants can be an interesting therapeutic alternative. *C. sylvestris* Sw. is popularly known by its antisnake capacity. Objective: To inquiry the pharmacological effect of methanolic fraction (MF) of *C. sylvestris* against the action of BthTX-I. Methodology: Thin layer chromatography was used to characterize the phenolic groups in MF. Polyethylene glycol 400 was used as solvent (3µL/mL) of MF (0,2µg/mL) to carry out biological assays with BthTX-I (45µg/mL) on mouse neuromuscular preparations using conventional myographic technique. Results: BthTX-I caused 50% of blockade in 16.8 ± 3.5 min (n=8), but when preincubated with MF kept the basal response of the preparation (n=6). Conclusion: *C. sylvestris* is able to avoid the neurotoxicity of BthTX-I and this activity is probably due to components with polar characteristics.

Financial Support: PROBIC/UNISO
Supervisor: PhD Yoko Oshima-Franco

PN011-ANTIMICROBIAL ACTIVITY OF ALCOHOLIC EXTRACT FROM *SYZYGIUM CUMINI* L. SKEELS (JAMBOLÃO) LEAVES

GUILHERME F. DE OLIVEIRA(PG)[1]; MARIA G. M. DE SOUZA(PG)[1]; ROSANGELA DA SILVA(PQ)[1]; CARLOS H. G. MARTINS (PG)[1]; MARCOS O. R. DOS REIS (PG)[1], ADRIANA H. C. VINHOLIS(PQ)[1]; TATIANE C. De CARVALHO (PQ)[1]; WILSON R. CUNHA(PQ)[1]; NIEGE A. J. C. FURTADO (PQ)[1]; JAIRO K. BASTOS(PQ)[2] AND MARCIO L. A. E SILVA(PQ)[1].

[1] Universidade de Franca – Av. Dr. Armando Salles de Oliveira, 201 – Franca –SP CEP 14404-600; [2] FCFRP-USP – Av. do Café s/n – Ribeirão Preto – SP CEP: 14030-000

Introduction: *Syzygium cumini*, a native species from India (Myrtaceae), has been used in popular medicine devoid of hypoglycemic activity. Nevertheless, the antimicrobial activity has been less investigated. Objective: The aim of this work was to evaluate the antimicrobial activity of alcoholic extract from *Syzygium cumini* leaves against bacteria and yeasts. Materials and Methods: Leaves (1Kg) were macerated with ethanol (3L) and left at rest (five weeks, room temperature). The material was filtered and the obtained crude extract was submitted to antimicrobial activity evaluation using the agar diffusion method. Results and Discussion: The alcoholic extract showed activity against *Staphylococcus aureus (*ATCC 25923), *Micrococcus luteus* (ATCC 9341), *Pseudomonas aeruginosa (*ATCC 27853), *Shigella flexneri* (ATCC 12022), *Candida albicans* (ATCC 23366), and *Candida krusei (*ATCC 6258). The activity against multi-resistent *Staphylococcus aureus* and *Pseudomonas aeruginosa* strains was higher than controls ($p<0,05$).

Financial Support: FAPESP, CAPES and CNPq
Supervisor: Prof. Dr. Márcio L. A. e Silva

PN012-SCREENING FOR ANTIMICROBIAL ACTIVITY OF PHYTOPATHOGENIC FUNGI

WILLIAN J. ANDRIOLI (IC)[1]; MARISA A. NOGUEIRA (PQ)[1]; GASPAR DIAZ (PQ)[2]; FABIANA A. FALCONI (PQ)[3]; JOSÉ R. STANGARLIN (PQ)[4]

Laboratórios de [1] Farmacognosia, [2] Química Orgânica, [3] Microbiologia, [4] Fitopatologia-Unioeste.

As part of an ongoing research for biological active secondary metabolites from phytopathogenic fungi, we detected antibacterial activity in fermentation ethyl acetate extracts of *Colletotrichum musae*, *Cladosporium fulvum* and *Septoria lycopersici* fungi. The production was carried out by inoculating 10^8 spore/mL in BDA medium at 28 ^oC in a shaking incubator at 150 rpm for 168 h. The cultures were filtered and submitted to the process of liquid-liquid partition, furnishing the dichloromethane and ethyl acetate extracts. The evaluation of antimicrocrobial activity of the extracts was performed by bioautography methods against the following microorganisms: *S. aureus, S. epidermidis, E. coli, B. cereus, K. pneumoniae, A. baumonii, E. aerogenes, P. aeruginosa, Salmonela sp, C. diversus, P. mirabilis* and *Plesiomonas*. The results showed that only the ethyl acetate extract was actives on some multi–drug resistant bacteria. In summary, ethyl acetate extracts of *C. musae, C. fulvum* and *S. lycopersici* fungi demonstrated moderate activity inhibiting action to growth of bacteria tested showing that fungi produced secondary metabolites that may be used like antibiotic agents or like prototypes of them.

Financial Support: Unioeste
Supervisor: Marisa Alves Nogueira

PN013-IN VITRO ANTIMICROBIAL ACTIVITY OF PLANTS FROM BRAZILIAN "CERRADO" AGAINST ORAL PATHOGENS.

LUIS CARLOS SCALON CUNHA(PG); CARLOS HENRIQUE GOMES MARTINS(PQ); MÁRCIO LUIS ANDRADE E SILVA(PQ); ADRIANA HELENA CHICHARO VINHOLIS(PQ); WILSON ROBERTO CUNHA(PQ)

Universidade de Franca – Av. Dr. Armando Salles de Oliveira, 201 – Franca –SP CEP 14404-600

Introduction. Several microorganisms are involved with pathogenesis of dental caries. Therefore, one of the strategies to prevent the development of dental caries is to control the growth of these oral pathogens.
Objectives. The aim of the present work was to evaluate the in vitro antimicrobial activity of three hydroalcoholic extracts of plants from Brazilian "cerrado" against oral pathogens.
Methodology. The extracts of the plants (*Birsonima intermedia*, *Aegiphila sellowiana* and *Solanum lycocarpum*) were obtained by maceration with ethanol/water (8:2 v/v). The antimicrobial activities were assessed by determination of Minimum Inhibitory Concentration (MIC).
Results. In the MIC assay, all extracts showed antimicrobial activity against the tested microorganisms. The microorganisms Streptococcus mutans and Enterococcus faecalis were the most resistant for all extracts.
Conclusions. The results of the present study showed inhibitory activities against several oral microorganisms, indicating that these plants are a valuable source for the development of new antimicrobial products against oral pathogens.

Financial support: FAPESP
Supervisor: Wilson Roberto Cunha

PN014-BIOREDUCTION OF DIBENZOYLMETHANE BY *DIPLODIA MAYDIS* AND *SCLEROTIUM ROLFSII* FUNGI

ANDRÉ R. DE LIMA DAMÁSIO (IC)[2]; GASPAR DIAZ (PQ)[1]; MARISA A. NOGUEIRA (PQ)[2]; FABIANA A. FALCONI (PQ)[3]; JOSÉ R. STANGARLIN (PQ)[4]

Laboratórios de [1] Química Orgânica, [2] Farmacognosia, [3] Microbiologia, [4] Fitopatologia-Unioeste.

Biocatalysis reactions carried out by fungi and bacteria are of great importance on the functionalization of certain positions in molecules, and inaccessible by using conventional chemical methods. As a resulted, biocatalysis emerged as a viable alternative to costly or difficult chemistry in the manufacturing of chiral drugs. In this work we reported the first results from an ongoing current microbial screening program using fungi that are able to making biotransformations. The bioreduction of dibenzoylmethane was carried out using the *Diplodia maydis* and *Sclerotium rolfsii* fungi employing whole cells during 240 hours in BDA medium. These results show that both fungi are bioreductors. The monoreducted product was obtained as major product, but was also produced the diol in minor proportion with a negligible amount of the remaining substrate for both cases. However, the stereogenic center of the monol was not yet establishments, this work it is ongoing in our laboratory and will be reported in due course.

Financial Support: Unioeste
Supervisor: Gaspar Diaz Muñoz

The authors did not follow the Scientific Committee's suggestion for an English language review

PN015-MORPHO-ANATOMICAL STUDY OF THE LEAF OF *SYNADENIUM GRANTII* HOOKER F. (EUPHORBIACEAE)

INGRID JURGENSEN (IC)[1]; MÁRCIA DO ROCIO DUARTE (PQ)[1]

[1]Laboratório de Farmacognosia, Departamento de Farmácia, Universidade Federal do Paraná

Synadenium grantii Hooker f. (Euphorbiaceae), commonly called African or Amazonian milkbush, is a shrub used in traditional medicine as anti-inflammatory by different populations. This study has investigated the morpho-anatomical characters of the leaf, in order to contribute for this species identification. The identified botanical material was fixed, either freehand sectioned or embedded in glycol methacrylate and sectioned by microtome, and stained with toluidine blue or astra blue and basic fuchsine combination. Histochemical tests and scanning electron analysis were carried out as well. The leaves are simple, alternate, obovate-lanceolate and coriaceous. The blade epidermis is uniseriate and coated with a thin and smooth cuticle and epicuticular wax. The leaf is amphistomatic and paracytic stomata predominate. Few pluricellular non-glandular trichomes are found, especially at the leaf margin. The mesophyll is dorsiventral and various collateral vascular bundles traverse the midrib and petiole. Numerous laticifers with thick cell walls, dense cytoplasm and lipophilic content are often seen associated with the vascular bundles.

Scholarship support: PIBIC/CNPq – UFPR
Supervisor: Márcia do Rocio Duarte

PN016-LEAF ANATOMICAL CHARACTERS OF *BRUNFELSIA UNIFLORA* (POHL) D. DON, SOLANACEAE

SAMANTHA WOLF(IC)[1]; MÁRCIA DO ROCIO DUARTE(PQ)[1]

[1]Laboratório de Farmacognosia, Departamento de Farmácia, Universidade Federal do Paraná

The Solanaceae family comprises about 147 genera and 2930 species worldwide distributed. *Brunfelsia uniflora* (Pohl) D. Don is a shrub native to the South America and used as anesthetics, diuretic and purgative. Aiming to contribute for the species identification, this study has analysed its leaf anatomy. The plant material was collected from cultivated specimens in Curitiba-PR, in August 2004. Mature leaves were fixed in FAA70, stored in ethanol solution, freehand sectioned transverse and longitudinally, and stained either with toluidine blue or astra blue/basic fuchsine. Usual histochemical tests and ultrastructure analysis were also applied. The leaf is hypostomatic, presenting anomocytic and predominantly paracytic stomata. The epidermis is uniseriate and coated with striate cuticle. The epidermal cells exhibit wavy shape in surface view. Non-glandular and glandular trichomes are found on both sides. The former is pluricellular and uniseriate, coated with a granular cuticle. The glandular trichomes have a short and curve stalk and a pluricellular ovoid head. The mesophyll is dorsiventral and the midrib is traversed by a bicollateral vascular bundle in open arc.

Scholarship support: PIBIC/CNPq – UFPR
Supervisor: Márcia do Rocio Duarte

PN017-ANTICANCER POTENTIAL OF MARINE SEAWEEDS FROM THE NORTHEASTERN BRAZILIAN COAST.

ALESSANDRA DE PAULA ALVES SOUSA(PG)[1]; MÁRCIA ROCHA TORRES(PQ)[1]; CLÁUDIA PESSOA(PQ)[1]; MANOEL ODORICO DE MORAES(PQ)[1]; LETÍCIA VERAS COSTA-LOTUFO(PQ)[1].

Department of Physiology and Pharmacology[1], UFC, Brazil.

Introduction: Many seaweeds extracts presented strong cytotoxicity on several tumor cell lines. Objective: The present study evaluated the antimitotic potential of 12 macroalgae from the northeastern Brazilian coast. Methodology: From the collected species it has been obtained 48 extracts (aqueous, dichloromethane, acetone and methanol extracts for each species). The extracts were tested for cytotoxicity using the brine shrimp lethality assay, sea urchin eggs assay, hemolysis assay and MTT assay using tumor cell lines. Results:. This study revealed that 9 among 12 tested species presented some activity in the applied assays, being that of the red algae *Botryocladia occidentalis* the most potent one The acetone extract obtained from *B. occidentalis* inhibited the growth of four out of five used tumor cell lines with an IC_{50} in the range of 5.0 to 24.5 mg/ml, possessed antimitotic activity on sea urchin eggs at concentrations up 100 mg/ml, with no hemolylic activity and moderate toxicity to brine shrimp nauplii. Conclusion: The results indicate that the extracts may act as antitumor agents.

Financial Support: FUNCAP, InCb.
Supervisor: LETÍCIA VERAS COSTA-LOTUFO.

PN018-CYTOTOXIC ACTIVITY OF PIPERINE AND PIPLARTINE FROM *PIPER* SPECIES

DANIEL PEREIRA BEZERRA(PG)[1]; CLÁUDIA PESSOA(PQ)[1]; MANOEL ODORICO DE MORAES(PQ)[1]; EDILBERTO ROCHA SILVEIRA(PQ)[2]; MARY ANNE SOUSA LIMA(PQ)[2]; FRANCISCA JULIANA MARTINS ELMIRO(IC)[2]; LETÍCIA VERAS COSTA-LOTUFO(PQ)[1].

Department of Physiology and Pharmacology[1] and Organic and Inorganic Chemistry[2], UFC, Brazil.

Introduction: Extracts of *Piper* species show significant activity in cancer cells lines. Piplartine and piperine are amides from *Piper* species. Objective: We studied the cytotoxic activity of the piplartine and piperine. Methodology: The substances were tested for their cytotoxicity on the brine shrimp lethality assay, sea urchin egg development, hemolitc assay and MTT assay using tumor cells lines. Results: Piperine showed higher toxicity in brine shrimp (DL_{50}=2.82±0.30µg/ml) than piplartine (DL_{50}=32.36±3.41µg/ml). Both piplartine and piperine inhibited the sea urchin egg development during all phases examined, first and third cleavage and blastulae, but in this assay piplartine was more potent than piperine. In MTT assay, piplartine was the most active with IC_{50} values in the range of 0.46 to 1.80 µg/ml. None of the substances induced hemolysis suggesting that its cytotoxicity were not related to membrane damage. Conclusion: The present result showed that the piplartine and piperine possess in vitro antimitotic activity.

Financial Support: CNPq, FINEP, InCb.
Supervisor: LETÍCIA VERAS COSTA-LOTUFO.

PN019-ANTITUMOR ACTIVITY OF PIPLARTINE AND PIPERINE, AMIDES FROM *PIPER* SPECIES

DANIEL PEREIRA BEZERRA(PG)[(1)]; FERNANDA OLIVEIRA DE CASTRO(IC)[(1)]; ANA PAULA NEGUEIROS NUNES ALVES(PG)[(2)]; CLÁUDIA PESSOA(PQ)[(1)]; MANOEL ODORICO DE MORAES(PQ)[(1)]; EDILBERTO ROCHA SILVEIRA(PQ)[(3)]; MARY ANNE SOUSA LIMA(PQ)[(3)]; FRANCISCA JULIANA MARTINS ELMIRO(IC)[(3)]; LETÍCIA VERAS COSTA-LOTUFO(PQ)[(1)].

Department of Physiology and Pharmacology[(1)], Clinic Odontology[(2)], and Organic and Inorganic Chemistry[(3)], UFC, Brazil.

Introduction: *Piper* species are traditional medicinal plants. Objective: We investigated the antitumor activity of piplartine and piperine in mice. Methodology: Sarcoma 180 cells were injected (2×10^6cells/animal/s.c.) in the left hind limbs in six groups (10mice/group). 24 h after the animals were treated i.p. with piplartine and, piperine (100 or 50mg/kg), 5-FU (25mg/kg) and, vehicle (DMSO 10%) respectively, for 7 days. 24 h after liver, kidney, spleen and tumor were weighed and submitted histopathology analysis. Results: There were significant reductions of tumor weight in both dose in piplartine-treated animals (52.3% and 28.7% respectively) and, piperine-treated animals (56.8% and 55.1% respectively) and 5-FU-treated animals (76.7%). Microscopic findings suggest that piplartine and piperine show only reversible toxic effects. Conclusion: The results indicate that piperine and piplartine may act as antitumor agents.

Financial Support: CNPq, FINEP.
Supervisor: LETÍCIA VERAS COSTA-LOTUFO.

PN020-ANTITUMORAL, ANTIPARASITIC AND ANTIMICROBIAL ACTIVITIES OF EXTRACTS FROM ENDOPHYTIC FUNGI ASSOCIATED WITH *TITHONIA DIVERSIFOLIA* AND *VIGUIERA ARENARIA*

WARLEY DE SOUZA BORGES (PG)[1]; DENISE OLIVEIRA GUIMARÃES (PG)[1]; AURO NOMIZO (PQ)[1]; GLAUCIUS OLIVA (PQ)[2]; OTÁVIO HENRIQUE THIEMAN (PQ)[2]; MÔNICA TALLARICO PUPO (PQ)[1].

[(1)]FCFRP-USP, [(2)]IFSC-USP

Comparing the main sources of lead compounds for discovery of new drugs (organic synthesis, natural products, combinatory chemistry and virtual libraries) the most wide chemical diversity are the substances from natural sources. EtOAc extracts were obtained after the culture of 39 endophytic fungi from *Tithonia diversifolia* and *Viguiera arenaria*. The 39 EtOAc extracts were evaluated in antimicrobial assays (agar diffusion) against *Staphylococcus aureus* (ATCC 25923), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853) and *Candida albicans* (ATCC 1023). These extracts were also assayed against Jurkat cells (human T leukemia) and against protozoal targets (enzymes GAPDH from *Trypanosoma cruzi* and APRT from *Leishmania tarentolae*). The results were satisfactory, especially in the antitumoral assays. Based on these results we can conclude that endophytes from Asteraceae are a promising source of bioactive compounds. The most promising are being fractionated in order to isolate the compounds.

Financial support: Fapesp and Capes
Supervisor: Mônica Tallarico Pupo

PN021-SCREENING FOR ANTIMICROBIAL ACTIVITY OF *DIPLODIA MAYDIS* PHYTOPATHOGENIC FUNGUS

MARISA A. NOGUEIRA (PQ)[1]; WILLIAN J. ANDRIOLI (IC)[1]; GASPAR DIAZ (PQ)[2]; FABIANA A. FALCONI (PQ)[3]; JOSÉ R. STANGARLIN (PQ)[4]

Laboratórios de [1] Farmacognosia, [2] Química Orgânica, [3] Microbiologia, [4] Fitopatologia-Unioeste.

The fungi are of great biotechnological interest in fermentative processes that culminate in the production of secondary metabolites that are important for search of new antibiotics. The aim of the present work was to evaluate the production of secondary metabolites from *Diplodia maydis* fungus with potential antimicrobial activities. The production was carried out by inoculating 10^8 spore/mL in BDA medium at 28 °C in a shaking incubator at 150 rpm for 168 h. The cultures were filtered and submitted to the process of liquid-liquid partition, furnishing the dichloromethane and ethyl acetate extracts. The evaluation of antimicrocrobial activity of the extracts was performed by bioautography methods against the following microorganisms: *S. aureus, S. epidermidis, E. coli, B. cereus, K. pneumoniae, A. baumonii, E. aerogenes, P. aeruginosa, Salmonela sp, C. diversus, P. mirabilis* and *Plesiomonas*. The results showed that only the ethyl acetate extract was actives on all tested bacteria with strongest activity on the multi–drug resistant bacteria. In summary, ethyl acetate extract of *D. maydis* fungus demonstrated a broader spectrum of inhibiting action to growth of all the bacteria tested showing that fungus produced secondary metabolites that may be used like antibiotic agents or like prototypes of them.

Financial Support: Unioeste
Supervisor: Marisa Alves Nogueira

PN022-ANTITUMORAL ACTIVITY OF CHAETOGLOBOSIN B ISOLATED FROM THE ENDOPHYTIC FUNGUS *CHAETOMIUM GLOBOSUM*

LUCIANO DA SILVA MOMESSO (PG); PATRICIA AYASHIDA RIBEIRO (IC); AURO NOMIZO (PQ); MÔNICA TALLARICO PUPO (PQ)

Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP

Chaetoglobosins are a sub-group of fungal secondary metabolites belonging to the general group of cytochalasins. Cytochalasins are remarkable in their biological activities, which includes the inhibition of movement and cytoplasmatic cleavage of mammalian cells. These biological activities can be accounted by an interaction with the common target protein actin, and they are unprecedented in any other group of compounds. We have already isolated and identified three chaetoglobosins from *C. globosum*, an endophytic fungus from *Viguiera robusta*. In this work we describe the antitumoral activities of chaetoglobosin B against leukemia (Jurkat) and melanoma (B16F10) cells, assessed by MTT method. Chaetoglobosin B showed 85.3% (1.0 mg/mL), 86.5% (0.5 mg/mL), and 89.5% (0.1 mg/mL) of citotoxicity against Jurkat cells. The positive control Gemzar showed citotoxicity of 41.4% (1.0 mg/mL). Chaetoglobosin B was also assayed against the more resistant B16F10 cells, and presented 81.0% (1.0 mg/mL), 85.1 (0.5 mg/mL), and 57.1% (0.1 mg/mL) of citotoxicity, while Gemzar showed 38.8% (1.0 mg/mL). Antitumoral activities of chaetoglobosin B were stronger than the positive control in both leukemia and melanoma cells.

Financial support: FAPESP
Supervisor: Mônica Tallarico Pupo

PN023-FLAVANONE FROM *VERNONIA TWEEDIEANA* BAKER

RICARDO BASSO ZANON(PG)[1]; DANIELLE F. PEREIRA(PG)[1]; GERALDO C. COELHO(PQ)[2]; MARGARETH L. ATHAYDE(PQ)[1]

[1]Universidade Federal de Santa Maria, [2]Universidade Regional do Noroeste do Estado do Rio Grande do Sul

Introduction: The genus *Vernonia* (Asteraceae) contains more than 500 species distributed in tropical and subtropical areas. In this genus the chemical constituents found are triterpenes, steroids and lignoids, but the more frequent compounds are sesquiterpenoid lactones and flavonoids. These two classes of compounds have been used as taxonomic markers of this genus. *Vernonia tweedieana* is used in Brazilian folk medicine as a herbal remedy in the treatment of gastritis and gastroduodenal ulcers and as expectorant. So far, no phytochemical and pharmacological study has been carried out on this plant. Objective: Phytochemical study of *V. tweedieana.* Methodology: The EtOAc fraction of the leaves was subjected to column chromatography on Si gel (CH_2Cl_2: EtOAc, gradient) to afford compound flavonoidic identified through ^1H NMR, ^{13}C NMR and DEPT spectrometric data. Results and conclusions: In this chemical investigation we report the isolation of the flavonoid 3,5,3´4´-tetrahydroxyflavanone (eriodictyol - $C_{15}H_{12}O_6$). This flavanone was previously isolated from V. *hindei* and *V. Syringifolia* and might therefore contribute to the overall phytochemical value of this plant.

Financial Support: CAPES
Supervisor: Margareth Linde Athayde

PN024-ANTIMICROBIAL ASSAY OF A TRITERPENE FROM *SENECIO SELLOI* SPRENG. DC.

GLORIA NARJARA SANTOS DA SILVA (IC) [1]; CARLOS AUGUSTO MALLMANN (PQ) [2]; SYDNEY HARTZ ALVES (PQ)[3]; BERTA MARIA HEINZMANN (PQ) [4].

[1] Graduação em Farmácia; [2]Departamento de Medicina Veterinária Preventiva/ UFSM; [3]Departamento de Microbiologia/ UFSM; [4]Departamento de Farmácia Industrial/ CCS/ UFSM

Introduction: The aerial parts of *Senecio selloi* Spreng. DC. furnish two triterpenes with an unknown skeleton, T1 and T2, as previously described. Objective: This work describes the isolation of T2 in order to evaluate its antimicrobial activity. Methodology: The dried ethanolic extract was dissolved in H_2O and extracted successively with hexane, CH_2Cl_2, EtOAc and BuOH. The hexane fraction was purified by silica gel CC to yield 50 mg of T2, which was identified by NMR and MS spectra. Its antimicrobial activity was assayed by the microdilution method (M27-A2/NCCLS). The microorganisms tested were *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923, *Pseudomonas aeruginosa* ATCC 27850, *Sacharomyces cerevisae* ATCC 2601, *Candida albicans* ATCC 44373, *C. glabrata* e *Prothoteca* sp. (clinical isolates). Results and Conclusions: T2 showed no antimicrobial activity at the tested concentrations (until 5 mg/mL).

Financial support: CNPq.
Advisor: Berta Maria Heinzmann.

PN025-ISOLATION AND IDENTIFICATION OF 2-PRENYL-4-VINYLPHENOL IN BRAZILIAN PROPOLIS SAMPLE AND ITS FREE RADICAL SCAVENGING ACTIVITY

GIUSEPPINA NEGRI(PQ)[(1)]; ANTONIO SALATINO (PQ)[(1)]; CELIA TOMIE KOBASHI (IC)[(1)]

[(1)]University of São Paulo, Institute of Biosciences, Department of Botany, São Paulo, SP

Introduction: Propolis, a complex mixture of sticky substances collected by honeybees from various plants sources, is used in the construction and adaptation of bee hives. Nowadays, propolis has also gained popularity as a health food in various parts of world where it is claimed to improve human health and prevent diseases, such as inflammation, hearth disease, diabetes and even cancer. Objective: Isolation of green propolis constituents and evaluation of their antioxidant activity. Methodology: Propolis constituents were analyzed by GC/EIMS and the structure of isolated compound was determined by EIMS, IR and ^{1}H NMR. The antioxidant activity were evaluated by 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging system. Results: 2-prenyl-4-vinylphenol was isolated from chloroform extract. Although its presence in propolis was related before, there was no biological activity related to it. In our study, the 2-prenyl-4-vinylphenol antioxidant activity ranged from 0,39 to 7,43% (to concentrations ranging from 3,125 to 50 mg/mL). Conclusion: Based on EIMS, IR and ^{1}H NMR data, we isolated a substance identified as 2-prenyl-4-vinylphenol, which showed a little antioxidant activity in DPPH free radical scavenging assay.

Financial Support: FAPESP
Supervisor: Antonio Salatino

PN026-PHYTOCHEMICAL AND TOXICOLOGICAL STUDY OF *ECHINODORUS GRANDIFLORUS*

ELISANGELA C. LIMA(PG)[1]; MARIA C. SANTOS(IC)[2]; JANINE S.CARDOSO(PQ)[3]; ALVARO A. C. LEITÃO(PQ)[3]; RICARDO M. KUSTER(PQ)[1,2]

[(1)]PBV/UFRJ;[(2)]NPPN/UFRJ;[(3)]IBCCF/UFRJ

Introduction *Echinodorus grandiflorus* is a Brazilian tradicional plant, popularly used as a diuretic and anti-inflammatory drug. There are little reports on literature about chemical and toxicological data on this specie. Objective The isolation of the major compounds of an aqueous extract of the leaves of *E. grandiflorus* and toxicological evaluation of the extract by a lysogenic induction test (inductest). Methodology 2 Kg of dried leaves were used to prepare an extract under ultrasound. After filtration, the solution was submitted to partition with EtOAc. This fraction was chromatographed on a Sephadex column with MeOH:$H_2$0 (1:1). The extract was evaluated in inductest according to Moreau *et. al.* (Proc.Natl.Acad Sci 73 3700-3704, 1976). Results Two flavonoids, orientin and isovitexin, were obtained, which were characterized by H^1 NMR and co-chromatography on TLC with authentic sample. In inductest was observed a ten fold increase of infective center induction over the background.Conclusions The compounds isolated were identified for the first time in the genus and the inductest showed to be the extract genotoxic. The preliminary toxicological result indicates that caution is necessary in medicinal plants usage.

Financial Support:FUJB,CNPq
Advisor:Ricardo M. Kuster

PN027-PLANT BIOTECHNOLOGY IN THE STUDY OF *BAUHINIA FORFICATA*

HALLINY S. RUELA (PG)[1]; ALBERTO S. JAPP(IC)[2]; NAOMI K. SIMAS(PQ)[3]; CELSO L. S. LAGE (PQ)[1], ALICE SATO (PQ)[1], FABIO S. MENEZES (PQ)[1]; RICARDO M. KUSTER(PQ)[1,2].

[(1)]PBV/UFRJ; [(2)]NPPN/UFRJ; [(3)]FIOCRUZ

Introduction Leaves of *Bauhinia forficata* are used in Brazil as a hypoglycaemic plant. Previous studies had determined the flavonoid kaempferitrin as the compound responsible for the pharmacological effect. This compound was isolated by us from a specimen acquired in pharmaceutical industry. However, it could not be found in extracts produced with a *B. forficata* maintained in garden at UFRJ. Objective Because of this result, we have started a seasonal study to determine a possible effect of season in the production of kaempferitrin. Methodology The leaves were collected in different seasons.1 g of the dried plant was extracted with 20 mL of water in ultrasound during 15 min. and analysed by HPLC/UV. Results However, no peak of the flavonoid was observed in the chromatogram. In fact, others flavonoids were produced, as we could see from the typical UV spectrum and different retention time of them when compared to kaempferitrin. Conclusions We are studying by *in vitro* culture, factors like temperature and luminosity and relate them with the biosynthesis of flavonoids. This study intends to give data for a future production of a standardized phytopharmaceutical product.

Financial Support: FUJB, CNPq, FAPERJ
Advisor: Ricardo M. Kuster

PN028-ALLELOPATHIC EFFECT OF DICHLOROMETHANE EXTRACT OF *TERMINALIA CATAPPA*'S FRUITS ON ROOT GROWTH OF *LACTUCA SATIVA*.

TATIANA G. BARATELLI[1] (PG); ANNE CAROLINE C. GOMES[1](IC); NAOMI K. SIMAS[2] (PQ); RICARDO M. KUSTER[1] (PQ) e ALFREDO M. O. FILHO[1] (PQ).

[(1)]NPPN/UFRJ; [(2)]FIOCRUZ;

Introduction Allelopathic compounds released by plants into the rhizosphere have effects on neighboring plants ranging from phytotoxicity to inducing organogenesis. Objective To investigate the allelopathic effect of *Terminalia catappa´*s fruit and isolation of allelopathic substances. Methodology The allelopathic effect of *T. catappa*'s fruit was evaluated on germination and root growth of *L. sativa* (lettuce) in Petri-dish bioassays using the quinone menadione as positive control. The allelopathic activity of quinones is a function of reactive radicals generated during redox cycling between quinone and hydroquinone states. Results The inhibitory concentration (IC_{50}) related to the root growth was established as 336 ppm for CH_2Cl_2 fraction of *T. catappa*'s fruits and 143 ppm for menadione. The bioassay-directed chromatography of dichloromethane extract resulted in three active fractions at 336 ppm. Conclusion These results stimulate the study of the allelophatic effect of *T. catappa*'s fruits for the isolation and identification of its allelochemical substances.

Financial Support: CAPES; FUJB.
Advisor: Ricardo M. Kuster.

PN029-ELLAGITANNIN OF *PENTACLETHRA FILAMENTOSA* WITH INHIBITORY ACTIVITY IN THE PROTEIN SYNTHESIS OF BACTERIA

IVANA C.R. LEAL (PG)[1]; KATIA R. N. SANTOS (PQ)[2]; PRISCILA V. COSTA (IC)[1]; IVALDO I. JR. (IC)[1]; ELIEZER M. PEREIRA(IC)[2]; GABRIELA M. MACEDO (IC)[2]; MARCIA GIAMBIAGI-DE-MARVAL (PQ)[2]; RICARDO M. KUSTER (PQ)[1]

[(1)]NPPN/UFRJ;[(2)]IMPPG/UFRJ;

Introduction *Pentaclethra filamentosa* have been used in the northern of Brazil for scarring. The search for natural products with antibacterial activity is increasing due to problems associated with resistant pathogens.Objective To study the antibacterial activity of this specie against hospital bacteria and the mechanism of action involved. Methodology Plant ethanol extract was fractioned and the antimicrobial activity of the fractions obtained was determined by the agar dilution method. The EtOAc active fraction was chromatographed on a Sephadex column and afforded an active tannin fraction. For the protein synthesis analysis, cells were labeled with [^{35}S]methionine and 250 µg/mL of the tannin was assayed. It was subjected to electrophoresis followed by exposure to X-ray film.Results Acid hydrolysis of this fraction afforded ellagic acid, identifying it as ellagic tannin, which prevented bacteria to incorporate [^{35}S]methionine. Conclusions Ellagitannins are responsible for the antibacterial activity of *P. filamentosa* and the mechanism of action involves the inhibition of protein synthesis.

Financial Support:FUJB, CAPES, PRONEX
Advisor:Ricardo M. Kuster

PN030-PHYTOCHEMICAL SCREENING OF *MYRCIARIA CAULIFLORA* LEAVES

TATIANA M. DE SOUZA(PG)[(1)]; RAQUEL R. D. MOREIRA(PQ)[(1)]; ROSEMEIRE C. L. R. PIETRO(PQ)[(1, 2)]

[(1)]Universidade Estadual Paulista–UNESP – Araraquara, São Paulo; [(2)]Universidade de Ribeirão Preto – UNAERP – Ribeirão Preto, São Paulo; Brasil.

Myrciaria cauliflora (Mart.) O. Berg., from Myrtaceae family, is a tree native from the south of South America whose fruits are cosmetible by the people. Its barks are astringent and used against diarrhea and skin irritation. In preliminary research its leaves extract showed antimicrobial activity. By the purpose to identify the compounds present in its leaves, the objective of this study was to search the following metabolites: alkaloids, antraquinones, flavonoids, saponins and tannins. The leaves were harvested at São Carlos - São Paulo on summer and winter, and the characterization of these metabolites were used chemical reactions specifics of precipitation, development of colour and fluorescence according Costa 1994 and Simões 2002. It was not detected the presence of alkaloids, antraquinones and saponins. The presence of tannis was detected by precipitate formation and flavonoids was detected by visualization at UV light. Thus, this search must be continued with the purpose to verify the relationship among these metabolites and the antimicrobial activity.

Supervisor: Prof[a] Dr[a] Rosemeire Cristina Linhari Rodrigues Pietro

The authors did not follow the Scientific Committee's suggestion for an English language review

PN031-THE TREATMENT OF POST-ERYSIPELAS' SKIN ULCER BY THE NATURAL LATEX BIOMEMBRANE - A CASE REPORT

FERNANDA GUZZO GOMES(PG)[(1)]; LUISIANE DE ÁVILA SANTANA(PG)[(2)]; MARCO ANDREY CIPRIANI FRADE(PQ)[(1)]

[(1)]Departamento Clínica Médica FMRP-USP; [(2)]Interunidades Bioengenharia(EESC-IQSC-FMRP)-USP

Introduction: Erysipelas is an infectious disease caused by *Streptococcus sp*. with several consequences including necrosis skin. The ulcer's healing corresponds to three phases: inflammatory, formation and remodeling tissue. A new dressing of the natural latex biomembrane (NLB) from rubber tree *Hevea brasilienses* has important healing properties as debridement and neoangiogenesis. Objective: To present the NLB treatment to post-erysipelas' ulcer in a patient treated in the School Health Center FMRP-USP. Methods: The treated case was a male patient, 54 years-old, smoker, with erysipelas on the left foot for 15 days. The consequent lesion was a large necrosis ulcer. The NLB dressing was applied in alternated days and photographed weekly to follow up by the images. Results: Initial ulcer measured was 24 cm x 11 cm, with 80% of granulation and 20% of fibrin. After 4 weeks, it was total granulated and a cellulose membrane was applied. More 4 weeks, the measure was 10cmx4cm. Conclusion: The NLB showed to be an important dressing with debridement and neoangiogenic properties accelerating the healing process in post-erisipelas'ulcer.

Financial Support: FAEPA-FMRP-USP
Supervisor: Marco Andrey Cipriani Frade

PN032-TRYPANOCIDAL CHROMENES FROM *PIPER GAUDICHAUDIANUM* AND *PIPER ADUNCUM* (PIPERACEAE)

JOÃO MARCOS BATISTA JUNIOR (IC)[1]; ADRIANA APARECIDA LOPES (PG)[1]; DANIELA LUZ AMBRÓSIO (PG)[2]; REGINA MARIA BARRETTO CICARELLI (PQ)[2]; VANDERLAN DA SILVA BOLZANI (PQ)[1]; MASSUO JORGE KATO (PQ)[3]; MAYSA FURLAN (PQ)[1]

[(1)] Instituto de Química de Araraquara – UNESP – R. Francisco Degni, s/n – Quitandinha, CEP: 14800-900, Araraquara-SP; [(2)]Faculdade de Ciências Farmacêuticas - Unesp- Rodovia Araraquara/Jaú Km 1 - CP 50214801-902 - Araraquara - S.P. [(3)]Instituto de Química – USP – Universidade de São Paulo, CP 26077, 05599-970 São Paulo, SP, Brazil

Introdution: Chagas disease is caused by the flagellate protozoan *Trypanosoma cruzi*, leading to 400,000 deaths per year. Products of plant origin have been studied as a source of new drugs against *T. cruzi*.
Objective: Investigation of trypanocidal activity of crude extracts and isolated chromenes from *Piper gaudichaudianum* (PG) and *Piper aduncum* (PA).
Methodology: The crude extracts from stems of PG and leaves of PA were subjected to chromatographic separations resulting in the isolation of four chromenes. The extracts and pure compounds were submitted to trypanocidal assay against epimastigotes forms of *T. cruzi* (stain Y).
Results: The crude extracts from PA, PG and isolated chromenes 1-4 showed IC_{50} 113.1; 412.0; 11.4; 36.0; 25.8 and 12.2; µg/mL respectively.
Conclusions: The samples tested showed potent *in vitro* activity.

Financial support: Fapesp
Adviser: Maysa Furlan

PN033-*IN VITRO* ACTIVITY OF SECONDARY METABOLITES FROM *PIPER CRASSINERVIUM* (PIPERACEAE) AGAINST *TRYPANOSOMA CRUZI*

ADRIANA APARECIDA LOPES (PG)[1]; JOÃO MARCOS BATISTA JUNIOR (IC)[1]; LUIS OCTÁVIO REGASINI (PG)[1]; DANIELA LUZ AMBRÓSIO (PG)[2]; REGINA MARIA BARRETTO CICARELLI (PQ)[2]; VANDERLAN DA SILVA BOLZANI (PQ)[1]; MASSUO JORGE KATO (PQ)[3]; MAYSA FURLAN (PQ)[1].

(1)Instituto de Química de Araraquara – UNESP – Francisco Degni, s/n – Quitandinha, CEP14800-900, Araraquara-SP; (2)Faculdade de Ciências Farmacêuticas – UNESP - Rodovia Araraquara/Jaú Km 1- CP 50214801-902 - Araraquara - S.P. (3)Instituto de Química – USP – Universidade de São Paulo, CEP 05599-970 São Paulo, SP, Brazil.

Introduction: Chagas disease is an important social and medicinal ailment for people living in the Americas. Some natural products of plant origin have been studied as a source of new drugs against *T. cruzi*.
Objective: Investigation of trypanocidal activity of a prenylated hydroquinone (1), prenylated benzoic acid derivative (2) and flavanones (3-4).
Methodology: The crude extracts from leaves of *P. crassinervium* were subjected to chromatographic separations resulting in the isolation of 1-4. The pure compounds (1-4) were submitted to trypanocidal assay against epimastigotes forms (stain Y).
Results: The IC_{50} for compounds 1-4 were 6.40; 67.8; 75.3 and 78.9 μg/mL respectively.
Conclusions: The isolated compounds showed hight *in vitro* activity, mainly prenylated hydroquinone.

Financial support: Fapesp
Adviser: Maysa Furlan

PN034-ANTIBACTERIAL EFFECTS OF THE ESSENTIAL OILS FROM FOUR SPECIES OF *BACCHARIS*

*ANGELA FLORÃO (PG); JEANINE MARIE NARDIN (PG); **FABIANA HERRERA ROCHA (IC); CYNTIA FADEL-PICHETH (PQ); ALMERIANE MARIA WEFFORT-SANTOS (PQ)

Programa de Pós-graduação em Ciências Farmacêuticas – UFPR – Curitiba, Brazil

INTRODUCTION/OBJECTIVE: The *Baccharis* genus (Asteraceae) comprises over 500 species distributed mainly in the tropical South America areas, with many of them widely used in the folk medicine for the treatment/prevention of several diseases. The aim of this study was to investigate the antibacterial effects of the essential oils extracted from *B. articulata*, *B. dracunculifolia*, *B. crispa,* and *B. gaudichaudiana.* METHOD: The agar diffusion method was performed using filter discs (6mm) impregnated with increasing concentrations (1.25 – 10ul) of the essential oils and set on Mueller-Hinton agar plates seeded with 10^8 CFU/ml of ATCC strains of *Staphylococcus aureus*, *Enterococcus faecalis*, *Escherichia coli* and *Pseudomonas aeruginosa*. RESULTS: Treatment with all *Baccharis* essential oils tested only inhibited the growth of gram-positive bacteria, producing rings of variable sizes according to the species assayed, which correlated with the concentration tested. CONCLUSIONS: The results indicate that the *Baccharis* essential oils tested are potent antibacterial agents through mechanisms that deserve further investigation.

Supervisor: A.M. Weffort-Santos
Financial support: *CAPES; **Fundação Araucária

PN035-ACTIVITIES OF *COPAIFERA* SPP. OLEORESIN AGAINST MYCOBACTERIA

VERA CASCON (PQ)[1]; MARIA AUXILIADORA C. KAPLAN (PQ)[1]; BENJAMIN GILBERT (PQ)[2]; ANNA GRAZIA MARSICO (PQ)[3]; GISELE BETZLER DE OLIVEIRA VIEIRA (PQ)[3]; EDUARDO WERNECK-BARROSO (PQ)[4]

[1]Núcleo de Pesquisas de Produtos Naturais/UFRJ; [2]Far-Manguinhos/FIOCRUZ; [3]Laboratório de Micobacteriologia-IDT/UFRJ; [4]Instituto de Pesquisa Clínica Evandro Chagas/FIOCRUZ

Introduction: The oleoresin obtained of *Copaifera* species, the popular "óleo de copaíba", has recognized anti-septic activity. Nowadays, the tuberculosis is the infectious-contagious disease that more causes deaths in Brazil. Objective: To test the activity of *Copaifera* spp. oleoresins against *Mycobacterium tuberculosis* and *M. avium*. Methodology: The commercial copaiba balsams: M, B and R, and the collected ones in the Amapá State: *Copaifera* sp., *C. reticulata* and *C. duckei*, in the concentration of 2,0 mg/ml, had been tested against H37Rv = *M. tuberculosis* standard strain, susceptible to all available drugs; MDR-TB = *M. tuberculosis* resistant to all drugs of the standard treatment (RMP, INH, PZA, EMB, ETH and SM); and *M. avium*. Results and Conclusion: All the copaiba balsams had shown 100% of activity against the *M. tuberculosis* strains and had not presented activity against *M. avium*. The presence of activity against MDR-TB points to a potential use of *Copaifera* spp. oleoresins as alternative drug in the treatment of patients with multidrug-resistant tuberculosis.

Financial Support: CAPES, CNPq
Supervisor: Benjamin Gilbert

PN036-PHYTOCHEMICAL SCREENING OF *SPONDIAS LUTEA* HARVESTED AT ARARAQUARA – SP

LUIZ ESTÊVÃO SALVAGNINI(IC)[1]; RAQUEL R. D. MOREIRA(PQ)[2]; LUIS EDUARDO SANTOS(PQ)[2]; HERIDA R. N. SALGADO(PQ)[2]; VERA L. B. I. RANGEL(PQ)[2]; ROSEMEIRE C. L. R. PIETRO(PQ)[2,3]

[1] Centro Universitário de Araraquara–UNIARA, SP, Brasil; [2]Universidade Estadual Paulista–UNESP – Araraquara, São Paulo; [3]Universidade de Ribeirão Preto – UNAERP – Ribeirão Preto, São Paulo.

Spondias lutea L. known as cajazeira is a tropical tree, 25 m. high whose fruits yellow, rounded and tasteful are eaten by people. The objective of this work was to search the presence of alkaloids, flavonoids, tannins, saponins, antraquinones, antraquinonic and cardiac glycosides in *S.lutea* fruits, cultivated at the "Horto de Plantas Medicinais e Tóxicas da Faculdade de Ciências Farmacêuticas de Araraquara-UNESP". Phytochemistry studies carried out with the fruits of this species describes the presence of tannins, flavonoids, terpenes and saponins. The presence of saponins was verified through the formation of persistent and abundant foam. In *S. lutea* fruits the specific characterization reactions for alkaloids, antraquinonic and cardiac glycosides and antraquinones presented negative results. The presence of condensed and hydrolyzable tannins as well as saponins may show a potential for future antimicrobial studies.

Support: FAPESP; PADC – FCF – UNESP
Supervisor: Profa. Dra. Rosemeire Cristina Linhari Rodrigues Pietro

PN037-PISOSTEROL INDUCES MONOCYTIC DIFFERENTIATION IN HL60 LEUKEMIA CELLS

MARNE CARVALHO DE VASCONCELLOS (PG)[1]; RAQUEL CARVALHO MONTENEGRO (PG)[1]; RÔMULO FEIO FARIAS (PG)[1]; FRANCIGLAUBER SILVA BEZERRA (PG)[2]; MANOEL ANDRADE NETO (PQ)[2]; MANOEL ODORICO DE MORAES (PQ)[1]; CLÁUDIA DO Ó PESSOA (PQ)[1]; LETÍCIA VERAS COSTA LOTUFO (PQ)[1]

[1] Departamento de Fisiologia e Farmacologia; Laboratório de Oncologia Experimental, UFC [2] Departamento de Química Orgânica, UFC

Introduction: Pisosterol, a triterpene isolated from the ectomicorrhizal fungus P*isolithus tinctoris* (Pers) Cok. & Couch, is strong cytotoxic against cancer cell lines *in vitro*. Objective: Our aim was to evaluate the differentiation induction by pisosterol (1, 2 and 5 µg/mL) in HL60 leukemia cells using Hematoxilin/Eosin staining, NBT, nonspecific esterase and cell growth inhibition assays. Methodology: TPA was used as positive control. After 72 hours of incubation pisosterol appeared to induce monocyte/macrophage characteristics, since HL-60 cells treated with this compound showed NBT reducing activity and non-specific esterase activity in a concentration-dependent manner. Results: Pisosterol (5 µg/mL) also induced morphological changes compatible with terminal differentiation and inhibited HL-60 proliferation. Conclusions: These data indicates a potentially therapeutic importance of pisosterol as an inducer of cell differentiation.

Supervisor: Letícia Veras Costa Lotufo
Financial Support: CAPES, CNPq, FINEP e BNB

PN038-BIOASSAY-GUIDED FRACTIONATION AND CYTOTOXICITY STUDIES ON FRACTIONS OBTAINED FROM IRCINIA FELIX

PAULA CHRISTINE JIMENEZ(PG)[1]; DIEGO VERAS WILKE(IC)[1]; CRISTIANE VASCONCELOS(PG)[2]; EDILBERTO SILVEIRA(PQ)[2]; CLAUDIA PESSOA(PQ)[1];MANOEL ODORICO DE MOARES(PQ)[1]; LETÍCIA VERAS COSTA LOTUFO(PQ)[1].

[1]Depto. de Fisiologia e Farmacologia-UFC; [2]Depto. de Química Orgânica-UFC

Introduction and objective: This study consisted on a bioassay-guided fractionation of a hidromethanolic extract from *Ircinia felix* (Porifera : Desmonspogiae) collected at Pedra da Risca do Meio, Ceará, and studies upon the cytotoxic activities presented by the active fractions. Methodology: Samples of *I. felix* were homogeneized in ethanol, partitionated in varies organic solvent and chromatographed in silica columns. The resulting fractions were tested for antiproliferative activity on 4 tumor cell lines using the MTT assay. 4 fractions showed good activity profile and were chosen for continued studies: IFE1-1, IFE1-Em, F48-51 and F51-60. Posterior cytotoxicity assays accessed proliferation, viability, death induction and morphology analysis on 24h treated HL-60 cells. Results: F 51-60 was slightly more potent. Along with F 48-50, F 51-60 presented cytostatic rather then cytotoxic activity, although both fractions had a residual necrotic action on higher concentrations. Conclusion: *I. felix* appeared as a good source of cytotoxic compounds.

Supervisor: Letícia Veras Costa Lotufo
Financial support: CNPq, BNB, FINEP

PN039-DIRECT INJECTION-MASS SPECTROMETRY OF *BYRSONIMA CINERA*

MARIA ELOÍSA FIGUEIREDO (IC)[1]; MIRIAM SANNOMIYA (PQ)[1]; LOURDES CAMPANER DOS SANTOS (PQ)[1]PAOLA MONTORO (PQ)[2]; SONIA PIACENTE(PQ)[2]; COSIMO PIZZA(PQ)[2]; WAGNER VILEGAS (PQ)[1]

[1]IQ-UNESP; [2]UNISA-Itália

Introduction: *Byrsonima cinera* is popularly consumed in fever treatment, gastric disfunctions and diarrhoeal. Despite the popular use there are no chemical data. Objectives: The main goal of this work was to investigate the potential of direct injection-mass spectrometry for the characterization of the very polar compounds present in the MeOH extract of the aerial parts of *B. cinera.* Methodology: The MeOH extract was analyzed on the Mass spectrometer fitted with an electrospray ionisation source. All mass spectrometry data were acquired in the negative ionisation and profile modes, the scan range varied according to the molecular weights of the parent compounds. Results: The MeOH extract analysis showed the presence of a quercetin-O-gluc-ara-rha $[M-H]^-$ 755, quercetin-Ogluc-ara $[M-H]^-$ 609, quinic acid $[M-H]^-$ 191, gallic acid $[M-H]^-$ 169. Conclusions: The informative fragments described can be contributed from the phytochemistry pointeview faciliting the screenings using selected ion monitoring. LC-MS was successfully applied for the tea analysis of catechins, flavonoids and poplyphenolic compounds by direct injection.

Financial Support: FAPESP
Supervisor: Miriam Sannomiya

PN040-ANTIMICROBIAL ACTIVITY OF MARINE INVERTEBRATE EXTRACTS

ANA CLAUDIA TREVIZAM MARTINS (IC) [1]; ELISSA G. O. SILVA (IC) [1]; GISLENE GARCIA FRANCO NASCIMENTO (PQ) [1]; ROBERTO B. S. BERLINCK (PQ) [2]

[1]Faculdade de Ciências da Saúde, Universidade Metodista de Piracicaba, Rodovia do Açúcar, km 156, CP 96, CEP 13400-901 Piracicaba, SP; [2] Instituto de Química de São Carlos/USP, CP 780, CEP 13560-970 São Carlos, SP

Brazilian biodiversity is an important source for the discovery of new substances with pharmacological properties. Therefore, the objective of this study is to evaluate the antimicrobial activity of 310 crude extracts of Brazilian marine invertebrates (sponges, ascidians, octocorals and bryozoans). In the evaluation of the antimicrobial activity through the agar diffusion method, 3 samples of sensitive microorganisms (1 yeast and 2 bacteria) and 11 antibiotic-resistant bacteria isolated in a hospital environment were used. The MIC was performed through the incorporation of extracts to a broth culture media. The results showed that 10.9% of the extracts had antimicrobial activity, mainly the sponge extracts: *Monanchora arbuscula* (15 to 20 µg/mL MIC range), *Pachicalina* sp and *Monanchora* sp (both with 100 to 200 µg/mL MIC range). The data obtained allowed us to conclude that more detailed studies on the therapeutic use of marine invertebrates must be carried out, specifically concerning antibiotic-resistant bacteria.

Financial Support: FAP/UNIMEP; CNPq
Supervisor: Gislene F. Nascimento

PN041-EVALUATION OF ANTINEOPLASTIC ACTIVITY OF COMPOUNDS ISOLATED FROM ANNONACEAE AND LAURACEAE

MARIA DE FATIMA C. MATOS (PQ)[(1)]; MÁRCIO H. MATSUBARA (IC)[(1)]; PATRÍCIA M. OGUMA (IC)[(1)]; JOÃO M. DE SIQUEIRA (PQ)[1]; DENISE B. DA SILVA (PG)[1]; MILENA MARTINS (PG)[1]; FERNANDA R. GARCEZ (PQ)[1]

[(1)] Universidade Federal de Mato Grosso do Sul, Brazil

Introduction – Alkaloids and butanolides are among the secondary metabolites with cytotoxic activity isolated from Annonaceae and Lauraceae.
Objectives – To evaluate the antineoplastic activity of two oxoaporphine alkaloids (lysicamine and lanuginosine) and a butanolide against a tumor cell line *in vitro*.
Methodology – The *in vitro* cytotoxicity was measured as inhibition of Hep_2 (larynx carcinoma) cell growth, using the sulforhodamine B stain.
Results – (–)-Epilitsenolide C_1 (*Aiouea trinervis*, Lauraceae) exhibited strong inhibitory activity against Hep_2 cell growth (IC_{50} = 3.23 micrograms/mL), whereas oxoaporphine alkaloids isolated from *D. glabriuscula* and *U. lindmanii* (Annonaceae) showed mild activity.
Conclusions – A strong antineoplastic activity was found for the butanolide (–)-epilitsenolide C1 against Hep2 cells. For the alkaloids assayed, however, further studies are required with additional tumor cell lines to identify their potential cytotoxic selectivity.

Financial support: FUNDECT-MS; PROPP-UFMS
Advisor: Maria de Fatima Cepa Matos

PN042-STUDY OF ANTIMICROBIAL ACTIVITY OF *PEDILANTHUS TITHYMALOIDES*

CRISTIANO DINATO DUTRA(IC)[1]; JOÃO PAULO NEVES MACEDO(IC)[1]; MARCOS ALBERTO ZOCOLER(PQ)[1]; VITOR JOSÉ MIRANDA DAS NEVES(PQ)[1]; ADRIANO CRESSONI ARAÚJO(PQ)[1]; ELEN LANDGRAF GUIGUER(PQ)[1].

[1]University of Marília-Brazil.

Introduction: *Pedilanthus tithymaloides* belongs to Euphorbiaceae family. Some plants pertaining to this family presents antimicrobial activity being this specie recognized like medical in India because of yours antiemetic, anti-rheumatic, and antianemic properties. Phytochemistry studies carried through *Pedilanthus tithymaloides* had demonstrated the presence of triterpene as predominant constituint. Objective: To test the activity antimicrobial organic extracts of *Pedilanthus tithymaloides*. Methodology: Tests of diffusion in plate for $Gram^+$ bacterium, $Gram^-$ bacterium and fungus had been carried through using paper discs impregnated with fluid extract hexanic and ethanolic of the aerial parts and root antibiotics's discs and solvent as control. Results: The gotten results had demonstrated that the ethanolic extract of the root was able to produce a halo of inhibition of 42% for $Gram^-$ bacterium. The other extracts had not presented antimicrobial activity. Conclusion: $Gram^-$ bacteriums they had been sensible to the rude ethanolic extract of the root, with perspectives of tests in raised concentrations. For fungus and $Gram^+$ bacterium tested, activity was not evidenced.

Supervisor: Elen Landgraf Guiguer(1)

PN043-ANTIMICROBIAL ACTIVITY OF *RHIZOPUS MICROSPORUS VAR. RHIZOPODIFORMIS*: EFFECTS OF FERMENTATION TIME AND CULTURE MEDIUM

ANA SILVIA CISCATO CAMILLO[1](PG); MARLEY GARCIA SILVA[1,2](PG); NIEGE ARAÇARI JACOMETTI CARDOSO FURTADO[1](PQ); JAIRO KENUPP BASTOS[1] (PQ).

[(1)]-Faculdade de Ciências Farmacêuticas de Ribeirão Preto– FCFRP-USP – Ribeirão Preto - SP
[(2)]-Centro Universitário de Formiga – Unifor-MG – Formiga- MG

A strain of *Rhizopus microsporus var. rhizopodiformis* isolated from Brazilian soil sample was submitted to different culture conditions to improve the production of antimicrobial metabolites. The fungus was first grown at 30°C with shaking (120 rpm) for 24 hours in seed medium. The produced biomass on seed medium was used to inoculate three different production media, which were found to influence antimicrobial metabolites production. After different incubation times, the culture broths were separated from mycelia by filtration and extracted with ethyl acetate and butanol in sequence. The separated mycelium biomass was extracted by maceration with methanol. The obtained extracts were submitted to antimicrobial activity evaluation by bioautography. The ethyl acetate extract from the culture developed in Jackson's medium for 192 hours of fermentation time was more active against *Staphylococcus aureus*, *Candida albicans* and *Micrococcus luteus*. None of the extracts showed activity against Gram-negative bacteria.

Supervisor: Prof. Dr. Jairo Kenupp Bastos

PN044-ANTITUMOR ACTIVITY OF PHYSALINS B AND D FROM *PHYSALIS ANGULATA*

HEMERSON IURY FERREIRA MAGALHAES(PG)[(1)]; ALESSANDRA DE PAULA ALVES SOUSA (PG)[(1)]; ANA PAULA NEGUEIROS NUNES ALVES(PG)[(2)]; MANOEL ODORICO DE MORAES(PQ)[(1)]; OTÍLIA DEUSDÊNIA LOIOLA PESSOA (PQ)[(3)]; MARIA LEOPOLDINA VERAS(PQ)[(3)]; MARCIA ROCHA TORRES(PG)[(1)]; LETÍCIA VERAS COSTA-LOTUFO(PQ)[(1)]; CLÁUDIA PESSOA(PQ)[(1)]

Department of Physiology and Pharmacology[(1)], Clinic Odontology[(2)], and Organic and Inorganic Chemistry[(3)], UFC, Brazil.

Introduction: *Physalis angulata* L. (Solanaceae), popurlarly known as "camapum", is a traditional medicinal plant. Objective: Investigation of the antitumor activity of physalin B and D in mice. Methodology: Sarcoma 180 cells were injected (4×10^6cells s.c.) in the left hind limbs in six groups (10mice/group). 24 h later the animals were treated i.p. with physalin B and D (10 and 25mg/kg), 5-FU (25mg/kg) and saline (vehicle DMSO 10%) for 7 days. Three days after liver, kidney, spleen and tumor were weighted and submitted to histopathology analysis. Results: Size of tumor reduced significantly in both dose (10 and 25mg/kg) in physalin B (52.5% and 43.2%) and physalin D (56 % and 35%) respectively and 5-FU-treated animals (66.5%). Microscopic findings suggest physalin B and D show reversible toxic effects. Conclusion: The results show that physalin B and D act as antitumor agents.

Financial Support: FUNCAP, FINEP, InCb, CNPq, BNB, FUNDECI.
Supervisor: CLÁUDIA PESSOA.

PN045-EVALUATION OF ANXIOLYTIC EFFECT OF SINGLE OR REPETITIVE ORAL ADMINISTRATION OF *PASSIFLORA ACTINIA* EXTRACTS.

LUIZ F. LOLLI(PG)[1], CID A. M. SANTOS(PQ)[2], RÚBIA M. W. DE OLIVEIRA(PQ)[1].

[1]Universidade Estadual de Maringá, [2]Universidade Federal do Paraná.

Introduction: *Passiflora actinia* extracts administered by *i.p.* route cause sedative effect in mice. Objective: To investigate the effects of *P. actinia* crude (CE) and methanolic (ME) extracts, by oral route, using the elevated plus maze (EPM). Methodology: Mice received acute or repetitive (7 days/ twice a day) oral administration of CE or ME, 30 min before submitted to the EPM. The number of open and enclosed arm entries and the time spent in both arms of the maze were recorded for 5 min. Results: Acute oral administration of CE or ME extract increased the % of entries (control= 8,6±2.4; CE 300 mg/Kg=29.3±2.5; CE 600 mg/kg=28.87±4.5; ME 30mg/Kg=24.01±4.3; ME 150 mg/Kg 28.21±2.9, $p<0.05$) and the % of the time spent in the open arms of the EPM (control= 4.1±1.4; CE 300 mg/Kg= 25.31±2.5; CE 600 mg/kg= 26.6±6.0; ME 30mg/Kg=16.03±3.3; ME 150 mg/Kg 22.3±3.1,$p<0.05$) without change the number of the enclosed arm entries ($p>0.05$). No significant effect was observed with repetitive administration of CE or ME. Conclusions: *P. actinia* CE or ME produce a selective anxiolytic-like effect in mice following acute oral administration; tolerance may occur with repetitive oral administration.

Financial Support: UEM
Supervisor: Rúbia M. W. de Oliveira

PN046-DETERMINATION OF TANNINS IN PLANT EXTRACTS BY TLC AND HPLC METHODS

MARILI VILLA NOVA RODRIGUES (PQ) [(1)]; ALINE SIVESTRE (IC) [(1)]; MARCOS NOPPER ALVES (PQ) [(2)]

[(1)] Division of Organic and Pharmaceutical Chemistry of CPQBA-UNICAMP [(2)] Agrotecnological Division of CPQBA-UNICAMP

Preliminary analysis by thin layer chromatography (TLC) of plant extracts samples have been evaluated for the presence of catechin, epigallocatechin, epigallocatechin gallate, epicatechin and epicatechin gallate, for posterior quantification by high performance liquid chromatography using diode array detector (LC-DAD). Qualitative analysis by TLC was performed on silica gel plates eluted with acetone / toluene / formic acid (3:3:1 v/v/v). and sprayed with anisaldehyde-acetic solution (heated 100 ^{o}C). Quantification analysis were performed by LC-DAD using gradient with formic acid and acetonitrile as mobile phase using a C-18 column. The compounds were detected at 275 nm with exception of the epigallocatechin that was detected at 237 nm. The compounds eluted in the increasing order: epigallocatechin (9.55 min); catechin (10.18 min); epigallocatechin gallate (12.21min); epicatechin (13.04 min) and epicatechin gallate (14.51 min). The method was applied for grape extract and different parts of barbatimão (bark, leaves, callus obtained by tissue culture). The TLC analysis supplied evidence of the presence of these compounds in plant extracts and the HPLC methodology presented robustness adjusted for quantification stage

PN047-EVALUATION OF THE GASTROINTESTINAL ACTIVITY OF *STRYCHNOS PSEUDOQUINA*

MARCELO A. SILVA(PG)[2]; JULIANA A. SEVERI(PG)[1]; HÉRIDA R. N. SALGADO(PQ)[1]; ALBA R. M. S. BRITO(PQ)[3]; WAGNER VILEGAS(PQ)[2]

[1]FCF-UNESP; [2]IQ-UNESP; [3]IB-UNICAMP

Introduction: *Strychnos pseudoquina* is a specie widely used to gastric and intestinal disturbances. Objectives: Evaluate the motility intestinal activity and liquid absorption in mice by intestinal system of MeOH extract of *Strychnos* leaves. Methodology: The study was made with groups of 10 animals, according JANSSEN & JAGENEAU (1957) and WONG & WAI (1981) methods. The distance traveled by the charcoal plug from the pylorus to the ceccum was determined and expressed as a percentage of the total length of the small intestine. Student's *t*-test was used to determine statistical significance ($P<0.05$). Results: The charcoal distance of control and leaves in treated groups were 51.2 and 54.75cm. The weights of intestines were 2.37 and 2.68g. Conclusions: The leaves *S. pseudoquina* extracts did not show significant activity the propulsive movement of intestinal contents in mice between control and treated groups. However we could observe significant differences between intestine weights of control and treated group. This aspect may explain the use of *S. pseudoquina* as a diarrhoeal agent in folk medicine, which may be due to a probable absorption of liquids inside intestines.

Financial Support: FAPESP
Supervisor: Wagner Vilegas

PN048-ANTIMICROBIAL ACTIVITY OF *BLEPHAROCALYX SALICIFOLIUS* H.B.K.

CARLA SPERONI CERON (IC)[1]; GUSTAVO LUIZ PARAGINSKI (IC)[1]; EVERTON DOLESKI DEON (IC)[1]; VANESA TEIXEIRA KUNZ (PG)[2]; JULIANE BORBA MÜLLER (PG)[2]; MELÂNIA PALERMO MANFRON (PQ)[3]

[1]Graduação em Farmácia; [2]Pós Graduação em Ciências Farmacêuticas/ UFSM; [3]Departamento de Farmácia Industrial/ CCS/ UFSM

Introduction: *Blepharocalyx salicifolius* H.B.K. belongs to Myrtaceae family is an arboreal species and it is recognized as medicinal. Objective: The goal of this work is to evaluate the antimicrobial activity of crude extract of the B. salicifolius leaves by bioauthography method. This assay is used to monitor the isolation of the active metabolites. Methodology: The microorganisms tested were *Staphylococcus aureus* ATCC 6538P, *Pseudomonas aeruginosa* ATCC 27853, *Salmonella choleraensius* ATCC 10708, *Escherichia coli* (clinical isolates), and Cefepime was used as standard antibiotic. Inoculum with about 10^6 UFC/ml was added to Mueller-Hinton agar mean. On Petri plates were disposed the chromatoplates developed in chloroform/methanol/amonia (50:9:1) and added the inoculated mean. After incubation, the plates were revealed with 2,3,5 triphenyl tetrazolium chloride (20 mg/ml) for detection of the inhibition halos. Results and Conclusions: *Blepharocalyx salicifolius* has significant antimicrobial activity against Salmonella choleraensius.

Financial support: DFI
Adviser: Melânia Palermo Manfron

PN049-PHYTOCHEMICAL SCREENING AND ANTIBACTERIAL ACTIVITY FROM MEDICINAL PLANTS

CRISTIANE FERNANDA FUZER GRAEL (PQ)[1]; DANIELLE CRISTINA FONSECA SANTOS (IC)[2]; THAÍS NÉRI DOS REIS (IC)[1]; WILSON MUANIS GODINHO (IC)[1]; FERNANDO PETACCI (PQ)[1]; PAULO HENRIQUE GRAZZIOTTI (PQ)[2]

[1] DFB;[2] DEF–FAFEID

Introduction: Ethnobotanical research in Diamantina (MG) showed a variety of native plants used for treatment of infections, wounds and edemas. Among those plants were selected for this research: (I) *Ageratum fastigiatum* (Asteraceae), (II) *Jacaranda caroba* (Bignoniaceae), (III) *Solanum lycocarpum* (Solanaceae). Objective: Investigation of the main micromolecule classes of extracts from plants and their antibacterial activity. Methods: The plants were collected in their blooming season. The ether and EtOH extracts were prepared with aerial parts or roots. The phytochemical screening was performed using standard tests and TLC. The dried extracts were impregnated in paper discs (500 µg/disc) and their activity evaluated in triplicate through the plate-well diffusion assay against different bacteria species. Results: The ether extract from roots of I and EtOH extract from aerial parts of I and II were the more active against Gram + bacteria ($P<0,05$). The active extracts presented micromolecule classes with bioactivity reported. Conclusion: The extracts evaluated are potential resources of molecules with antibacterial action.

Financial support: FAPEMIG
Supervisor: Cristiane Fernanda Fuzer Grael

PN050-COMPARISON OF THE CHROMATOGRAPHIC PROFILES FROM *MELISSA OFFICINALIS* AND *LIPPIA ALBA* BY HPLC

JOSE LUIZ PINTO FERREIRA(PG)[1,2,3]; RENATA BASTOS DE ARAUJO(PQ)[1]; ELIANE VELASCO SIMÕES(PQ)[1]; KAÍZA MARTINS PORTO DE HOLLANDA CAVALCANTI(PQ)[1]; NAOMI KATO SIMAS(PQ)[1]; RICARDO MACHADO KUSTER(PQ)[2]; ANA CLAUDIA FERNANDES AMARAL(PQ)[1]

[1]Farmanguinhos (FIOCRUZ); [2]NPPN (UFRJ); [3]Laboratório de Farmacognosia (UFF)

Introduction: some vegetal species called "erva cidreira" are widely used by the brazilian population as sedative, antispasmodic and digestive. The most used are *Melissa officinalis*, of european origin, and *Lippia alba*, growing spontaneously all over the Brazil. Objective: the present study compare the chromatographic profile of the *M. officinalis* and *L. alba* leaves. Methodology: crude extracts made by decoction of the dry leaves and submitted to reverse phase HPLC/DAD analysis on a HIBAR C-18 column with 0.05% TFA + water and CH_3CN gradient from 90:10 to 30:70 v/v in 55 min. Results: the analysis of the chromatographic profiles at 305 nm together with the individual peaks in UV spectra showed a substantial variation of phenylpropanoid content. Glycoside esters of caffeic acid and rosmarinic acid were main constituents of *L. alba* and *M. officinalis*, respectively. Conclusions: these results permit a fast comparison between two "erva cidreira" species by HPLC analysis.

Financial Support: Farmanguinhos and FUJB
Supervisor: A.C.F. Amaral and R.M. Kuster

PN051 - MEDICINAL PLANTS AND ELDERLY PEOPLE: WHAT IS THE RELATIONSHIP?

JAQUELINE DOS SANTOS MARTINS (IC)[1]; PATRÍCIA V. SOUSA (IC)[1]; MARINA P. N. LAVERS (IC)[1]; MARCOS F. O. COSTA (PQ)[1]; RENATA MAZARO E COSTA (PQ)[1].

[1] ICB - DCIF-UFG.

Introduction: Older Brazilians have been using medicinal plants; this is a regional and economic situation in many cities like Tambaú, in São Paulo State. Objective: this study evaluated the use of medicinal plants in an elderly community and collected data to elaborate a municipal health project based on phytotherapy. Methodology: 136 questionnaires were applied at the Social Service Program, named S.O.S., in Tambaú, city with 22,000 inhabitants, 10% are elderly. Results: Average age is 62 years (women 82%; 39% are homemaker). 57% are not retired. 82% are using medicaments for chronic diseases: hypertension (49%; nifedipine, captopril); diabetes (9.5%, clorpropamide); menopause (9.5%, estrogens conjugated), chronic backache (8.8%) and depression (8.5%). 79% have been using medicinal plants, 85% believe in the cure by plants and in its safety. Most cited plants are: *Cymbopogon citratus; Mentha sp; Vernonia condensata; Foeniculum vulgare; Mikania sp; Eclipta alba; Baccharis trimera; Mentha pulegium; Melissa officinalis; Enterolobium shomburgkii and Arnica montana*. Conclusion: Older people have been using medicinal plants, not as the only recourse. They believe in the safety of plants and approve the use although there is necessity to instruct them for risk of the use.

Supervisor: Renata Mazaro e Costa

PN052-PHARMACOGNOSTIC STUDY IN SPECIES FROM ASTERACEAE FAMILY USED AS ANTIINFLAMMATORY IN A TRADITIONAL COMMUNITY IN PARACATU – MG

SIMONE CASTELUCCI(PG)[(1)]; ALEXANDRE DE PAULA ROGERIO(PG)[(1)]; SIMONE POSSEDENTE LIRA(PG)[(2)]; LÚCIA HELENA FACCIOLI(PQ)[(1)]; FERNANDO BATISTA DA COSTA (PQ)[(1)]

[(1)]FCFRP/USP;[(2)]IQSC/USP

The community living in the Special Protection Area of Paracatu keep the tradition of using plants as antiinflammatory. Fumo-bravo (Fb)(*Elephantopus mollis* HBK), Orelha-de-carneiro (Oc)(*Eremanthus sf mollis* Sch Bip) and Espinho-agulha (Ea)(*Sasyphyllum brasilienses* (Spreng) Cabrera). The raw extracts were prepared according to community instructions. We have analyzed the antiinflammatory activity of these species in mice injected i.p. with F1 (Alkali-insoluble fraction of the *Histoplasma capsulatum* cellular wall). Four groups of animals injected with F1 were daily treated with water, Fb, Oc or Ea (100 mg/kg, p.o.). The control group was injected i.p. with PBS. The mice were killed 24 hours after the i.p. stimulus and the total and differential number of cells in the peritoneal cavity was determined. In the animals treated with Ea there was inhibition of neutrophil, eusinophil and mononuclear cells recruitment. In the animals treated with Fb and Oc there were no significant alterations. Our studies are important in order to validate that traditional communities can serve as a reference in the search for new bioactive substances.

Financial support: CAPES
Supervisor: Fernando B. da Costa

PN053-HPTLC-DENSITOMETRIC METHOD TO COMPARE THREE SPECIES OF GENUS *HIMATANTHUS.*

THALIA ROCHA SAMPAIO[1](IC); CARLA JUNQUEIRA MORAGAS[2](PG); ANA CLAUDIA FERNANDES AMARAL[2](PQ); RICARDO MACHADO KUSTER[2](PQ).

[1]Farmanguinhos-FIOCRUZ; [2]NPPN-UFRJ.

Introduction: *Himatanthus* have been popularly used in northern region of Brazil for the treatment of gastritis and cancer. This wide application spectrum has waken the interest to the local population where *Himatanthus sucuuba* is most commonly used as infusions, decoctions and poultices prepared from stem barks, leaves and latex. Objective: analyze two species of genus *Himatanthus*: *H. drasticus* and *H. obovatus,* by comparison between their hexane fractions with *H. sucuuba* by HPTLC-densitometric method. Methodology: the standard solution of the main triterpene, lupeol acetate, was prepared containing 9µg/ml and diluted to 7, 5, 3 and 1mg/ml to obtain de calibration curve. The HPTLC silica plates were developed with hexane: toluene (3:7) as mobile phase and scanned at 208nm. Main results: the major concentrations of the lupeol acetate were found at the barks: 0,88% (*H. drasticus*) 2,61% (*H. obovatus*) and 3,5% (*H. sucuuba*). The hexane fraction from the leaves showed 0,32% (*H. drasticus*) and 1,23% (*H. obovatus*) of this triterpene. Conclusions: these results showed the great similarity between these species and justify in part, the use of them to the same medicinal purpose.

Financial support: CNPq.
Supervisor: A.C.F. Amaral and R.M. Kuster.

PN054-CHEMICAL COMPOSITION OF THE POPULAR ANTICANCER MEDICINE, *EUPHORBIA TIRUCALLI* LATEX

RICARDO M. KUSTER(PQ)[1,2];MARCIA C.B.N. VARRICCHIO (PG)[1]; CELSO L.S.LAGE (PQ)[1,3] MARCIA A.M.CAPELLA (PQ)[3]; MORGANA LIMA (PQ)[4]

[(1)]PBV/UFRJ;[(2)]NPPN/UFRJ;[(3)]IBCCF/UFRJ;[(4)] Anatomy and Histology Department/UFRJ

Introduction *Euphorbia tirucalli* (aveloz) latex is popularly used in Brazil to treat cancer. People use 3-4 drops of it diluted in 2 litre of water and swallow the solution in small portions in a day. No evidence is reported on scientific literature about the anticancer activity attributed to the plant. Objective To characterize the components of the latex. Methodology 1 mL of the latex was collected from the plant by incision of the aerial parts. To it were added 10 mL of methanol. The suspension was centrifuged in 7000 g during 10 min and the resulted solution was decanted and concentrated. Results It was obtained 500 mg of a white amorphous solid. ^{1}H-NMR and ^{13}C-NMR (CD_3OD) of this sample showed no chemical shift related to phorbol esters, substances known to be co-carcinogenic. Conclusions Scientific literature dissuades people to use *Euphorbia tirucalli* as a medicine due to its content in phorbol esters. However, in a preliminary study, we did not find this class of diterpene in a sample of latex.

Financial Support: FUJB
Supervisor: Ricardo M. Kuster

PN055-IN VITRO CYTOTOXIC ACTIVITY OF CASEARINS FROM *CASEARIA SYLVESTRIS* SW.

PAULO MICHEL PINHEIRO FERREIRA (PG)[(1)]; SABRINA OLIVEIRA RAMOS (IC)[(1)]; PATRÍCIA MARÇAL DA COSTA (PG)[(1)]; ANDRÉ GONZAGA DOS SANTOS (PG)[(2)]; CARLA CRISTINA PERES(PG)[(1)]; ARISTEU GOMES TININIS (PG)[(2)]; ALBERTO JOSÉ CAVALHEIRO (PQ) [(2)]; MANOEL ODORICO DE MORAES (PQ)[(1)]; LETÍCIA COSTA-LOTUFO (PQ)[(1)]; CLÁUDIA PESSOA (PQ)[(1)].

Department of Physiology and Pharmacology[(1)], UFC, Brazil
Department of Organic Chemistry - Chemistry Institute [(2)], UNESP, Brazil.

Introduction: *Casearia sylvestris* Sw. (Flacourtiaceae) is a medicinal plant found in Latin America that has shown significant activity in cancer cells lines. Objective: Evaluate cytotoxic and hemolytic activity of 9 casearins isolated from leaves of *C. sylvestris*. Methodology: These substances were tested for their cytotoxicity on MTT assay using 9 tumor cells lines: CEM, HL-60, K562, MDA-MB435, MDA-MB231, PC-3, HCT-8, B16, SF-295. Hemolysis assay was determined on mouse erythrocytes. Results: Four of them (F22 Cas26, F22 Cas30, A1B3C3, A1B3C2D2) showed strong citotoxic activity in all tumor cell lines tested with $IC_{50} < 4$ µg/mL. None of the casearins induced hemolysis, even on maximum concentration of 200µg/mL, suggesting its cytotoxicity was not related to membrane damage. Conclusion: Substances described above possess high citotoxic potential and no hemolytic activity.

Financial Support: CNPq, InCb, FAPESP, BNB/FUNDECI e FINEP.
Supervisor: Cláudia do Ó Pessoa

PN056-PHTYOCHEMICAL STUDY OF *HANCORNIA SPECIOSA* GUIDED BY ANGIOTENSIN CONVERTING ENZYME INHIBITION ASSAY

DENISE COUTINHO ENDRINGER (PG)[1]; CRISTIANE MOTA SOARES (IC)[1]; PRISCILLA VALADARES CAMPANA RODRIGUES (IC)[1]; FERNÃO CASTRO BRAGA (PQ)[1]

(1) Laboratório de Fitoquímica, Faculdade de Farmácia, Universidade Federal de Minas Gerais

Hancornia speciosa (Apocynaceae) is a plant species found in cerrado, popularly known as mangaba. The plant is traditionally used to treat several diseases, including hypertension. We have previously reported the angiotensin converting enzyme (ACE) inhibitory activity of this species, indicating its potential anti-hypertensive acitivity. The goal of the present work was the fractionation of *H. speciosa* guided by the ACE inhibition colorimetric assay. The ethanol extract of *H. speciosa* leaves (EHS), prepared by percolation, was chromatographed on a silica gel column. EHS and several derived fractions showed ACE inhibition rates > 50%, at the concentration of 0.10 mg/ml. From the EtOAc:MeOH (1:1) fraction (80% of ACE inhibition), two compounds were isolated and identified by spectroscopic methods as rutin and 1-*O*-methyl-*myo*-inositol. Both compounds showed ACE inhibition rates < 20%, at the concentration of 0.10 mg/ml. These results suggest the presence of other ACE inhibitory active compounds in the fraction, or a synergistic effect between its constituents.

Financial Support: CNPq / PRPq UFMG
Supervisor: Fernão Castro Braga

PN057-SPASMOLYTIC ACTION OF THE CHLOROPHORM EXTRACT FROM *TYPHA DOMINGENSIS* PERS. INVOLVES BLOCKADE OF CA^{2+} INFLUX IN RAT UTERUS

XIRLEY PEREIRA NUNES (PG)[1]; JULIANELI TOLENTINO LIMA (PG)[1]; MARCOS ANTONIO ALVES MEDEIROS (PG)[1]; MARCELO CAVALCANTE DUARTE (IC)[1]; GABRIELA LEMOS AZEVEDO (IC)[1]; JOSÉ MARIA BARBOSA FILHO (PQ)[1,2]; BAGNÓLIA ARAÚJO SILVA (PQ)[1,2]

[1]Laboratório de Tecnologia Farmacêutica - LTF/UFPB; [2]Depto. de Ciências Farmacêuticas - UFPB

Introduction: *Typha domingensis* Pers. is an herbaceous plant known in Brazil as "taboa". Previous studies showed that *T. domingensis* exhibits spasmolytic action in trachea and guinea-pig ileum. Objective: We decided to investigate a possible spasmolytic effect of the chlorophorm extract obtained from the aerial parts of *T. domingensis* (TD-$CHCl_3$) in rat uterus. Methodology: The tissues were suspended in organ bath chambers (6 mL) and the isometric and isotonic contractions were monitored. Results: TD-$CHCl_3$ inhibited (n=3) in a concentration-dependent manner 10^{-5} M carbachol- (IC_{50} = 69.5±1.1 µg/mL) and 10^{-2} UI/mL oxytocin phasic contractions (IC_{50} = 120.8 ±7.8 µg/mL) and relaxed (n=3) 60 mM KCl-(EC_{50} = 59.7 ±0.2 µg/mL)-induced tonic contractions. Conclusions: TD-$CHCl_3$ presents non-selective spasmolytic effect in rat uterus. The fact of TD-$CHCl_3$ to relax the rat uterus pre-contracted by contractile agent used suggests that this relaxation might be due to the blockade of Ca^{2+} influx.

Financial Support: PIBIC/CNPq, CAPES.
Supervisor: Bagnólia Araújo Silva.

PN058-PHYTOCHEMISTRY INVESTIGATION AND BIOLOGICAL ANALYSIS OF AMPELOZIZYPHUS AMAZONICUS AGAINST MALARIA

GEONE M. CORRÊA (PG)(1); JUNIOR C. RIBEIRO (IC)(1); JEFFERSON ROCHA DE A. SILVA (PQ)(1); ANA CLAUDIA F. AMARAL (PQ)(2)

(1) Universidade Federal do Amazonas (UFAM-AM); (2) FIOCRUZ-RJ/ Farmanguinhos

Since the 70s, the world health organization (WHO) has recognized the true importance of folk medicine, because sometimes just the traditional formulas represent the only alternative of treatment. The root of *Ampelozizyphus amazonicus* (Rhamnaceae), known commonly as "saracura-mirá" or "Indian beer", is among the several plants used in Brazil to treat malaria and this specie is the only representative of genus *Ampelozizyphus*. The root and fine twigs were collected in november 2004 at the Adolpho Ducke Reserve and dried at room temperature. The plant samples were extracted by maceration with hexane, dichloromethane and ethanol 70%. The hexane and dichloromethane extracts were analyzed by GC/MS and it allowed identifying, using the Wiley library and literature values, as main constituents triterpenes (40 to 50%) such as, Taraxasterol and steroids (stigmasterol and Sitosterol). In the other hand, analysis by HPLC/DAD of the ethanolic extract revealed presence of some saponins, substances frequently found in Rhamnaceae in a lot of quantity, and phenylpropanoids.

Financial support: CNPq/PADCT, FINEP, FAPEAM/AM
Supervisor: Jefferson Rocha de Andrade Silva

The authors did not follow the Scientific Committee's suggestion for an English language review

PN059-OPTIMIZATION OF SYNTHESIS AND PREPARATIVE CHROMATOGRAPHIC SEPARATION OF CAFFEOYLQUINIC DERIVATIVES

STELA COSTA COMPARINI(IC)[(1)]; LEONARDO GOBBO-NETO(PG)[(1)]; MICHEL DAVID SANTOS(PG)[(1)]; NORBERTO PEPORINE LOPES(PQ)[(1)]

[(1)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP

Introduction: Caffeoylquinic acids are plant derived compounds which posses a broad spectrum of pharmacological activities, such as analgesic, anti-inflammatory, antioxidant and anti-HIV.
Objective: Optimization of a fast and cheap method to synthesise a range of caffeoylquinic derivatives and its preparative chromatographic separation.
Methodology: di-*O*-acetylcaffeoyl chloride synthesis: 1) acylation of caffeic acid with Ac_2O in pyridine; 2) obtained di-*O*-acetylcaffeic acid was purified by liquid-liquid extraction and reacted with oxalyl chloride in toluene to afford the acid chloride. HPLC preparative separation was optimized using standards (3,5-di-*O*-[*E*]-caffeoylquinic, 4,5-di-*O*-[*E*]-caffeoylquinic and 3,4,5-tri-*O*-[*E*]-caffeoylquinic acids) obtained previously from plant extracts. Obtained structures were confirmed by spectroscopic methods.
Results and conclusion: Until the moment, a suitably protected and activated caffeic acid (di-*O*-acetylcaffeoyl chloride) was obtained to be used to synthesise caffeoylquinic derivatives by esterification with quinic acid. Concomitantly, a method for preparative separation of caffeoylquinic derivatives was developed.

Financial Support: FAPESP, CNPq
Supervisor: Norberto P. Lopes

PN060-INDUCTION OF CASPASE-INDEPENDENT CELL DEATH BY POMOLIC ACID

JANAINA FERNANDES (PG)[1]; RACHEL O. CASTILHO (PQ)[2]; KLAUS-MICHAEL DEBATIN (PQ)[3]; SIMONE FULDA(PQ)[3] & CERLI R. GATTASS(PQ)[1].

[1]Instituto de Biofísica Carlos Chagas Filho and [2]Núcleo de Pesquisas em Produtos Naturais, UFRJ, Rio de Janeiro. [3]University Children's Hospital, Ulm, Germany.

Introduction: In previous studies we showed that pomolic acid (PA) induced apoptosis of leukemia cell lines. Objective: In this work we investigated the effect of PA in a cell line with high expression of the IAP Survivin. Methods: LN229, a human glioma cell line was treated with different concentrations of PA and viability was assessed by MMT. Variations of mitochondrial membrane potential (MMP), cell cycle analysis and cytochrome c release were assessed by FACS. Activation of caspases was analyzed by western blot. Optical microscopy was used for morphological analysis. Results and conclusions: Although PA inhibited the growth of LN229 cells (80%), it induced low levels of DNA fragmentation, suggesting the occurrence of necrosis rather than apoptosis. This was confirmed by morphological analysis. PA also induced loss of MMP (60%) and release of cytochrome c (49%), but there was no activation of caspases. Thus PA induced caspase-independent cell death in LN229, being effective even when the apoptotic machinery is partially blocked by high expression of survivin.

Supported by: FAPERJ, CNPq, PRONEX.
Supervisor: Cerli R. Gattass.

PN061-EFFECTS OF EUSCAPHIC ACID ON HUMAN CANCER CELL LINES

GLEICE G. ROCHA (IC)[1]; RODRIGO RODRIGUES (PQ)[2]; MARIA AUXILIADORA C. KAPLAN (PQ)[2] and CERLI R. GATTASS (PQ)[1].

[1]Instituto de Biofísica Carlos Chagas Filho and [2]Núcleo de Pesquisas em Produtos Naturais, UFRJ, Rio de Janeiro.

Introduction: In recent years, natural products were recognized as an important source of new anti-cancer agents. Objective: To investigate the tumoricidal activity of Euscaphic Acid (EA), a triterpene isolated from *Cecropia lyratiloba*. Methods: Human cancer cell lines were treated with different concentrations of EA and their viability was assessed by MTT. Apoptosis was quantified by flow cytometry (FL2), measuring the Sub-G1 peak of the cell cycle in cells stained with Propidium Iodide (PI). Variations of mitochondrial membrane potencial (MMP) were assessed by flow cytometry (FL-1) using cells stained with $DIOC_6(3)$. Results and conclusions: EA decreased the viability of all cell lines in a dose-dependent way. It also killed Lucena1, a leukemia MDR line. Quantification of the sub-diploid nuclei population, showed that induction of DNA fragmentation was also dose-dependent. As no alterations of mitochondrial membrane potential were observed, participation of the extrinsic pathway (Fas/FasL) is under investigation. Our data suggested that EA is a promising experimental agent for cancer treatment including MDR tumors.

Supported by: FAPERJ, CNPq, PRONEX.
Supervisor: Cerli R. Gattass.

PN062-FRAGMENTATION STUDIES ON MONENSIN BY ELECTROSPRAY IONIZATION TANDEM MASS SPECTROMETRY

JOSÉ NERÍ DE SOUSA JUNIOR(PG)(1); PAUL J. GATES(PQ)(2); NORBERTO PEPORINE LOPES(PQ)(1)

(1) Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo.
(2) School of Chemistry, University of Bristol, Cantock's Close, Bristol, UK BS8 1TS.

Introduction: Monensin is an polyether ionophore antibiotic widely used in veterinary medicine as an anticoccidial drug in poultry. Monensin is a potent human toxin and reliable methods for its detection is essential to food safety. *Objective:* To study the fragmentation of the monensin anion by negative mode electrospray ionization tandem mass spectrometry. *Methodology:* Monensin A and B are studied by electrospray ionization (ESI-MS, ESI-MS-MS) in the negative mode on a Quattro LC triple-quadrupole mass spectrometer (Micromass, UK). The spectra were acquired and processed using MassLynx software version 3.5 (Micromass, UK). *Results and Conclusion:* The ESI-MS-MS spectra of the monensin A and B anions ($[(M - Na)]^-$ = *m/z* 669 and 655 respectively) showed some significant fragmentation. The fragmentation seems to be initiated by the loss of several simple neutrals (MeOH, CO_2 and H_2O) followed by the elimination of mass 136 resulting in the formation of fragment ion *m/z* 439. The results presented will be of significant use for future identification of monensin metabolites.

Financial Support: FAPESP, CNPq
Supervisor: Norberto P. Lopes

PN063-SPECTROPHOTOMETRIC DETERMINATION OF TANNINS IN *SCHINUS TEREBINTHIFOLIUS* RADDI BY THE FOLIN DENIS METHOD

E.A F. VASCONCELOS (PG)[1]; T.F.A. MOURA (PQ)[1]

[1]Pharmacy Department/CCS/UFRN Natal– RN Brazil.

The development and validation of analytical methods represent one of the most important requirements in the quality control applied to phytopharmaceuticals. The aim of this study was to establish experimental parameter to validate a spectrophotometric method for determining polyphenols (PT) and total tannin (TT) contents in hidroalcoholic extract from *Schinus terebinthifolius* Raddi. There are several colorimetric techniques to determine tannins in plant extracts. One widely used is the Folin Denis method that procedures a blue color with phenolic compounds. The PT and TT were determined in hydroalcoholic extracts, using gallic acid as reference substance. The PT and TT contents were determined at 750 nm. The regression analysis of the calibration curve of standard and extractive solution showed to be linear (R^2=0,9994 and 0,9967, respectively). The PT and TT content in hidroalcoholic extract were 29,54g% and 26,14g%, respectively, expressed as gallic acid. The method presented good repeatability (RSD<1,5%) and reproducibility (RSD<5%). The analytical methodology adopted in this work can be further applied, mainly to the spectrofotometrical PT and TT contents determinations in phytopharmaceutical products containing extracts from *Schinus terebinthifolius* Raddi.

PN064-FRAGMENTATION OF GOYAZENSOLIDE CONGENERS USING ESI-MS/MS

DAYANA R. GOUVEA (IC)[(1)]; ANTÔNIO E. M. CROTTI (PQ)[(2)]; JOÃO LUIS C. LOPES (PQ)[(1)], NORBERTO P. LOPES (PQ)[(1)]

[(1)] Departamento de Física e Química, Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Brazil.
[(2)] Núcleo de Pesquisa em Ciências Exatas e Tecnológicas, Universidade de Franca, Brazil.

INTRODUCTION: Goyazensolide type of furanoheliangolides are commonly isolated from native Brazilian species, such as *Lychnophora* ("false arnica"). Interest for these compounds is because their biological activities (i. e., antiinflammatory and analgesic).
OBJETIVE: This study is to understand the fragmentations reactions of goyazensolide congeners under ESI and CID conditions.
METHODOLOGY: Structurally related compounds were analyzed by ESI-MS/MS using collision induced dissociation (CID) at low resolution.
RESULTS: Loss of CO_2 and R^2CO_2 from protonated compounds exhibiting a hydroxyl group and an acyloxy group at C-8, respectively, are due to different hydrogen migrations upon CID conditions. Further fragmentation is resulting of consecutive losses of H_2O and CO from a same structural moiety.
CONCLUSIONS: Although MS^n and accurate-mass data are needed, our results can be useful for assisting in the structural identification and metabolomic profile studies on native Brazilian species that goyazensolide congeners have been isolated from.

Financial Support: CAPES, CNPq and FAPESP
Supervisor: Prof. Dr. Norberto P. Lopes

PN065-EVALUATION OF THE GASTROINTESTINAL ACTIVITY OF *QUALEA* SPECIES

MARCELO A. SILVA(PG)[2]; ANA L. M. NASSER(PG)[2]; JULIANA A. SEVERI(PG)[1]; HÉRIDA R. N. SALGADO(PQ)[1]; ALBA R. M. S. BRITO(PQ)[3]; WAGNER VILEGAS(PQ)[2]

[1]FCF-UNESP; [2]IQ-UNESP; [3]IB-UNICAMP

Introduction: *Qualea parviflora* (Qp) and *Qualea grandiflora* (Qg) are species used to gastric and intestinal disturbances. Objectives: Evaluate the motility intestinal activity and liquid absorption in mice by intestinal system of MeOH extract of Qp and Qg barks. Methodology: The study was made with groups of 10 animals, according JANSSEN & JAGENEAU (1957) and WONG & WAI (1981) methods. The distance traveled by the charcoal plug from the pylorus to the ceccum was determined and expressed as a percentage of the total length of the small intestine. Student's *t*-test was used to determine statistical significance ($P<0.05$). Results: The charcoal distance of control and barks in treated groups were 53.09(control), 45.55(Qp) and 45.50(Qg)cm. The weights of intestines were 2.61(control), 2.77(Qp) and 2.47(Qg)g. Conclusions: The barks of Qp and Qg extracts did not show significant differences between intestine weights of control and treated groups. However we could observe significantly difference between control and treated groups in activity the propulsive movement of intestinal contents in mice. This aspect may explain the use of Qp and Qg as anti-diarrhoeal agents in folk medicine

Financial Support: FAPESP
Supervisor: Wagner Vilegas

PN066-EVALUATION OF THE GASTROINTESTINAL ACTIVITY OF *INDIGOFERA SUFFRUTICOSA*

JULIANA A. SEVERI(PG)[1]; TAMARA R. CALVO(PG)[2], HÉRIDA R. N. SALGADO(PQ)[1]; ALBA R. M. S. BRITO(PQ)[3]; WAGNER VILEGAS(PQ)[2]

[1]FCF-UNESP; [2]IQ-UNESP; [3]IB-UNICAMP

Introduction:*Indigofera suffruticosa* (IS) is used to intestinal disturbances. Objectives:Evaluate the motility intestinal activity and liquid absorption in mice by intestinal system of MeOH(A) and $CHCl_3$(B) extracts of IS leaves. Methodology:The study was made with groups of 10 animals, according JANSSEN & JAGENEAU (1957) and WONG & WAI (1981) methods. The distance traveled by the charcoal plug from the pylorus to the ceccum was determined and expressed as a percentage of the total length of the small intestine. Student's *t*-test was used to determine statistical significance ($P<0.05$). Results:The charcoal distance of controls were 51.20(A) and 44.4cm(B); of leaves in treated groups were 42.75(A) and 38.06(B)cm. The weights of intestines were 2.37(A), 2.17(B)g to controls; 2.51(A), 2.19(B)g to test. Conclusions:The leaves from IS extracts did not show significant difference among intestine weights of control and treated groups. However we could observe significant differences among control and treated groups in the propulsive movement of intestinal contents. This aspect showed liquid absorption by intestinal system and it could explain the use of IS as an anti-diarrhoeal agent in folk medicine.

Financial Support:FAPESP
Supervisor:Wagner Vilegas

PN067-EFFECTS OF DIETARY CHOLESTEROL (DC) AND *TAMARINDUS INDICA* L. (TI) ON COLONIC PRENEOPLASTIC LESIONS IN HAMSTERS

FLÁVIA MARTINELLO (PG)[(1)]; SHEILA MARIA SOARES (PG)[(1)]; JOÃO JOSÉ FRANCO (TC)[(1)]; SÉRGIO BRITTO GARCIA (PQ)[(2)]; SÉRGIO AKIRA UYEMURA (PQ)[(1)]

[(1)]FCFRP-USP, [(2)]FMRP-USP

It has been observed that DC increases DNA oxidative damage by free radicals, event related to the increased risk for cancer development. Consumption of fruits and vegetables like TI has been suggested to produce health benefits including anticarcinogenic effects. The aim of this study was evaluate if TI or DC could act independently on the colonic mucosal (CM), and/or facilitate the chemical carcinogen dimethylhydrazine (DMH)-mediated cellular damage. Hamsters were treated with TI (in drinking water), DC and/or DMH. Aberrant crypt foci (ACF)/cm^2, number of aberrant crypts per foci (AC/F) and proliferative cell nuclear antigen (PCNA)-labeling index were determined. DC or TI did not modify CM in groups non treated with DMH. DC reduced PCNA and ACF formation in DMH-induced group. Significant increase in the PCNA, ACF/cm^2 and AC/F was observed in DMH-induced/TI fed group when compared with its control group. Therefore, this study indicates that DC does seem to protect the initiation and early promotion stages of DMH-induced colon cancer (CC). Although TI has an antioxidant activity and does not stimulate CC itself, it showed a co-stimulatory effect on DMH-induced CC.

Support: FAPESP
Adviser: Sérgio A. Uyemura, PhD

PN068-TETRAHYDROFURAN LIGNANS FROM *PEPEROMIA BLANDA* (PIPERACEAE)

LIDIANE GASPARETO (IC)[1]; DEBORA CRISTINA BALDOQUI BERGAMO (PQ)[1]; VANDERLAN DA SILVA BOLZANI (PQ)[1], MASSUO JORGE KATO (PQ)[2]; MAYSA FURLAN (PQ)[1]

[(1)]Instituto de Química de Araraquara – UNESP – R. Francisco Degni, s/n – Quitandinha, CEP: 14800-900, Araraquara-SP; [(2)]Instituto de Química – USP – CEP: 05599-970, São Paulo, SP, Brazil

Introduction: *Peperomia* is the less studied genus from Piperaceae, and the most noteworthy compounds that have been isolated are the secolignans, the cyclobutane, acylphloroglucinol and phenolic with long aliphatic chains. *Peperomia blanda* is an herb perennial, usually terrestrial, that grows up in wet rocks. No previous phytochemical study has been made on this species.
Objective: Isolate the constituents of medium polarity extract from *P. blanda* and evaluate antioxidante activity.
Methodology: The CH_2Cl_2-soluble part of EtOAc extract of *P. blanda* leaves was subjected to chromatographic separations, resulting in the isolation of three tetrahydrofuran lignans.
Results: The compounds isolated were identified as grandisin, rel-(7R,8R,7'R,8'R)-3',4'-methylenedioxy-3,4,5,5'-tetramethoxy-7,7'-epoxylignan and rel-(7R,8R,7'R,8'R)-3,4,3',4'-dimethylenedioxy-5,5'-dimethoxy-7,7'-epoxy-lignan. All compounds showed potential antioxidante activity.
Conclusions: The tetrahydrofuran lignans have been isolated at the first time in this genus.

Financial support: FAPESP
Adviser: Maysa Furlan

PN069-ANTIMICROBIAL ACTIVITY OF *LUEHEA DIVARICATA* MARTIUS

JULIANE DE BORBA MÜLLER (PG)[1]; MELÂNIA PALERMO MANFRON (PQ)[1]; CARLA SPERONI CERON (IC)[1]; PATRÍCIA RECKZIEGEL (IC) [1]

[1]Department of Industrial Pharmacy – Federal University of Santa Maria

Luehea divaricata Mart. is an arboreal specie of Tiliaceae. The aim of this work was to evaluate the antimicrobial activity of the extract of the leaves of this specie by the bioauthography method. The extraction was carried out with methanol, hexane, chloroform, ethyl acetate and butanol. The assay was also used to follow the isolation of active metabolites. The following microorganisms were tested: *Klebsiella pneumoniae* ATCC 10031; *Escherichia coli* ATCC 11103; *Staphylococcus aureus* ATCC 6538P; *Staphylococcus epidermidis* ATCC 12228; *Sacharomyces cereviseae* ATCC 1600; *Candida albicans* ATCC 10231. Amoxicillin and nystatin were used as standards for bacteria and yeast, respectively. The inoculum containing about 10^8 UFC/ml was added to the Mueller-Hinton and Sabouraud dextrose agar media. The chromatoplates were developed with chloroform/methanol (85:15) and placed on Petri dishes. The medium inoculated was poured in the Petri dishes and incubated. After incubation, the plates were revealed with 2,3,5 triphenyl tetrazolium chloride for detection of the inhibition zones. The results demonstrated the activity of all the extracts of *L. divaricata* against the microorganisms tested.

Financial support: PPG/CF
Supervisor: Melânia P. Manfron

PN070-CHEMICAL AND MICROBIOLOGYCAL ANALYSIS OF ESSENTIAL OILS OF *EUCALYPTUS CINEREA* F. M., MYRTACEAE

JOCELINE FRANCO (PG)[1]; LUZIA FRANCO (IC)[2]; TOMOE NAKASHIMA (PQ)[2]; CHRISTIAN BOLLER (PG)[1]; GUSTAVO BERTOL (IC)[2].

1 – Programa de Pós-Graduação em Ciências Farmacêuticas (UFPR)
2 – Curso de Farmácia (UFPR)

Eucalyptus cinerea is a species native from Australia and also known as "silver dollar tree", it has an ornamental utility due to its seeds format. This species has an essential oil, raw materia to 1,8-cineole and other components. Studies with this eucalypt are rare. The aim of this work was the chemical, physical-chemistry and antimicrobial analysis of the essential oil from this species. It was investigated the yield of the essential oil extracted during three hours and fragmented in four different fractions, such as chemical analysis using GC/MS, physical-chemistry and antimicrobial analysis by broth dilution methods. It was observed more concentration of 1,8-cineole in the fraction collected in a quarter of hour and one hour. The mainly components investigated in the essential oils by GC/MS were: 1,8-cineole, α-pineno, limoneno e α-terpineol. The research of CIM by broth dilution presented that the fractions collected at two and three hour after the beginning of the extraction had antimicrobial activity with less concentration than other fractions and than essential oil, special against *Pseudomonas aeruginosa*.

Supervisor: Tomoe Nakashima

PN071-FLAVONOIDS DETECTION IN MELXI® SYRUP USING HPLC

MARIA ISAURA PEREIRA DE OLIVEIRA(PQ)[1]; MARIA DO CARMO DE BARROS PIMENTEL(PQ)[1]; JOSÉ LUIZ DE LIMA FILHO(PQ)[1]

[1]LIKA / UFPE, Av. Prof. Moraes Rego, s/n, Recife, CEP: 50670-910, Brasil.

Introduction: The flavonoids pharmacological activities justify the interest in quantifying them in phytopharmaceutical formulations, mucolytic syrup (pineapple juice+honey) for respiratory diseases. Objective: This study reports, the separation and quantification of flavonoids in syrup Melxi® using HPLC. Method: Syrup Melxi® sample (50 ml) was diluted using 75 ml of ethyl acetate/water/methanol (100:50:25, v/v) mixture. After 2 hour at room temperature was obtained separation of the phase. Less dense phase was collected and stirred for 3 min at 50 ºC. The final extract was diluted with methanol and filtered using nylon membrane filter 0.45 mm. Mobile phase: solvent A [water-acetic acid (97:3, v/v)] and B (methanol). Results: This method permitted identification of these flavonoids: quercetin (338.26 MW), kaempferol (286.20 MW), apigenin (270.24 MW) and pinocembrin (256.26 MW) respectively, retention times: 60.49, 59.47, 60.49 and 64.74 min. At $\lambda = 350$ nm was shown the maximum absorption for quercetin and apigenin and 290 nm for kaempferol and pinocembrin. Conclusion: The system was able to measure flavonoids in citrus juices and honey, with better detection limit and short time consumption.

Financial support: CNPq, FACEPE, HEBRON.
Supervisor: José Luiz de Lima Filho

PN072-ANTIMICROBIAL ACTIVITY OF HYDROALCOHOLIC EXTRACT FROM *STRYPHNODENDRON ADSTRINGENS*

SANDRA C. ORLANDO(PG)[1]; ROSANGELA DA SILVA(PQ)[1]; CARLOS H. G. MARTINS (PQ)[1]; EVELINE S. COSTA (IC)[1], ADRIANA H. C. VINHOLIS(PQ)[1]; TATIANE C. De CARVALHO (IC)[1]; WILSON R. CUNHA(PQ)[1]; NIEGE A. J. C. FURTADO (PQ)[1]; JAIRO K. BASTOS(PQ)[2] AND MARCIO L. A. E SILVA(PQ)[1].

[1]Universidade de Franca – Av. Dr. Armando Salles de Oliveira, 201 – Franca –SP CEP 14404-600; [2]FCFRP-USP – Av. do Café s/n – Ribeirão Preto – SP CEP: 14030-000

Introduction: S*tryphnodendron adstringens* is a native species of Brazil, well-known as Barbatimão, which grows abundantly in the cerrado. Objective: The aim of this work was to evaluate the antimicrobial activity of Barbatimão's crude hydroalcoholic extract against standard strains (ATCC) and field multi-resistent strains (FSMR). Materials and Methods: The biological assay was carried out with crude hydroalcoholic extract at the concentration of 300 mg/mL, using the agar diffusion method. Results and Discussion: The hydroalcoholic extract showed activity against all the evaluated strains, except for *E. coli* (14948). The values of inhibition halos varied between 13.7 ± 0.6 and 28.0 ± 1.0 mm. Conclusions: The analysis of the obtained results suggested that Barbatimão presents antimicrobial potential against bacteria and yeast.

Financial Support: FAPESP, CAPES and CNPq
Supervisor: Prof. Dr. Márcio L. A. e Silva

PN073-CYTOTOXIC ACTIVITY OF *DIDEMNUM PSAMMATODES*

RENATA TAKEARA (PG)[1]; PAULA CHRISTINE JIMENEZ (PG)[2]; CLÁUDIA PESSOA (PQ)[2]; MANOEL ODORICO DE MORAES (PQ)[2]; JOÃO LUIS CALLEGARI LOPES (PQ)[1]; NORBERTO PEPORINE LOPES (PQ)[1]; LETÍCIA VERAS COSTA-LOTUFO (PQ)[2]

[1] Departamento de Física e Química, FCFRP/USP; [2] Departamento de Fisiologia e Farmacologia, FM/UFC

Depsipeptide B obtained from marine ascidian was the first marine natural product to reach human clinical trials as an anticancer agent, increasing the attention to this class of marine organisms. The methanolic extract from *Didemnum psammatodes*, collected in Icapui. was fractionated by chromatographic techniques and afforded 2'-deoxyuridine, 2'-deoxyinosine, 2'-deoxyguanosine, thymidine, cholesterol, stigmasterol and b-sitosterol. These compounds were identified by spectroscopic methods and gas chromatography comparing the obtained data with those of the literature and standards. The methanolic extract showed a strong inhibition of the sea urchin egg cell cycle during both phases examined, with an IC_{50} of 120.1 µg/mL for first cleavage and 231.8 µg/mL for blastula. 2'-deoxyuridine was active at a concentration of 100 µg/mL presenting 63.9% of normal cells for first cleavage and 69.3% of normal cells for blastula. 2'-deoxyguanosine was active at same concentration presenting 40.6% of normal cells for first cleavage and 38.3% of normal cells for blastula.

Financial Support: FAPESP
Supervisor: Prof. Dr. João Luis Callegari Lopes

PN074-PROFILE OF *MENTHA X VILLOSA* HUDSON OIL FROM NATAL – BRAZIL

ALAIZE DE PAIVA MARTINS(PQ)[1]; AFRÂNIO A. CRAVEIRO(PQ)[2]; MARIA IRACEMA L. MACHADO(PQ)[2]; TÚLIO FLÁVIO A. DE L. E MOURA(PQ)[1]

[1]Departamento. Farmácia – UFRN; [2]Padetec – UFC

The volatile compounds from the *Mentha x villosa* Hudson oil, commonly known as small leaved mint or creeping mint, were identified by GC/MS analysis. Fresh leaves were collected at the medicinal plant garden of the Cidade da Esperança in Natal RN, chopped and subjected to hydrodestilation using a Clevenger apparatus modified. The oil obtained (0,1%) was dried over anhydrous sodium sulfate and stored at 4ºC. The GC/MS analyses were carried out (in triplicate) at the Padetec laboratory. From the 25 compounds 13 are monoterpenes, 10 sesquiterpenes, 1 phenylpropanoide, and 1 ester. The main constituents are α-Pinene (0,67%), Sabinene (1,38%), β-Myrcene (2,05%), 2,6-Dimethyl-Heptanol-2 (0,57%), Limonene (2,60%), 1,8-Cineole (3,48%), T-Ocimene (2,10%), P-Cymenene (0,40%, Linalool (0,40%), Octanol-2-acetate (0,42%), Endo-borneol (0,37%), Thymol acetate (6,38%), Anethole (0,84%), Piperitenone oxide (35,35%) the major one, β-Elemene (1,21%), Piperitone (9,64%), T-Caryophyllene (3,36%), β-Cubebene (0,52%), α-Humulene (0,51%), δ-Cadinene (2,20%), ³-Muurolene (8,47%), Germacrene B (0,64%), ´-Cadinene (1,01%), Cubenol-1,10-di-epi (0,42%) and T-Muurolol (0,79%). The oil density was 0,9349 g/mL at 25ºC. Descritive statistics of the data, were calculated.

Supervisor: ALAIZE DE PAIVA MARTINS – Farmacêutica Departamento de Farmácia – UFRN - alaize@ufrnet.br

PN075-CONSTITUENTS OF BRAZILIAN *MIKANIA CORDIFOLIA* (L.F.) WILLD

CARLOS ALEXANDRE CAROLLO (PG)[1]; ARNILDO POTT (PQ)[2]; DIONÉIA CAMILO RODRIGUES DE OLIVEIRA (PQ)[1]

[1] Faculdade de Ciências Farmacêuticas de Ribeirão Preto; [2] Embrapa, MS, Brazil; *e-mail:* carollo@fcfrp.usp.br.

M. cordifolia is a widespread species, used in traditional medicine as anti-inflammatory and against snakebite and fever. The present work describes a phytochemical study of a Brazilian species. 2.100g of dried plant was percolated with ETOH 95% and this extract was partitioned in the fractions HX, DCM, ACOEt and n-butanol. The HX and DCM fractions were submitted to several purifications. From HX fraction were obtained β-amirin (1), α-amirin (2), taraxasteryl (3), pseudotaraxasteryl (4), β-amirin acetate (5), ±-amirin acetate (6), taraxasteryl acetate (7), pseudotaraxasteryl acetate (8), campesterol (9), stigmasterol (10) and β-sitosterol (11). From DCM fraction were isolated the melanfolides 3e (12), 3g (13) and 3f (14), which were previously isolated[1], 7-methoxylluteolin (15), stigmasterol-3-O-b-D-glucoside (16) and β–sitosterol-3-O-β-D-glucoside (17). The substances 1-11 were identified by NMR ^{1}H, ^{13}C and comparison whit authentic samples in GC; 12-17 by NMR ^{1}H, ^{13}C and HMQC. 8 and 15 are been described for the first time in the genus *Mikania* and 7, 15 and 16 for the first time in the *M. cordifolia*.

[1] Gutiérrez, *Phytochemistry*, 26, 2315-20, 1987.

Support: FAPESP; CNPq
Supervisor: Dionéia C. R. de Oliveira

PN076-ANTIMICROBIAL ACTIVITY OF GERMACRENE-D-1-HYDROPEROXIDE

LEANDRO N. FRANCESCATO(PG)[1]; SYDNEY H. ALVES(PQ)[1]; ADOLF NAHSTEDT(PQ)[2]; BERTA M. HEINZMANN(PQ)[1]

[1] Programa de Pós-Graduação em Ciências Farmacêuticas, CCS/UFSM; [2] Institut für Pharmazeutische Biologie und Phytochemie, Universität Münster, Germany

Introduction: Natural peroxides are usually sesquiterpene derivatives and show antimicrobial, antimalarial, antihelmintic and cytotoxic activities. Objective: This work describes the antimicrobial evaluation of germacrene-D-1-hydroperoxide (1) obtained by photooxidation of germacrene D. Methodology: The antimicrobial activity of 1 was determined by the microdilution method based on M27-A2/NCCLS and adapted to test bacterial strains. Concentrations between 0.025 and 5 mg/ml were assayed. The microorganisms tested were *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27850, *Saccharomices cerevisiae* ATCC 2601, *Staphylococcus aureus* ATCC 25923, *Candida tropicalis* and *Prototheca zoopfi* (clinical isolates). Results: 1 inhibited the growth of *S. cerevisiae* (MIC of 2.5 mg/ml). For *P. zoopfi* there was a partial inhibition of 80% and 50% (5 mg/ml and 2.5 mg/ml, respectively). For *C. tropicalis*, *E. coli*, *P. aeruginosa* e *S. aureus* no inhibition was observed (until 5 mg/ml). Conclusion: 1 showed antifungal activity against *S. cerevisae* and inhibited partially the growth of the algae *P. zoopfi*.

Financial Support: CNPq, FAPERGS, DAAD.
Advisor: Berta M. Heinzmann

PN077-DISSOLUTION STUDY OF DRY EXTRACT FROM *AESCULUS HIPPOCASTANUM* L.

JANINE DE SOUZA ALMEIDA (PG); RENAN ARAÚJO GÓIS (IC); TATIANE PEREIRA DE SOUZA (PQ); ERYVALDO SÓCRATES TABOSA DO EGITO (PQ); LUIZ ALBERTO LIRA SOARES (PQ).

Department of Pharmacy - Universidade Federal do Rio Grande do Norte

INTRODUCTION: *Aesculus hippocastanum* L. also known as horse chestnut is widely used by the pharmaceutical industry, and commercialized throughout Brazil due its effectiveness as vasodilator and anti-edema. OBJECTIVE: The aim of this study is the development of dissolution methodology for capsules containing dry extract from *A. hippocastanum* (ADE). METHOD: The solubility of the ADE was tested in different mediums [pure water, HCI 0.1 N, phosphate buffer (pH = 7,4) and mediums containing sodium lauryl sulfate (SLS) from 0.5 to 2.5 % (w/v)]. The release ADE from capsules (n = 6) was determinate in an apparatus according with the USP 25 specifications (using baskets, 37.5°C ± 0.5 and 100 rpm). The ADE concentrations were measured at each 5 min until 60 min, and the dissolved ADE was determinate by spectrophotometry at 267 nm. RESULTS: Higher solubility was observed when a SLS solution 1.0 % was used, and the pH of medium showed no interference on the solubility. At this condition the capsules containing ADE showed total dissolution at 15 min. CONCLUSION: Satisfactory condition for dissolution of dry extract from *A. hippocastanum* was achieved using a 1.0 % of sodium lauryl sulfate.

Supervisor: Luiz Alberto Lira Soares

PN078-NEW ISOLATED CONSTITUENTS FROM *MIKANIA GLOMERATA* SPRENG

SILVIO MIRÓ FRANCHI(PQ)[2]; RICHARD T. BROWN(PQ)[3]; MÁRCIA R. DUARTE(PQ)[1]; CID A. M. SANTOS(PQ)[1]

(1) Universidade Federal do Paraná; (2) Centro Universitário Positivo (UNICENP); (3) The University of Manchester

Mikania glomerata Sprengel is a native species from Brazilian Flora, belonging to Asteraceae family, known in the folk medicine as guaco. A morpho-anatomic study of the leaves, isolation and characterisation of chemical constituents and determination of anti-inflammatory and analgesic activity were done, using the crude hydro-alcoholic extract. The isolation of the constituents was made by fractionating the crude extract using column chromatography and purification techniques. The pharmacology assays were oriented by using general activity test and DL 50 determination, in mice. Three compounds were isolated and identified by spectroscopic methods: cumarin, 2-acyl-trans-cinnamic acid and 4-hydroxy-3,5-dimethylbenzaldehyde, also known as syringaldehyde. The pharmacology studies suggest that the crude extract shows low toxicity orally and intraperitonially, as well as antinociceptive and antiedematogenic activities, with potential antiinflammatory activity.

Financial support: Universidade Federal do Paraná
Supervisor: Cid Aimbiré de Moraes Santos

PN079-NATURAL SUBSTANCES WITH ANXIOLYTIC EFFECT

FERNANDO DE S. OLIVEIRA (PG), MARCELO D. DE MOURA (PG), JOSÉ MARIA BARBOSA-FILHO (PQ), REINALDO N. DE ALMEIDA (PQ)

Laboratório de Tecnologia Farmacêutica / Universidade Federal da Paraíba

Anxiety is today a brazilian and worldwide serious public health problem, which ignores social classes, religion and race. The discovery of new drugs with low cost, less aggressive collateral effects and efficacy in treatment of the anxiety is a permanent search for the scientific community. The objective of the present work was to review in literature about the application of natural products with anxiolytic effects. The focus was to capture information in a way to provide data for those who search about natural products related with this effect and also to promote a new survey. The key-word used was "anxiolytic" which was done in Biological Abstracts and NAPRALERT (trademark, Natural Products ALERT) databases. The scientific magazines referenced in this abstract were consulted. We observed that among 41 substances searched, there were 45 positive effects over anxiety. One of these effects was tested on human beings. The majority of the substances found belong to the class of alkaloid. We concluded that there is a small number of researches in this field, although there is a great variety of plants and micro-organisms in our planet.

Financial Support: CNPq
Supervisor: Reinaldo N. de Almeida

PN080-OPTIMIZATION OF TOTAL FLAVONOIDS ASSAY FOR AQUEOUS EXTRACTIVES FROM *BAUHINIA MONANDRA* K.

ANA JOSANE D. FERNANDES (PG)[1]; FABÍOLA P. DA COSTA (IC)[1]; ANDREZA KALINE SOARES DANTAS (IC)[1]; TATIANE P. DE SOUZA (PQ)[1]; ADRIANA A. DE RESENDE (PQ)[2]; LUIZ ALBERTO L. SOARES (PQ)[1]

[1]Department of Pharmacy-UFRN; [2]Department of Clinical Analysis-UFRN

INTRODUCTION: *Bauhinia monandra* ("pata-de-vaca") is widely used in the traditional medicine as hipoglicemiant. Although the active substances of this medicinal plant are not yet known, flavonoids can be used as chemical markers for quality control purposes. OBJECTIVE: The purpose of this study was the evaluation of the influence of reaction time and development of a flavonoid assay for *B. monandra* aqueous extracts. METHODOLOGY: The influence of the reaction time and concentration of $AlCl_3$ on method response was evaluated on aqueous extract (decoction 15% w/v; 15 min) through the central composite design, based in a factorial 2^2 ($AlCl_3$: 2.5% and 7.5%; time: 15 and 35 min). The absorbances were measured at 410 nm. RESULTS: The statistical analysis of the mathematical model demonstrated that it was able to explain more than 99% of the experimental variance (r^2= 0.9989), and the test-t for the coefficients demonstrated that only the terms related to the reaction time had been significant. CONCLUSION: The optimum conditions, choosing from response surface, were 1.5% (w/v) for $AlCl_3$ and 25 min. for reaction time.

Supervisor: LUIZ ALBERTO L. SOARES

PN081-THE METABOLITE PRODUCTION BY THE ENDOPHYTE *COLLETOTRICHUM GLOEOSPORIOIDES* IS INFLUENCED BY THE CARBON SOURCE

LAIANI FISCHER DE OLIVEIRA (IC)[1]; SURAIA SAID (PQ)[2]; MÔNICA TALLARICO PUPO (PQ)[2]

[(1)]FFCLRP-USP; [(2)]FCFRP-USP

Endophytes are a promising and under explored source of bioactive compounds and novel chemical entities. As part of our bioprospecting program on endophytes from Asteraceae, *Colletotrichum gloeosporioides* was isolated from the leaves of *Viguiera robusta*. The fungus was cultivated in a two-step culture using glucose as carbon source. The EtOAc extract obtained from the culture broth inhibited 50% the activity of the enzyme adenine phosphoribosyltranferase (APRT) from *Leishmania tarentolae*. Other three cultivation experiments were conducted using sucrose and glucose as carbon sources. The EtOAc extracts were analyzed through HPLC (reverse phase) and ^{1}H NMR spectra. The chemical profiles showed significant qualitative and quantitative differences in the produced metabolites, depending on the carbon source.

Financial support: Fapesp
Supervisor: Mônica Tallarico Pupo

PN082-SYNTHESIS AND BIOLOGICAL ACTIVITY OF A NEW PALLADIUM(II) COMPLEX WITH A SULFUR-CONTAINING AMINO ACID

LILIAN PATRICIA B. SABEH (IC)[1]; PEDRO P. CORBI (PG)[2]; FLÁVIA CAGNIN (IC)[2]; ANTONIO C. MASSABNI (PQ)[2]; CLAUDIO M. COSTA-NETO(PG)[1].

[1]Dep Bioq. Imunol. FMRP/USP, Ribeirão Preto; [2]Dep Quím. Geral Inorg. IQ/UNESP, Araraquara/SP

Introduction. Cisplatin is largely used in many human cancers. Since 1965, when its antiproliferative property was described, different research groups have been seeking for new biologically active metal complexes.
Objective. Analyze the cytotoxic activity of a new metal-amino acid complex.
Methodology. The complex was synthesized by the reaction of an alcoholic solution of Li_2PdCl_4 with one of the amino acid salt. The powder obtained was dissolved in PBS. HeLa cells were cultured at 37^{o}C with 5% of CO_2, using DMEM with FCS and gentamicin. HeLa cells were plated in a 48-wells tray, the complex or the vehicle were added and incubated for 48h. Inhibition of cell growth was assessed using a tetrazolium salt (MTT) colorimetric assay.
Results. The obtained data from dose-response curves show a potent cytotoxic effect of the complex, with IC50 at 2M.
Conclusions. About 70% of all compounds tested at the National Institute of Cancer-USA do not present any cytotoxic effect in mammalian cells. Thus, the potent cytotoxic effect of this new metal complex prompts us to perform further in vitro and in vivo antitumoral analysis.

Support: FAPESP
Supervisor: Claudio M. Costa-Neto

PN083-EVALUATION OF ACUTE ORAL TOXICITY OF FRUITS OF *DIMORPHANDRA MOLLIS* BENTH. (LEGUMINOSAE)

SILVIANE ZANNI HUBINGER(PQ)[2]; RAQUEL REGINA DUARTE MOREIRA(PQ)[2]; GEORGINO DE OLIVEIRA(PQ)[2]; VERA LUCIA BORGES ISAAC RANGEL(PQ)[1].

[2]Department of Medications; [2]Department of Natural Active Rudiments and Toxicology - Faculdade de Ciências Farmacêuticas - UNESP-Araraquara.

The plants have been a valious source of natural products to keeping the human health. The Brazilian flora is rich in species and the toxic activity of some plants is well reconized. Dimorphandra mollis, popularly known as "faveiro" is a common tree in the Brazilian cerrado. The fruit is used to treat ulcer due to presence of flavonoids (10-15%). In this work, three extractive partitions (ethanol, chloroform and hexane) of the drug were prepared. The extracts were administered in a 2000 mg/kg dose to each rat. Animals were observed during 14 days and sacrificed to morphometric analysis of vital organs. Comportamental alterations were observed to animals treated with chloroformic and ethanolic extracts. With the 5000 mg/kg dose to the same extracts were observed the lost of the danger sense when the rats were put on a platform with 1 m high during three minutes. The ethanolic extract showed effect more intense, but the effect of chloroformic extract was longer. It hasn't been observed significant alterations of the analyzed organs.

Supervisor: Raquel Regina Duarte Moreira

PN084-PHYTOCHEMICAL STUDY OF *ACRITOPAPPUS LONGIFOLIUS* (GARDNER) R. KING & H. ROBINSON.

DIONÉIA CAMILO RODRIGUES DE OLIVEIRA(PQ)[(1)]; EDUARDO HENCK MARTURANO(IC)[(1)]; FERNANDA PERES FERREIRA(IC)[(1)]; CARLOS ALEXANDRE CAROLLO(PG)[(1)]

(1)Departamento de Fisica e Química, Faculdade de Ciências Farmacêuticas de Ribeirão Preto - USP

Introduction
The plant *Acritopappus longifolius* belongs to family Asteraceae, tribe Eupatorieae and subtribe Ageratinae.
Objective
Isolation, purification and identification of chemical constituents of the plant *A. longifolius*.
Methodology
By maceration of the powdered plant, were obtained the methanolic and dichloromethanic extracts. The substances were isolated and purified by liquid-liquid extractions and various chromatographic methods and the structural identification by UV and IR spectroscopy, ^{1}H and ^{13}C NMR and MS.
Results
From the dichloromethanic extract were isolated a labdanic diterpene with skeleton not yet described in literature, and the stigmasterol-3-O-β-*D*-glycoside. From the methanolic extract were identified the amino acid *N*-methyl-4-hydroxy-*trans*-proline, rutin, another glycosylated flavonoid derived from quercetin and aglycones of flavonoids in mixture.
Conclusions
The identified substances match the phytochemical profile of the genus, such the labdanic diterpene. Substances that hadn't been described in the species until now were also found (flavonoids and saponin).

Financial Support: FAPESP, CAPES, CNPq
Supervisor: Dionéia Camilo Rodrigues de Oliveira

The authors did not follow the Scientific Committee's suggestion for an English language review

PN085-GENOTOXIC EFFECTS OF *SOLIDAGO MICROGLOSSA* EXTRACTS ON *ALLIUM CEPA* CELL CYCLE

MARGARETE DULCE BAGATINI (IC)[1]; SOLANGE BOSIO TEDESCO(PQ)[2]

[(1), (2)] Universidade Federal de Santa Maria

Introduction: Medicinal plants are used in alternative medicine as teas in Brazil. However, their abusive use may be harmful to human health. *Solidago microglossa* (Asteraceae) is a medicinal plant, known as erva-lanceta or Brazilian arnica, used for stomach disorders. Objective: Three populations of *S. microglossa* were collected in order to check the effects of aqueous extracts of erva-lanceta (from Rio Grande do Sul state, Brazil) on the cell cycle of *Allium cepa* (onion). Methodology: The extracts were prepared by using *in natura* leaves in infusion for five minutes, as used in alternative medicine and at 2, 3 and 4 times more concentrated: 3.5g/2L, 3.5g/L, 3.5g/1/2L and 3.5g/1/4L, respectively. We used 4 groups of 6 onion bulbs to root in water, 2 control bulbs remained in water, and the others were placed in extracts for 24 h. The root-tips were fixed and stained in order to count 6000 cells from each group and to calculate the mitotic index (MI). Results: Statistical difference between the control group and the one in the more concentrated extracts by the X^2 test at the 5% level was found. Conclusion: The analyses indicated cytotoxic activity of this species, displayed by the inhibition of the cell division of *Allium cepa*.

Financial support: CNPq - PIBIC
Supervisor: Solange B. Tedesco

PN086-EVALUATION OF THE GASTROINTESTINAL ACTIVITY OF *BAUHINIA FORFICATA* LINK.

JULIANA A. SEVERI(PG)[(1)]; MARCELO A. SILVA(PG)[(2)]; JULIANA S. A. SUMITANI(IC)[(2)]; HÉRIDA R. N. SALGADO(PQ)[(1)]; MARIA T. PEPATO(PQ)[(1)]; WAGNER VILEGAS(PQ)[(2)]; LOURDES C. DOS SANTOS(PQ)[(2)]

[(1)]FCF-UNESP; [(2)]IQ-UNESP.

Introduction:*Bauhinia forficata* Link.is the *Bauhinia* species most used as an anti-diabetic herbal remedy in Brazil. Objectives:To evaluate the intestinal motility and liquid absorption in the intestinal system of mice after administration of the MeOH extract from the leaves of *B. forficata*. Methodology:The study was made with groups of 10 animals, according JANSSEN & JAGENEAU (1957) and WONG & WAI (1981) methods. The distance traveled by the charcoal plug from the pylorus to the ceccum was determined and expressed as a percentage of the total length of the small intestine. Student's *t*-test was used to determine statistical significance ($P<0.05$). Results:The charcoal distance of control and leaves in treated groups were 51.2 and 47.4cm. The weights of intestines were 2.37 and 2.72g. Conclusions:The MeOH extract from the leaves of *B. forficata* extracts did not show significant activity on the propulsive movement of intestinal contents in mice amongst control and treated groups. No significant differences between intestine weights of control and treated group were observed. This result may have implications on the bioabsorption of this herbal drug.

Financial Support: FAPESP
Supervisor: Wagner Vilegas

PN087-THE TOXIC PROPERTIES OF ABORTIVE PLANT EXTRACTS

ADRIANA JANUÁRIO (PQ)[1], CARLA ROBERTA SALATA (IC) [1], SARAZETI IZÍDIA VAZ PEREIRA (IC) [2], SUZELEI DE CASTRO FRANÇA (PQ) [2] , ANA HELENA JANUÁRIO (PQ) [2].

[1] Centro Universitário Claretiano, Batatais, São Paulo, Brasil,[2] Universidade de Ribeirão Preto-UNAERP, Ribeirão Preto, São Paulo, Brasil

Even it is forbidden, the pregnancy interruption has been an important birth-rate control method for thousands of people in Latin America. This pattern stimulates the search of clandestine abortificent habits, increasing the risk of dangerous and potentially lethal interventions. It is considered that one million of clandestine abortions happen every year among Brazilian people. Approximately 250.000 women are hospitalized every year in health public hospitals because of incited abortions. The aim of this work was to evaluate the toxic potential of aqueous extracts of the *Punica granatum* and *Datura suaveolens*. For that, *Lactuca sativa* seed growth and germination inhibition bioassays were made, as well as toxicity bioassay using *Dugesia gonocephala.* The results obtained show us that aqueous extracts of the *Punica granatum* and *Datura suaveolens* inhibited the *Lactuca sativa* seed growth and germination in a dependent dose way and that they incited the *Dugesia gonocephala* mortality, suggesting that these extracts may perform cytotoxic activities or cell growth difficulty, which could be harmful to the embryonic development.

Supervisor do trabalho: Ms. Adriana Januário

PN088-ANTIMICROBIAL ACTIVITY AND CONSTITUENTS OF *XYRIS PTERYGOBLEPHARA*

KELLER GUILHERME GUIMARÃES (PG)*, CLAITON PIRES VENTURA (PQ)*, BETÂNIA BARROS COTA (PQ)*; ALAÍDE BRAGA DE OLIVEIRA (PQ)*; FERNÃO CASTRO BRAGA (PQ)*.

*Laboratório de Fitoquímica, Faculdade de Farmácia, Universidade Federal de minas Gerais.

Several *Xyris* species are found in the Serra do Cipó region (MG), being popularly named "sempre-vivas". Some are collected for ornamental purposes and for medicinal uses, to treat eczemas and dermatitis. The chemistry of *Xyris* is poorly studied as are its biological activities. The aim of this work was to investigate the antimicrobial activity and chemical composition of *X. pterygoblephara.* The ethanol extract of *X. pterygoblephara* aerial parts (EXP) was assayed by the agar diffusion method and direct bioautography on silica gel plates against standardized microorganism strains. EXP was active against *Micrococcus luteus, Staphylococcus aureus*, *Aspergillus niger* and *Fusarium oxysporum*. It was fractionated by two differents mathods. A portion of EXP was dissolved in MeOH/H_2O (1:1) and sequentially partitioned with *n*-hexane, DCM and EtOAc. A triterpenoid was obtained from the *n*-hexane fraction. In the second method, EXP was directly extracted with DCM, resulting in the isolation of an aromatic derivative. Structural elucidation of these compounds is being undertaken.

Financial support: CNPq
Supervisor: Fernão Castro Braga

PN089-ANTIMICROBIAL ACTIVITY FROM *DRECHSLERA SP.*, AN ENDOPHYTIC FUNGUS FROM *VIGUIERA ROBUSTA* (ASTERACEAE)

DANIELA PAULA REGO BONOMO (IC); MÔNICA TALLARICO PUPO (PQ)

FCFRP-USP

Endophytes are a promising source of novel bioactive natural products. In our bioprospecting program on endophytes from Asteraceae, *Drechslera sp*. was isolated from the leaves of *Viguiera robusta*. The fungus was cultivated in a two step fermentative process (rich medium, 48h, 30ºC, 120 rev/min, followed by poor media, 144h, 30ºC, 120 rev/min), yielding an EtOAc extract from the culture broth. The EtOAc extract was assayed against *Staphylococcus aureus* (ATCC 25923), *Candida albicans* (ATCC 1023), *Escherichia coli* (ATCC 25922) and *Pseudomonas aeruginosa* (ATCC 27853) by agar diffusion method. The fungus was also cultivated in solid rice medium, yielding a MeOH extract, which was active against *Micrococcus luteus* (ATTC 9341) by bioautography method. The results showed that *Drechslera sp.* was able to produce active compounds when cultivated in both liquid and solid media. The fractioning of MeOH extract has been monitored by antimicrobial assays, affording more purified active fractions. Therefore, *Drechslera sp.* is a promising source of antimicrobial compounds.

Financial support: Fapesp
Supervisor: Mônica Tallarico Pupo

PN090 - INHIBITORY EFFECT ON LEUKOCYTE MIGRATION PRODUCED BY ACETONIC EXTRACT (AC) FROM *ANACARDIUM OCCIDENTALE* (CAJUEIRO) ANACARDIACEAE

DAVID DO CARMO MALVAR(IC)[(1)]; WELLINGTON DA SILVA CÔRTES(PQ)[(1)]; HIGOR FRUTUOSO LANDIM(PQ)[(2)]; FÁBIO FAGUNDES DA ROCHA(PQ)[(2)]; ELSON ALVES COSTA(PQ)[(3)]; GERALDO VIEIRA JUNIOR(PQ)[(3)]; LÉCIA GARCIA MATOS(PG)[(3)]; MARIA APARECIDA MEDEIROS MACIEL(PQ)[(4)]; TERESA NEUMA DE CASTRO DANTAS(PQ)[(4)]; CAMILA DE SOUZA SILVA(IC)[(4)]; FREDERICO ARGOLLO VANDERLINDE(PQ)[(1)]

[(1)]UFRuralRJ; [(2)]UBM; [(3)]UFG; [(4)]UFRN

Acetonic extract (AE 0.1-1g kg^{-1},*p.o.*) obtained from *Anacardium occidentale* (cajueiro) barks produced antinociceptive effects in abdominal constriction and formalin (2^{nd} phase) tests, and also inhibited croton oil oedema formation. AE was ineffective in hot plate test (SPMB-Manaus 2004 p.163). To evaluate the influence on leukocyte migration after oral administration of AE (1g kg^{-1}), the inflammatory model of carrageenin-induced pleurisy was assessed. The results demonstrated that, comparatively to vehicle group (6.4±0.3 leukocytes x 10^6), AE and positive control dexamethasone (2mg kg^{-1}) produced a significant reduction of leukocyte migration (36.6±3.7% and 50.9±4.2% respectively). These results indicated the involvement of anti-inflammatory mechanisms in the AE-induced antioedematogenic and antinociception effects and may account for the popular use of *A. occidentale* in pain and inflammatory diseases.

Financial Support: CNPq
Supervisor: Frederico Argollo Vanderlinde

PN091-CHARACTERIZATION OF PUNICA GRANATUM LEAVES

MARIANNE NEVES DOS ANJOS (IC)[(1)]; SILMARA GARCIA DANTAS (IC)[(1)], ALAIZE PAIVA MARTINS (PG)[1]

Universidade Federal do Rio Grande do Norte[1] - Gen. Gustavo Cordeiro de Faria St; s/n. Petrópolis - Natal/RN - 59010-180

Punica granatum L. belongs to Punicaceae family and is a little fructiferous tree with ornamental and pharmacological application. The aim of this work was to analyze microscopic, macroscopic and organoleptic characteristics of *Punica granatum* leaves, in order to supply information to the pharmacognostical identification of this medicinal plant. The samples used in this study were collected in Natal/RN, Brazil, and microscopic analysis was made with powder obtained from dry leaves, which were grinded and sieved in a 40 mm sieve. Slides were also prepared with cuts of fresh material. Organoleptic analysis revealed aromatic leaves with consistence of paper, bitter and astringent taste, smooth and glabrous surface. Macroscopic analysis revealed elliptic blade, acute base, pinatt venation and entire but slightly sinuous margin. Its short petiole posses stipule and there is no axillary bud. In microscopy, it was observed a large number of unicellular and non-glandular trichomes, numerous prismatic crystals and druses. It was also observed upper and lower epidermis and vascular bundle. This work made possible the recognition of characteristics which are relevant to the diagnosis of the specie.

Supervisor: Maria Cleide Ribeiro Dantas Carvalho(PQ)[1]

PPN092 - ESSENTIAL OIL ANALYSIS AND BIOLOGICAL STUDY OF *ACHILLEA MILLEFOLIUM* EXTRACTS

CHRISTIAN BOLLER (PG)[(1)]; JOCELINE FRANCO (PG) [(1)]; CRISTIANE BAGGIO (PG) [(1)]; MARIA CONSUELO DE ANDRADE MARQUES (PQ) [(1)]; TOMOE NAKASHIMA (PQ) [(1)]

[(1)]Universidade Federal do Paraná

Achillea millefolium L., Asteraceae, is a herbal plant native of Europe and Asia. Preview researches have shown that aqueous extract of *Achillea millefolium* reduces the activity of the enzyme H^+/K^+. The aims of this work were the evaluation of hydroalcoholic extracts of *Achillea millefolium* on the H^+/K^+ATPase activity and analysis of the essential oil obtained by steam destillation. The essential oil extraction was accomplished in two stages, and resulted in an essential oil of dark blue color and strong characteristic scent, varying its concentration from 0,6 to 0,2 mL%. It presented, by CG/MS analysis, azulene (10 %), 1,8-cineol (8,20 %), caryophyllene (8,0 %) as majority components. Phytochemical analysis revealed the presence of steroids and/or triterpenes, condensed and hydrolysable tannins, flavonoids, fixed acids and aminogroups. In relation to the ATPasic activity, three hydroalcoholic extracts were prepared (EH90, EH70 and EH50), using aerial parts of *Achillea millefolium*. The EH70 showed as more active and was submitted to liquid/liquid extration, from which five different samples were obtained. All of them were tested and the chloroformic fraction showed the best activity. This fraction did not show any of the previous metabolities and, after hydrolysis, it was observed the presence of aminogroups, suggesting the presence of amide like compounds.

Supervisor: Profª Drª Tomoe Nakashima

PN093-INVESTIGATION OF *ALOE BARBADENSIS MILLER* BIOLOGICAL ACTIVITY AND TUMOR GROWTH INTERFERENCE IN RATS

GIULIANO KENRO ALVES DE CAMPOS(IC)[(1)]; CARLOS DE ALMEIDA BARBOSA(IC)[(2)]; CLAUDIA CONSUELO DO CARMO OTA(PQ) [(2)]

Toho Laboratório Industrial[(1)]; Universidade Tuiuti do Paraná[(2)]

Introduction: *Aloe*'s compounds include complex polysaccharides with imunostimulant activity that had shown efficiency in experiments with different ills (Kemp, 1989). Objetive: This experiment intend to investigate therapeutical effects of oral administration of different *Aloe barbadensis* Miller extracts at tumor reduction in rats. Methodology: Experiment with 80 male adult Wistar rats inoculated subcutaneously with Walker 256 tumor cells investigate the therapeutical effects of oral administration of different extracts from *Aloe barbadensis* M. For different study subjects, the mucilaginous portion and the green portion of extracts from *Aloe barbadensis* M. with concentrations at 74,3 mg/dL and 59,9 mg/dL respectively were administrated daily throughout ten days since third day from inoculation. The animals were sacrificed between the 14th and 16th days. *Ex vivo* samples were taken for gravimetry and spectrometry. Results: The tumor growth in the treated subjects are 5% less than in non-treated subjects. Conclusions: There are tumor growth and cachexia interferences with oral administration of *Aloe barbadensis* M. extracts.

Financial Support: Toho Laboratório Industrial
Supervisor: Claudia Consuelo do Carmo Ota

PN094 - BIOLOGICAL ACTIVITY OF TRADITIONALLY PREPARED HERBAL INFUSIONS ON ORAL MICROBIOTA STRAINS

AMIM KHALIL (IC)[1]; EMMANUEL SANTOS SOUZA (IC)[1]; OMAR ARAFAT KDUDSI KHALIL (PQ)[1]; LUÍS FERNANDO LANDUCCI (PQ)[1]; ELERSON GAETTI-JARDIM JÚNIOR (PQ)[2]

[1]Centro Universitário de Rio Preto (UNIRP), São José do Rio Preto-SP, Brazil
[2]Universidade Estadual Paulista (UNESP), Araçatuba-SP, Brazil

Introduction: Oral diseases, such as dental caries and periodontal disease, affect millions of Brazilians. Various synthetic products are used as treatment for dental caries, but recent attempt has been conducted to search for natural products due to their decreased side effects. Objective: The purpose of this study was to identify Brazilian plants with antimicrobial activities on oral pathogens *S. mutans* and *F. nucleatum*. Materials and Methods: Antimicrobial activity of the aqueous extracts of eleven plants was evaluated by paper disc method. *S. mutans* (ATCC 35688 and ATCC 1910) and *F. nucleatum* (ATCC 10953 and ATCC 25556) were strains used. All infusions were prepared at the same concentration. Results: extract of *P. cattleianum* inhibited all strains tested. Conclusion: These results confirm that traditional herbal remedies could be employed as potential natural antibacterial agents for preventing dental caries and periodontitis.

Financial Support: UNIRP and UNESP
Supervisor: Omar Arafat Kdudsi Khalil

The authors did not follow the modifications suggested by the Scientific Committee

PN095 - PROBABLE CORRELATION BETWEEN ANTIOXIDANT AND ANTICANCER ACTIVITIES OF NATURAL ANTIOXIDANTS

ANTONIO, MARIA EMMA CONTIN OLIVEIRA (PG); SANTOS, CID AIMBIRÉ MORAES DOS (PQ); SATO, MAYUMI ELIZA OTSUKA (PQ)

Department of Pharmacy, UFPR

Cancer is a generic term for a variety of malignant neoplasms, due to unknown and probable multiple causes, arising in all tissues composed of potencially, and resulting in adverse effects on the host through invasive growth and metastases. The oxidative hypothesis of carcinogenesis claims that many carcinogens in such varied processes as chemical and radiation injury, oxygen and other gaseosus toxicity, cellular aging, microbial killing by phagocytic cells, inflamatory damage, tumor destruction by macrophages, and others, can generate free radicals that damage cells, setting these cells to malignant changes, causing mutations and by stimulating cell division. Antioxidants play an important role in inhibiting and scavenging radicals, thus providing protection to humans against infections and degenerative diseases. The aim of this work was to review the scientific literature about natural antioxidant, searching for relationships which are able to justify the fact that they shall be promising anti-cancer agents. Herbal plants that possess flavonoids and phenolic compounds with antioxidant activities and antimutagenic properties were analized as well as the influence of enviromental factors, diet, age and of several types of carcinogens, establishing their proper interference in the action of oxidant carcinogens.

Supervisor: Mayumi Eliza Otsuka Sato

The authors did not follow the modifications suggested by the Scientific Committee

PN096-EFFECTS OF TREATMENT WITH EXTRACT OF *ERYTHRINA FALCATA* B.*(*EHE) ON GENE EXPRESSION IN THE RAT BRAIN SUBMITTED TO ELEVATED PLUS MAZE (EPM).

DANIELA RODRIGUES DE OLIVEIRA(IC)[(1)]; JANETE MARIA CERUTTI(PQ)[(2)] SUZETE MARIA CERUTTI(PQ) [(1)].

[(1)] PROPEP, USF
[(2)] UNIFESP

Introduction: The formation of long-term memory (LTM) requires gene expression. The transcription factor cAMP response element binding protein (CREB) and GAP-43 play a fundamental role in molecular mechanisms underlying LTM. Objective: Examine differential expression gene CREB and GAP-43 in rats using real time RT-PCR in brains after 8 or 21 days treatment with EHE and submitted to EPM test. Methods: Rats, Wistar, males, adults were assigned in 8 groups (n=10), according (i) drugs: EHE 0,25g/Kg and 0,5g/Kg, Control Tween 80-12% and Diazepam 4mg/Kg; and (ii) treatment. The rats were decapitated 3 hours after behavioral test for analysis gene expression. Results: The EPM results showed prolongation of transfer latency all groups received EHE and Diazepam compared to Tween group ($p<0.05$). The mRNA expression these data led us to assume that these genes were less expressed in rats brains treated for 8 days ($p<0.05$), and more expressed at rats received EHE for 21days.Conclusion: Differential gene expression is decreased in rats brains with spatial memory impairments. Additionally, suggest that different mechanisms are involved in the LTM.

Financial Support: FAPESP, PROBAIC/USF
Supervisor: Suzete Maria Cerutti

The authors did not follow the Scientific Committee's suggestion for an English language review

PN097-SPECIES OF OLACACEAE FAMILY USED IN BRAZILIAN FOLK MEDICINE AND THEIR CHEMICAL PROFILE.

ANA VALÉRIA DE MELLO CRUZ (PG)[1]; MARIA AUXILIADORA COELHO KAPLAN (PQ)[1]

1. Núcleo de Pesquisa em Produtos Naturais, NPPN, UFRJ, Rio de Janeiro, Brasil.

Introduction:The Olacaceae family comprises about 25 genera and 250 species distributed mainly in the tropics and subtropics, whose habit ranges from shrubs to trees, with some lianas and parasitic species. The chemical profile consistes of free long chain fatty acids, which are widely found in the family; triterpenoids; alkaloids and essential oils. In Brazil, they are used in folk medicine mainly in the north and northeast regions. Objective: A survey was performed to find out the medicinal use of plants from Olacaceae family in Brazil and their phytochemical feature. Methodology: Data on the occurrences of secondary metabolites in the family as well ethnobotanical data were collected from specialized literature. Results: Species of the genera *Ximenia* are used for diarrhea, menorrhagia, hemorrhoids and as diuretic. The genera is rich in essential fatty acids and has varying levels of unsaturated higher fatty acids as eicosatrienoic, erucic and nervonic acids. It has also saponins, cyanogenic glycosides, flavonoids and tannins. The root bark of *Ptychopetalum olacoides* Benthan known as "Muira Puama" or Marapuma is used popularly to treat asthenia, sexual impotency, central nervous system disorders, paralysis, chronic reumatism and gastrointestinal disorders. The plant is rich in free fatty acid as behenic, arachidic and melissic acids. Conclusion: Although the family has few species in Brazil known as medicinal, they are a rich source of secondary metabolites.

Financial support: CAPES
Supervisor: Maria Auxiliadora Coelho Kaplan

PN098 - APPROACH TO THE SYNTHESIS OF NIAZIMIN A

PATRICIA RIGLOSKI MENEZES (PG)(1); GUILHERME SASSAKI (PQ)(2); RICHARD T. BROWN (PQ)(3); CID AIMBIRÉ M. SANTOS (PQ)(1)

(1) Programa de Pós-Graduação em Ciências Farmacêuticas, UFPR; (2) Departamento de Bioquímica, UFPR;
(3) Chemistry Department, The University of Manchester, UK.

INTRODUCTION: Substances with acyl radicals have frequently been isolated from plants and most of them present biological activities of interest to the pharmaceutical industry. Niazimin A is a carbamate glycoside isolated from leaves of *Moringa oleifera* Lam. (Moringaceae). Biological assays show that the intravenous administration of niazimin A (3mg/kg) reduces the arterial pressure about 35 to 40%. OBJECTIVE: Proposal of a synthetic route for obtaining niazimin A. METHODOLOGY: To obtain, separately, the glycone (4-acetyl-α-L-rhamnopiranosyde) and the aglycone (4-hidroxybenzyluretane) moieties, followed by a glycosilation reaction. RESULTS: The aglycone was obtained from 4-methoxyaniline in two steps. The glycone presents one acetyl group at C4, as in niazimin A, and it has been synthesized through protection and deprotection reactions of the hydroxyl groups of L-rhamnose. The glycosilation will be achieved by a reaction catalysed with boron trifluoride. CONCLUSIONS: The approach presented seems to be efficient to the synthesis of niazimin A and it will be useful for obtaining analogous structures.

Supervisor: C.A.M. Santos
Financial support: Fundação Araucária/CAPES

PN099-CHROMATOGRAPHIC PROFILES AND *IN VIVO* ACTIVITY OF A PHTYTOPHRMACEUTICAL PRODUCT ON LIPID METABOLISM

YDIA MARIELLE VALADARES (PQ)(1), LEIDA MARIA BOTION(2), JÚLIO ANTÔNIO LOMBARDI(3) (PQ), ALAÍDE BRAGA DE OLIVEIRA(1) (PQ), FERNÃO CASTRO BRAGA(PQ)(1)

(1) Faculdade de Farmácia, UFMG
(2) Departamento de Fisiologia e Biofísica, ICB, UFMG
(3) Departamento de Botânica, ICB, UFMG

The herbal product Ierobina® is indicated for the treatment of dyspepsia. It is composed by the fluid extracts of *Jacaranda caroba, Remijia ferruginea, Solanum paniculatum* and *Erythraea centaurium*, species popularly used to treat gastro-intestinal disorders. The aim of this study was to obtain chromatographic profiles (HPLC and TLC) for reference samples of the four plant species and commercial extracts employed in Ierobina® formulation. The phytochemical composition of the samples was evaluated by TLC analysis, employing specific spray reagents for detection. The efficacy of the product on dyspepsia was assayed in rats fed with a high fat (HF) diet. Chromatographic and phytochemical analysis indicated similar profiles for the commercial extracts and the corresponding reference plant materials. Triacylglycerol (TAG)-rich lipoprotein uptake, estimated by measuring total lipoprotein lipase activity in epididymal adipose tissue, was accompanied by TAG increase in HF-fed rats, after Ierobina® administration, suggesting the efficacy of product on dyspepsia.

Financial support: CNPq
Supervisor: Fernão Castro Braga.

PN100-DERIVATIVES OF LAPACHOL SHOW SPASMOLYTIC EFFECT IN GUINEA-PIG ILEUM.

ROSIMEIRE FERREIRA DOS SANTOS (PG)[1]; FABIANA ANDRADE CAVALCANTE (PG)[1,2]; MARCOS ANTONIO ALVES MEDEIROS (PG)[1]; SILVIA SIQUEIRA (IC)[1]; RITA DE CÁSSIA MENESES OLIVEIRA, (PG)[1,3]; CELSO DE AMORIM CAMARA (PQ)[1]; TICIANO PEREIRA BARBOSA, (PG) [1]; BAGNÓLIA ARAÚJO SILVA (PQ)[1,4]

[1]LTF/UFPB; [2]FSO/CCBi/UFAL;[3]DBF/CCS/UFPI; [4]DCF/UFPB

Introduction: lapachol, α- and β-lapachones have shown some biological actions, amongst them the spasmolytic. Aim: investigate spasmolytic actions of derivatives of lapachol: nor-lapachone (I), α (II) - and β (III) -nor-lapachone and hidroxihidro-nor-lapachol (IV) on guinea-pig ileum. Methods: the tissues were suspended in a organ bath containing Krebs solution at 37 °C Isometric and isotonic contractions were monitored. Results: I, II, III and IV relaxed significantly the guinea-pig ileum pre-contracted by KCl 40 mM (EC_{50}=2.6±0.8, 1.6±0.3, 0.8±0.1 and 6.9±2.0x10^{-5}M, respectively), histamine 1 μM (EC_{50}=2.7(0.1, 1.2(0.3, 1.2(0.1 and 3.2(0.8x10-5M, respectively) and ACh 1 (M (EC50=2.4(1.0, 8.8(1.2, 4.5(0.2 and 2.1(0.7x10-5M, respectively).Only II and III inhibited the phasic contractions induced by ACh 1 (M (IC50=1.2(0.2x10-4 and 2.7(0.1x10-5M) and histamine 1 (M (IC50=9.8(2.9 and 3.1±0.6x10^{-5}M, respectively).Conclusion: I, II, III and IV showed non-selective spasmolytic activity in guinea-pig ileum. These results are inedited.

Financial support: CAPES; CNPq.
Supervisor: Bagnólia Araújo Silva.

PN101 - PREPARATION OF FORMULATION AND STUDY ACTIVITY ANTIINFLAMMATORY OF *SHINUS TEREBENTIFOLIUS,* RADDY IN THE ROUTINE OF MATERNIDADE ESCOLA JANUÁRIO CICCO, UFRN

VERÔNICA DA SILVA LOPES (PG)*,**; TEREZA NEUMA DE CASTRO DANTAS (PQ)**; EVERLANE FERREIRA MOURA(PQ)**; ZÉLIA MARIA SILVA ASSIS (PG)*; IAPERI ARAÚJO (PQ)*;VANUZIA GALDINO DE SOUZA (IC)*.

*Maternidade Escola Januário Cicco (MEJC), UFRN veronicalopes@ufrnet.br
** Depto. Química, UFRN)

This paper has the aim the preparer of formulation of identifying clinical action of anti-inflammatory, analgesic and cicatrizing effects of an aqueous extract of the steam bark of *Shinus terebentifolius*, Raddy (AEST). Clinical evaluation of AEST was performed to 423 patients with skin lesions (SL, caused by injury and disease) and mucous lesions (ML, vulva and uterus erosion). The patients were randomly separated in two groups, e.g. A (GA, with 363 adult persons) and B (60, allopathic medication) and were attended at the MEJC. AEST (6% = 0, 24% principle active) yields an emulsion preparation that were prescribed to GA to treat and cure SL and ML. The whole period of treatment ranged from 3 to 20 days, depending of each inflammation process. The safe use of AEST was proved by the reductions of the characteristic lesions symptoms growing to the total lesions cure, without any single registration of side effects or adverse reactions.

Supervisor: Tereza Neuma de Castro Danta

The authors did not follow the Scientific Committee's suggestion for an English language review

PN102-SHORT-TIME EVALUATION OF HYPOLIPEMIC EFFECTS OF *TAMARINDUS INDICA* (TI) ON HYPERCHOLESTEROLEMIC HAMSTERS

PATRICIA VIDOTTI GOMES PASCHOARELLI (IC); FLÁVIA MARTINELLO (PG); SHEILA MARIA SOARES (PG); JOÃO JOSÉ FRANCO (TC); SÉRGIO AKIRA UYEMURA (PQ).

FCFRP-USP - DACTB

High consumption of fruits and vegetables like TI may reduce significantly cardiovascular diseases risk factors, including hypercholesterolemia. This study was addressed to compare the prevention and treatment of hypolipemic effects of TI and to observe how long it takes to return to basal levels after discontinuing the treatment with TI. In a group, the TI treatment was done after hypercholesterolemia development (G1). In another one, hamsters were fed simultaneously with atherogenic diet and TI (G2) for the same period of time, and after interruption of the treatment with TI, the lipidic profile was monitored for 60 days. During treatment, G2 showed a 38.6% and 41.8% reduction on total cholesterol and non-HDL cholesterol levels *versus* 25.14% and 28.9% in G1, respectively. The triglycerides (TG) levels presented the highest reduction percentual in both groups. Fifteen days after stopping the treatment with TI, cholesterol levels returned to control levels, however TG levels were monitored for 60 days and did not return to control levels. These evidences indicate a high potential of TI extract activity against the risk of the development of atherosclerosis.

Financial Support: CNPq
Supervisor: Prof. Dr. Sérgio Akira Uyem

PN103-GLANDS IN THE BRAZILIAN SPECIES OF *INDIGOFERA* L. (LEGUMINOSAE)

FLÁVIA S. MARQUIAFÁVEL (IC)[1]; DANIELA P. MORAES (IC)[1]; GISELLE M. C. CANAVACI (IC)[1,2]; SIMONE P. TEIXEIRA (PQ)[1]

[(1)] FCFRP/USP; [(2)] Centro Universitário Barão de Mauá.

Introduction. *Indigofera* is a well-known genus because of its great amount of species and the pharmacological properties its representatives bear. Objective. The current work deals with distribution, structure and histochemistry of the glands found in only two out of the nearly 13 Brazilian species – *I. microcarpa* and *I. sabulicola*. Methods. Flowers, leaves and fruits have been examined with SEM and sectioned for the building of histological slides. Results. Three types of glands have been found: isodiametric head and short peduncle – occurs on leaves, sepals and fruits in both species, as well as standards in *I. sabulicola*; cylindrical head and short peduncle – sepals of *I. microcarpa*; isodiametric head and long peduncle – bracteoles of *I. sabulicola.* Glands produce only oil in flowers and fruits, but oil, alkaloids and phenolic compounds in leaves. Conclusions. Distribution and gland types differ between species and these can be used as diagnostic characters. Phytochemical studies that have identified new arilbenzofuranes and nitrogen compounds in *I. microcarpa* and the presence of different types of secretory structures suggest that such species may have pharmacological potential.

Financial Support: Fapesp
Supervisor: Simone P. Teixeira

PN104-ANGIOTENSIN CONVERTING ENZYME INHIBITORY ACTIVITY OF *MANSOA HIRSUTA* FRACTIONS

PRISCILLA RODRIGUES VALADARES CAMPANA (IC)[1]; DENISE COUTINHO ENDRINGER (PG)[1]; ALAÍDE BRAGA DE OLIVEIRA (PQ)[1]; FERNÃO CASTRO BRAGA (PQ)[1]

[1]Departamento de Produtos Farmacêuticos, Faculdade de Farmácia - UFMG

Mansoa hirsuta DC (Bignoniaceae) is a plant species found in the Atlantic Forest. A literature search indicated no ethnopharmacological use described for the plant. In a previous work, we have reported the *in vitro* angiotensin converting enzyme (ACE) inhibitory activity for the ethanol extract from *M. hirsuta* leaves (EMH), which showed 54% inhibition at the concentration of 0.33 mg/ml, indicating a potential anti-hypertensive effect. The aim of the present study was to fractionate EMH, guided by the ACE inhibition colorimetric assay. The ethanol extract of *M. hirsuta* leaves, obtained by percolation, was submitted to chromatography on a silica gel column. Fractions eluted with EtOAc:MeOH (95:5) and EtOAc:MeOH (90:10) showed ACE inhibition rates of 96 ± 11% and 94 ± 12%, respectively, in the concentration of 0.10 mg/ml. RP-HPLC and TLC analysis of these fractions suggested they are composed by polyphenols, especially proanthocyanidins. Isolation of the ACE inhibiting compounds from these fractions is being undertaken, employing size exclusion chromatography.

Suporte Financeiro: CNPq / PRPq UFMG
Supervisor: Fernão Castro Braga

PN105-STRUCTURE AND CYTOCHEMISTRY OF POLLEN GRAINS IN BRAZIL WOOD

FLÁVIA R. DE PAOLI (IC) (1); SIMONE P. TEIXEIRA (PQ) (1)

(1) FCFRP-USP

Introduction. Air pollution directly affects both the surface and protean content of pollen grains and strengthens its allergenic potential. Objective. In the current work the surface and cytochemistry of brazil wood pollen grains (*Caesalpinia echinata*, Leguminosae) have been studied. The allergenic potential within polluted areas has been evaluated once this species has been growingly used in urban tree planting. Methods. Pollen grains of cultivated individuals from polluted areas (São Paulo) have been compared to the grains of cultivated individuals from non-polluted areas (Estação Ecológica de Moji-Guaçu) by making use of SEM and light microscopy. Results. Releasing pollen grains present a reticulate surface with granules inside lumen, two gamete cells and one vegetative cell with protean grains. Oilplasts have been found only throughout the vegetative cell cytoplasm. Walls have lipid drops, protean granules and are PAS-positive. Conclusions. Air pollution does not affect the shape, surface or protean content of the brazil wood pollen grain. This suggests that such structure does not accumulate pollutant particles so heavily. Current results may enhance the planting of brazil wood in parks, public squares and boulevards so that the growing decline of its populations in Brazil can be minimized.

Financial Support: Fapesp
Supervisor: Simone P. Teixeira

PN106-STUDIES ON THE CYTOTOXICITY OF CUCURBITACINS ISOLATED FROM *CAYAPONIA RACEMOSA* (CUCURBITACEAE)

IVANA NOGUEIRA FERNANDES DANTAS (IC)[1]; GARDENIA CARMEN GADELHA MILITÃO (PG)[1]; DAVINA CAMELO CHAVES (PG)[2]; FRANCISCO JOSÉ QUEIROZ MONTE (PQ)[2]; CLÁUDIA Ó PESSOA (PQ)[1]; MANOEL ODORICO DE MORAES (PQ)[1]; LETÍCIA VERAS COSTA-LOTUFO (PQ)[1]

[1] Department of Pharmacology and Physiology; [2] Department of Inorganic and Organic Chemistry - UFC

Introduction: The search for stronger and more specific anticancer agents led us to study natural products from plants with cytotoxic potential. Objective: We report the cytotoxic activity of Curcubitacin P (CP), deacetylpicracin and the yet non-identified CRF-PIR-5 isolated from *C. racemosa*. Methodology: The compounds were tested in the brine shrimp lethality assay, sea urchin development assay, hemolytic assay and MTT assay using tumor cell lines. Results: CP showed the highest toxicity on MTT and brine shrimp lethality assay, with IC_{50} of 0.80, 0.64, 0.99, 0.96 and 1.71µg/mL for CEM, HL-60, B-16, HCT-8 and MCF-7 respectively and LD_{50} of 29.6µg/mL. CRF-PIR-5 presented a moderate activity with IC_{50} of 1.89, 1.35, 2.22, 1.68 and 3.58µg/mL for CEM, HL-60, B-16, HCT-8 and MCF-7, respectively, and LD_{50} of 38.79µg/mL. None of them presented activity on sea urchin assay and hemolytic assay. Conclusion: The compounds tested present potent citotoxicity against tumor cells.

Financial Support: CNPq, InCb, FINEP, BNB, FUNDECI
Supervisor: LETÍCIA VERAS COSTA-LOTUFO

PN107-INVESTIGATION OF THE USE OF MEDICINAL PLANTS IN BARRETOS – SP, BRAZIL

GILMARCIO ZIMMERMANN MARTINS (PQ)[1]; CAROLINE ZANARDO MOUSSA (IC)[1]; JOSEGUERI CELERI (IC)[1]; JULIANA NUNES MACHADO (IC)[1]; SAMANTHA MALUMBRES DE SALLES (IC)[1]; MARIA AUXILIADORA BRIGLIADOR CONTI (PQ)[1];

[1] Faculdades Unificadas da Fundação Educacional de Barretos - UniFEB

Due to the lower utilization of herbs in the beginnings of the XX century and the secondary effects of the artificial drugs, ecologists are stimulating a return to the "natural", and because of this, it's happening a fantastic renascence of herbs utilization. This research had the objective to make a qualitative and quantitative survey of the most used plants with medicinal finalities by people from Barretos – SP and evaluate the use, described by people with scientific information. The valuation was accomplished, in which can be told more than one plant. Among of the mentioned plants, the tree most used were: *Melissa officinalis*, *Coleus barbatus* and *Mentha piperita*, with 22 %, 18 % and 15 % of frequency, correspondingly. Other mentioned plants were: *Chinopodium ambrosioides*, *Mikania glomerata*, *Matricaria chamomilla* and *Baccharis gaudichaudiana*, all between 7 to 9 % of frequency. The use as therapy, of medicinal plants, coincides with proved scientific effects in specific literature. It was possible to observe, that old people prefer to use medicinal plants as therapy, which are collected in the backyard of their houses, and the youngers don't know this kind of treatment.

Financial Support: UniFEB
Coordinators: Gilmarcio Zimmermann Martins and Maria Auxiliadora Brigliador Conti

PN108-PHYTOCHEMICAL AND ANTIOXIDANT EVALUATION OF LEAVES FROM EXOTIC FRUITS (ACEROLA, CAMU-CAMU AND STAR FRUIT)

RICARDO MATHIAS ORLANDO(PQ)[1]; DAMIANI GISLAINE GOMES GRITTI(IC) [1]; ROSEMARY MATIAS(PQ)[1]; FRANCISCO ANTÔNIO ZPEVACK(PQ) [1]; ERIC DE SOUZA GIL(PQ) [1].

[1]Universidade para o Desenvolvimento do Estado e da Região do Pantanal

The use of natural products in cosmetic formulations has been gained more acceptation by consumers and professionals of the cosmetology area. Because of that, fruits deserve great attention owing to their inherent potential as font of useful ingredients for cosmetic proposals like vitamins, oligoelements and phytoantioxidants. However, the research is generally restricted on the fruits, and has few attention over the other parts of the fruit bearing plants. At the present work extracts of leaves from the three fruit bearing recognized by the high level of ascorbic acid in their fruits were analyzed by classic and chromatographic methods,: camu-camu (*Myrciaria dubia*), acerola (*Malphigia glabra L*) and star fruit (*Averrhoa bilimbi*). Among the assays done, can be outstanding the assessment of antioxidant activity by DPPH and classical phytochemistry methods and ascorbic acid by HPLC. The phytochemistry analysis found the presence of saponins in the three samples and flavonoids in the camu-camu sample. It was determined the high antioxidant activity in the three samples, and the camu-camu with the highest of three what could be match with the presence of flavonoids. The HPLC analysis determinate the presence of vitamin C in the three samples analyzed with levels of 13,07; 2,82 and 5,06 mg/ g of leave to acerola, camu-camu and star fruit respectively.

Finalcial Support: UNIDERP
Supervisor: Eric de Souza Gil.

The authors did not follow the Scientific Committee's suggestion for an English language review

PN109-EVALUATION OF ANTINOCICEPTIVE AND ANTIINFLAMMATORY ACTIVITIES OF *DAVILLA RUGOSA* (DILLENIACEAE)

JUSSARA JÚLIA CAMPOS (PG)[1];ADOLFO DE OLIVEIRA AZEVEDO (PQ)[2,3]; IGOR DIMITRI GAMA DUARTE (PQ)[2]; ANDRÉIA DE CASTRO PERES (PQ)[2]; ROSE LISIEUX JÁCOME (PQ)[1];FERNÃO CASTRO BRAGA(PQ)[1]

1. Departamento de Produtos Farmacêuticos FAFAR-UFMG; 2. Departamento de Farmacologia ICB-UFMG; 3. Departamento de Farmacologia UNILAVRAS (Centro Universitário de Lavras)

Davilla rugosa (Dilleniaceae) is a species found in the Brazilian cerrado, popularly used to treat inflammatory disorders. The ethanol extract from *D. rugosa* leaves (EDR) was studied for its antinociceptive (licking time in the formalin test) and antiinflammatory (carrageenan-induced paw edema model) effect in Swiss mice. EDR was active in the second phase of the nociceptive reaction, presenting a ID_{50} = 188mg/kg. The development of acute induced paw edema was also reduced ($p < 0.05$) by EDR at the same dose. These results corroborate the popular use of the plant as an antiinflammatory agent. The fractionation of EDR is in course, aiming to isolate the compound(s) responsible for the observed activity.

Financial support: CNPQ
Supervisor: Fernão Castro Braga

PN110-EVALUATION OF THE SEASONAL ROLE ON THE CHROMATOGRAPHIC PROFILE OF THE ESSENTIAL OIL OBTAINED BY GAS CHROMATOGRAPHY FROM A CULTIVATED POPULATION OF *BACCHARIS DRACUNCULIFOLIA*

JOÃO PAULO BARRETO DE SOUSA (PG)[1]; RENATA FABIANE JORGE (IC)[1]; ADEMAR ALVES DA SILVA FILHO (PG)[1]; CARMEN LUCIA QUEIROGA (PQ)[3] ADEMILSON ESPENCER EGEA SOARES (PQ)[2]; PEDRO MELILLO DE MAGALHÃES (PQ)[3]; JAIRO KENUPP BASTOS (PQ)[1].

(1) Faculdade de Ciências Farmacêuticas de Ribeirão Preto – USP; (2) Faculdade de Medicina de Ribeirão Preto – USP; (3) Centro de Pesquisas Químicas, Biológicas e Agrícolas - UNICAMP.

Introduction: *Baccharis dracunculifolia* is a shrub from central parts of Brazil. The leaves of this plant bear glandular trychomes and secretory glands which produce and store essential oil.
Objectives: To quantify the major constituents of the samples of *B. dracunculifolia* collected along of one year.
Methods: The essential oil was obtained by steam distillation of the aerial parts of the plant, using a Clevenger apparatus. The oil was extracted by partition using hexane containing the internal standard peperonal. The hexane fraction was analyzed by GC using detection by FID.
Results: Fifteen compounds were quantified and it was observed qualitative and quantitative variation of the essential oil components along of the year.
Conclusion: It was observed that between the months of August and December, *B. dracunculifolia* displayed the best qualitative and quantitative profile of the essential oil.

Financial support: FAPESP
Advisor: Prof. Dr. Jairo Kenupp Bastos

PN111-COMPLEMENT ACTIVITY IN HYPERCHOLESTEROLEMIC HAMSTERS: EFECT OF THE EXTRACT OF TAMARIND (*TAMARINDUS INDICA L.*) PULP.

ANA PAULA LANDI-LIBRANDI (PG) [(1*)]; TAÍS NADER CHRYSOSTOMO (IC) [(1*)].; SÉRGIO AKIRA UYEMURA(PQ) [(1**)]; ANA ISABEL DE ASSIS PANDOCHI (PQ) [(1**)].

[(1)] University of São Paulo, College of Pharmaceutical Sciences of Ribeirão Preto, *Department of Physics and Chemistry** Department of Clinical, Toxicological and Bromatological Analysis.

Complement system (CS) is involved in atherogenesis. We evaluated CS in hamsters receiving diet rich in cholesterol (CD), and the effect of the extract of tamarind pulp (ExT) in this condition. Methods: Hamsters were treated with ExT plus normal diet (ND) or CD for 15-60 days. Other groups included treatment with ND or CD. Classical pathway (CP) of CS was evaluated by hemolytic assay. ExT action on CS was investigated also *in vitro.* Results: hamsters receiving CD showed increased lytic activity after 30 and 45 days. CD associated to ExT leads to CP activity similar to that of ND group. *In vitro* ExT reduced alternative pathway (AP). Reduction or increase of CP occurred depending of ExT concentration. Conclusions: CD increases CS activity, ExT abolishes this effect, and affects CS *in vitro*. This ExT activity may be related to its action reducing cholesterol levels in hypercholesterolemic hamsters (Martinello et al, submitted). ExT can be a tool to study the role of CS in atherosclerosis.

Finacial Support: CNPq
Supervisor: Ana Isabel de Assis Pandochi

PN112-SEASONAL DETERMINATION OF THE BETULINIC ACID IN LEAVES FROM *EUGENIA FLORIDA* BY GC.

BRUNO M. LESSA[1] (IC), CARINE F. SILVEIRA[1](IC), LEANDRO S. BARBOSA[1] (IC), CAROLINA S. LUNA[2] (IC), ANTÔNIO C. SIANI[1] (PG), ANA C.F. AMARAL[1] (PG), ALAÍDE S. BARRETO*[1] (PG).

[1] Farmanguinhos – *FIOCRUZ.*

Betulinic acid (1) has been identified in several plants including *E. florida*. This compound has been shown inhibiting virus HIV and melanoma-specific cytotoxic in both cell culture: *in vitro* and *in vivo* studies. Although 1 has been a promising new lead compound for use against human melanoma, its isolation is based in extraction of the bark and cerne the plants, synthetic methods and biotransformations. Therefore are necessary the discovery of new natural sources with high yields of 1. Considering the high yields of 1 found in the leaves during the study in *E. florida* and its importance, we decide to determine the seasonal concentration (2002 august – 2003 july). For this purpose an GC method has been developed for the detection and quantification of 1 in material. GC quantification was carried out using a Agilent 6890-N equipped with a HP-5 column (30m; carrier gas He, flow of 2mL/min; split (1:20). The programme was: 70^0C - 5^0C/min - 290^0C with 5min isothermal. The highest concentration was found in octobre (33.21%), whilst smaller in january (11.59%). The study has demonstrated that the leaves of *E. florida* is an important source of 1.

Financial Support: Farmanguinhos.
Supervisor: Alaíde S. Barreto

PN113-MANUFACTURE AND EVALUATION OF THE DRIED EXTRACTS OF *UNCARIA TOMENTOSA* BY SPRAY DRIER

LIDIA M. C. MATOS (IC); ROGÉRIO R. ALMEIDA (IC); MARCELO ANTUNES(IC); EDÉLCIO ARAÚJO JR (IC); VANESSA PROFÍCIO (IC); RUBIANA F. BOTT (PG)*; CLÁUDIA R. F. SOUZA (PG)*; WANDERLEY P. OLIVEIRA (PQ)*

*Departamento de Ciências Farmacêuticas (FCFRP-USP)

INTRODUCTION:Nowadays, several studies have been carried out aiming to the production of dried extracts of medicinal plants such as *Uncaria tomentosa* (cat's claw). Besides being an expensive method, spray drier has the advantage of producing powdered and uniform particles with low degradation of active substances. OBJECTIVES/METHODS: The aim of this study was to evaluate the rate of this degradation using 5 groups of extracts (crude extract without drying aids and extract plus starck or maltodextrin 5 and 20% in 2 different inlet air temperature (100 and 150ºC). The particle size distribution, the total polyphenol content and the process efficiency were measured. RESULTS: In both temperatures, starck 20% was the best drying aid and at 100ºC the rate of degradation was smaller. CONCLUSION: Spray-drier was effective in the production of the dried extract of cat's claw.
Palavras-chave: spray-drier, Uncaria

Supervisor: Wanderley Pereira de Oliveira.

PN114-CELLULAR PROFILE OF MYOSIN-V IMMUNOREACTIVE MYENTERIC NEURONS FROM THE ILEUM OF DIABETIC RATS AFTER GLUTAMINE SUPPLEMENTATION

ELEANDRO APARECIDO TRONCHINI(PG)[1]; IVAN DOMICIO DA SILVA SOUZA(IC)[1]; ENILZA MARIA ESPREAFICO(PQ)[2]; ROBERTO BARBOSA BAZOTTE(PQ)[1]; JACQUELINE NELISIS ZANONI(PQ)[1].

[1] Universidade Estadual de Maringá. [2] Universidade de São Paulo.

Introduction: The neuronal degeneration in the diabetes mellitus (DM) is due to the high level of glucose that increases the levels of free radicals. The supplementation with glutamine is likely to present some neuroprotector effect, since it is the precursor of glutathione. The glutathione is an endogenous antioxidant that in the presence of the oxidative stress related to the DM shows reduced levels. Aims: Assess the effect of the glutamine supplementation on the neuronal profile of myosin-V immunoreactive myenteric neurons in the ileum of diabetic rats. Methods: Twenty rats, aged 90 days, divided into three groups: normoglicemic (N), diabetic (D), and diabetic treated with glutamine (DG). 1% of glutamine was added to the chow. The animals were sacrificed at 210 of age. We employed the immunohistochemical technique myosin-V to stain the neurons. 500 neurons were measured per group. Results: The mean cellular profile (mm^2) for groups N, D and DG was 273.5 ± 17.17, 286.6 ± 11.59 and 285.5 ± 21.16, respectively ($p>0.05$). Conclusion: Glutamine treatment did not change the cellular profile of the myosin-V myenteric neurons.

Supervisor: Jacqueline Nelisis Zanoni.

PN115 - FRACTIONATION AND BIOLOGICAL ACTIVITY OF ESCARGOT MUCUS

LARISSA DEADAME DE FIGUEIREDO, [1](IC); ANA ISABEL DE ASSIS-PANDOCHI,[1](PQ); IEDA RAZABONI PRADO, [1](PQ); ANA ELISA CALEIRO SEIXAS AZZOLINI,[1](PQ); MARIA DE FÁTIMA MARTINS,[2](PQ); PEDRO PACHECO,[2](PQ); CAREM GLEDES VARGAS-RECHIA, [1](PQ)

[1]DFQ - FCFRP-USP - Ribeirão Preto-SP, [2]Heliciário Experimental FMVZ-USP - Pirassununga-SP.

The mucus of the escargot *A. monochromatica* has been studied for the treatment of injuries. This work evaluated the activity of this mucus on complement (CS) and characterized compounds responsible for this activity. The water soluble fraction (FSM) contained protein (90 %) and neutral sugar (5 %). The monosaccharidic composition was determined by GC, showing Rha:Man:Xyl in the molar ratio of 2.4:1.2:1.0. FSM was fractionated in DEAE-Cellulose in phosphate buffer and NaCl gradient (0.1-1.0M). Six fractions (M1-M6) were isolated. The effect of FSM and M1 to M6 on CS activity was evaluated *in vitro* using human serum. The FSM, M1, M2 and M4 inhibited (10, 18, 25 and 55 % respectively) CS classical pathway (CP) and presented 21, 13 and 15 µg/mL of total sugar, and 43, 17,and 28 µg/mL of proteins, respectively. These results indicated that FSM and its fractions interact with the CS, and its healing properties may involve CS.

Financial Support: CNPq/PIBIC
Supervisor: Carem Vargas-Rechia

PM116-CONVECTIVE DRYING OF *CISSAMPELOS SYMPODIALIS* EICHL. FRESH LEAVES

CLÉSIA OLIVEIRA PACHÚ (PG)[1]; OSVALDO SOARES DA SILVA (PQ)[1]

[1]Federal University of Campina Grande -UFCG

The plant. *Cissampelos sympodialis* Eichl., popularly known as “milona”, grows in Northeast Brazil and widely used for the treatment of asthma, bronchitis and rheumatism, among other inflammatory diseases. In the present work it was investigated the drying kinetics of fresh leaves of “milona” as first step to the development of phytotherapic products. The solid pharmaceutical forms are adequate storing and conserving active ingredients. Nevertheless, few data are found in the literature including the effects of temperature and moisture content on the physical properties of the leaves. In this work the influence of temperature and moisture content on the size, density and bed porosity of *Cissampelos sympodialis* leaves was studied along the thin layer convective drying. The leaves were dried in a convective dryer with 1.5 m/s air velocity at temperatures 40 °C, 50 °C and 60 °C. The drying kinetics was modeled by means of a Fickian model, considering five terms of the mathematical series. The found results showed a good agreement between the fitted curves and the experimental data. These results demonstrate that convective drying “milona” leaves is an efficient technique to obtain dried extracts.

Financial Support: SEBRAE/PB and BNB
Advisor: Odelsia Leonor Sánchez de Alsina

PN117-INHIBITION OF THE ACTIVITIES OF TRIPSIN, BHTL AND *BOTHROPS NEWVIED PAULOENSIS* SNAKE VENOM BY THE FRACTIONS OF THE AQUEOUS EXTRACT FROM SEEDS OF *SCHIZOLOBIUM PARAHYBA*

MIRIAN MACHADO MENDES(PG)[1]; AMÉLIA HAMAGUCHI(PQ)[1]; MARIA INÊS HOMSI-BRANDEBURGO(PQ) [1] ; FABIO OLIVEIRA(PQ)[2]; VERIDIANA DE MELO RODRIGUES ÁVILA(PQ) [1].

[1] Instituto de Genética e Bioquímica– [2] Instituto de Ciências Biomédicas –Universidade Federal de Uberlândia

Introduction: The seeds of the Leguminosae family contain inhibitors proteins of proteases. Objective: This study reported the partial purification of a proteinase inhibitor (PI) of *S. parahyba* (Leguminosae) and inhibition of tripsin and BHTL (a new serine proteinase from *B. moojeni* snake venom) by your sub-fractions. Methodology: The seeds were grinded and mixed with water, the material was filtrated and fractionated by ammonium sulfate precipitation into three fractions. The fraction of 90% was purified by chromatography in Sephadex G-75 eluted with ammonium bicarbonate buffer 0.05 M pH 8,0. The subfractions were dialyzed. The sterasic activity on TAME was assayed with Tripsin and BHTL. The coagulant activity was assayed with crude venom of *B. neuwiedi pauloensis*. Results: Both activities were inhibited when carried out with the third subfraction at ratio 1:10 (enzyme: inhibitor, w/w). Conclusions: *S. parahyba* have important clinical implications against snakebite.

Financial support: CNPq and UFU
Supervisor: Veridiana de Melo Rodrigues

PN118-BROMELIA ANTIACANTHA RIPE FRUITS: INVESTIGATIONS ON CHEMICAL AND BIOACTIVITY PROFILE

VANESSA N.C.SANTOS (IC)[1]; RILTON A.FREITAS (PQ)[1]; FRANCISCO C.DESCHAMPS (PQ)[2]; MAIQUE W.BIAVATTI (PQ)[1]

1. Universidade do Vale do Itajaí (UNIVALI), Itajaí/SC, 2. Empresa de Pesquisa Agropecuária (EPAGRI), Itajaí/SC

Bromelia antiacantha fruits (popularly called Banana-do-mato) are used to treat cough also mouth and skin ulceration's and remains scientifically unexplored. Possible properties as antioxidative, cytotoxic, and the fruit profile were investigated in this work. The extract of Banana-do-mato was prepared boiling the ripe fruits with water, and freeze drying. Methanol extract (ripe fruits exhaustively macerated and dried in rotary evaporator) and soxhlet extraction with ether-toluene was also prepared.
The antioxidant potential was accessed *in vitro* by spectrophotometric reduction of DPPH and phosphomolibdenum complex, the cytotoxicity through *Artemia salina*. The phenolics (HPLC/PDA) and fatty acids (GC/FID) composition were also investigated. The antioxidant activity was not expressive, no activity detected under 5 mg/ml. No cytotoxic activity was observed under 500 ¼g/ml. LC fingerprint of phenolics and carotenoids was developed, showing presence of few flavonoids and carotenoids (lutein and b-carotene); the GC analysis of fatty acids indicated the presence of the palmitic and linoleic in equal amounts (30 % each), oleic 20%, α-linolenic 8%, among others.

Financial support: IFS

PN119-HISTOLOGICAL STUDY AND LEUCOCYTE COUNTS IN WISTAR RATS TREATED WITH AN AQUEOUS EXTRACT FROM SEEDS OF *SYZYGIUM CUMINI*

MARIA PAULA GAROFO PEIXOTO (PG)[(1)]; ÉRIKA VITALIANO GARCIA DA SILVA (PQ)[(2)]; AURO NOMIZO(PQ)[(3)]; SÉRGIO ZUCOLLOTO[(4),] LUÍS ALEXANDRE PEDRO DE FREITAS[(5)] (PQ)

(1), (2), (3), (5) FCFRP-USP; (4) FMRP-USP

Introduction: *Syzygium cumini* is largely used in tradicional medicine for its hypoglicemic properties. In order to achieve the phytoterapic medicine standard, studies regarded to both efficiency and safety are necessary. Many plants with antidiabetic properties are related to hepatotoxic effects. Objective: Histological and leukocytes counts in normal and alloxan-diabetic rats treated with *Syzygium cumini* aqueous extract. Materials and Methods: Normoglycemic rats were feed with 100, 200, 400 and 800 mg/kg/day while the diabetic animals were feed 200 mg/kg/day during 30 days. The total leukocytes counts were performed by microscopy using a Neubauer chamber. The histological analysis of liver, kidney and pancreas were carried out by microscopy using Rosenfeld and Hematoxylin-Eosin stainings. Results: No significant alterations were found in the total and differential blood leukocytes numbers and in the tissues and organs analyzed. Conclusion: The results indicate that aqueous extract from seeds of *Syzygium cumini* shows absence of cellular and tissue toxicity at the doses studied.

Financial Support: CNPq
Advisor: Luis Alexandre Pedro de Freitas

PN120-OPTIMIZATION OF VICENIN-2 EXTRACTION FROM *LYCHNOPHORA ERICOIDES* LEAVES USING FACTORIAL DESIGN.

ANDREA DINIZ (PG)[1]; NORBERTO PEPORINE LOPES (PQ)[2]; FABIO YAMASHITA (PQ)[1]

[1] Universidade Estadual de Londrina; [2]Faculdade de Ciências Farmacêuticas de Ribeirão Preto - USP

In order to improve the efficiency of extractive methods we need to study the influence of the many variables involved on the process. The aim of this work was to determine the best conditions to vicenin-2 extraction from *L. ericoides* leaves that were previously reduced in a knife mill. The extractive variables evaluated were maceration time, solvent and ratio plant:solvent and the response was vicenin-2 concentration per g of plant. A HPLC method was employed to quantify the flavonoid. A two-level factorial design with two repetitions at central point was employed and the levels were 24 (-), 48 (0) and 72 h (+) for maceration time, the alcoholic grade 40°(-), 60° (0) and 80°GL (+), and plant:solvent ratio were 1:3 (+), 1:2 (0) and 1:1 (-) w/v. The main effects and their interactions were calculated using the Experimental Design module of Statistica 5.0® software. The best conditions were plant:solvent ratio 1:3 and alcohol 40°GL providing a vicenin-2 concentration of 786±110 µg/g. Maceration time have no influence and was kept at 24 h and there was an negative interaction effect between alcoholic concentration and plant:solvent ratio.

Supervisor: Prof. Dr. Norberto Peporine Lopes

PN121-EXTRACT OF *MIKANIA GLOMERATA* INFLUENCED GENOTOXICITY INDUCED BY DOXORUBICIN WITHOUT ALTERS LIPID PEROXIDATION AND ANTIOXIDANTS LEVELS

CAMILA A DE PAULA(IC)[(1)]; MARIÂNGELA D DE MORAIS(IC)[(1)]; MURILO C S FERREIRA(IC)[(1)]; LÍLIAN C BARBOSA(PG)[(1)]; ALCEU A JORDÃO JR(PQ)[(2)]; HELIO VANNUCCHI(PQ)[(2)]; ANDRÉA DE O CECCHI(PQ)[(1)]

[(1)]University of Franca, Franca-SP, Brazil; [(2)]Nutrition Division, Faculty of Medicine, University of São Paulo, Ribeirão Preto-SP, Brazil

Introduction: *M. glomerata*, known as guaco, has been used in folk medicine probably due its antioxidant properties.
Objectives: The effects of extract of guaco (EX.G) against doxorubicin (DXR)-induced micronucleated polychromatic erythrocytes (MNPCEs) in Swiss mice and the liver contents of malondialdehyde, vitamin E and glutathione.
Methods: Mice were treated for 30 days with EX.G (0,035 mg coumarin/ml, drinking water), associated or not with antitumoral DXR (90 mg/kg bw, intraperitoneal), injected 24 h before analysing.
Results: EX.G significantly increased the frequency of MNPCEs induced by DXR. This increase was not accompanied by lipid peroxidation and antioxidants depletion.
Conclusions: Despite the presence of antioxidants in extract, adverse effect can be found, probably consequence of the interaction with other chemicals, and that this synergistic effect was not by causing oxidative stress.

Financial support: University of Franca
Supervisor: Andréa de Oliveira Cecchi

PN122-NEUROPHARMACOLOGICAL EFFECTS OF AQUEOSE EXTRACTS OF *LOPHANTHERA LACTENCENS* DUCKE

M. T. S. NETO (PG) [(1)]; J. C. FONTANELLA (PG)[(2)]; H.S. ABREU (PQ)[(3)];M. R. FERRAZ (PQ)[(2)]

[(2)]UERJ, Dep. Farmacologia e Psicobiologia
[(1)]UFRJ, Dep. Farmacologia Básica e Clínica.
[(3)]UFRRJ, Dep. Produtos Florestais.

Lophanthera lactencens (LL) has been used in treatment of malaria. In this study we evaluate the sedative-hypnotic and anticonvulsive activities of LL.
The peel of LL was dried, macerated and heated until ebullition. After cooling this aqueous extract (AE) was filtered and diluted in 5% and 10%. To evaluate the sedative-hypnotic effects of LL male mice was administered saline (controls, n=10), AE 10% (n=10) or AE 5% (n=10) after 60min Sodium Pentobarbital 40mg/Kg was administered i.p. and the sleep time was measured. Anticonvulsive activity of LL was availed by convulsion induced by picrotoxine. In this method, picrotoxine was administered i.p and the convulsion latency and the number of convulsions in 30 min was measured.
The sleep time was 48.2±10.8 min. in control group, 156±32.8* min in AE 5%, and 187.7±61.6* min in AE 10%. The number of convulsions was not altered by the treatment with AE5% or AE10%. The convulsion latency was enlarged from 25±0.49 in control to 20.7±0,7min in AE 5% and 23.3±3,07min in AE 10%. This result suggests that the AE of LL evoked dose dependent sedative effects and can protect against convulsion induced by picrotoxine.

Financial Support: FAPERJ
Supervisor: Dr. N.A. Pereira

PN123-EVALUATION ON AMAZONIAN MEDICINAL PLANTS: *VISMIA CAYENNENSIS*

DOMINIQUE FERNANDES DE MOURA (IC)[(1)]; JEFFERSON ROCHA DE A. SILVA (PQ)[(1)]; ANA CLAUDIA F. AMARAL (PQ)[(2)].

[(1)]Universidade Federal do Amazonas (UFAM); [(2)]Farmanguinhos/FIOCRUZ-RJ

Infections of protozoa of the genus *Leishmania* are a major health problem, with high endemicity in developing countries. According to etiological agent, the illness can come in different clinical forms: cutaneous, mucocutaneous or visceral. As part as of the attempts to discover a novel antileishmanial agents of plant origin, the barks of *Vismia cayennensis* were subjected to phytochemical investigation. The barks were extracted with ethanol 95%. This extract was submitted to HPLC/DAD analysis on a C-18 column with water (with 0.05% TFA):CH_3CN gradient. The chromatographic profile at 254 nm together with the individual UV spectra indicated the flavonoids as main constituents. The ethanolic extract, after evaporation, was suspended in EtOH/H_2O (7:3) and partitioned with hexane. This apolar fraction was active against leishmania and after the analysis by GC/MS showed the presence of: ethyl hexadecanoate (17.53%), ethyl oleate (5.61%), fridelin (45.38%), stigmasterol (50.29%) and sitosterol (49.71%). Further analysis may contribute to the search of natural agents against leishmaniasis.

Financial support: CNPq, PADCT, FAPEAM/AM
Supervisor: Jefferson Rocha de A. Silva

PN124-MICRONUCLEUS FREQUENCY INDUCED TO ACUTE, SUBACUTE AND CHRONIC TREATMENT WITH PROPOLIS EXTRACT (EPP-AF) TO BURN PATIENTS.

ALINE R. S. RODRIGUES(IC)[1] , JULIANA M. SENEDESE(IC)[1] , ANDRESA A. BERRETTA(PG)[2,3] , JULIANA M. MARCHETTI(PQ)[2], DENISE C. TAVARES(PQ)[1]

[(1)] Universidade Franca; [(2)]Faculdade Ciências Farmacêuticas Rib. Preto-USP; [(3)]Apis Flora Indl. Coml. Ltda., Brazil.

Introduction: Nowadays, we observed an increasing interest in natural products to topical application. Many kinds of some skin inflammatory diseases, burns and wound healing are being treated with propolis extract. Propolis is a resinous hive product collected by honeybees from various plant sources. Objective/methodology: The present work studied the genotoxic potential of gels with propolis standardized extract (EPP-AF) to use in burn patients, using micronucleus analyze (MN) in peripheral blood of wistar rats. The animals, after dorsal lesions, were studied with acute, subacute and chronic treatment, with gels containing different concentrations of propolis extract (1,2%, 2,4% and 3,6% w/v). Laminas of peripheral blood were done 24 hours, 7 days and 30 days after gels application into animal´s dorsal lesions. Results/Conclusion: Results obtained showed that animals treated with different concentrations of propolis didn't show any increase in MN´s frequency when compared to negative control or with gel without propolis in treatments studied.

Financial support: Apis Flora Ltda
Supervisor: Juliana M. Marchetti

PN125-ANTIDEPRESSANT PROPERTIES OF AQUEOSE EXTRACTS OF *LOPHANTHERA LACTESCENS* (DUCKE)

M. T. S. NETO (PG) [(1)]; J. C. FONTANELLA (PG)[(2)]; O.M.M.S. ALMEIDA (PQ)[(2)];M. R. FERRAZ (PQ)[(2)]

[(2)]UERJ, Dep. Farmacologia e Psicobiologia
[(1)]UFRJ, Dep. Farmacologia Básica e Clínica.

Lophanthera lactencens (LL) has been used in treatment of malaria. In this study we evaluate the antidepressant properties of LL. The tree stamp of LL was dried, macerated and heated until ebullition. After cooling this aqueous extract (AE) was filtered and diluted the 30%. To evaluate antidepressant effects of LL male rats was administered saline (controls, n=10), AE 30% (n=10) and amitriptyline 20 mg/Kg (AT) was administered v.o. and the immobility time was measured. Antidepressant activity of LL was availed by forced swimming test (Porsoult's test). The immobility time was 220.7±19.9 s in control group, 134.6±10.8* s in AT, and 172.7±16.4* s in AE. The immobility time was reduced by the treatment with AT. The treatment with AE 30% reduced the immobility time in a non significant way ($p < 0.056$). This result suggests that the AE 30% may have antidepressant properties.

Financial Support: FAPERJ
Supervisor: Dr. N.A. Pereira

The authors did not follow the Scientific Committee's suggestion for an English language review

PN126-INHIBITION OF BIOLOGICAL AND ENZYMATIC ACTIVITIES OF *BOTHROPS NEUWIEDI PAULOENSIS* SNAKE VENOMS BY *SCHIZOLOBIUM PARAHYBA* AQUEOUS EXTRACT.

LUIS HENRIQUE FERREIRA DO VALE (PG)[1]; MIRIAN MACHADO MENDES(PG)[1]; RENATA SANTOS RODRIGUES(PG)[1]; JOHARA BOLDRINI FRANÇA(IC)[1]; GUILHERME ROCHA LINO DE SOUZA(PG)[1]; AMÉLIA HAMAGUCHI(PQ)[1]; MARIA INÊS HOMSI BRANDEBURGO(PQ)[1]; VERIDIANA DE MELO RODRIGUES(PQ)[1].

1-Instituto de Genética e Bioquímica, Universidade Federal de Uberlândia.

Animal venoms are complex mixtures of enzymatic proteins including phospholipases A2 (PLA2) and others. Plant extracts are rich in pharmacologically active compounds and have been shown to antagonize the activity of some venoms. The aim of this work was study inhibition of biological and enzymatic activities of *Bothrops neuwiedi pauloensis* (Bnp) snake venoms by *Schizolobium parahyba* (SP) aqueous extract. For inhibition assays venom solutions were mixed with SP at room temperature immediately before the test.The extract was ineffective to inhibit the bactericidal activity of Bnp at 1: 50 ratio (Bnp:SP w/w), only Bnp venom was able to inhibit the activity. PLA2 activity was determined by the indirect hemolysis, the extract was able to neutralize 81% at 1:20 ratio (Bnp:SP w/w). These results suggest that compounds from this extract are able to interact with animal venoms and could be useful tools for the elucidation of the action mechanism of toxins.

Financial Support: CAPES and CNPq.
Supervisor: Veridiana de Melo Rodrigues

PN127-SUGAR CONTENT IN NECTAR FLOWERS OF ORANGE (CITRUS SINENSIS L. OSBECK) IN THE NORTH-WEST OF PARANÁ STATE

VALENTIM SALA JUNIOR[1], FRANCYELLE CRISTINE BULA[1], VALÉRIA RODRIGUES CELLOTO[1], JOSÉ EDUARDO GONÇALVES[2], REGINA APARECIDA CORREIA GONÇALVES[1], ARILDO JOSÉ BRAZ DE OLIVEIRA[1]

[1]Laboratório de Química Farmacêutica, Depto. de Farmácia e Farmacologia. Universidade Estadual de Maringá - Av. Colombo 5790, 87020-900, Maringá, PR, Brasil; [2] Centro Universitário de Maringá- CESUMAR. E-mail: sala_junior@hotmail.com

Honey from orange flowers is one of the most appreciate kind because its pleasant taste and medicinal proprieties. The nectar composition is very important not only for the honey quality, but also sugar concentrations which are related to pollinator type, flower anatomy, geographic conditions. These aspects make nectar chemical composition an important factor for the environmental impact studies. The aim of this study was to determine the total and individual nectar sugar concentration through spectrophotometry of the commercial orange plantation in Atalaia in the north-west of Paraná State. The total sugar concentration was 6,97 ± 1,47 mg/flower. It was also determined individual sugar concentrations (sucrose:glucose:fructose) using spectrophotometry being the relative sugars rates 1:7:23.These results indicate that hexose is dominant in these species that can interfere in pollinators sorts.

Financial Support: Fundação Araucária; CAPES
Advisor: Arildo J. B. Oliveira

PN128-ANTINOCICEPTIVE ACTIVITY FOR FLOWER METHANOLIC EXTRACT OF *ESTERHAZYA SPLENDIDA*

GLÁUCIA DE MELO REIS(IC)*; REGINA BRAGA DE MOURA(PG)**; ANAIZE BORGES HENRIQUES(PQ)**; MARIA APPARECIDA ESQUIBEL(PQ)**; PATRÍCIA DIAS FERNANDES(PQ)* AND MARIA ELINE MATHEUS(PQ)*.

* Departamento de Farmacologia Básica e Clínica, ICB, UFRJ.
**Laboratório de Fisiologia do Desenvolvimento Vegetal e Fitoquímica, IB, PBV, UFRJ

Esterhazya splendida (Es) can be found in “restingas”, in high altitude and also in rupestres’ Brazilian fields. This study evaluated the mechanisms involved in the antinociception of the Es. In the formalin test (2.5% 20 mL/paw), Es (100mg/kg, *p.o*) inhibited reactivity (re)of mice by 36,86% (52 ±0,77 sec) during phase 1 and by 22,03 % (90,83 ± 2,63 sec) in phase 2 of nociception, compared to the control group PBS (82,36±1,057 and 116,5±1,027 sec respectively). Indomethacin (10mg/kg, *p.o*), positive control to the phase 2, did not modify re in phase 1 (67,98±0,927 sec) and reduced by 48,63% (59,85 ± 0,961 sec) the re during phase 2. The fentanyl (300mg/kg, *s.c*) inhibited both phases (28,37±0,53 and 71,83 ± 0,83 sec). In the Tail Flick Test, Es amplified the re time to heat stimulus after 40 and 60 min (2,45±0,04 sec ; 3,16 ± 0,10 sec)respectively, compared to the control group (1,80 ± 0,05 sec; 1,79±0,04 sec). Naloxone (3mg/kg, *s*.c) inhibited this effect of Es. These results suggest an antinociceptive effect of Es with a possible opioid participation.

Financial support: Capes/FUJB

PN129-ANTIOXIDANT ISOFLAVONES FROM IN VITRO CULTURES OF *DIPTERYX ODORATA*

RENATA S FERNANDES (PG); MIRIAM V LOURENÇO(PQ), SUZELEI C FRANÇA(PQ), ROSEMEIRE CLR PIETRO (PQ), PATRICIA G ROBERTO(PQ), JOSÉ F LIMA (IC), SARAZETE IV PEREIRA(IC), ANA H JANUÁRIO (PQ)[1]

Biotecnologia - UNAERP- Ribeirão Preto-SP

Isoflavonoids, actives in the prevention of cancer, osteoporose and reduction of seric cholesterol level are oxigenated compounds of potential use as phytoestrogens and antioxidants against peroxidation of lipids and proteins. Cell cultures of *D. odorata* are valuable sources of isoflavones, allowing the continuous production of these compounds under controlled culture conditions. The antioxidant activity of *D.* odorata cell extracts and some of their constituents was investigated. Crude chloroform extracts from cell suspension cultures (C4), 7-hydroxy-4',6-dimethoxy-isoflavone (1) and 5',7-dihydroxy 4',6-dimethoxy-isoflavone (2) were evaluated for their ability as radical scavengers through the DPPH oxi-redox spectrometric assay. Obtained results showed that C4 and isoflavone 2 inhibited 70,72% and 59,54% of oxidant activity, respectively, while isoflavone 1 showed no significant antioxidant activity (1,09%). Antioxidant activity exhibited by Isoflavone 2 suggests that it depends on the pattern of substitution in the B ring, being the presence of a hydroxyl group in 5' position responsible for the increased activity.

Finnacial support: CAPES, CNPq, UNAERP
Supervisor: Ana H Januário

PN130-ANTIMICROBIAL ACTIVITY OF *BYRSONIMA* CRASSA NIEDENZU (IK)

Daniele Carvalho Michelin (PG)[(a)], Miriam Sannomiya(PQ)[(b)], Hérida Regina Nunes Salgado(PQ)[(a)], Wagner Vilegas(PQ)[(b)]

[a] Departamento de Fármacos e Medicamentos, FCF,– UNESP –Araraquara – SP – Brasil
[b] Departamento de Química Orgânica, Instituto de Química, UNESP – Araraquara – SP – Brasil

Introduction: *Byrsonima crassa* Niedenzu (IK) is a native specie from Brazil, which is popularly known as 'murici-cascudo' or 'murici-vermelho'. There are several properties attributed to *B. crassa* including indications as anti-emetic, diuretic, antiulcer, gastritis and diarrhoea. Objecitve: the aim of this work was to evaluate the antimicrobial activity of *B.crassa* extracts obtained from the leaves. Methodology: The extracts were obtained by maceration with methanol, methanol/water and EtOAc/H_2O. The antimicrobial activity was evaluated through agar diffusion method against *Bacillus subtilis*, *Bacillus cereus*, *Shigella*, *Sthaphylococcus epidermidis*, *Proteus mirabilis*, *Salmonella*, *Enterococcus faecalis* and *Candida albicans*. The determination of MIC was evaluated through the incorporation of extracts into broth culture media. Results: Our results indicate that EmeOH, EMeOH 80% and EmeOH/EtOAc were the most effective agents against the microbial species tested.

Financial support: CNPq and FAPESP – Brasil.
Supervisor: Hérida Regina Nunes Salgado

The authors did not follow the Scientific Committee's suggestion for an English language review

PN131-PHARMACOGNOSTIC STUDY OF THE BARKS OF STEM OF *ASPIDOSPERMA SUBINCANUM* MART.

CLEVIA FERREIRA DUARTE GARROTE[1] – PQ; JOSÉ REALINO DE PAULA[1] – PQ; MARIA TERESA FREITAS BARA[1] – PQ; IRANI FERNANDES CAMPOS[2] – PQ; LEONARDO GOMES DE SOUZA[1] – IC; ROBERTA CAMPOS LINO[1] – IC; RUBIA BARASUOL[1] – IC; ISABELA GOMES PEREIRA[1] – TFC; ENEIAS LEONARDO BORGES[1] – TFC.

1- Faculdade de Farmácia ; 2- Instituto de Ciências Biológicas – Universidade Federal de Goiás

Aspidosperma subuncanum Mart. barks are used in Goiás traditional medicine, as hypoglicemic and antihiperlipemic. However, no have cientific facts that confirm this effects and neither models of quality control in the species. The objective of this work is to obtain the models of the quality control. Two sample the plant, were collected in the Goiânia's botanic garden and achieved pharmacognostic study. The phitochemistry results was positive to alcaloids, steroids and triterpenoids, coumarins and resins. The microscopic analysis in the histologic cut showed the presence in the secretorys ducts with lipides, fiber, grain of starch and prismatic crystals. The tenor of total ashes was of 9,5% and humidity of 8,9%. The dates obtained, showed to be of value for the quality control of this herbal medicine.

Financial Support: Faculdade de Farmácia/UFG
Supervisor: Clévia Ferreira D. Garrote

The authors did not follow the modifications suggested by the Scientific Committee

PN132-ANTIBACTERIAL ACTIVITY OF ASTERACEAE EXTRACTS FROM DIAMANTINA

WILSON MUANIS GODINHO (IC)[(1)]; THAÍS NÉRI DOS REIS (IC)[(1)]; VÂNIA APARECIDA SÁ (IC)[(2)]; FERNANDO PETACCI (PQ)[(1)]; NAJEH MAISSAR KHALIL (PQ)[(1)]; PAULO HENRIQUE GRAZZIOTTI (PQ)[(2)]

[(1)] DFB; [(2)] DEF – Faculdades Federais Integradas de Diamantina[2]

Introduction: Asteraceae is the more representative botanical family among all in the "campos rupestres" in the Diamantina region. This family comprises approximately 23.000 species. Biological activities of this family are reported by several authors, including bactericidal activity. Objectives: The aim of this work was investigate the potential of eleven Asteraceae ethanolic extracts against *Escherichia coli*, *Staphylococcus aureus* and *Bacillus cereus*. Methods: Plants were collected in their blooming season and the extracts prepared with fresh leaves (ethanol 2 weeks). The dried extracts were impregnated in paper discs (500 µg/disc) and their in vitro antibacterial activity evaluated through the plate-well diffusion assay against the bacteria's cited above. The assays were performed in triplicate and results expressed as diameter of inhibition (mm). Results: *Argeratum fastigiatum* (0.9, 6.0, 13.1), *Lychnophora* sp (0.8, 10.8, 12.7) and *Mikania* sp (0.7, 5.7, 3.9) were the most actives extracts against *E. coli*, *S. aureus* and *B. cereus*, respectively. Conclusion: We report here a great potential of the studied plants in the discovery of new antibiotic.

Financial support: FAPEMIG
Supervisor: Fernando Petacci

The authors did not follow the Scientific Committee's suggestion for an English language review

PN133- HEPATOPROTECTIVE EFFECTS OF ZEDOARIA RHIZOMA ON ACETAMINOPHEN – INDUCED LIVER IN RATS.

MARGARIDA KUGA (PG) [1]; MARIA C. PETRELLIS (PG) [2]; GUSTAVO TEIXEIRA (PG) [1]; RICARDO POMBO (PG) [1]; ANTÔNIO C. PRIANTI (PG) [1]; FLÁVIO AIMBIRE (PQ)[1]; RODRIGO MARTINS (PQ)[1]; JOSÉ C. COGO (PQ)[1]; WELLINGTON RIBEIRO (PQ)[1].

[1]Department of Pharmacology, IP&D, Univap, S. J. dos Campos, SP, Brazil; gton@univap.br; [2]Cartesius Analytical Unit, Department of Pharmacology, ICB I, USP, São Paulo, Brazil.

Curcuma zedoaria (Cz) is used as a herbal medicine to promote blood circulation. From the experience of Chinese Medicine, it has been shown that the sesquiterpenes constituents from Cz exibited hepatoprotective activites. The aim of the present study was to investigate the hepatoprotective effects of cetonic extract of Cz on acute liver damage induced by acetaminohen (APAP) in rats. Cz (300mg/kg) was administrated p.o to experimental animals model followed by a single dose of APAP (650mg/kg). Hepatoprotective activity was monitored by estimating sAST, sALT, sALP levels and histopathological changes of liver sections for different treatment groups. Our results indicated that Cz at a dose 300mg/kg exibited a significant protective ($p<0.001$) by lowering the serum levels of sAST, sALT and sALP induced by high doses of APAP. In addition histopathological observation supported the results obtained from enzyme assay and confirmed that Cz at a dose (300mg/kg) reversed an extent hepatic lesion produced by APAP.

Finnancial Support: FVE.

PN134-*IN VITRO* EFFECT OF *TAMARINDUS INDICA* L. EXTRACTS ON CARIOGENIC FACTORS OF *STREPTOCOCCUS MUTANS*.

MATEUS FREIRE LEITE(PG)[(1)]; VIVIANE K. S. KAWATA(IC)[(1,3)]; ANA C. M. POLIZELLO(PQ)[(1)]; DENISE P. S. LEITÃO(PQ)[(1)]; SÉRGIO A. UYEMURA(PQ) [(2)]; AUGUSTO CÉSAR C. SPADARO(PQ)[(1)].

[(1)]Depto Física e Química, FCFRP/ USP; [(2)]Depto Análises Clínicas, FCFRP/USP; [(3)]FORP/USP.

S. mutans triggers dental caries establishment in part, by synthesis of organic acids which demineralize dental enamel. In this work, we have evaluated the effect of ethanolic (EE), hidroethanolic (EH) and aquous (EA) crude extracts of *T. indica* (Ti) as well as Hexanic (FH), Cloroformic (FC), Ethyl acetate (FAE) and aquous (FA) fractions from the EE on the acidogenic potencial of *S. mutans*. The inhibitory effect on bacterial acid production was evaluated through the potentiometric measurement of pH from bacterial suspensions treated with serial concentrations of EE, EH and EA (2.0–12.0mg/mL), and fractions from the EE of Ti (0.05-1.50mg/mL), incubated with excess of glucose at 37ºC for 1h. For the antibacterial activity assay, the MIC and MBC were determined. The inhibitory effect values obtained for the bacterial acid production were 4.04–39.15% for EH, zero–82.77% for EE and zero–85.32% for FH. FC and FAE stimulated the acid production. EA and FA did not display significant inhibitory effect. The MIC value for FH was 120mg/mL, at this concentration the extract was also bactericidal. The others extracts did not display any bactericidal effect at the concentrations tested herein. Only EE and FH displayed significant activity upon the evaluated parameters suggesting the presence of apolar active components in these fractions.

Supervisor: Augusto César C. Spadaro.

PN135 - PHENOLIC COMPOUNDS IN EXTRACTS OF LEAVES OF *CASEARIA SYLVESTRIS* SW. OBTAINED BY TWO DIFFERENT METHODS: PERCOLATING AND DYNAMIC MACERATION

ARAUJO, ROBERTA B (IC).; LAROCI, ELOISE A. F.(IC); ANDREO FILHO, NEWTON (PQ); SILVA, MAGALI G.(PQ)

University. of Sorocaba

Introduction: *Casearia sylvestris* Sw. is known as guaçatonga, and is used against simple herpes, gastric ulcer, etc. Phenolic compounds are used as its markers, being that its incomes in extracts depending on the employed processes. Objective: determination of the parameters of quality control of vegetable extracts and of the amount of phenolic compounds in fluid extracts of the leaves of *C. sylvestris* Sw. Methodology: the extracts were prepared by percolating or dynamic maceration, both with ethanol 70%. The tenor of phenolic compounds was determinated by spectrophotometric method. Another parameters analyzed were: dry residue (105ºC), density (picnometer, 20ºC) and viscosity (Ostwald viscometer). Results: The results obtained by total phenolic compounds, dry residue, density and viscosity were respectively, for the percolating method, 3.00g%; 26.48g%; 0.994g/mL; 10.68cP; and for maceration, 2.94g%; 23.14g%; 1.009g/mL and 5.85cP. Conclusion: Dynamic maceration process can substitute percolating, for this drug and respective analyzed parameters, mainly in industrial level, once this method presents a great economy of time in the obtaining of extracts.

Financial Suport: Uneversity of Sorocaba
Supervisor: Magali Glauzer Silva

PN136 - A NEW APPROACH TO OBTAIN PHYSALINS

IVONE MARIA RIBEIRO(PQ)[1];THEREZINHA COELHO BARBOSA TOMASSINI (PG)[1]

[1] LAB. PROD. NAT.PN [2] FARMANG /FIOCRUZ -RJ

Introduction: Physalins are compounds obtained from plants of *Physalis* spp. (Solanaceae) which are characterized as polyoxygenated molecules known as 13,14-seco-16,24-cyclosteroids.Several papers have described the biological activities of physalins B and F as antitumoral (Chiang, H. 1993), physalins B, F and G as immunomodulator (Soares, M.2003), physalins B and D as an antimicrobial agent, (Januário,H.2003). Recently the cytotoxicity of physalins has been described (Kawai, M. 2003). Objective: The main aim of this study is to describe a new approach to obtain physalins. Methodology and Results: *Physalis angulata* L. was collected in Belém, Pará, Brasil and identified by Dra Lucia de Carvalho from the Rio de Janeiro Botanical Garden. A voucher (RFA23907/8) is deposited at the Federal University of Rio de Janeiro. Stems (340g) dried and powdered were extracted with a buffer solution (NaCl) pH 7,2-7,4, stirred at 34^0C, for 5 h. The solution obtained (9,0 L) was partitioned three times with ethyl acetate (9,0 L). The organic phase was washed with distilled water (4,0 L), filtered with $MgSO_4$ and evaporated under reduce pressure giving 1,7g of a physalin fraction (pool). This pool was separated by MPLC under the following condictions: adsorvent Silica gel activated with methanol, eluate system: hexane - ethyl acetate 7: 3, flow rate: 2ml/ min, affording 1,44g of physalins B, D, F and G. (patent BRPI 0404635-8, 2004) Conclusions: The new procedure gave an overall yield of 0,41% on dry stems wich is ten times higher than the literature value 0,04% (Kawai, M.1996).

Financial support: FARMANG - PDTIS/FIOCRUZ

PN137-ANTIMICROBIAL POTENTIAL OF EXTRACTS OF *DIPTERYX ODORATA*.

JAQUELINE V. DARROZ(IC)[(1)]; JANINE D. SOUZA(IC)[(1)]; FLÁVIA C. F. CUSTÓDIO(IC)[(1)]; RENATA S. FERNANDES(PG)[(1)]; ANA H. JANUÁRIO(PQ)[(1)]; MIRIAN V. LOURENÇO(PQ)[(1)]; DAISY N. SATO(PQ) [(2)]; SUZELEI C. FRANÇA(PQ) [(1)]; ROSEMEIRE C. L. R. PIETRO(PQ) [(1,3)] .

[(1)]Universidade de Ribeirão Preto-UNAERP, Ribeirão Preto-SP,Brasil; [(2)]Instituto Adolfo Lutz; [(3)]Universidade Estadual Paulista-UNESP, Araraquara-SP, Brasil

The antibacterial activity of several plant species has been reported in many countries. The purpose of this work was to evaluate the antimicrobial activity of the crude chloroform extract, methanolic extract of aerial parts, callus and methanolic extract of seeds of *Dipteryx odorata*. The method used was microdilution against *Staphylococcus aureus* (ATCC 25923), *Staphylococcus epidermidis* (ATCC 1228), *Escherichia coli* (ATCC 10536), *Bacillus subtilis* (ATCC 6633), *Mycobacterium tuberculosis* H37Ra (ATCC 25177) and *Mycobacterium tuberculosis* H37Rv (ATCC 27294). The results showed that aerial part and seed extracts did not present good antibacterial activities, however the callus culture presented high antimicrobial activity to all strains, except to the mycobacteria. In a parallel search was detected isoflavonoids in callus. The data obtained suggest that detailed studies of callus extract must be intensified to elucidate its total composition.

Financial Support: UNAERP / CNPq
Supervisor: Profa. Dra. Rosemeire C. L. R. Pietro

The authors did not follow the Scientific Committee's suggestion for an English language review

PN138-ANTIFUNGAL PYRIDOCARBAZOLE ALKALOIDS AND LUPEOL-DERIVED BUTANOLIDES FROM *ASPIDOSPERMA OLIVACEUM*

DULCE SILVA (PQ)[1]; FERNANDO CARNEIRO (PG)[1]; RENATA LEMOS (IC)[1]; ANGELA ARAUJO (PQ)[1]; M. CLAUDIA YOUNG (PQ)[2], VANDERLAN DA SILVA BOLZANI (PQ)[1], ANA M. ALMEIDA (PG)[3], MARIA JOSE SOARES MENDES GIANNINI (PQ)[3]

[1] NuBBE, IQ-UNESP-CP 355-14800-900-Araraquara-SP-BRAZIL.
[2] S. Fisiol. Bioq. Plantas, Inst Bot, São Paulo
[3] FCF UNESP, C.P. 502-14801-902-Araraquara.

-*Aspidosperma olivaceum* belongs to Apocynaceae, a family known for its bioactive alkaloids. Pentacyclic triterpenes are also widespread in *Aspidosperma* species and present several bioactivities.
-This led us to search for bioactive compounds from *A. olivaceum.*
-The EtOH extract (EE) from leaves of *A. olivaceum* showed positive results when screened for antitumoral (modified strains of *Saccharomyces cerevisae*) and antifungal (bioautography on TLC) activities.
-Phytochemical work on the $CHCl_3$ phase of EE led to the isolation of uvaol, lupeol and ursolic acid derivatives in addition to 3 new lupeol-derived butanolides, identified after extensive NMR studies, ESI/HRMS. The EtOAc phase afforded steroidal glycosides, besides pyridocarbazole alkaloids olivacine, olivacine *N*-oxide and *N*-methyl-guatambuine, which have been tested for antifungal activity. The alkaloids showed strong activity against *Candida albicans* and *C. parapsilosis* and phytopathogens *Cladosporium cladosporioides* and *C. sphaerospermum*.

Financial support: CNPq/Biota-FAPESP
Supervisor: Dulce H. S. Silva

PN139-MORPHOLOGICAL ASPECTS OF NERIUM OLEANDER LEAVES

FRANCISCO A. A. DE ALMEIDA (IC)[1]; MELINA G. CARVALHO (IC)[1]; KLEYTON T. C. DE CARVALHO (IC)[1], ILANA A. DE A. FONSECA(IC)[1], ALAISE PAIVA MARTINS(PG)[1]

Universidade Federal do Rio Grande do Norte[1] - Gen. Gustavo Cordeiro de Faria St; s/n. Petrópolis - Natal/RN - 59010-180

INTRODUCTION: *Nerium oleander* (Apocynaceae) is used for ornamentation, however, its pharmacological application is limited due to its high toxicity. OBJETIVE: The aim of this work is to characterize morphologically the leaves of *N. oleander*, which were collected in Nata/RN, Brazil. METHODOLOGY: Microscopic analysis was made with samples of dry plants obtained after grinding and sieving in a 40 mm sieve. Fresh cuts were also used for analysis. RESULTS: Organoleptic analysis showed that the leaf is bicolor, flexible and rough, has leather aspect and nauseous smelling. Its length vary from 3 to 16,4 cm and its width from 0,5 to 2,8 cm. The petiole measures from 0,2 to 1,1cm of length, is straight and has lateral insertion. There is no axillary bud. Microscopy showed palisade and lacunose parenchyma beside druses and crypts, which contain many non glandular trichomes and a large number of stomatas. Upper epidermis contains cuticules and poliedric cells while lower epidermis presented stomatas. CONCLUSION: This study was very important since it contributed to a better identification and characterization of the specie in northeast region.

Financial support: none
Supervisor: Maria Cleide Ribeiro Dantas Carvalho (PQ)[1]

PN140 - CROMATOGRAPHIC EVALUATION OF FORMULATIONS FROM AMPELOZIZYPHUS AMAZONICUS

JUNIOR R. CARVALHO (IC)[(1)]; GEONE M. CORREA (PG)[(1)]; JEFFERSON ROCHA DE A. SILVA (PQ)[(1)]; MARIA L. B. PINHEIRO (PQ)[(1)] ANA CLAUDIA F. AMARAL (PQ)[(2)].

[(1)]Universidade Federal do Amazonas (UFAM); [(2)]Farmanguinhos/FIOCRUZ-RJ

Malaria is a tropical disease caused by protozoa of genus *Plasmodium,* the parasite's resistance is the main factor that guide the continuous search of new drugs. To prevent malaria, the population has used an amazonian medicinal plant, *Ampelozizyphus amazonicus*. The objective of this work was to evaluate the chromatographic profiles using HPLC-DAD of the aqueous (infusion) and ethanolic extracts from the fresh leaves of *A. amazonicus*. The botanic material was collected at experimental farm of UFAM. The HPLC chromatograms of the aqueous and ethanolic extracts were obtained on a RP-18 column (250 x 4.6 x 5 mm). The elution was made with water (with 0.05% TFA):CH_3CN gradient from 90:10 to 30:70 v/v in 45 min. The results obtained in the chromatographic profiles indicated the presence of saponins, phenylpropanoids and flavonoids in the both extracts. In the infusion predominated phenylpropanoids (52.7%), while in the ethanolic extract the main substances were flavonoids (38.5%). In conclusion, the results demonstrated that HPLC is a useful tool in the future pharmaceutical formulations studies from this plant.

Financial support: CNPq, PADCT, FAPEAM/AM
Supervisor: Jefferson Rocha de A. Silva

PN141 - COMPARATIVE STUDY OF VARIATION OF SPF IN DIFFERENT FORMULATIONS AND *ACHYROCLINE SATUREOIDES* DC. AND *JUGLANS REGIA L*. EXTRACTS.

JOCEANA SOARES SPEROTTO (PQ)[1]; ANDRESSA FRIZZO PHILIPPSEN (IC)[1]; RENATO ANDRETTA (IC)[1]; MARCOS ANTÔNIO CORRÊA (PQ)[2]; SIMONE CEREZER (PQ)[1]

1 Universidade Regional Integrada-URI/Erechim
2 Universidade Estadual de São Paulo-UNESP/Araraquara.

The use of natural products as sunscreens is an excellent alternative, also can be associate with other types of filters, being able to modify the final protection of the product.The aim of study was to compare the varation of the Sun Protector Factor (SPF) by spectroscopy UV (290-320nm) and Mansur's Formula, between the sunscreens preparations, adding *Achyrocline satureoides* DC. and *Juglans regia* L. extracts. For this, had compared glycolic and crude hidroalcoholic extracts (CHE).The samples were prepared with sunscreens formulations (lotion and gel), followed of the addition of vegetal extracts in the concentrations of 1%, 3%, 5%, 7% e 10%. The values of SPF of the samples that contend CHE decreased, when compared with the control. Still, it was observed that the reduction of the SPF that contend CHE, was bigger in percentage, when compared with the samples that contend glycolic extract. In conclusion, this study showed that the SPF of the samples analyzed were modified when added extracts in the sunscreens formulations.

Supported by: PIIC/URI
Adviser: Joceana Soares Sperotto

The authors did not follow the Scientific Committee's suggestion for an English language review

PN142-EFFECTS OF *ERYTHRINA FALCATA* B. IN ACQUISITION AND EXTINCTION IN CONDITIONED FEAR

PRISCILA FUMIE SANADA(IC)[(1)]; DANIELA RODRIGUES DE OLIVEIRA(IC)[(1)]; FRANCISCO BARBOSA FILHO(PG)[(1)]; SUZETE MARIA CERUTTI(PQ)[(1)].

[(1)] PROPEP, USF

Introduction Recent findings in our laboratory suggest that extract from *Erythrina falcata* B. (EHE) induced impairment in transfer latency learning in rats evaluated in the elevated plus maze. Objective To investigate the effect of the EHE extract in the conditioned emotional response (CER). Methods Rats, Wistar, male, adults were assigned in 4 groups (n=10), according (i) drugs: EHE 0,25g/Kg and 0,5g/Kg, control (Tween 80-12% and Diazepam 4mg/Kg); and (ii) treatment: 7 days. In classical fear conditioning, rats learn to associate conditioned stimulus (CS-tone) with aversive, unconditioned stimulus (US-foot shock). 48h after training, in test session, the CS itself becomes able to elicit fear response. The means of suppression ratio (SR) was calculated for each rat, in 6 attempts. SR approaching 0.0 indicates complete suppression. Results Greater SR for control groups in first attempt ($0.10 \pm 0.05 p < 0.05$) was shown. The measurements for the six attempts didn't differ ($p > 0.05$). For EHE group SR was 0.39. Conclusions Our data suggests that EHE may interfere in acquisition of CER. There was a decrease in expression of CER in all groups submitted to treatment for 7 days.

Financial support: FAPESP
Supervisor: Suzete Maria Cerutti

PN143-DEVELOPMENT OF MICROPLATE ASSAY FOR STUDYING THE EFFECT OF NATURAL COMPOUNDS ON HUMAN NEUTROPHIL ELASTASE RELEASE

JOEL G. SOUZA (IC), ALEXANDRE KANASHIRO (PG), LUCIANA M. KABEYA (PG), ANA ELISA C. S. AZZOLINI (PQ), YARA M. LUCISANO-VALIM (PQ)*.

Depto. Física e Química, FCFRP/USP, *yaluva@usp.br

Neutrophils (PMNs) play an important role in body defense, which is mainly mediated by oxidant generation and degranulation. PMNs granules contain a wide variety of proteolytic enzymes, among which the serine protease elastase seem to have the greatest potential to act as mediator of tissue destruction in inflammatory diseases where intense PMNs infiltration is observed. Therefore, searching for compounds that inhibit elastase activity or its release from PMNs is an important task in the screening of anti-inflammatory drugs. In the present study, a microplate assay was developed for evaluating the effect of natural compounds on elastase release. After pre-incubation of human PMNs with cytochalasin B and the flavonoid quercetin (standard compound), degranulation was initiated by n-fMLP addition. Elastase activity was measured spectrophotometrically by p-nitroaniline formation. Quercetin exhibited a concentration-dependent inhibitory effect on elastase release. In conclusion, the proposed method can be useful for large-scale screening of natural compounds.

Financial Support: FAPESP, CNPq/PIBIC

PN144-PHYTOCHEMICAL STUDY OF *ERYTHROXYLUM* GENUS FROM THE NORTHEAST OF BRAZIL

ROBERTA ÉRIKA DE SOUZA SILVA (IC); CLÁUDIO COSTA DOS SANTOS (PG)

Universidade Federal do Ceará - UFC.

Plants belonging to the *Erythroxylum* genus (Erythroxylaceae) are well known as cocaine-producing species and have attracted commercial interest and considerable attention on their agronomic and phytochemical analysis. Previous studies of species from this genus revealed the presence of tropane and nor-tropane derived alkaloids and flavonoids as chemotaxonomic markers, besides a prolific source of assorted terpenoids. In our phytochemical studies of *Erythroxylum barbatum* O. E. Schulz, a small tree native of Northeastern Brazil, we have recently reported the isolation from its roots of prenylated chalcones, steroid, coumarin, pterocarpans and the devadarane diterpene erythoxydiol X, widely reported for species of this genus. In continuation of our studies we report now the phytochemical study of the leaves from *Erythroxylum sp*. Chromatography using silica gel from the hexane and EtOH extracts allowed the isolation of the triterpenes lupeol and ethyl linoleate , and of the flavonoids quercetine and quercetin-3-O-α-L-rhamnopiranoside of the leaves from *Erythroxylum* sp. The structural characterization of the isolated compounds were performed by the use of IR, MS and a series of 2D NMR experiments including ^{1}H,^{1}H-COSY, HMQC and HMBC.

Financial Support: CNPq/PRONEX/CAPES
Supervisor: Mary Anne Sousa Lima

PN145-CELL CULTURE AVALIATION OF PHARMACOLOGIC ACTIVITY OF *CALENDULA OFFICINALIS* L. EXTRACT AND DEVELOPMENT OF SEMI SOLID FORMULATION

LUIZA H. A. CARMO (PG) [1] ; ANDRÉIA C.D. RODAS (PG)[2]; MÕNICA BEATHRIZ MATHOR (PQ)[2].; WALCY DIASTEODORO (PQ)[3]; IDA CARAMICO SOARES, I (PQ)[1].

[1]Faculdade de Ciências Farmacêuticas USP/SP; [2]-Instituto de Pesquisas Energéticas e Nucleares – IPEN/SP; [3]Faculdade de Medicina USP/SP

Introduction: The concept of herbal drugs is not only limited to the pharmacopoeial identification of the drug, it also comprises the quality of the final medication obtained from active ingredients and excepients. It involves physical characteristics of formulations, microbiological contamination, bioavailability of active principles and stability under various storage conditions. *Calendula Officinalis L.* is a European plant found all over the world which bears antiseptic, cicatrization and anti-inflammatory properties. Objectives:This work has aimed at evaluating the cicatrization activity of this species through studies that utilize techniques of cellular culture as well as the development and observation of emulsion formulation stability containing the herbal extract. Results Our results show that there are differences in terms of quantity and quality amidst the extracts of *Calendula Officinalis L* that have been studied. The extract from the plant cultivated in Brazil in concentrations of 2,0, 6,0 and 8,0 µl/ml presented an increase of mitochondrial activity, but significant influence has not been observed in the surge of human fibroblasts and in the production of collagen Type 1. The multifactor planning applied to the development of formulations with non-ionic wax with a minimum content concentration (FNI1) has proven to be more stable. The addition of *Calendula* extract in the formulations has not been influential to spreadability, centrifugal stability, rheology and viscosity.

Finacial support: CNPq
Supervisor: Profa. Dra. Ida Caramico Soares

PN146-EFFECTS OF GINGER ON DNA DAMAGE AND NEOPLASTIC LESIONS INDUCED IN A MOUSE BLADDER CARCINOGENESIS MODEL.

LUCAS T. BIDINOTTO[(1,2)](IC*); ANA L.T. SPINARDI-BARBISAN[(2)] (PQ), DAISY M.F. SALVADORI[(2)](PQ); LUÍS F. BARBISAN[(1,2)](PQ).

[1]Department of Morphology- IB and [2]Department of Pathology-FM UNESP, Botucatu-SP, Brazil

Introduction: Ginger (*Zingiber officinale* Roscoe) extracts are rich in gingerols and shogaols that exhibit antioxidant, anti-inflammatory, analgesic and anti-carcinogenic proprieties both *in vivo* and *in vitro* systems. Objective: The present study was aimed to verify the modifying potential of a ginger extract on DNA damage and development of bladder cancer induced by N-butyl-N-(4-hydroxybutyl)-nitrosamine (BBN) in male Swiss mouse. Methodology: Groups G1 to G3 were given 500 ppm of BBN in drinking water for 18 weeks and four injection i.p. of N-metyl-N-nitrosourea (MNU) (30 mg/kg, b.w.) at 1, 3, 10 and 18 weeks of experiment. Additionally, G2 and G3 and G4 groups were fed with diet containing ginger extract at 1.0% and 2.0% and G1 and G5 group fed with basal diet, respectively. Four hours after each MNU application, samples of peripheral blood were collected to DNA damage analysis (comet assay). At the end of experiment, the animals were killed and the urinary bladder was removed, fixed and routinely prepared for histopathologic evaluation.
Results: Ginger meal not altered DNA damage levels induced by BBN/MNU treatments as evaluated by tail moment and tail intensity parameters in comet assay. The incidence of urothelial carcinoma was not significantly different between ginger-treated groups (G2 and G3) and only BBN/MNU-treated group (G1). Conclusion: The results suggest that dietary ginger did not alter the development of *in vivo* chemically-induced urinary bladder tumor.

Financial Support: FUNDUNESP, TOXICAN and *FAPESP (04/08035-9)
Supervisor: Barbisan, L.F.

PN147-NEUTRALIZATION OF *BOTHROPS MOOJEN*I VENOM BY EXTRACT FROM *CASEARIA GRANDIFLORA*

DANILO SIQUEIRA FORTUNATO(IC)[1]; LUIS HENRIQUE FERREIRA DO VALE (PG)[1], RENATA SANTOS RODRIGUES(PG)[1], VERIDIANA DE MELO RODRIGUES(PQ)[1]; MARIA INÊS HOMSI-BRANDEBURGO(PQ)[1], AMÉLIA HAMAGUCHI(PQ)[1]

1-Instituto de Genética e Bioquímica, Universidade Federal de Uberlândia-MG.

Introduction/objective: Several plants have been tested against snakebites. This work aims to neutralize phospholipase and coagulant activities of *B. moojeni* crude venom (CV) by *C. grandiflora* (Cg) aqueous extract (AE), ethanol soluble fraction (ES) and ethanolic pellet fraction (EP). Method: Leaves of Cg were mixed in water or ethanol (97º) and centrifuged to prepare AE, ES and EP. Phospholipase and coagulant activities were assayed by the indirect hemolysis method and bovine plasma clotting time, respectively, by using CV and Cg at 1:10 ratio (w/w). Result: Hemolytic activity of CV (20μg) was neutralized in about 71.7% , 17,8% and 75% by AE, ES and EP, respectively. Coagulant activity of CV (5mg) was inhibited in about 100% by AE and EP, but ES did not show this inhibition activity. Conclusion: These results suggest that leaves of *C. grandiflora* contain compounds that are soluble in water but not in ethanol, that neutralize PLA2 and thrombin-like enzymes of venom from *B.moojeni*.

Financial support: CAPES and CNPq.
Supervisores: Amélia Hamaguchi, Maria Inês Homsi-Brandeburgo e Veridiana de Melo Rodrigues.

PN148 - IMPROVING THE PROFESSIONAL PERCEPTION ON WASTE DISPOSAL

FILIPE G. FERREIRA (IC)[1]; SILVIO L. T. DE LIMA (PQ)[1]; NEWTON ANDRÉO F[O](PQ)[1]; LEONARDO F. FRACETO (PQ)[1]

[1]University of Sorocaba

Introduction: Nowadays, there is a general concern about many skills that a professional, mainly in pharmaceutical fields, must detain. Among them, skills related to waste disposal should deserve special attention in the undergraduate courses, once the universities produce lots of chemical wastes, from their teaching and research laboratories, which must be properly discarded.
Objective: It was intended to implement a program for residues management at UNISO and to develop/establish educational strategies to ensure the recruitment of all laboratory staff.
Methodology: Educational activities and routine procedures were used in the treatment of the waste in order to make students and the academic staff aware of the importance of proper waste disposal.
Results: The educational activities and protocols led to a significant reduction in the volume of residues produced due to the cooperation among teachers, technicians and students. The students have manifested great interest on how to properly dispose the waste.
Conclusions: The results achieved are promising in both environmental and educational point-of-view, leading to professionals with an active position in the environment preservation, serving as lively examples for undergraduate students.

Financial support: PROBIC/UNISO
Supervisor: Dr L. F. Fraceto

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Química e Biologia de Fármacos / *Chemistry and Biology of Drugs* (QB)

QB001- EVALUATION OF DARK TOXICITY OF CHLORINE$_{E6}$ IN CELL LINE J774-A

PATRÍCIA PEREIRA MACAROFF (PG)[1]; ANTONIO CLAUDIO TEDESCO (PQ)[1]

[1]Departamento de Química, FFCLRP-USP

Traditional cancer treatments, including surgery, radiation and chemotherapy, all established as well known protocols, present generally uncontrollable side effects normally associated with loss of normal cell function. Photodynamic Therapy (PDT) has been used since the 80's as a potential protocol in the treatment of a variety of oncological and nononcological diseases, with minimal side effects. In its present status, more than 4000 patients have been treated. The current PDT agents under basic and clinical studies have reveled high photodynamic action and low dark toxicity. In this study, with PDT we used the photosensitiser Chlorine$_{e6}$ in the concentration range from 5 to 25μM, a compound was previously selected based on the PS photophysical properties. The methodology used to investigate Chl$_{e6}$ dark toxicity was based on the classical MTT assay. The results showed that toxicity to the J774-A cell line was 2, 22, 60, 75 and 80% respectively for 5, 10, 15, 20 and 25 μM Chl$_{e6}$. A higher dose of Chl$_{e6}$ also presented higher aggregation process. For dark toxicity studies, the lower concentration was selected (5μM) for use *in vitro* studies, in association with other agents to induce photodynamic action under PDT protocols.

Financial Support: FAPESP
Advisor´s names: Antônio Claudio Tedesco

QB002-SPECTROSCOPIC STUDY OF LIPOSOMAL FORMULATION OF CROWNED PORPHYRINS.

A.C.PELEGRINO(PG)[1]; M. C.A.F. GOTARDO (PG)[1]; M. D.ASSIS (PQ)[1]; A.C.TEDESCO(PQ)[1]

[1]Departamento de Química, FFCLRP-USP

Considerable efforts have been devoted to the development of new photosensitizers with higher tumor selectivity and photodynamic activity. These goals led us to study amphiphilic porphyrins with potential application for PDT. In this work, we evaluated the crowned ether porphyrins (5,10,15,20-tetrakis[4-(1,4,7,10,13-pentaoxacyclopentadecane-2-aminomethyl)2,3,5,6-(tetrafluoro)-phenyl]-porphyrin (H_2C_4P) and Zn(II)5,10,15,20-tetrakis[4-(1,4,7,10,13-pentaoxacyclopenta-decane-2-aminomethyl)2,3,5,6-(tetrafluoro)-phenyl]-porphyrinate (ZnC_4P) in small unilamellar liposomes and organic medium, by steady-state (absorbance and emission fluorescence) photophysical techniques. The absorption spectra of ZnC_4P (6 μM) and H_2C_4P (6 μM) in liposome medium display maximum absorption at 432 nm and 428 nm, respectively. We have observed an 8 nm shift of the bands for the same dye in organic medium. Particle size analysis led to values around 115 nm for the liposome drug delivery system. New *in vitro* studies will allow us to evaluate how the crown ether framework could act in the damage maximization in tumor cells after light treatment, and how this will act upon the Na^+ and K^+ ions homeostasis.

Financial Support: Fapesp
Supervisor: Antonio Claudio Tedesco

QB003-STUDY OF ACTION ANTI-INFLAMMATORY MECHANISM OF THE (-)-CUBEBIN DERIVATIVES

THAIS C. LIMA(IC)[1]; ROSANGELA DA SILVA(PQ)[1]; VANESSA A. DE SOUZA(IC)[1], ANA C. PEREIRA(IC)[1]; VANESSA DE A. ROYO(PG)[1 2]; ADEMAR ALVES FILHO(PG)[2]; WILSON R. CUNHA(PQ)[1]; JAIRO K. BASTOS(PQ)[2] AND MARCIO L. A. E SILVA(PQ)[1].

[(1)]Universidade de Franca – Av. Dr. Armando Salles de Oliveira, 201 – Franca –SP CEP 14404-600; [(2)]FCFRP-USP – Av. do Café s/n – Ribeirão Preto – SP CEP: 14030-000

Cubebin and many of its derivatives belong to the dibenzylbutyrolactone lignans, which are widely distributed in the plant kingdom and have been investigated by researchers for their different biological activities. The aim of this work was to study the anti-inflammatory action mechanism of (-)-cubebin derivatives obtained by partial synthesis. The carrageenan induced rat paw edema was used, and PGE2 (50 µg/paw) and histamine (50 µg/paw) were used as mediators of the edema formation. It was observed that the orally administration of 30 mg/kg of the samples, inhibited the edema induced by PGE2 and histamine ($p<0.05$). However, the derivatives 3 and 6 (44 and 30%, respectively) were more efficient to reduce the edema induced by PGE2, while, the derivatives 4 and 5 (28 and 25%, respectively) were less active. Compound 3 inhibited histamine induced-edema (55%), and this effect was similar to the one obtained for ciproeptadine (49.4%). So, the compounds 2, 4, 5 and 6 showed 44, 30, 33 and 33%, respectively. On the basis of these investigations, it may be suggested that 1, 2, 3, 4, 5 and 6, are possible acting by blockading the histamine and prostaglandin receptors.

Financial support: FAPESP, CAPES and CNPq
Supervisor: Márcio Luís Andrade e Silva

The authors did not follow the Scientific Committee's suggestion for an English language review

QB004-PREPARATION OF HINOKININ ENTRAPPED IN A SOLID MATRIX BY SOL-GEL PROCESS

LUCAS A. ROCHA(PG)[1]; VANESSA A. ROYO(PG)[1,2]; BRUNO L. CAETANO(PG)[1]; EDUARDO F. MOLINA(PG)[1]; THAIS C. LIMA(IC)[1]; FRANCIELI R. C. MORAES(IC)[1]; KATIA J. CIUFFI(PQ)[1]; EDUARDO J. NASSAR(PQ)[1]; MARCIO L. A. SILVA(PQ)[1]; JAIRO K. BASTOS(PQ)[2].

[1-]Labquim da Universidade de Franca – UNIFRAN;
[2-]Laboratório de Farmacognosia da FCFRP – USP.

Introduction: The encapsulation of enzymes and other proteins into inorganic host materials using sol-gel processing has attracted considerable attention. Studies have clearly established that biological molecules encapsulated in inorganic matrices retain their characteristic chemical and biochemical functionality as oxidation/reduction and enzymatic activity. The molecular system acts as active species while the sol-gel acts as a structural matrix for rigidity, stability, and addressability. The hinokinin is a dibenzylbutyrolactone lignan found in the extract from seeds of *Piper cubeba* or as oxidation product of the cubebin and the interest in the study your action mechanism is due to results promising in biological activities such as trypanocidal activity. Objective: Preparation of hinokinin entrapped in an inorganic polymeric matrix. Methodology: The materials were prepared by the sol-gel route. Results and Conclusions: UV-Vis spectra show that hinokinin was entrapped and makes possible the investigation of the trypanocidal activity.

Financial Support: CAPES and FAPESP
Supervisor: Kátia J. Ciuffi and Jairo K. Bastos

QB005-SYNTESIS OF HETEROGENEOUS METALLOPORPHYRIN AS BIOMIMETIC SYSTEM OF CYTOCHROME P450 IN OXIDATION OF DRUGS

RAFAEL A. ROCHA(IC); LIZIANE MARÇAL(IC); GUSTAVO P. RICCI(IC); LUCAS A. ROCHA(PG); KATIA J. CIUFFI(PQ); EDUARDO J. NASSAR(PQ).

Universidade de Franca – UNIFRAN

Introduction: Cytochrome P450 is a member of the monoxygenase family of heme enzymes that plays an important role in metabolizing biomolecules and xenobiotics. Particularly the alkane hydroxylation is a key process by which the heme enzyme cytochrome P450 metabolizes xenobiotics. The synthetic metalloporphyrins is used as model of these heme enzymes. Besides of mechanistic studies, these metalloporphyrin synthetic systems can be used for the investigation of metabolic reactions of different drugs. The biomimetic oxidations can be considered a powerful medicinal chemistry tools when supporting pharmacokinetic studies. Objective: The purpose of the present work is to develop a simple method for the preparation of an efficient biomimetic catalyst. Methodology: The Fe(TDCPP)NO_2^+ was entrapped in a silica matrix in the form of spherical particles by the sol-gel route using the Stober methodology. Results and Conclusions: The efficiency of this catalyst was tested in oxidation of cyclohexane, (Z)-cyclooctene and acetominophen. The results of this study showed that synthetic conditions influence the catalytic activity and must be carefully chosen to obtain an efficient P-450 model.

Financial Support: CAPES and FAPESP
Supervisor: Katia J. Ciuffi

QB006-PHOTODEGRADATION OF NEUROLEPTIC DRUG IN HOMOGENEOUS MEDIUM

MARIANA ROBERTO GAMA (IC); ROBERTO DE CARVALHO (PQ); ROSE MARY Z. G. NAAL (PQ)

Departamento de Física e Química- FCFRP - USP

Thioridazine (THD) is a neuroleptic drug used for the treatment of psychiatric disorders. However, photoalergic and phototoxic reactions are frequently reported as adverse effects of THD administration, which justify the importance of this drug photostability study. The aim of this work is to investigate THD photodegradation, in homogeneous environment, to contribute to the comprehension of the phototoxicity mechanisms of this drug. Solutions of THD 10, 40 and 100 μM were prepared in water and irradiated in a Nd-YAG laser system, model Surelite I-10, using the third harmonic of the laser (λ=355 nm) as excitation source. The photodegradation behavior, after irradiation, was monitored by fluorescence spectroscopy (λ_{ex}=262 nm and λ_{em}=465 nm). For 10 and 40 μM concentrations was observed a reduction of the maximum emission of fluorescence, at 465nm, with simultaneous appearance of an emission band at 380 nm, which is attributed to the photodegradation product. For THD 100 μM, it occurs an initial increase in maximum emission, at 465 nm, until the energy irradiation of 17,5 J. After that, it is observed a similar behavior of 10 and 40 μM, suggesting drug aggregation for high concentration. These aggregates were confirmed by absorption spectroscopy.

Financial Support: FCFRP-USP
Advisor: Profa. Dra. Rose Mary Zumstein Georgetto Naal

QB007-PHOTOPHYSICAL PROPERTIES OF FOSCAN® ASSOCIATED WITH NANOEMULSIONS (NE) FOR THE PHOTODYNAMIC THERAPY OF SKIN CANCER

PRIMO, F. L.(PG)[1]; MICHIELETO, L.(IC)[1], TEDESCO, A. C.(PQ)[1]

[1]FFCLRP – Universidade de São Paulo, Brasil.

Photodynamic Therapy (PDT) is a promising treatment for a variety of oncological, cardiovascular, dermatological, and ophthalmic diseases. PDT is based on the use of photosensitizer drugs, which are preferentially taken up and/or retained by neoplasic tissues. Upon photoactivation (with visible light at the appropriate wavelength), the photosensitizer leads to the generation of cytotoxic species, such as reactive oxygen species, acting in the irreversible destruction of the tumoral tissues. The present work focuses on the evaluation of the photophysical properties of the Foscan® nanoemulsion (NE) drug delivery system (DDS), developed for topical application to treat different skin cancers. Results clearly indicate that the fluorescence quantum yield (Φ_f) for Foscan® decreases in NE DDS, compared with that in organic medium. The maximum fluorescence emission can be observed at 650 nm, with excitation at 430 nm. The fluorescence lifetime present a biexponential decay (t_1 = 8,3 ns and t_2 = 3,4 ns), indicanting different locations for the photosensitizer in the nanocolloidal system. These results support the *in vitro* and *in vivo* profile for the use of Foscan® associated with NE in skin cancer PDT protocols.

Financial: FAPESP, CNPq
Supervisor: Prof Dr A. C. Tedesco

QB008- NEW PHBPE MICROSPHERES FROM *BURKHOLDERIA CEPACIA* AS BIODEGRADABLE DRUG DELIVERY SYSTEMS (DDS) FOR PHOTODYNAMIC THERAPY.

I. P. M. CASTRO(IC)[1]; A. R. SIMIONI(PG)[1]; A. C. TEDESCO(PQ)[1]; M. I. RÉ(PQ)[2]; M. F. A. RODRIGUES(PQ)[2]; E. S. SILVA(PG)[2]; MARCELO MIGUEL MARTIN PELISSON (PQ)[3]

1 Universidade de SãoPaulo, FFCLRP-USP, RibeirãoPreto – SP, Brazil
2 Instituto de Pesquisa Tecnológica do Estado de São Paulo, São Paulo – SP, Brazil
3 Universidade do Vale do Paraíba – IP&D, São José dos Campos-SP, Brazil

Photodynamic Therapy (PDT) is a non-invasive treatment for neoplastic diseases that is currently being used around the world. In this work, NzPC, a new photosensitizer has been investigated, and was incorporated into the microspheres of PHBPE as a DDS. The photophysical and photochemical properties of the NzPC-microspheres were determined after the incorporation of this dye into the microspheres prepared by spray drying techniques. The maximum absorption and fluorescence emission are located at 682 and 700 nm, respectively. The *in vitro* dark toxicity (MTT assay) for NZPC-PHBPHPE microspheres was reported, using J774A cell line as a model. The dark toxicity found was 24%, compared to 14.9% for NzPC alone. On the other hand, the use of PHBHPE microspheres and laser light in cells showed increased toxicity reaching a maximum of 60 % of cell death at the fluency of 10J/cm^2. This value is in agreement with drug know as a good photo sensitizers for PDT protocol.

Financial Support: CNPq
Supervisor: A.C.Tedesco

QB009- INCLUSION COMPLEXES OF b-CYCLODEXTRINE/PRIMAQUINE: AVALIATION OF STABILITY

MARIA PERPÉTUA FREIRE MORAIS DEL LAMA (PQ); ROSE MARY ZUMSTEIN G. NAAL (PQ)

Departamento de Física e Química, FCFRP – USP

Primaquine is an efficient drug used for the treatment of rheumatoid arthritis and ischemia but the therapeutic doses are very close to the limit of toxicity causing serious side effects mainly for patients exposed to sun light. Nowadays, there is significant interest in cyclodextrins (CDs) as drug carriers systems which are able to minimize these side effects. The objective of our work is to investigate the influence of incubation time on the stability of the inclusion compounds. Since the drug is fluorescent, binding constants (K_b) of primaquine with β-CD can be determined by fluorescence spectroscopy (λ_{exc}=354 nm e λ_{em}=475 nm). Primaquine stock solution (1 x 10^{-5} M) was stirred overnight in phosphate, or acetate buffer (pH 5, 7 and 13) in the presence of 20 mM of β-CD. Several dilutions were made for β-CD using drug solution. The fluorescence was measured 0, 1, 2, 6, 10 and 15 days after preparation. K_b values were determined using Benesi-Hildebrand equation assuming stoichiometry of 1:1. The results showed good stability for the inclusion complexes, mainly for pH 13, until 2 days after preparation. After that, it is observed a K_b decrease suggesting the primaquine/β-CD complex slowly dissociates.

Financial Support: FCFRP-USP.
Advisor: Profa. Dra. Rose Mary Zumstein Georgetto Naal

QB010-INCORPORATION OF ANTI-MALARIAL DRUG INTO MEMBRANE MIMETIC SYSTEMS

MARCELA DE SOUZA SANTOS (IC); BEATRIZ M. P. GIROLINETO (IC); MARIA PERPÉTUA F. M. DEL LAMA (PQ); ROSE MARY ZUMSTEIN GEORGETTO NAAL (PQ)

Departamento de Física e Química, FCFRP - USP

Anti-malarial drug efficiency depends on cell membrane interaction and later accumulation in the food vacuole of the parasite to prevent its growth. Chloroquine is a fluorescent anti-malarial drug that changes its photophysical properties when incorporated to a mimetic system. So, the change of spectroscopic properties of the drug, in ionic micellar systems, and β-cyclodextrin, can be used as a tool to investigate its incorporation on biological membranes. The goal of this work is to study the chloroquine incorporation on membrane mimetic systems by using fluorescence spectroscopy. The fluorescence emission spectrum of the drug (1 x 10^{-5} M) at citrate-borate-phosphate buffer, were registered at pH range of 4 to 13, in the presence of β-cyclodextrin and surfactants SDS, SDTMA, CTAB and CTAS, using λ_{exc} and λ_{em} equal to 330 and 390 nm, respectively. The fluorescence emission spectrum of the drug has shown considerable shifts at studied pH range studied, mainly for anionic micelles. Those shifts were used to determine the chloroquine pka. The better drug interaction, evaluated by pKa values, occurs with anionic micelles and this behavior does not depend on the surfactant counterion.

Financial Support: FCFRP-USP.
Advisor: Profa. Dra. Rose Mary Zumstein Georgetto Naal

QB011-MICROWAVE INDUCED SYNTHESIS OF COBALTICENIUM SALTS

BRUNA JULIANA MOREIRA(IC)[1]; ÁUREA DONIZETE LANCHOTE BORGES (PQ)[1]; ALBERTO FEDERMAN NETO(PG)[1]

(1) Faculdade De Ciências Farmacêuticas de Ribeirão Preto, USP

Introduction: $(Cp)_2Co^+$ salts(1) are stable organometallic compounds, related with ferrocenes(2), but less studied, due to their not facile synthesis(1-3). They are obtained in multisteps, by reaction of cobalt salts with cyclopentadienide ions, generated from dicyclopentadiene via thermal cracking(3) and deprotonation with bases.
Objective, Methodology, Results: We are currently developing chemical methods using microwaves. During this work, we developed a new and facile method for preparation of cobalticenium salts by heating or microwave irradiation of the mixture of dicyclopentadienes (CpH or CpMe), $CoCl_2$ and piperazine, a solid (suitable for use in microwave ovens) organic base(4).
The cracking, deprotonation and metalation steps occurs all together, forming the cobalticenium salts.
Microwave irradiation improves yields (thermal: 49-63 ; microwave: 100 %) and reduces time from 9 hs. to minutes.
Conclusions: A new and very easy one step method for the synthesis of cobalticenium salts is described.
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Financial Support: FCFRP
Supervisor: Alberto Federman Neto

QB012-JACOBSEN'S CATALYST AS P-450 BIOMIMETIC MODEL FOR THE OXIDATION OF AN ANTIEPILEPTIC DRUG

TATIANA C. O. MAC LEOD (PG)[1]; MARIA EUGÊNIA Q. NASSUR (PQ)[1]; MARILDA D. ASSIS (PQ)[1]

[1]Universidade de São Paulo, FFCLRP-USP, 14040-901, Ribeirão Preto-SP, Brazil

The major metabolic pathway of carbamazepine (CBZ) is the formation of the carbamazepine 10,11-epoxide (CBZ-EP) by cytochrome P-450. This reactive metabolite is further deactivated by the action of epoxide hydrolase to give inactive carbamazepine trans-diol (CBZ-DiOH), which is then partially conjugated with glucuronic acid and excreted in the urine. Several other minor metabolites have also been identified with CBZ. The understanding of its oxidation mechanisms stimulated numerous studies using biomimetic chemical catalysts. In this work, results for the oxidation of CBZ by m-chloroperbenzoic acid (m-CPBA) and tert-butyl hydroperoxide (t-BOOH) using Jacobsen's catalyst as P-450 biological model will be presented. Oxidation products were analyzed by HPLC-UV. Results show that the Jacobsen's catalyst is able to efficiently catalyze the oxidation of carbamazepine, producing only CBZ-EP, with yield around 70% when m-CPBA is used as oxidant. However, t-BOOH is ineffective for the CBZ epoxidation. These results indicate that the generation of the high-valent Mn(V) oxo salen cation radical intermediate in the reactions of m-CPBA and t-BOOH is affected by the acidity of the oxidant.

Financial Support: FAPESP
Supervisor: M.D.Assis

QB013 - CHROMATOGRAPHIC PROFILE OF FLAVONOIDS OF ETHANOLIC EXTRACT OF *PEPEROMIA PELLUCIDA* (L.) H.B.K.

SANCLAYVER CORRÊA ARAÚJO(IC)[(1)]; GILBERTO VIANA CORDOVIL [(1)]; WAGNER LUIZ RAMOS BARBOSA(PQ)[(1)]

[(1)]Universidade Federal do Pará- Centro de Ciências da Saúde- Laboratório de Fitoquímica

Introduction: *Peperomia pellucida* (L.) H.B.K. is a Piperaceae that occurs in regions with equatorial weather. In brazillian north region, it is popularly known as "erva-de-jaboti" or "comida-de-jaboti" or "coraçãozinho" in the northern region. It's reported a traditional used as anti-hipertensive and antidiahroeacal in a research on Igarapé-miri city (BARBOSA, 2001). In asiatic countries, the vegetable has traditional use since headache, until breast cancer and other infectious diseases, passing through mental disorders. Aim: Determinate the chromatographic profile of ethanolic extract in trying to stablish a pattern of future analysis. Methods: The whole vegetable was harvest and washed under current water, and then put in a stove to be dried. A exsicata was prepared and sent to identification by Dr. Mario Jardim from MPEG (Museu Paraense Emilio Goeldi). The method used to prepare the extract, follows the Brazilian Pharmacopoeia IV (FARMBRAS IV). The extract was then filtered and concentrated under vacuum and reduced pressure at temperature of 45ºC. After that, the dried extract was tested for qualitative detection of secondary metabolites in triplicate by humid way prospection. Also, samples were prepared for analysis by thin layer chromatography (TLC) and high performance liquid chromatography (HPLC). The two first, were the crude extract solved in methanol in the concentration of 1m mg/mL (sample 1) and the sample 1 filtered in reversed phase silicagel (sample 2). Also, a chromatographic column of sephadex 254 was prepared. The sample was 6g of the crude extract solved on 100 mL of methanol/water 9:1 eluting system, and this solution wash with hexane to remove the nonpolar compounds. After the treatment, the sample was applied in the column to separate by molecular weight. Either the samples of TLC or the fractions collected were analysed by TLC and HPLC. The chromatograms were developed in standard plates Merck® of normal and reversed phases. in TLC analysis, and columns of reversed phase were used in HPLC analysis, both in proper eluting systems. Results: The 7,5Kg of fresh vegetable had a weight of 369,75g, so a loss of water of 95%. 329,75g of the vegetable drug used in extract preparation, gave a yelding of 9%. The phytochemical screening detected the presence of reductor sugars, steroids and triterpenoids, carotenoids, flavonoids and coumarins derivated. The chromatographic profile of the TLC analysis.

Support: CNPq
Supervisor: Dr. Wagner Luiz Ramos Barbosa

QB014-CYTOTOXIC ACTIVITY OF 3,4,4',5-TETRAMETHOXYBENZOPHENONE AN ANALOGUE OF RESVERATROL

MARNE CARVALHO DE VASCONCELLOS (PG)[1]; DIEGO VERAS WILKE (IC)[1]; RAQUEL CARVALHO MONTENEGRO (PG)[1]; RODRIGO ROTTA (PG)[2]; DÊNIS PIRES DE LIMA (PQ)[2]; MANOEL ODORICO DE MORAES (PQ)[1]; LETÍCIA VERAS COSTA LOTUFO (PQ) [1];CLÁUDIA DO Ó PESSOA (PQ)[1]

[(1)] Departamento de Fisiologia e Farmacologia; Laboratório de Oncologia Experimental, UFC; [(2)] Departamento de Química/ CCET - UFMS

Introduction: Resveratrol (3,42 ,5-trihydroxy-*trans*-stilbene), a naturally occurring compound present in grapes and other plants provides cancer chemopreventive effects for different systems based on its striking inhibition of diverse cellular events associated with tumor initiation, promotion and progression. Objective: the aim of this work was to study the cytotoxic activity of a synthetic analogue of resveratrol 3,4,4', 5-tetramethoxybenzophenone. Methodology: MTT assay in tumor cell lines proliferation, the inhibition in embryos of the sea urchin *Lytechinus variegatus* and lysis of mouse erythrocytes. Results: 3,4,4',5-tetramethoxybenzophenone lacked activity on mouse erythrocytes, was active in sea urchin eggs development and strongly inhibited the growth of all eight tested tumor cell lines. Conclusions: the compound was as active is the chemotherapeutic agent used as the positive control.

Financial Support: CAPES, CNPq, FINEP e BNB
Supervisor: Cláudia do Ó Pessoa

QB015 - SYNTESIS AND ANTIMICROBIAL ACTIVITY OF NEW 1-ALKYL(ARIL)- 2 ALKYL(ARIL) AMINO- 5-TRIFLUOROACETYL- 1, 2, 3, 4-TETRAHYDROPYRIDINE

FABIANE N. NACHTIGALL(PG)[(1)]; SYDNEY H. ALVES(PQ)[(2)]; NILO ZANATTA(PQ)[(1)]; TATIANA B. SPADER(IC)[(2)]; HELENA S. COELHO(PQ)[(1)]; HELIO G.BONACORSO(PQ)[(1)]; MARCOS A. P. ARTINS(PQ)[(1)]

(1)NUQUIMHE, Departamento de Química, (2)LAPEMI, Departamento de Microbiologia Universidade Federal de Santa Maria, 97.105-900 Santa Maria, RS, Brasil

Pyridines are basic structural of a variety of heterocyclics which present great biological properties. However, available methodologies to produce 1, 2, 3, 4-tetrahydropyridines usually envolve extense synthetic routes, low reaction yields and the isolation of a complex product mixture. Based on that, we have developed a new, simple and regioespecific synthetic strategy to obtain 5-trifluoroacetyl-1, 2, 3, 4-tetrahydropyridines from 4-alcoxy- 5-trifluoroacetyl- 2H- 3, 4-dihydropyranes and primary amines in excelent yield. The in vitro antimicrobial activities are evaluated to pathogenic microorganisms such gram-positive cocci, gram-negative rods, yeas like fungi and alga methods according to bioautography described by Rahalison et al. The compound 3h showed a significant activity to Candida glabrata, Cryptococcus neoformans, Saccharomyces cereviseae, alga Prototheca zopfii and against bacterial patogens Staphylococcus aureus and Escherichia coli.

Financial Support: CAPES, CNPq
Advisor: Sydney H. Alves, Nilo Zanatta

QB016-EFFECTS OF HIGH T3 LEVELS ON THE ALTERNATIVE PATHWAY OF THE COMPLEMENT SYSTEM

CLAUDIA DA SILVA BITENCOURT–PG[1]; ANA ELISA C. S. AZZOLINI–PG[1]; ANA ISABEL DE ASSIS PANDOCHI–PG[1]

[1]Depto. de Física e Química, FCFRP-USP, Ribeirão Preto, SP

Introduction: previous studies have shown that hypothyroidism affects the complement system (CS), increasing the lytic activity of the alternative pathway (AP). Objective: in accordance to this observation the aim of the present study was to investigate if the hyperthyroidism induced in rats by triiodotironine (T3) would also affect complement. Methodology: rats received 0.15 to 50µg of T3 by gavage during periods of 3-14 days. The lytic activity of CS was evaluated by hemolytic assay measuring time required for 50% of lysis to occur (t1/2). Results: the lytic activities of classical/lectin pathways were not significantly altered at any time or T3 dose evaluated. The dose of 0.15µg reduced AP activity (increased t 1/2 values) after 7 and 14 days of treatment. These alterations showed statistical significance (Annova and Dunnet test). The effect on AP activity was dependent on the dose and the period of treatment. Conclusions: hyperthyroidism induced by T3 affects CS reducing AP lytic activity; this effect is opposite to that observed in hypothyroidism. The effect of the T3 level on CS may be considered in certain conditions such as in autoimmune processes involving the thyroid gland.

Financial Support: CAPES
Supervisor: Ana Isabel de Assis Pandochi

QB017 - CHARACTERIZATION OF A ROPIVACAINE:β-CYCLODEXTRIN INCLUSION COMPLEX

LEONARDO F. FRACETO(PQ)[1,2]; DANIELE R. DE ARAÚJO(PG)[2]; FERNANDA D.G.F. CARVALHO(PG)[2]; ENEIDA DE PAULA(PQ)[2]

[1] Univ. of Sorocaba; [2] Dep.Biochem./Unicamp

Introduction: Ropivacaine (RVC) is a local anesthetics introduced in the 90ths as an alternative for the clinical use. The development of formulations for RVC in carriers such as β-cyclodextrins (β-CD) offers the possibility to control drug-delivery biological systems.
Objective: The present work comprises the structural characterization of a RVC:β-CD complex using several analytical techniques.
Method: The complex was prepared at different molar ratios with RVC and b-CD suspended in water and then lyophilized for further characterization by such as nuclear magnetic resonance (NMR), UV-Vis absorption, differential scanning calorimetry (DSC) and scanning electron microscopy (SEM).
Results: The UV-Vis spectra revealed an increase in RVC solubility upon complexation with β-CD and an association constant of 10 M^{-1}. The stoichiometry of complexation was determined by NMR and UV-Vis. DSC data revealed the characteristic loss of the anesthetic melting point (117.6 °C) and β-CD dehydration temperature (141.8 °C) upon complexation and SEM pictures revealed that complex formation leads to changes in the morphology of the crystals of pure RVC and β-CD.
Conclusion: This work suggests that RVC:β-CD complex may be a promising novel formulation to enhance the pharmacokinetics of RVC preparations used for pain relief.

Financial Support: FAPESP/UNISO
Supervisor: E. de Paula

QB018- *IN VITRO* METABOLISM STUDY FOR HCQ USING RAT AND MOUSE LIVER MICROSOMES

CARMEM DICKOW CARDOSO (PG)[12]; PIERINA SUELI BONATO[3] (PQ)

[1] Universidade Católica de Pelotas; [2] Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto/USP; [3]Faculdade de Ciências Farmacêuticas de Ribeirão Preto/USP

Hydroxychloroquine (HCQ) is used in the treatment of rheumatoid arthritis and systemic lupus erythematosus and as an antimalarial. It is administered as a racemic mixture [*rac*-HCQ] of two enantiomers, *R*(-)-HCQ and *R*(+)-HCQ and its hepatic metabolism generates three active metabolites, desethylchloroquine (DCQ), desethylhydroxychloroquine (DHCQ) and bisdesethylchloroquine (BDCQ), which are also chiral molecules. We report here an *in vitro* metabolic study for this drug carried out with rat and mouse liver microsomes. The time of incubation, the amount of microsomes homogenate and the concentration of HCQ were optimized. The enantiomers of DCQ and DHCQ metabolites were separated and quantified by HPLC, using an one-step chiral method. The enantiomers of BDCQ metabolite were separated and quantified by CE (capillary electroforesis) chiral method. The metabolic study demonstrated that HCQ metabolism is stereoselective. The major metabolites formed in the incubation of racemic HCQ were *R*(-)-DCQ and *R*(-)-DHCQ, for both animal species.

Financial Support: FAPESP, CNPq, UCPel

QB019-CHROMATOGRAPHIC AND SPECTROMETRIC EVALUATION OF PORCINE MONOSIALOGANGLIOSIDE

PEDRO GONÇALVES DE OLIVEIRA(PQ) [1]

[(1)] Faculdade de Ciências Farmacêuticas e Bioquímicas "Oswaldo Cruz"

Monosialoganglioside, also called ganglioside GM1, is a glycosphingolipid used in the treatment of stroke and spinal cord injury. The pharmaceutical products containing this kind of molecule have used raw material obtained from bovine brains. Recently, Chemedica International concluded the development of an extraction process to obtain GM1 from porcine sources. In this case, it is important to evaluate the reproducibility of that in order to generate the same product, emphasizing its identity. The aim of this work is the chromatographic and spectroscopic evaluation of three batches of porcine GM1. The chromatographic profiles were performed by thin layer chromatography technique, using four solvent systems, and an isocratic high performance liquid chromatography method. The spectroscopic evaluation considered infrared, ultraviolet-visible, mass and nuclear magnetic resonance spectrums. The results were compared with those obtained from bovine GM1 standard, supplied by Sigma, and with data available in the scientific literature. Chromatograms and spectrums resulted from each batch were equivalents and compatible with standard values. The identity of three batches is similar and this means that the extraction process is reproducible concerning that characteristics.

QB020-SOLID STATE CHARACTERIZATION OF POLYMORPHISM IN DRUGS: OXCARBAZEPINE (OXC) AND MEBENDAZOLE (MBZ).

SONIA FAUDONE(PG)*,JAVIER ELLENA(PQ)**,ALEJANDRO P. AYALA(PQ)+,YVONNE P. MASCARENHAS(PQ)**, SILVIA CUFFINI(PQ) *

*Agencia Córdoba Ciencia. Ceprocor. Argentina;** Instituto de Física de São Carlos, USP, SP. Brasil; +Departamento de Física, UFC, CE, Brasil. E-mail: scuffini@ceprocor.uncor.edu

The polymorphic behavior of drugs is a major concern of the pharmaceutical industry as it may have considerable formulation, therapeutic, legal and commercial implications. It is crucial to be able adequately to identify and characterize different polymorphic forms of drugs. The aim of the present study was to show the solid state characterization of APIs like OXC, a new-generation anticonvulsant [1] and MBZ, a broad spectrum antihelmintic active[2]. The methodology used was single crystal and powder X-ray diffraction, FTIR and Raman Spectroscopy and dissolution techniques. The results reported crystal structure and spectroscopic characterization of OXC and MBZ. The difference between OXC and CBZ were not only with the structure and H-bonding but also with dissolution and stability properties. Raw materials and final products of MBZ were analyzed and it was detected Pol. C (ACITVE API) and Pol. A (INACTIVE API).
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[2] E. Swanepoel, W. Liebenberg, B. Devarakonda and M.M. de Villiers. Pharmazie 2003; 58 (2)117-121.

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Supervisor: Dra. Silvia Cuffini

QB021-SYNTHESIS OF 1,4-BIS-(3,4,5-TRIMETHOXYPHENYL)BUT-2-IN-1,4-DIOL AND 1,4-BIS-(3,4,5-TRIMETHOXYPHENYL)1,4-BUTANEDIOL AS POTENTIAL TRYPANOCIDAL DERIVATIVES.

LÍLIAN SIBELLE CAMPOS BERNARDES (PG)[1]*, PÉTERSON DE ANDRADE (IC) [1], SÉRGIO ALBUQUERQUE (PQ)[2], IVONE CARVALHO (PQ) [1]

[1]DCF, FCFRP/USP; [2]DACTB, FCFRP/USP - * lscamber@fcfrp.usp.br

Our continuing interest in the synthesis of neolignans derivatives, such as grandisin 1 and veraguensin 2, isolated from *Virola surinamensis*, led us to prepare potential trypanocidal 1,4-bis-(3,4,5-trimethoxyphenyl)but-2-in-1,4-diol 31 and 1,4-bis-(3,4,5-trimethoxyphenyl)1,4-butanediol 38. The synthetic strategy involves the condensation of carbinol compounds with the corresponding aldehyde in order to prepare symmetrical diaryl acetylenic glycol 31, being the former prepared by reaction of substituted benzaldehydes with lithium acetylide ethylene diamine complex. The treatment of 31 with platinum oxide allowed the hydrogenation of the triple bond, giving the desired compound 38. The "in vitro" biological activity was carried out with different strains of *Trypanosoma cruzi*, such as Y and Bolívia strain. The IC50 of 31 and 38 were, respectively, 0,11 mM (Y strain), 0,14 mM (Bolívia strain) and 0,10 Mm (Y strain), 0,11 Mm (Bolívia strain), which were assessed by measuring the percentage of trypomastigotes lyses.

Financial Support: FAPESP
Supervisor: Profa. Dra. Ivone Carvalho

QB022 - SYNTHESIS AND GLYCOSIDASE INHIBITORY ACTIVITY OF CYCLITOL DERIVATIVE

ADRIANE DA SILVEIRA GOMES (PG)*; IVONE CARVALHO (PQ)

Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP * drigomes@fcfrp.usp.br

Cyclitols are important constituents of many biologically active molecules and exhibit different biological effects, for example, selective inhibition of enzymes, such as glycosidases. This work reports a new synthetic route, with only four steps, to obtain the key-intermediate (3/2,4)-2,3,4-tri-O-benzyl-5-hydroxy-cyclohexanone 1 in 52% yield. This compound was conveniently hydrogenated in the presence of Pd-black, which afforded the desired cyclitol 2,3,4,5-tetra-hydroxy-cyclohexanone 2. Thus, the compound 2 was evaluated against a-D-glycosidase *of Saccharomyces cerevisiae*. Preliminary tests with 2 have shown inhibition of 20% of enzyme activity. In order to improve the activity against glycosidases, new cyclitols derivatives are being synthesized

Financial Support: FAPESP
Supervisor: Profa. Dra. Ivone Carvalho

QB023-ANTIOEDEMATOGENIC ACTIVITY AND INHIBITORY LEUKOCYTES MIGRATION PRODUCED BY 1,5-DIFENIL-3-HIDRAZINOPIRAZOL (DHP)

JULIO CESAR MARIANO FARIAS(PG)[(1)]; ANTONIO CARLOS CARRERA FREITAS(PQ)[(2)]; JOÃO CARLOS MARTINS MAFRA(PG)[(3)]; ELSON ALVES COSTA(PQ)[(4)]; LÉCIA GARCIA MATOS(PG)[(4)]; MARIA APARECIDA MEDEIROS MACIEL(PQ)[(5)]; DAVID DO CARMO MALVAR(IC)[(6)]; WELLINGTON DA SILVA CÔRTES(PQ)[(6)]; FREDERICO ARGOLLO VANDERLINDE(PQ)[(6)]

[(1)]ABF; [(2)]UNIG; [(3)]UFRJ; [(4)]UFG; [(5)]UFN; [(6)]UFRuralRJ

The compound DHP (1-10mg kg^{-1},*p.o.*) produced antinociceptive effects in abdominal constriction and formalin (2nd phase) tests while in hot-plate test was ineffective (FeSBE 2004-resume 17.012). To assess the antioedematogenic effect of DHP, croton oil-induced mice ear oedema method was used and DHP inhibited croton oil oedema formation. The difference of right and left ear weight obtained in control group was 8.5±1mg, and DHP (10mg kg^{-1},*p.o.*) or positive control dexamethasone (0.5mg kg^{-1},*p.o.*) inhibited the oedematogenic response by 54.1% and 55.3%, respectively. In inflammatory model of carrageenin-induced pleurisy, comparatively to vehicle group (13.6±0.2 leukocytes $x10^6$), oral administration of DHP (3, 10 or 30mg kg^{-1}) produced a dose-related reduction of leukocyte migration (11.8±1.7%, 39±2.9% and 53.7±4.1% respectively), while positive control dexamethasone (2mg kg^{-1},*p.o.*) inhibited 72.7±3.9%. These results indicated antiinflammatory activity of DHP.

Financial Support: CNPq
Supervisor: Frederico Argollo Vanderlinde

QB024-KINETICS OF ELECTRODEGRADATION OF OXYTETRACYCLINE

MARCELO AZEVEDO OLIVEIRA (IC)[1]; LUÍS ANTÔNIO DA SILVA (PQ)[1]; VALÉRIA ALMEIDA ALVES (PQ)[1]; DANILO DE OLIVEIRA SANTOS E ASSIS (IC)[1]; ALEXANDRE ROSSI (PQ)[1]

[(1)] Faculdades Federais Integradas de Diamantina / FAFEID – Diamantina - MG

The presence of polluent antibiotics in waters, even after the processes of treatment in the Stations of Treatment of Sewers (STSs), have demanded new technologies to degrade these drugs. The electrochemical processes have shown to be efficient and promising in the electrodegradation of antibiotics. Thus, it was investigated the kinetics of electrodegradation of the oxytetracycline (OTC) (2,17 mmol dm^{-3}) in solutions of different pH values (1,46; 3,70; 4,70 and 6,80), applying a constant current of +100mA to the ruthenium oxide anode (Ti/RuO_2) during 1 h, using a Potenciostate/Galvanostate (Micro-Química). It was collected 1,0 mL of the OTC solutions before the electrodegradation and after 10, 20, 30 and 50 minutes of electrolysis. The samples were diluted and analyzed using a UV-Vis spectrophotometer (Micronal). All experiments were carried out at room temperature. It was verified that the OTC electrodegradation is pH-independent. The kinetics law is of first-order with respect to OTC concentration; the value of the reaction constant rate was $1{,}28.10^{-4}$ s^{-1}.

Financial Support: FAFEID, FAPEMIG
Supervisor: Prof. Dr. Alexandre Rossi

QB025-SYNTHESIS AND EVALUATION OF NEW CANDIDATES TO TRICOMONICIDAL AGENTS PLANNING FROM SAFROL

LUCIANA C. NASCENTE (IC)[1]; LARISSA C. MALUF (IC)[1]; VALÉRIA F. CERIPES (IC)[1]; FABRÍCIO FERNANDES (IC)[2]; SANDRA E. S. CARVALHO (PG)[2]; CAMILA L. CORREIA (IC)[2]; JAQUELINE RODRIGUES (IC)[2]; AUGUSTO SIMÕES-BARBOSA (PQ)[2]; OCTAVIO L. FRANCO (PQ)[2]; LUIZ A. S. ROMEIRO (PQ)[1]

[1]NQBM/UCB-DF; [2]Centro de Análises Proteômicas e Bioquímicas, PGCGB/UCB-DF

Introduction: *Trichonomas vaginalis* is an urogenital protozoan that parasites humans, causing trichomoniases, a sexually transmissible disease with a worldwide impact. Objective: We describe the synthesis and evaluation of new trichomonicidal candidates e.g. TCH-Ox (1), TCH-Al (2), TCH-Al-NO_2 (3) , TCH-ETA (4), and TCH-MF (5), planning from safrol. Methods: Compound stock solutions were stored (16μg.mL^{-1}, distilled water), and added at several standard concentrations to Diamond broth and after 24 hours, *T. vaginalis* individuals were counted in Neubauer chambers. Results and Conclusions: 3 showed a remarkable inhibition of 98.6% (8.45x10^{-3}M), 4 decreased 100% the protozoan growth (1.2x10^{-3}M), and 5 have caused mortality of 69.7% (2.75x10^{-3}M). By contrast, 1 and 2 did not cause any deleterious effects. As a positive control, metronidazole 0,12 μM was used, causing 100% mortality. Our results showed relevant structural features involved in the lethal activity toward *T. vaginalis*.

Financial Support: UCB and CNPq.
Supervisor: Luiz A. S. Romeiro

QB026-ENCAPSULATION OF ANTIMYCOBACTERIAL IN BIODEGRADABLES POLYMERS MICROPARTICLES

MARUSKA NEUFERT(PG) [1]; PRISCYLA D. MARCATO (PG)[2] NELSON DURÁN(PQ)[12]

[1] Universidade de Mogi das Cruzes; [2] Unicamp

Introduction
Polymeric microparticles (MP) have become an important area of research in the field of drug delivery. The most widely used polymers for MPs have been PLA,PGA,PLGA,PHBV and PCL. Several drug delivery systems have been developed to improve the efficiency of drugs and minimize toxic side effects.
Objective
To encapsulate an antimycobacterial (AB) in MPs using differents polymers and to characterize a size and morphology of them.
Methodology
The PLGA, PCL and PHBV were used. The preparation MPs were accomplished by double emulsion (w/o/w) technique. Briefly, the AB was dissolved in distilled water and emulsified in an organic phase containing the polymer under magnetic stirring. Thereafter, this first emulsion was poured into PVA aqueous solution and homogenized. After solvent evaporation, the MPs were isolated by centrifugation before lyophilization.
Results and Conclusions
The MPs were characterized by scanning electron microscope (SEM). The particle size distribution was 10-40 mm in diameter. In the PLGA and PCL MPs showed a smooth surface, but in the PHBV MPs were not appeared a smooth surface. A particle morphology of MPs were different. It was possible caused by different properties of the polymers and surfactants interactions.

Financial Support: Rede de Nanotecnologia, CNPq and Fapesp
Supervisor: Nelson Durán

The authors did not follow the Scientific Committee's suggestion for an English language review

QB027-SYNTHESIS AND EVALUATION OF NEW CANDIDATES TO SUNSCREENS PLANNING FROM CASHEW NUT SHELL LIQUID

EMELI MOURA DE ARAÚJO (PG)[(1)]; SHEILA GARCIA (PQ)[(1)]; ELISABETE PEREIRA DOS SANTOS (PQ)[(1)]; GISELA D. ORTIZ (PQ)[(1)]; CÉLIA S. SILVA (PQ)[(1)]; ALVARO A. C. LEITÃO (PQ)[(1)]; ZAIDA MARIA FARIA DE FREITAS (PG)[(1)]; MARIA L. DOS SANTOS (PQ)[(2)]; LÚCIO P. L. LOGRADO (PQ)[(2)]; ANA P. C. RODRIGUES(IC)[(3)]; LUIZ A. S. ROMEIRO (PQ)[(3)];

[(1)]Faculdade de Farmácia – UFRJ; [(2)]Instituto de Química, UnB-DF; [(2)]NQBM,UCB-DF

Introduction: The photoprotection is an important public health subject in face of the problems related to skin cancer. Objetive: In a research field aiming the design, synthesis and evaluation of new candidates to photoprotector agents useful as sunscreens we report the evaluation of new esters planning from cashew nut shell liquid. Methods: To verify the Sun Protector Factor (SPF) an *in vitro* method based on spectrophotometry was applied, using the mathematics equation developed by Mansur. In addition some tests preconized by ANVISA to assure that these substances are safe *e.g.* phototoxicity (*in vivo* and *in vitro*), mutagenicity, genotoxicity, skin and mucous irritancy were also applied. Results and Conclusions: The SPF values found were: V32 (9,5), V33 (5,2), V34 (1,7), V35 (3,3), V36 (7,7), and these substances also demonstrated to be non-phototoxic, non-genotoxic, non-mutagenic and non-irritant, validating the structural planning of this class of compounds.

Financial Support: UCB and CNPq
Supervisor: Sheila Garcia

QB028-DELETERIOUS EFFECTS OF SYNTHETIC COMPOUNDS TOWARD HOSPITAL INFECTION GRAM-NEGATIVE BACTERIA

VALÉRIA F. CERIPES (IC)[1]; LUCIANA C. NASCENTE (IC)[1]; THIAGO C. SANTOS (IC)[2]; THAINA DE A. LIMA(IC)[2]; OCTAVIO L. FRANCO (PQ)[2]; LUIZ A. S. ROMEIRO (PQ)[1]

[(1)]Núcleo de Química Bioorgânica e Medicinal, UCB-DF; [(2)]Centro de Análises Proteômicas e Bioquímicas - Pós-Graduação em Ciências Genômicas e Biotecnologia, UCB-DF

Introduction: One main problem faced by hospital patients in Brazil is the increasing of bacterial resistance to antibiotics. *Klebsiella* sp is a human pathogen that could cause pneumonia, renal and neural infections. Objective: We report the evaluation of new compounds synthesized from cardanol (ANF-1 and ANF-ED1) and anacardic acid as for their bactericidal activity. Methods: Compound stock solutions were stored at a concentration of 200 $\mu g.ml^{-1}$, dissolved in distilled water and added at several standard concentrations to Luria Bertani broth and after 3 hours, wherin optical densitometry were measured at 530 nm. Results and Conclusions: Anacardic acid showed a remarkable inhibition of 91.1%, while ANF-ED1 decreased 62% the *Klebsiella* growth. By contrast, ANF-1 compound did not cause any deleterious effects. As a positive control, cloranfenicol $40\mu g.ml^{-1}$ was used, causing 100% mortality. Our results demonstrated relevant structural features involved in the lethal activity toward gram-negative bacteria.

Financial Support: UCB and CNPq.
Supervisor: Octavio L. Franco

QB029 - SYNTHESIS OF NEW CANDIDATES FOR ALPHA-1 ADRENERGIC ANTAGONISTS, USEFUL FOR TREATMENT OF THE BPH

RENATA O. SILVA (IC)[1]; CARLOS A. M. FRAGA (PQ)[2]; ELIEZER J. BARREIRO (PQ)[2]; LUIZ A. S. ROMEIRO (PQ)[1]

[1]Núcleo de Química Bioorgânica e Medicinal/UCB-DF, [2]LASSBio – Faculdade de Farmácia/UFRJ

Introduction: The benign prostatic hyperplasia (BPH) is a of nonmalignant tumor more commonly found in men. Our group has working in the development of new adrenergic antagonists based on lead compounds LASSBio 772 and LASSBio 772B, which showed subnanomolar α_{1A}/ α_{1D} profile. Objective: In this work we describe the synthesis of new *N*-phenylpiperazinic compounds aiming to obtain insight of the structural requirements for α_1-AR recognition. Methods: The new compounds were synthesized by the use of classical chemistry procedures including microwaves Friedel-Crafts acylation microwave irradiation and catalyzed by $ZnCl_2$, Willgerodt-Kindler reaction to obtain a thioamide derivate, hydrolysis and reduction with metallic hydrides, conversion to methanesulfonates and nucleophilic bimolecular substitution of the corresponding mesylates by 2-methoxyphenylpiperazine under reflux. Results and Conclusion: The compounds were obtained in 40-81% overall yield and characterized by spectroscopic methods NMR , IR. Binding assays and functional experiments will be carry outbin order to validate the structural planning of this class of compounds.

Financial Support: UCB and CNPq
Supervisor: Luiz A. S. Romeiro

QB030 - UV SPECTROPHOTOMETRIC PROFILE OF OCTYLMETHOCINNAMATE AND A NEW PHENOLIC ESTER FROM CASHEW NUT SHELL LIQUID

LAIANNA DE OLIVEIRA SILVA (IC)[1]; LUIZ ANTONIO SOARES ROMEIRO (PQ)[1]; SILVIA KELI DE BARROS ALCANFOR (PQ)[1]

[1]Curso de Química, UCB-DF.

Introduction: Octylmethoxycinnamate is a filter usually used in cosmetic preparations, reaching about 10% of its concentration. The maximum absorbance was found in 310 nm. However, the absorbance intensity and the maximum wavelength depend on the solvents and on the composition of different kind of sunscreens. Objective: In this work we describe the absorbance profile of octylmethoxycinnamate in different solvents in order to develop a standard referential to evaluate new UV protector agent (V36) synthesized at the UCB as for their SPF and the critic wavelength (λc). Methods: Solutions of octylmethoxycinnamate (5%) (1) were prepared in methanol (A), ethanol (B), hexane (C), THF (D), chloroform (E), isopropanol (F), *n*-butanol (G) and DMSO (H) and V36 (5%) (2) only in H. They were individually evaluated as for their UV spectrophotometric features. Results and Conclusions: The better SPF value to 1 were observed in A and C (9,0), while B, E and H showed SPF value 7,0 and the others solvents between 3,0 and 4,0. The λc observed to 1 stayed in the range of 318 to 330 nm (UVB range). 2 showed SPF value 7,0 with λc 352 nm, compatible with UVA/UVB protection range.

Financial Support UCB and CNPq
Supervisor: Silvia Keli de Barros Alcanfor

QB031-ELECTROCHEMICAL OXIDATION OF SULPHITE BY FERROCENECARBOXILIC ACID COVALENTLY ATTACHED TO GRAPHITE: PH INFLUENCE.

EDGAR T. SUZUKI YAMAMOTO (IC)[1]; ALBERTO FEDERMAN NETO (PQ)[2]; ZEKI NAAL (PQ)[1].

1.Depto.de Física e Química, FCFRP/USP; 2. Depto.de Ciências Farmacêuticas, FCFRP/USP.

There is a great deal of interest in new methodologies for the covalent modification of redox mediators that will allow for maximal retention of stability regards on its lixiviation in various solutions. Recently, we have been involved in the development of preparation strategies of graphite (GF) surface modification by Friedel-Crafts acylation (F-CA). Ojani et al. reported sulphite (SP) analysis using ferrocene carboxylic acid (Fc) as a mediator in solution pH 8. Since the SP analysis is pH dependent it is a great deal to study the electrochemical behavior of GF-Fc, obtained by F-CA, in different pH values. In this work, we have showed the electrochemical behavior of the GF-Fc as an electrodic material in phosphate buffer solutions at pH 3, 7 and 8 in absence and presence of SP. Therefore, in addition of SP, the electrode exhibits an enhancement in the current response for the peak centered at +0.35 V ($Ag/AgCl/NaCl_{sat}$). The amplitude of the catalytic current (in a cyclic voltammogram at 10 mV/s) is proportional to the solution concentration of SP for values of up to 5 mM. The results obtained indicate that the SP oxidation has higher sensitivity at pH 7 and 8.

Financial Support: FAPESP
Advisor: Zeki Naal

QB032 - MICROBIAL MODELS OF ANIMAL METABOLISM: APPLICATION TO A STUDY OF THE METABOLISM OF LASSBIO 873

EMMANUEL DE OLIVEIRA CARNEIRO (IC) [(1)]; VALÉRIA DE OLIVEIRA (PQ) [(1)]; RICARDO MENEGATTI (PG) [(2)]; CARLOS A. MANSSOUR FRAGA (PQ)[(2)]; ELIEZER J. BARREIRO(PQ)[(2)]

[(1)] Universidade Federal de Goiás-UFG; [(2)] Universidade Federal do Rio de Janeiro-UFRJ

LASSBIO 873 **(**1-methyl-7-(4-nitrophenyl)-3-phenyl-3,6,7,8-tetraidropyrazolo [3,4-d] pyridine 6,8-dione) is a new heterotricyclic compound recently developed, which was structurally designed by using zolpidem. The biological assays (sleeping time and hot plate) of the LASSBio 873 were performed *in vivo* showing hypnotic profile with DL_{50} = 42.6 mðg/Kg and moderate analgesic activity. It was thus a good opportunity to apply the concept of "Microbial Models of Mammalian Metabolism", in order to make some prediction about the nature of formed metabolites, to prepare a significant amount of the main ones for structure identification and as authentic chromatographic specimens for the analysis of animal metabolites, and if needed, to produce sufficient amounts of some of them for new pharmacological studies. LASSBIO 873 was incubated in a liquid medium with various strains of filamentous fungi and five different metabolites were detected by HPLC in the incubation supernatants, then separated and purified. These results demonstrated the interesting potential of such methods, compared to animal models.

Financial Support: CNPQ; SECTEC
Supervisor: Valéria de Oliveira

QB033-MORPHOANATOMICAL CONSIDERATION OF *PFAFFIA GLOMERATA*

ROSILDA MUSSURY(PQ); KELEN HOFFMANN(IC); BRUNA GOMES(IC); KASSIA PEREIRA(IC); ELISANGELA NUNES(IC)

Centro Universitário da Grande Dourados,UNIGRAN,Dourados-MS

INTRODUCTION
Pfaffia glomerata is one of the brazilian ginseng species used as medicinal plant
OBJECTIVE
The present work had as its objectives the morpho-anatomical characterization of vegetative organs
METHODOLOGY
Leaves were sectioned on medium of the third part in different stadiums of development and they were analyzed anatomically. Anatomical of the subterranean system and stem were simultaneously analyzed
RESULT AND CONCLUSION
P. glomerata initial morphology is epigeous-foliaceous, root is axial type. The subterranean system consists of tuberous root and another region being formed starting from the hypocotyl thickness from where aerial branches are emitted. It was observed that in the root the secondary growth results of an initial establishment of a normal vascular cambium and the diameter increase of the root is due to the additional cambia with a limited activity, which are initially formed from plurisseriate pericycle and later from the division of parenchym cells, which are placed outside the secondary phloem. Secondary growth of the stem begins with the installation of a typical cambium, which increase of stem diameter is a result of installation of accessory cambiums. The mesophyll in every type of studied leaves is dorsiventral and anomocitic stomata.

Supervisor: Rosilda Mussury

The authors did not follow the Scientific Committee's suggestion for an English language review

QB34 - PHYTOCHEMICAL AND BIOLOGICAL EVALUATION OF *SAPINDUS SAPONARIA* L.

IZABEL CRISTINA PILOTO FERREIRA (PQ)[4]; PAULA AKEMI HONDA (IC)[1]; JOYCE KARLA TSUZUKI (PG)[2]; MARIA VALDRINEZ CAMPANA LONARDONI (PQ)[3]; DIÓGENES APARÍCIO GARCIA CORTEZ (PQ)[4]

(1) Acadêmica de Farmácia-UEM; (2) Acadêmico do Curso de PG-Ciências Farmacêuticas-UEM; (3) Docente do DAC-UEM; (4) Docente do DFF-UEM.

Introduction: The necessity of finding new drugs against leishmaniasis lend us study *Sapindus saponaria* L. According to previores biological studies on *Sapindus* its crude extract is believed to have molluscicide, antifungal and antiulcer activities. The most extensive studies have been made on *S. mukurossi* e *S. delavayi*. Purpose: Isolating saponins, triterpenes, tannins and flavonoids of *Sapindus saponaria* L. and to evaluating its biological potentials as molluscicide, antifungal and anti-protozoan activity through a phytochemical study of its crude extract. Methods: The chromatographic methods used were both column of adsorção of silica gel and exclusion in Sephadex LH-20. Results: The hydroalcoholic crude extract was submitted to leishmanicide and molluscicide test, being the superior joined values 320 μg/ml and about 200ppm respectively, while butynoic extract presented leishmanicide inhibition of only 20% at the same concentration. Conclusion: These preliminary studies of *Sapindus saponaria* extract have indicated biological potential to the leishmanicide action.

Supervisor: Izabel Cristina Piloto Ferreira

QB035- STUDIES ON THE INCLUSION COMPLEX OF NICLOSAMIDE/β-CYCLODEXTRIN: PREVIOUS EXPERIMENTS

[1] ROSANE MARIA BUDAL(PQ); [2] MARIA DA GRAÇA NASCIMENTO (PQ) ; [3] AIDA JOVER RAMOS (PQ);[2] ROSENDO A. YUNES (PQ);[3] JOSÉ VÁZQUEZ TATO (PQ).

(1) Departamento de Ciências Farmacêuticas, Universidade Federal de Santa Catarina (UFSC); (2) Departamento de Química, UFSC; (3) Departamento de Química Física, Faculdade de Ciências, Universidade de Santiago de Compostela (USC).

Cyclodextrins are a group of cyclic oligosaccharides which can change the physicochemical properties of the guest molecule, such as solubility, stability and bioavailability, by forming inclusion complexes. This ability has been largely exploited in pharmaceutical applications. In this work, we studied the niclosamide/β-CD system. Niclosamide is an antiparasitic drug used to treat helminthiasis and in the Shistosoma mansoni control, with little solubility in water and susceptible to hydrolysis. Previous experiments like NMR, ultraviolet and fluorescence, as well kinetic methods were used to try to evaluate the formation of niclosamide/β-CD inclusion complexes. It was not possible to establish the formation of the complex by NMR or fluorescence. The results propose that the kinetic approach could be the most reliable way to determine the formation constant of the niclosamide/β-CD complex and it could be the choice method for compounds unstable in aqueous media.

Financial Support: UFSC, CAPES, USC
Supervisor: José Vázquez Tato

QB036- ACUTE TOXICITY $(LD)_{50}$ DETERMINATION OF THE POTENTIAL ANTICHAGASIC HIDROXIMETILNITROFURAZONE.

MARA FILOMENA FERREIRA DE MELO[1](PG); RICARDO VIAN MARQUES[1](IC); ELIZABETHE IGNE FERREIRA[2](PQ); MARIA DO CARMO LONGO[1](PQ); MAN CHIN CHUNG[1](PQ).

[1]Faculdade de Ciencias Farmaceuticas, UNESP
[2]Faculdade. de Ciências Farmacêuticas, USP.

Current therapy of the Chagas´ disease in Brasil is based on benznidazol, which are mostly efective in the acute phase of the disease and may cause serious adverse side effects. The hydroxymethylnitrofurazone (NFOH) showed high antichagasic ativity with decreased mutagenic activity related to nitrofurazone (NF) in studies "*in vitro"*. The purpose of this study was to determine acute toxicity (LD_{50}) of the NFOH (*p.o* and *i.p* route) and NF (*i.p.*) in mice. The sample was prepared from NFOH (Lapdesf batch 001, obtained by reacting NF with formaldehyde in pH 7,4, 24 hs) and NF (batch 064K2513, Sigma). The doses of NFOH were 150,250,300,400,600 and 1000,1500,2000,2500 and 3000 mg/kg for *i.p* and *p.o.* route, respectively, and the doses of NF were 98,200,250,300 and 400 mg/kg, total n=120, adults and males.
The Lethal Average Dose was calculated through probitos. The results showed for NFOH LD_{50}:2500 mg/kg (*p.o*) and 327mg/kg (*i.p*.). The derivative NFOH showed lower values of toxicity than NF (DL_{50} literature 590 mg/kg *p.o*, obtained 197,1 mg/kg *i.p*.), suggesting that NFOH can continue the preclinical studies.

Financial Support: CAPES
Supervisor: Chung Man Chin

QB037 - RESEARCH OF NATURAL ANTIDEPRESSANTS BY CAMCORDER TAIL SUSPENSION ASSAY

KEIDI UJIKAWA (PQ); HERIDA REGINA NUNES SALGADO (PQ)

Faculdade de Ciências Farmacêuticas – Unesp- Araraquara

A program of study of nutritional and environmental factors, that cause or cure moody disorders, is being carried out. The tests with animals are sensitive to various environmental conditions. Low infrastructure laboratories can not avoid many these interferent factors. The objective of this work was to characterize nutritional and phytopharmaceutical factors that influences mood disorders. Seventy two Swiss male mice (*Mus musculus*) were housed in twelve cages , six individuals per cage. The substances tested were extracts of *Pfaffia glomerata* in 2% glycerin, glycerin 2%, extracts of *Pygeum africanunn* and *Urtica dioica*, stevioside and Stevia rebaudiana all diluted to 500 ml with water. Also it was carried out a blank test with water. After the treatments, the tail suspension assay was performed in two sessions of three groups simultaneously by the usual method, but using fish hooks and Sony TRV328 camcorder. The mean results (n=12) were respectively 81.83, 58.16, 94.50, 82.18, 106.90 and 104.54 seconds. The calculated SD were 36.22, 48.27, 45.29, 40.15, 56.91 and 63.08, respectively. The t values were 0.45, 0.07, 1.00, 0.73, 0.72 and 1.00. Our results can sugest that tested substances did not change significantly the mood when compared to untreated control mice. Moreover, the tested groups showed a high SD values despite the abbeviation of test time.

Financial support – CNPq

QB038-PHOTOPHYSICAL STUDIES OF LIPOSSOMAL ZINC-PHTALOCIANINE (ZNPC) IN THE PRESENCE OF AN ADDITIVE, FOR USE IN SKIN CANCER PHOTODYNAMIC THERAPY

MICHIELETO,L.(IC);PRIMO,F.L.(PG);TEDESCO,A.C.(PQ)

Lab de Fotoquímica e Fotobiologia, Depto de Química, FFCLRP – USP, SP

Photodynamic Therapy (PDT) is a modality for the treatment of various cancer deseases. PDT is based upon the administration of a photosensitive compound (photosensitizer, PS), followed by its activation with light of appropriate wavelength. The resulting photodamage to the neoplasic cell comes from biochemical reactions induced by reactive oxygen species, leading to cell inactivation. In this work, we evaluated the interference of Monoolein (MO), a good enhancer, in the lipossomal photophysical characteristics of ZnPC, by steady-state spectroscopic tecniques and time–related fluorescence. The results clearly show that the spectral properties in the stationary state (absorption and fluorescence emission) are not affected by the presence of MO, being most of the photophysical properties of the drug preserved in this drug delivery system. Time-related fluorescence studies indicate there is no difference in the singlet excited state profile decay, but an increase in its lifetime (t_1=1,49 ± 0,02ns and t_2=6,1 ± 0,09ns to t_1=2,54 ± 0,03ns and t_2=8,66 ± 0,2ns) in the presence of MO, which fortunately is not considerably high for PDT, but appropriate for photodyagnosis protocol.

Financial: FAPESP/CNPq
Supervisor: Prof Dr A.C. Tedesco

QB039-PLASMA HYDROLYSIS STUDY OF THE HYDROXYMETHYLNITROFURAZONE PRODRUG

ELIANA OMETTO PAVAN SERAFIM (PG)[2]; MARIA LÚCIA RIBEIRO (PQ)[2]; ELIZABETH IGNE FERREIRA (PQ)[3]; ROSÂNGELA GONÇALVES PECCININI MACHADO (PQ)[1]; MAN-CHIN CHUNG (PQ)[1]

[1] Faculdade de Ciências Farmacêuticas / UNESP – Araraquara.
[2] Instituto de Química / UNESP – Araraquara.
[3] Faculdade de Ciências Farmacêuticas / USP – São Paulo.

Trypanosoma cruzi infection causes significant morbidity and mortality. Chagas Disease morbi-mortality in Brazil is significant, killing 20% or more of the infected individuals, which acquire chronic heart disease, able to kill, at least, 15.000 persons/year in Latin America. The present study investigate the half life time of hydroxymethylnitrofurazone (NFOH), a prodrug of nitrofurazone (NF), with antichagasic activity. The hydrolysis study of NFOH was performed at 37 °C in a pool of human plasma (pH 7.4) and serial samples were collected in the 144 h interval. NFOH and NF were extracted using ethyl acetate (pH 10) and analyzed by HPLC using a RP18 column and UV detector set at 365nm. The study shows that NFOH is stable till the first 12 h. After this time, the hydrolises occurs at the rate of 80% at 144 hours. This results shows that this prodrug can be used because its not cleaved to the parent drug immediatly.

Financial suport: CAPES.
Supervisor: Maria Lúcia Ribeiro.

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SP001-CORONARY ARTERY DISEASE: STUDY IN PEOPLE OF FIFTY YEARS OLD AND ABOVE, CONCERNED TO THE RISK PERCEPTION FACTORS AND THE PHYSICAL ACTIVITY

THIAGO HENRIQUE ALVES DO AMARAL QUADROS(IC)[1]; SEBASTIÃO RIBEIRO DA SILVA JÚNIOR(IC)[2]; ANGELA PIERAZO DOS SANTOS(IC)[3].

(1)(2)(3)Centro Universitário Barão de Mauá.

Introduction: The increase in the incidence of the cardiovascular illnesses (CI) was described for the first time in the decade of 50 in a classic study. The same it that the CI highly are related the risk factors. Currently 250 factors of risk had been described. It refers to a quantitative research type descriptive Survey. Objective: identify the diseases occurrence, medication use, cardiovascular surgery and the practicing physical activity, as well to measure the perception in people of fifty years and above, referring to the contribution of the risk factors to the coronarian disease. Methodology: The instrument of collection of data was applied in 200 pertaining individuals to the age of 50 years or more. Results: showed that 78,5% of the interviews developed any kind of disease, 69,5% took any kind of medication, 6,5% had had cardiac surgery and 54,0% practiced physical activity. Of all the factors, the perception of the HA as risk factor is what it has higher average and shunting line lower standard. Conclusion: It was observed that the entire group didn't notice the risk factors in its absolute risk.

Supervisors: Simone S. Belluzo, Nilza Teresa Rotter Pelá.

The authors did not follow the Scientific Committee's suggestion for an English language review

SP002-THE INFLUENCE OF THE PROFIT MARGIN AND THE FINAL PRICE FOR THE CONSUMER ON THE COMMERCIALIZATION OF MEDICATIONS

LUCIANE CRUZ LOPES(PQ)[1]; SILVIO BARBERATO FILHO(PQ)[1]

(1)University of Sorocaba

[Introduction] In Brazil, where access to medications constitutes a serious public health problem, their commercialization still lacks regulation. [Objective] To identify the variation of the profit margin and the final price for the customers in certain reference medicines, generic and similar ones, and to discuss the relation between these variations and the commercialization of medications under the ethical and legal perspective. [Methodology] Fourteen chemical substances and 295 specialties were included. A profit margin (PM) in each segment was calculated based on the real purchase prices (RPP) of the medications and the maximum price for the consumer (MPC). [Results] For reference medicines, the PM varied between 30-36%; for the respective generic ones, the PM was between 51-58%; and similar medicines between 32-71%. The MPC also presented high variations, exceeding 70% in the case of amoxicilin, omeprazole and ranitidine. [Conclusion] These results, combined with increased competition in the pharmaceutical market and with the social-economic conditions of most of the Brazilian population, have consolidated practices that are very distant from those preconceived by the rationality of science and by the social commitment inherent in the commercialization of medicines.

SP003-THE USE OF MEDICATION AMONG ELDER PEOPLE IN A FAMILY HEALTH PROGRAM IN RIBEIRÃO PRETO, SP

MARIANA HONORATO GIARDINI

(1)Department Social Medicine, Medical School of Ribeirão Preto, University of São Paulo

Introduction: The patients' knowledge on their medication is crucial to their proper use.. The World Health Organization (WHO) recommends to be the prescription used as a parameter to characterize medicines use among the population. Objectives: Identify the features of medical prescriptions and the knowledge of elderly patients. Methodology: This cross-sectional study used the WHO prescription indicators as reference in the verification of 100 elderly patients´prescription as well as through the administration of a questionnaire on their knowledge . Results: The mean of prescribed medicines for patient was 2,8, 89,5% of them were dispensed, 91,4% were prescribed by generic name and 90,9% according to the standard list of medicines. It has been prescribed 0,36% of antibiotics and 0,72% of injectable medications. Out of one hundred interviewees, 44% showed to have good knowledge about their medicines, 22% had an average knowledge and 34% showed bad knowledge. Conclusion: The Family Health Program has a good performance regarding the use of medicines by old-aged patients although there is some room for improvement in the pharmaceutical care.

Supervisor: Elisabeth Meloni Vieira

SP004-DRUG INTERACTIONS IN PRESCRIPTIONS WITH HIGH-ALERT MEDICATIONS AT A HOSPITAL

HESSEM M. NEIVA (PQ)[1]; MÁRIO BORGES ROSA (PQ)[1]; EDSON PERINI(PQ)[1]; TÂNIA A. ANACLETO (PQ)[1]

(1) Group of Studies of Safety in drug Use, Minas Gerais-UFMG

Introduction: Drug interactions can be prevented and their detection and adequate management rationalize drug use. Objective: To research frequency and interaction profile involving high-alert medication. Methodology:Cross-sectional study carried out at a hospital, including prescriptions with high-alert medications, during 30 days, in 2001, recording interactions between high-alert medications. Results and Conclusions: A total of 4026 prescriptions were evaluated and 680 drug interactions of clinical importance were recorded in 10,9% of prescriptions. Among them, 89,9% were originated in the Intensive Care Units, Internal Medicine and Neurology. Digoxin, pancuronium, warfarin, heparin, dopamine and midazolam concentrated 92,9% of interactions. Interactions with higher severity (type 1) were originated in 83,0% of cases in the Intensive Care Units, Internal Medicine and Neurology. Interactions with medium severity (type 2) also concentrated on these areas with 95,1% of cases. There were 39 interactions type 3 representing 5,7% of the total. Data help to provide measurements such as implantation of differentiated policy in areas where most interactions were originated, considering as top priority those medications more frequently involved in such events.

SP005 - CLINICAL EFFICACY AND SIDE EFFECTS OF SIBUTRAMINE AND METFORMIN IN THE TREATMENT OF OBESITY

LEONARDO RÉGIS LEIRA PEREIRA(PQ)[(1)]; REGINA HELENA COSTA QUEIROZ (PQ)[(1)]; NÉLSON IUCIF JÚNIOR(PQ)[(2)]; MARIA DE LOURDES PIRES BIANCHI(PQ)[(1)]; DERMEVAL DE CARVALHO(PQ)[(2)].

[(1)] Departamento de Ciências Farmacêuticas (FCFRP-USP).
[(2)] Universidade de Ribeirão Preto.

Introduction: Obesity is a serious medical condition that, like other chronic diseases, requires treatment. Research has shown that weight loss decreases the co-morbidity associated with obesity. Sibutramine is a serotonin and noradrenaline re-uptake inhibitor. Metformin is an antidiabetic drug that reduces insulin resistance and induces weight loss. Objectives: The clinical efficacy of sibutramine and metformin and possible side effects were assessed in obese patients treated with the drugs. Methods: 16 patients with a BMI above 30 kg/m^2 were divided into 2 groups submitted to treatment with sibutramine or metformin for a period of 90-day. The volunteers were submitted to regular anthropometric evaluations and received a dietary reeducation plan. Results: The data demonstrated that sibutramine presented better results in the anthropometric tests such as a 7.91% reduction of the abdominal circumference and a 9.65% reduction in adipose tissue. However, metformin induced a lower number of side effects. Conclusions: In general, the two drugs can be considered safe as long as they are prescribed in a rational manner.

SP006- ANALYSIS OF THE ADVERTISING OF PRESCRIBED MEDICATION

PATRÍCIA APARECIDA MACHADO(PQ)[1]; DIRCE SOFIA FABBRI DE ALMEIDA VERDE DOS SANTOS (PQ)[1]

[1]Industrial Pharmaceutics – University of Uberaba – MG

Introduction: The quality of the information in medication advertising is important because medication advertising is used as a source of technical upgrading by those who prescribe drugs. Objective: Evaluate the quality of the technical information in the advertising of prescribed medication. Methods: From August/2004 to March/2005, 48 types of printed advertisement available in doctor and dentist offices, public and private hospitals, pharmacies and drugstores were analyzed by using the VERIFICATION OF MEDICATION ADVERTISING CONFORMITY GUIDE (RDC 102/2000). An analysis of the technical information was conducted, comparing it to the information found in scientific literature. Results: 20% did not give information on all the side effects, 13% omitted the warnings and 19% only partially mentioned them. 12% gave the incorrect dosages and 7% omitted them, 16% failed to give information on adverse reactions and 13% omitted information. Conclusion: The technical information that was found, presented insufficient quality so as to make the advertisement a source of technical upgrade for those who prescribe drugs.

Financial Support: UNIUBE, ANVISA
Supervisor: Dirce Sofia Fabbri de Almeida Verde dos Santos

SP007-THE USE OF CALENDULA (*CALENDULA OFFICINALIS L.)* AND CONFREI (*SYMPHYTUM OFFICINALE*) MEDICINAL PLANTS BY THE POPULATION

ANA CAROLINA BATISTA DE OLIVEIRA(PQ)[1]; ANA CAROLINA FIDELIS(PQ)[1]; BARBARA COSTA VILLEFORT(PQ)[1]; GLADIS MACHADO MALACARNE(PQ)[1]; MARIO TEIXEIRA NETO (PQ)[12]; THAIS ANGELICA CARDOSO(PQ)[1]

[(1)]Centro Universitário Newton Paiva; [(2)]Doutor

The objective of this paper was to answer the following questions: What is the information level regarding the use of medicinal plants CALENDULA and CONFREI by people, and Which is the best interventional method for rational use of those plants by the population. The used method for this study consists of direct method, indirect method and qualitative method, with fiscal surveys. One hundred and one random interview with people at an open medicinal plant market in Belo Horizonte was done from 11/05/05 to 19/04/05. Several direct and indirect questions were used to assess the use of those plants by people. The results shows that 34% of people used the plants in a different way that is described in the literature, and 58% of people started to use the plants by informal indication. We advise a public orientation campaign for the rational use of those medicinal plants by people, showing the popular names, photographs illustrating each kind of plant, the benefits and side effects.

Supervisor: Doutor Mario Teixeira Neto

The authors did not follow the Scientific Committee's suggestion for an English language review

SP008-SEMI-INDUSTRIAL DRUGS PRODUCTION IN HIGH DEMAND HOSPITAL: A COST DECREASE STRATEGY.

CAMILA ALVES AREDA (PG)[1]; LUIZ MAÇAO SAKAMOTO (PQ)[2,3]; VANIA PASSARINI TAKAHASHI (PQ)[1]; OSVALDO FREITAS (PQ)[1]

[1]FCFRP-USP; [2] HCFMRP-USP; [3] UNAERP

Introduction: the ultimate goal in health sectors is reducing costs without losing quality. In this context, the hospital industrial pharmacy, which produces similar drugs to those commercially available, offers lower price and exclusive formulations, not available in the market. Objective: evaluate the drug production at the Industrial Activities Service (SAI) of HCFMRP-USP during the year 2004 and its correlations with trade industrialized drugs. Methods: SAI output from 01/01/2004 to 12/31/2004 was documented and classified into two types. Group I: drugs similar to commercially distributed products, Group II: exclusive formulations for routine consumption. Cost of production were assessed and compared with market prices for Group I. Results: 54,92% of total manufacture orders represented Group I and 45,08% Group II. When compared with market prices, tablets of Group I indicated saving of about 44%. The social benefit promoted by the production of exclusive formulations not available at market, as dialysis solutions, is important to be considered. Conclusion: the observed saving supports the contention that manufacture of pharmaceutical formulations by SAI is a cost-effective alternative.

Financial Support: CNPq
Supervisor: Osvaldo de Freitas

SP009-SALMONELLOSIS VERSUS FOOD SAFETY

ALZIRA MARIA MORATO BERGAMINI(PQ)[1]; ELIANA GUIMARÃES ABEID RIBEIRO(PQ)[1]; SUELI APARECIDA FERNANDES(PQ)[2]; ANA TEREZINHA TAVECHIO(PQ)[2]; MARIA APARECIDA DE OLIVEIRA(PQ)[1]

[1]Adolfo Lutz Institute - Ribeirão Preto;[2]Adolfo Lutz Institute - São Paulo

Salmonellosis represents an important problem of Public Health worldwide, including Brazil. The aim of the present study was to evaluate the presence of *Salmonella* spp. in food samples collected by municipal Public Health Surveillance, from 1995 to 2004. The samples were processed as proposed by Flowes et al. (1992) in Adolfo Lutz Institute – Ribeirão Preto/São Paulo State - Brazil and the serotyping was characterized at Adolfo Lutz Institute – São Paulo/Brazil, according to Popoff & Le Minor (1997). Salmonella was isolated from 157(3,3%) of 4795 samples. Of this total 48(30,6%) were involved in 34 distinct foodborne illness outbreaks. *Salmonella* Enteritidis was detected in 33(97,8%) outbreaks and *Salmonella* 4:d:- in only 1(2,2%). The food outbreaks were associated from ready-to-eat egg products, delicatessen products, poultry and pork meats, showing the food importance as probable illness sources. Food safety education for the population should be priority by govern, based on developed programs with potentially impact in schools, restaurants, supermarkets, home, food processors. Food safety must be a constant practice in Public Health.

SP010 - DRUGS COMMERCIALIZED IN NON-PHARMACEUTICAL ESTABLISHMENTS LOCATED IN THE DISTRICT OF JARDIM UNIVERSITÁRIO AND NOVA CIDADE (CASCAVEL, PR).

GRACIELE C. M. MÂNICA (IC); JORGE J. T. VIEIRA (PQ); EDUARDO B. DE MELO (PQ).

School of Pharmacy – Universidade Estadual do Oeste do Paraná

In Brazil, the commerce of drugs is allowed in pharmacies, drugstores and drug posts. However, it is common to find drugs for sale in establishments such as supermarkets, restaurants and gas stations. These facts stimulate the self-medication, favour drug intoxication and expose the consumers to products of doubtable quality. Aiming to trace the characteristics of this parallel market in the city of Cascavel, PR, 33 non-pharmaceutical establishments, located in the districts of Jardim Universitário and Nova Cidade, were visited. All drugs commercialized were registrated. Only OTCs (over-the-counter) drugs, which prescription is not needed, were found. 60% of all visited places used to sell these drugs. However, 9.09% refused to answer the questionnaire. Drug class mostly found were analgesics, anti-thermics and anti-inflammatories (68.12%), followed by antiacids (27.54%). The most found salt was acetylsalicylic acid (20.69%), dipirone (14.48%), sodium bicarbonate and citric acid (13.10%). Despite the illegality of the practice, the drug commerce was noticed in the majority of the establishments visited.

Supervisor: Eduardo B. de Melo.

SP011-PREVALENCE OF DEPRESSION IN PARKINSON'S DISEASE PATIENTS IN UBERLÂNDIA.

ANNA PAULA DE SÁ BORGES; GILMA D. FERREIRA; RITA ALESSANDRA CARDOSO

Centro Universitário do Triângulo – Unitri

Introduction: Parkinson's Disease (PD) is a neurological disorder characterized by bradykinesia, rigidity, tremor and postural instability. Depression is a common problem in patients with PD and may have a negative impact on quality of life of those patients. Diagnosis of depression in PD patients may present some difficulties, since many symptoms of both disorders overlap. Objective: The aim of this study was to investigate the prevalence of depression in PD patients in the city of Uberlândia. Methodology: A retrospective study of medical records of patients treated at the Unidade de Atendimento Integrado Planalto, which gives medical support to patients with neurological disorders in the city of Uberlândia. After discharging 8 medical records due to insufficient information or duplicated records, 23 medical records were analyzed. Results: 47,8% of patients with PD were diagnosed with depression. Among them, 54,5% presented depression after PD symptoms, and 45,5% presented depression before PD symptoms. Conclusions: These findings suggest that depression has been properly identified in PD patients in Uberlândia. PD and depression seem to have a bi-directional relationship, where PD might be a risk factor for depression as well as depression might be a risk factor for PD.

Supervisor: Rita A. Cardoso

SP012-USE OF MERCURY IN ODONTOLOGY: A THEORETICAL-PHILOSOPHICAL REFLECTION

ALINE DA SILVA OLIVEIRA (PG)[1] ; JAMYLE CALENCIO GRIGOLETTO (PG)[1] ;SUSANA INÉS SEGURA MUÑOZ (PQ)[1] ; ANGELA MARIA MAGOSSO TAKAYANAGUI (PQ) [1].

(1) Escola de Enfermagem de Ribeirão Preto da Universidade de São Paulo- EERP/USP. Departamento Materno-Infantil e Saúde Pública. Laboratório de Saúde Ambiental.

This article presents a theoretical-philosophical reflection on the use of mercury for dental amalgams in dentistry and their potential toxicological risks in terms of occupational exposure and for patients. Our study results from a discussion about this subject in a graduate course on biohazardous waste management, held at EERP-USP, and is based on a bibliographic review. We also report on some national and international position on the use of this amalgam, which reveal that it continues being frequently used and that there is a need for better rules and technical guidelines on its use.

Financial support: FAPESP e CNPq
Supervisor: Susana Inés Segura Muñoz e Angela Maria
Magosso Takayanagui.

SP013-FACTORS RESPONSIBLE FOR THE CERVICAL CANCER

RACHEL DE LIMA(IC)[1]; DAIANE DOS SANTOS SOARES(IC)[1]; MARGARETE DULCE BAGATINI(IC)[1];CALIZE OLIVEIRA DOS SANTOS(IC)[1];

[(1)]Universidade Federal de Santa Maria

Introduction: In the world more than 500000 new cases of cervical cancer happen every year. It is shown as an alteration on the lap of the womb's surface cells as time goes by and it will be able to become a cancer. However, it is a tumor that can be prevented, once it has a relatively slow progression and it is easily detected in routine gynecological exams. Its epidemic profile is of a disease related to the sexual activity. Objective: In order to evaluate the epidemic profile of the cervical cancer's occurence diagnosed in the University Hospital of Santa Maria (HUSM), within August 2002 and August 2004, a collection of data in the patients's handbooks research was developed. Methodology: We evaluated the degree of correlation between the disease and: age of the first sexual relation, number of children, number of sexual partners, and infection by HPV. Results: High levels of diagnosed cases were in women: in the beginning of a precocious sexual activity, rise in the number of children, larger diversity of sexual partners and infection for HPV. Conclusion: These are the main topics responsible for the cervical cancer.

Financial Support: FIPE
Supervisor:Gilda Maria Dias Tavares

SP014-OCCURRENCE OF DIPHYLLOBOTHRIASIS IN RIBEIRÃO PRETO CITY, SP, BRAZIL.

DIVANI MARIA CAPUANO(PQ)[1]; MADALENA H. T. OKINO(PQ)[1]; GERALDO M. DE ABREU(PQ)[1]; MARIA JOSÉ DO C. B. BETTINI(PQ)[1]; DOMINGAS M. A. G. V. TORRES (PQ)[1]; HERCÍLIA R. M. DE MATTOS(PQ)[2]

[(1)]Adolfo Lutz Institute; [(2)]Health Municipal Service of Ribeirão Preto

Diphyllobothriasis, a disease caused by the fish taenia, is registered in North America, Europe, Asia, Japan, Chile, Peru and Argentina. In Brazil, the first autochthonous cases occurred in 2004 in São Paulo State, reaching 44 cases till May 2005. Human infection occurs by the ingestion of raw or rare fish with the infective larva, which is fixated in the small intestine and becomes an adult taenia. In general the infection is asymptomatic, but complications may occur, such as megaloblastic anemia and intestinal obstruction. We have attempted to record the first case of diphyllobothriasis in Ribeirão Preto, SP. After the spontaneous elimination of proglottides, a 22-year-old male patient looked for the public health service, reporting symptoms of nausea, flatulence, diarrhea, fever, weakness, and weight loss. He also reported that he used to ingest raw salmon sashimi twice a week. Feces and proglottides laboratorial analysis done at Instituto Adolfo Lutz, confirmed the diagnosis of diphyllobothriasis. The patient was treated with praziquantel. The authors stress the need of making fecal examinations in patients with history of raw fish ingestion.

SP015-HEPATITIS B AND ITS PROFILAXIS THROUGH ACTIVE IMMUNIZATION

ÊNIO JOSÉ BASSI (PET)[1], ANA MARIA SELL(PQ)[1], DENNIS ARMANDO BERTOLINI(PQ)[1]

[(1)]Universidade Estadual de Maringá

Hepatitis B is an infectious hepatic disease of great worldwide prevalence, caused by hepatitis B virus, an hepatotropic DNA virus. The blood and corporal liquids of infected people are the most important reservoir of infection and the virus is mainly parenterally and sexually transmitted. This work had as objective to review the hepatitis B and its prophylaxis by immunization, approaching disease aspects, HBV virus and its transmission, epidemiology and clinical aspects, as well as hepatitis B vaccine, how its indication, production, dosage, administration ways and collateral effects. For in such away, it was realized a bibliographic survey in the printed and virtual sources. In Paraná state, hepatitis B is a disease of the great epidemiologic importance, being observed intermediated the high one prevalence in the Southwestern region of the State. Although to be an extremely contagious disease, the prevention is extremely simple and occurs through hepatitis B vaccine, which contains the HBV surface antigen, synthesized by technique of DNA-recombinant, inducing protection in more than 90% of the adults. The government's incentive and investment in vaccination and awareness of the population are the best ways to avoid the propagation of this big problem in the world health.

Supervisor: Ana Maria Sell

SP016-RELATION BETWEEN INCOME AND MEDICINES ACCESS IN NATAL/RN-BRAZIL

KLEYTON T. C. DE CARVALHO (IC)[1], MELINA G. CARVALHO (IC)[1], FRANCISCO A. A. DE ALMEIDA (IC)[1], ILANA A. DE A. FONSECA (IC)[1]

Universidade Federal do Rio Grande do Norte [1]- Gen. Gustavo Cordeiro de Faria St; s/n. Petrópolis - Natal/RN - 59010-180

Health is one of the human rights, without distinction of race, religion as well as political, economic or social condition. This work intends to show the effects of unequal social conditions on the use of medicine by population. 500 families were randomly visited in Natal between May and October, 2004 to an interview concerning access to health service and medicine. A comparative study was done, classifying families into three groups according to their income: under R$1000,00(ID1), between R$1000,00 and R$2500,00(ID2) and; over R$2500,00(ID3). There was no significant difference on generic medicine acceptance among the classes but it was verified that medical service was more used by richer families. In addition, a higher number of medicine was found in the houses whose families had higher incomes (ID1=0,98; ID2=2,05; ID3=2,86 product/person). Analgesic was the pharmacological group more frequently found, independent of the social class. On the other hand, the number of products for digestive system and dermatological drugs had a direct relationship with income. This way, it is essential to adopt measures to avoid the inequalities observed and to improve health system.

Financial support: none
Supervisor: Ana M.M. de A. Marinho

SP017-MEDICATION PROFILE AND EXPENSES INCURRED BY THE MUNICIPAL CENTER OF HEALTH OF BELO HORIZONTE, MG, 1999-2004

SANTUSA PEREIRA SANTANA (PQ)[1]; AUGUSTO A. GUERRA JR. (PQ²; SIMONE A. VALE (PQ)²

[1]NEWTON DE PAIVA UNIVERSITY CENTER; [2]MUNICIPAL CENTER OF HEALTH OF BELO HORIZONTE

Introduction: The number of court injunctions brought against public health services in order to obtain medication is growing. Objective: Characterize the medication profile and expenses incurred with court injunctions by the Municipal Center of Health of Belo Horizonte (MCH/BH). Methods: Transversal study, researching registers of the Therapeutical Assistance Unit, Legal Aid Dept. and Licitations and Purchasing Sector of the MCH/BH. Results: A total of 286 court injunctions were analyzed. Approximately 55.6% of the medication was not available under the free government distribution programs. Of the 44.4% which belonged to some program, 29.2% belonged to the Exceptional Medications program and 43.7% belonged to the list of essential medication. The number of court injunctions for medication per year increased 64% in the period from 1999 to 2004. In 2003, it represented 3.5% of the total spent by MCH/BH on medication. Conclusion: The population has sought to obtain its rights through the legal system. It is up to the Sole Health System administration to seek of ways to obtain means and funds to achieve improved access to essential medication and better quality of pharmaceutical assistance services for society.

SP018-A STUDY OF THE CHAGAS DISEASE PREVALENCE AND ITS VARIABLES IN THE CITIES OF THE 14TH REGIONAL HEALTH COORDINATION (CRS) FROM SANTA ROSA - RS.

LUZIELI DA CRUZ MURARI (PQ)[1]; MARILEI UECKER (PQ)²

(1) Farmacêutica Bioquímica em Análises Clínicas; (2) Departamento de Ciências da Saúde - UNIJUI

Introduction: Despite of the Chagas Disease Control Program introduced in Brazil in 1975, it is estimated that even nowadays there are 20 millions of people under risk of getting contaminated by the *T. cruzi*. This study reports the Chagas Disease (DC) prevalence and its variables on the cities of the 14th CRS of Santa Rosa. Objective: This study aims at verifying the DC prevalence and its variables during the period from January of 2000 to September of 2004 on the cities previously mentioned. Methodology: It consists of a documental research based on the data obtained from the individual control chart, which contains the requests of the exams that are able to provide the diagnosis of DC. Results: from 1067 investigated patients, 367 (34%) were infected. The majority of the DC cases had been undertaken to a transfusion. During the study, there was not any acute case of DC in the investigated context. Conclusions: According to the data, the intensification of the means of DC control may diminish considerably the relevant rates of prevalence on such context.

SP019-EVALUATION OF ELDERLY PATIENTS ASSISTED AT THE PADRE EUSTÁQUIO SECONDARY REFERENCE UNIT

ADRIENNE MARIE DA SILVEIRA (PQ)[1]; BIANCA G. VELOSO (PQ)[1]; KARLA C. GIACOMINI[2]; SIMONE A. VALE (PQ)[3]

[1]SRU PADRE EUSTÁQUIO; [2]MUNICPAL CENTER OF HEALTH OF BELO HORIZONTE; [3]NORTHEASTERN DISTRICT PHARMACY

Introduction: The [2]Municpal Center of Health of Belo Horizonte develops an integral program of assistance to the elderly. A good part of the patients of the Padre Eustáquio secondary reference unit (SRU-PE) is elderly. Objective: Trace an elderly user profile at the SRU-PE considering multi-pharmacy services as risk criteria. Methods: Tranversal study conducted at the SRU-PE, using data of medication prescription for the elderly at risk (in use of 5 or more medications) in a period of one year. Results: There were 2,126 registries at the pharmacy, with 38% by the elderly, of which 64% were women and 7% used five or more medications. For 49% of the latter, standardized medicine for the elderly was not used, being prescribed by distinct physicians in different levels of attention for the same disease. Conclusion: It was observed that there is lack of knowledge of medication standardization, disarticulation among the levels of attention and lack of management of attention by the medical assistant. The pharmacist plays an essential role as a collaborator in the assistance of these patients, especially in the follow up of medication usage.

SP020-THE DOSAGE INFLUENCE OF NO ADHESION OF PATIENTS TO THE PROGRAM OF HANSEN'S DISEASE

LUÍS CLÁUDIO FRANÇA PINTO (PQ)[1]; SYLVIA DE FÁTIMA DOS SANTOS GUERRA(PQ)[2]; SUSIE FERNANDES NEGRÃO(PQ)[3].

(1)Universidade do Estado do Pará; (2)UFPA; (3)CEFET/PA; (4)Núcleo de Epidemiologia do Estado do Pará.

In 1981, was implemented a Polychemotherapy (PQT), a therapeutics made for three (3) kind of drugs (rifampicina, clofazimina e dapsona), that avoid the dosage resistance (Brasil,2002) and decrease relatively the treatment period. In Pará state, in the 90s, there were 25% rate of the treatment dereliction; that glare the existence of a barrier created by the patient to engage to the Hansen's disease control program (HDCP). The goal is to connect the dosage influence of no adhesion of patients to the HDCP, from September to December of 2003. Have been interviewed people into the program at Marambaia and Jurunas HCUs. Have been selected 35 patients from the HCU. It has been done a domiciliary visit and applied a questionnaire. All of them, we got to interview only 17,14%. 60% of them, related that a great barrier to accept the treatment was the reaction of the medicines, and 40% said that it was the main reason to stop it. They related that the undesirable symptoms stopped them to go on with their routine, including their family support. It is a concerning data, since PQT means the heal of the disease.

Supervisor: Ângela Maria Rodrigues Ferreira(4); Co-author: Maria Helena Cunha Oliveira (PQ)[4]

SP021-A MULTIPROFESSIONAL TEAM WORK: A CASE-REPORT OF A DIABETIC AND HYPERTENSIVE PATIENT

RITA BENTO; FERNANDA TORRESAN;REGINA SIMÕES; LUCIANE CRUZ LOPES

Chronic diseases such as hypertension, diabetes and obesity are public health problems with high mortality rates. Their treatments require life style change from food to hygiene, disease control with pharmacotherapy and regular exercise. Since 1998, UNIMEP has been supporting projects for patient care and in 2004 a project involving multiprofessional team (nutrition, pharmacy, physical practices, and psychology) to promote self-care was created to implement orientation and education programs. Four interrelated intervention moments are precompiled: pharmaceutical care, orientation to and application of exercises, weekly and monthly meetings. We have a study case with a 53-year old female (M.A.). The data are glycemia, weight, and blood pressure charts and a home visit. She has DM2 for 23 years and hypertension. Anxious and worried with overweight, she participates of physical exercises and meeting. With the team work has started to take medications correctly. The PharmCare records analysis has shown the need for multiprofessional team work.

SP022-TECHNICAL AND LEGAL ASPECTS IN CONDUCTING RELATIVE BIOAVAILABILITY/ BIOEQUIVALENCE STUDIES OF HORMONE-BASED DRUGS

KYUNG HEE CHANG(PQ)[1]; PAULA MACEDO CERQUEIRA(PQ)[1]; MÁRCIA MARTINI BUENO(PQ)[1]; SÍLVIA STORPIRTIS(PQ[12]

[(1)]Unidade de Avaliação de Bioequivalência–GEMEG/GGMED/ANVISA/MS; [(2)]FCF/USP

Since the publication of the Law nº 9787/99, which established generic drugs in Brazil, all related areas from the pharmaceutical technology to the clinical trials (relative bioavailability/bioequivalence-BA/BE) had a great development that supports the therapeutic equivalence between reference and generic drugs. Some therapeutic classes were excluded from Brazilian generic market by the necessity of previews implementation of the National Medicine Policy. The hormone-based drugs, included in these classes, required technological improvement from both the Research Centers and the Regulatory Agency, that were reached within the 5-year experience. The objective of this work was to describe and clarify the technical and legal basis to conduct BA/BE trials of hormone-based drugs intended to be registered as generic or similar products in Brazil, based on the international experience of USA, Canada and Europe. The BA/BE studies of hormones must be carried on as stated at the General Guidance, nevertheless, some peculiarities have to be considered as the bioanalytical and clinical issues.

Financial Support: ANVISA/MS
Supervisor: Sílvia Storpirtis

SP023-DIFFERENCES IN THE MANAGEMENT OF ASTHMA IN PRIMARY AND SECONDARY LEVELS OF CARE IN A HEALTH DISTRICT OF BELO HORIZONTE, MG.

SIMONE ALVES DO VALE (PQ)[1]; EDSON PERINI (PQ)[2]; MARIA J. F. FONTES (PQ)[3]; CIBELE C. CÉSAR (PQ)4

[1]MUNICIPAL CENTER OF HEALTH OF BELO HORIZONTE; [2]PHARMACY SCHOOL/UFMG; [3]MEDICAL SCHOOL/UFMG; [4]ICEX/UFMG

Introduction: The local program for children with asthma (Programa Criança que Chia) was organized to follow up patients with respiratory diseases at the basic units of health and by pneumologists at the units of secondary reference at Belo Horizonte. Objective: To compare health care directed to children in use of inhalatory therapy at the basic units of health and units of secondary reference. Methodology: Cross-sectional study using clinical and therapeutic data from charts at the basic units of health and units of secondary reference of the North-west Health District. Results: Male was predominant, higher [1]at secondary level, for first crisis before one year old (83%) and for moderate asthma, especially at the units of secondary reference (83%) where average of hospitalizations, emergency visits and use of oral corticosteroids were higher. Evolution in severity to mild clinical conditions after inhalatory corticosteroids was significative, mainly at the units of secondary reference. Initial dose of inhalatory corticosteroids at basic units of health was higher than the prescribed dose at the units of secondary reference and, in the end of the period, the latter presented the highest reduction of dose. Conclusions: Care provided by specialists in the program is more adequate considering recommendations of guidelines. Results reinforce the need of permanent education for the basic units of health professionals.

SP024 - ANALYSIS OF CAPTOPRIL AND ASA SAMPLES DISTRIBUTED BY FARMÁCIA BÁSICA DE CASCAVEL, PR.

PAULO R. STOEF(IC); GRACIELE C. M. MÂNICA(IC); JANAÍNA F. DA ROZA(T); EDUARDO B. DE MELO(PQ).

Curso de Farmácia - Universidade Estadual do Oeste do Paraná

From 1999 to 2003, 29% of the medicines apprehended by the ANVISA showed quality deviations. It represents a serious problem of public health, especially for the poor population that depends on these public health services. Seeking to determinate the quality of the products acquired and distributed by the public system of Cascavel, we carried out, between 06/2004 and 04/2005, the sampling and analysis of tablets of captopril 25mg and acetylsalicylic acid (ASA) 100mg (3 lots each). According to Brazilian Pharmacopoeia, we accomplished appearance analysis, hardness, friability, uniformity of weight and drug content. For aspirin, we also determined the free salicylic acid (SA). All captopril samples showed to be among the specified limits. Otherwise, all ASA samples showed quality deviations (three in apparance, two in free SA, one in friability and one in drug content), confirming what was exposed in the introduction. With the continuation of this work, we expect that the obtained information could help the municipal district in the next purchases of medicines.

Acknowledgment: Farmácia Básica de Cascavel; Farmacêuticos Mario Godoi e José A. Zanluti Filho
Supervisor: Eduardo B. de Melo.

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Síntese de Fármacos / *Drug Synthesis* (SF)

SF001 - SYNTHESIS OF MUTUAL PRODRUG DERIVATED OF NAPROXEN FOR THE TREATMENT OF RHEUMATHOID ARTHRITES (AR)

EDNIR DE OLIVEIRA VIZIOLI (PG)[1]; LÚCIA FIORAVANTI DE CASTRO (PG)[1]; ANTONIO GIBERTO FERREIRA (PQ)[2]; MAN CHIN CHUNG (PQ)[1]

[(1)]Faculdade de Ciências Farmacêuticas/UNESP –Araraquara.
[(2)]Instituto de Química, UFSCar –São Carlos.

The AR involves mediators as TNF-a,ILs and cytokinas have been modified by treatment with anti-inflammatory, which naproxen has been used over the past 20 years, showing a special tolerance, in a long period of treatment. Taurine is an aminoacid with properties of PGE_2 inhibition, as well as the reducing the excitation of the nitric oxide synthesis and the COX-2 expression, reducing also the production of superoxide anion that would stop tissue lesions. The purpose of this work was to synthesise mutual prodrug of taurine and naproxen for the treatment of AR. The synthesis was carried out using equimolar quantity of naproxen and taurine coupled by a) THF/MeOH and pyridine; b) CH_2Cl_2 and DMAP; c) DMF and DMAP, all at 40ºC. The result showed that using CH_2Cl_2 and DMAP, the synthesis is fast and easy to isolate. The obtained compound were purified by column chromatography using silica gel and identified by IR,UV,NMR.

Financial Support: Capes
Supervisor: Chung Man Chin

SF002 - TRYPANOCIDAL AND LEISHMANICIDAL EVALUATION OF THE CRUDE HYDROALCHOOLIC EXTRACTS FROM BARK, LEAVES AND FLOWERS OF *TABEBUIA AVELLANEDAE*

MARCELO D. FERRARI(PG)[(1)]; ROSANGELA DA SILVA(PQ)[(1)]; DANIELE DA SILVA FERREIRA(PG)[(2)]; EVELINE S. COSTA (IC)[(1)], ADRIANA H. C. VINHOLIS(PQ)[(1)]; SÉRGIO DE ALBUQUERQUE(PQ)[(2)]; ADEMAR A.S. FILHO(PG)[(2)]; WILSON R. CUNHA(PQ)[(1)]; ÍCARO E. F. DA SILVA (PG)[(1)]; ANDRÉIA DE A. ROCHA(PQ)[(1)]; JAIRO K. BASTOS(PQ)[(2)] AND MARCIO L. A. E SILVA(PQ)[(1)].

[(1)]Universidade de Franca – Av. Dr. Armando Salles de Oliveira, 201 – Franca –SP CEP 14404-600; [(2)]FCFRP-USP – Av. do Café s/n – Ribeirão Preto – SP CEP: 14030-000

Introduction: Phytotherapy has been a great interest option for the new pharmaco development, united to that, Brazil holds one of the largest, if not the biggest, natural pharmacy of the world. Objective: The aim of this study was evaluated the trypanocidal and leishmanicidal activities of *Tabebuia avellanedae*. Materials and Methods: Three different concentrations (8, 32 and 128 µg /ml) of hydroalcoholic crude extract of *T.* avellanedae bark, leaves and flowers were assayed in vitro against strains of *Trypanosoma cruzi* (Y) and *Leishmania braziliensis*. Results and Discussion: It was observed that *T. avellanedae* hydroalcoholic extract of bark was relatively active within the tested concentrations for L. (V.) braziliensis and *T. cruzi* (IC_{50} 250.0 µg /ml and 325.6 µg /ml, respectively), but inactive against *T. cruzi* and L. (V.) braziliensis for the leaves and flowers crude extracts. Conclusion: Despite the fact that both protozoan belong to the Trypanosomatidae family, we suggest that the difference observed for activity should be related to the biological differences between the two parasite species.

Financial Support: FAPESP, CAPES and CNPq
Adviser: Márcio L. A. e Silva

SF003 - NEW AROMATIC REACTIONS AND FUNCTIONAL GROUP MODIFICATIONS OF ARYSTOL AND DITHYMOL.

MAÍRA ROSATO SILVEIRA (IC)[1]; ALBERTO FEDERMAN NETO(PQ)[1]; ÁUREA DONIZETE LANCHOTE BORGES(PQ)[1].

(1) Universidade de São Paulo, Faculdade de Ciências Farmacêuticas de Ribeirão Preto.

Introduction: Recently, we reported(1) the preparation of the antiseptic Arystol and their use as intermediate in the synthesis of dithymol (thymol biphenyl dimer), useful substrate for SEAr reactions(2).
Objective, Methodology, Results, Conclusion: Here, we described new reactions: A) Nitration of Arystol. The presence of I atoms protects the OH groups from oxidation and control their level of reactivity. B) The reaction of dithymol phenolates with alkylating agents gives their new aromatic ethers. C) The reaction of dithymolates with $FeCl_3$ or $CuCl_2$ gives new phenolate complexes. These mat. are useful in Pharm. or Mat. Scienc.
(1)*Quim. Nova*, submitted, 2005. (2)*12º SIICUSP*, 2004.

Financial Support: FAPESP, PIBIC/CNPq
Supervisor: Alberto Federman Neto

The authors did not follow the modifications suggested by the Scientific Committee

SF004 - SYNTHESIS OF PRECURSORS OF FUNCTIONALIZED PHTHALOCYANINES

LUIZ EDUARDO CARDOSO (PG)[1]; MILTON BELTRAME JUNIOR (PQ)[1]; MARCELO MIGUEL MARTINS PELISSON (PQ)[1]

(1) Universidade do Vale do Paraíba, Av. Shishima Hifumi 2911, São José dos Campos / SP, 12244-000.

Introduction: Here we describe the preparation of two different precursors for the synthesis of new phthalocyanines (PCs), for use in the photodynamic therapy of cancer. Objective: The PCs may have four or eight galactose molecules as peripheral groups, with a silicon atom at its inner position. Methodology: 1,2-dicyano-4,5[bis-methylbromide]benzene (1) was prepared from *o*-xylene by reactions with Br_2, NBS and copper(I) cyanide. 1,2-Dicyano-4[1-*O*-hexyl-6-*O*-*p*-toluenesulfonyl]benzene (2) was prepared from 4-nitrophthalonitrile by reactions with 1,6-hexanediol and tosyl chloride. Results: Starting from *o*-xylene, (1) was obtained in three steps, and has two peripheral groups at positions 4 and 5. Starting from 4-nitrophthalonitrile, (2) was obtained in two steps, and has one peripheral group at position 4. Conclusions: The two synthetic routes yielded different precursors, which allow to prepare symmetrical and assymmetrical PCs, with different kind and number of groups, at different positions. The precursors will be used for reactions with galactose, to get the desired products.

Financial Support: FAPESP / Univap
Supervisor: Milton Beltrame Junior

SF005 - HG(TCA)2 – REAGENT FOR THE SYNTHESIS OF BENZENIC ORGANOMERCURY COMPOUNDS.

MILENA ARAÚJO TONON(IC)[1]; ÁUREA DONIZETE LANCHOTE BORGES(PQ)[1], ALBERTO FEDERMAN NETO(PQ)[1]

(1) Universidade de São Paulo, Faculdade de Ciências Farmacêuticas de Ribeirão Preto.

Introduction: Some years ago, we reported the synthesis of $Hg(TCA)_2$ - mercury(II) trichloroacetate, and their use in the permercuration of ferrocene (1). In previous communications (2), the use of $Hg(TCA)_2$ for the mono and dimercuration of ferrocene was described. $Hg(TCA)_2$ is a strong metalating agent, and economical in comp. with the classical $Hg(TFA)_2$.
Objective, Methodology, Results, Conclusion: Now, we extended the use of methanolic or ethanolic solutions of stabilized $Hg(TCA)_2$ for the direct Dimroth electrophilic mercuration of benzenes (benzene itself, phenol, benzoic acid, mesithylene, toluene, salicylic acid, biphenyl ,anisole) using $Hg(TCA)_2$ in adequate proportions, forming the corresponding mono or permercury organometallic compounds – $RPh(HgCl)_n$, in low to moderate yields. We found that $Hg(TCA)_2$ is better stabilized by an small excess of HgO, instead of $CaCO_3$, used in the original procedure (1).
(1) FEDERMAN NETO et al., *Synth React Inorg, Met-Org Chem*, 27, 1543, 1997 and ref. cited. (2) TONON et al.,*12⁰ SIICUSP-Simpósio Internacional de Iniciação Científica da USP*, number 4220, 2004 and comm. cited.

Financial Support: FAPESP, CNPq
Supervisor: Alberto Federman Neto.

The authors did not follow the Scientific Committee's suggestion for an English language review

SF006 - TOTAL FLAVONOIDS CONTENT IN *BAUHINIA MONANDRA* K. DRUG MATERIAL

ANA JOSANE DANTAS FERNANDES (PG)(1); FABÍOLA PESSOA DA CUNHA (IC)(1); ANDREZA KALINE SOARES DANTAS (IC)(1); ADRIANA AUGUSTO DE RESENDE (PQ)(2); TATIANE PEREIRA DE SOUZA (PQ)(1); LUIZ ALBERTO LIRA SOARES (PQ)(1)

(1)Department of Pharmacy/UFRN; (2)Department of Clinical Analysis/UFRN

INTRODUCTION: *Bauhinia monandra* ("pata-de-vaca") is widely used in the traditional medicine as hipoglicemiant. Although the active substances of this medicinal plant are not yet known, flavonoids can be used as chemical markers for quality control purposes. OBJECTIVE: The aim of this work was to develop a total flavonoid assay for the drug material of *B. monandra*. METHODOLOGY: Different amounts of the drug material dried and grounded (0.25 to 1.25g), were extract by reflux (3x 30min) with: water, ethanol and ethanolic solutions (40, 60 and 80%; v/v). The total flavonoids content was determinate at 410 nm after reaction with $AlCl_3$ 5% (w/v) by 25 min at 410 nm. RESULTS: Increasing in method response was observed for both studied variables (drug amount and ethanolic concentration). However, no linearity could be observed. Additionally, the process showed lower variability. CONCLUSION: The method is able to evaluate the total flavonoid of the drug. The optimum conditions were 0.5g of drug and ethanol 80% (v/v) as solvent. The relative standard deviation (2.2%, n=5) showed the higher repeatability of the method.

Supervisor: Luiz Alberto Lira Soares.

SF007 - SYNTHESIS AND BIOLOGICAL EVALUATION OF BORONATED POLYGLYCEROL DENDRIMERS AS POTENTIAL AGENTS FOR NEUTRON CAPTURE THERAPY

ALVARO ANTONIO ALENCAR DE QUEIROZ (PQ)[1]; GERALD SARAIVA SILVA (PG)[2]; MARIA APARECIDA PIRES CAMILLO (PQ)[2] ; OLGA ZAZUCO HIGA[2]

(1) Departamento de Física e Química/Instituto de Ciências Exatas, Universidade Federal de Itajubá, 37.500-903, Itajubá/MG, Brasil. E-mail: alencar@efei.br.
(2) Laboratório de Biologia Molecular, Instituto de Pesquisas Energéticas e Nucleares. Av. Professor Lineu Prestes, 2242, 05508-000 -São Paulo/ SP, Brasil.

Successful treatment of cancer by boron neutron capture therapy (BNCT) requires the selective delivery of ^{10}B to constituent cells within a tumor. The slow evolution of effective drug-targeting methodologies for the selective delivery of sufficient amounts of boron to cancer cells remains as an important obstacle to the development of this therapy. In the present study we have investigated the potential use of 3rd generation boronated poly(glycerol) dendrimers (^{10}B-PGLD) to obtain ^{10}B concentrations necessary for BNCT treatment. The PGLD dendrimer was synthesized by using a polyglycerol as core functionality followed by covalently coupling of decaborate clusters. In vitro and in vivo studies have shown that the enriched boron-10 polyglycerol dendrimers exhibits lower cytotoxicity suggesting that ^{10}B-PGLD might be a useful drug for BNCT.

Financial Support: Fapemig, Capes
Supervisor: Maria Aparecida Pires Camillo

The authors did not follow the Scientific Committee's suggestion for an English language review

SF008 - SYNTHESIS OF ORGANIC AND ORGANOMETALLIC DI-CHALCONES, WITH HYDROXYLATED SUBSTITUENTS.

CLÁUDIO BATTISTON LOUREIRO (IC)[1]; ÁUREA DONIZETE LANCHOTE BORGES (PQ)[1]; ALBERTO FEDERMAN NETO (PQ)[1]

(1) College of Pharmaceutical Sciences of Ribeirão Preto - USP

Chalcones can be defined as ±,ß-unsaturated ketones, in witch or the carbonyl, or the olefinic, or both moieties, are aromatic groups. The majority of organic chalcones is of natural origin, found in superior plants. However, many are synthetic now. Natural or synthetic chalcones, can possess a large spectrum of biological activity: anti-inflammatory, antimalarial, tripanocidal etc., being therefore a good target for the research of new drugs.
This research has for objective to study new methods for make new organic/organometallic di-chalcones with hydroxyl groups, because it's known that hydroxyl groups may enhance biological activities.
For the synthesis of chalcones, the Claisen-Schmidt Condensation proc. was modified, either using diss. aldehydes and/or ketones and KOH in absolute ethanol as cat./solv. (instead of the NaOH in CH_3OH/H_2O,"Claisen's alkali") The isolation proc. was modified, in order to easy app. to water soluble products.
This new results suggests that the method is good for the routine synthesis of water soluble, hydroxylated bis-chalcones, in good or high yields.

Financial support: PIBIC – CNPq
Supervisor: Alberto Federman Neto.

SF009 - SYNTHESIS OF SOLUBLE DERIVATIVES OF ESCIN

CAROLINA DE BARROS FRANCO ARAUJO (PG)[1]; NADIA RUSCINC (PG)[1]; CARLA APARECIDA PEDRIALI (PG)[1]

BIOCHEMICAL AND PHARMACEUTICAL TECHNOLOGY DEPARTMENT – FCF / USP(1)

Introduction: The beta-escin is a widely used product, as much in the herbal form as in the topic form, as phlebotomic and circulation activator. For being little soluble in water, its manipulation and incorporation in liquid pharmaceutical forms, especially for topical use, are very difficult. Objective: The objective of this study is to synthesize soluble derivatives from the beta-escin, keeping its anti-inflammatory and phlebotomic characteristics. Methodology: The new derivatives had been synthesized from reaction with succinic anhydride and phtalic anhydride in different concentrations and submitted to solubility and inflammation in balb C mices. Main Results and Conclusion: The preliminary results show that the synthesized derivatives possess better characteristics of solubility and keep the anti-inflammatory and phlebotomic characteristics.

MAIN LEADER: BRONISLAW POLAKIEWICZ

The authors did not follow the Scientific Committee's suggestion for an English language review

SF010 - TRYPANOCIDAL ACTIVITY OF PIRANOQUINOLINE DERIVATIVES

LUIZ C. SILVA FILHO(PG)[1]; ROSANGELA SILVA(PQ)[2]; MAURICIO G. CONSTANTINO(PQ)[1]; SÉRGIO ALBUQUERQUE(PQ)[2]

(1)FFCLRP-USP (2) FCFRP-USP / Ribeirão Preto-SP-Brazil

INTRODUCTION - Tetrahydroquinoline derivatives are an important class of compounds which displayed a wide range of biological activity.[1]
OBJETIVE - *In vitro* trypanocidal activity evaluation of pyranoquinoline derivatives against trypomastigote forms of Y strain of *T. cruzi*.
METHOD - The evaluation of the trypanocidal activity of the compounds was performed as described by Muelas-Serrano .[2]
RESULTS - (4a*R**,5*S**,10b*S**)-5-Phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-c]quinoline (1) and 11 derivatives (2-12) were synthesized and evaluated.
Table 1 show the trypanocidal activity of compounds with IC_{50} lower than 70μM. Compound 1 in the more active (IC_{50}=25.5 μM). Compound 7 showed value of IC_{50} above 100μM and the compound 9 have the lower value of IC_{50}= 52.7 μM in the second group.

Table 1. Determination of % lysis and IC_{50} obtained against *T. cruzi*

Compounds	% lysis X concentration (μM) ± S.D.)			IC_{50} μM
	8,0	32,0	128,0	
1	41.6± 3.6	44.7± 5.0	71.6± 5.7	29,5
9	41.1± 2.9	42.1± 1.1	57.9± 3.6	52,7

+control–violet gencian to 613,5 μM (IC_{50}=76μM)
-control-infected blood+5% of DMSO

CONCLUSION - The results suggest that the stereochemistry of compound 1 is important for trypanocidal activity.

Reference
1) Magesh CJ *et al. Bioor. Med. Chem. Lett*. 2004, *14*,2035.
2) Muelas-Serrano S, *et al*. *Parasitol Res*. 2000, *86*,999.

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Supervisor: Mauricio Gomes Constantino

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Tecnologia Farmacêutica/ Farmacotécnica /
Pharmaceutical Technology /Pharmacotechinique (TF)

TF001 - GLYCEROL MONOOLEATE/WATER GELS AS TRANSDERMAL DELIVERY SYSTEM FOR NICOTINE

MÔNICA MINUCCI DALLA TORRE(IC)[1]; GISLAINE RIBEIRO PEREIRA(PQ)[1]

[1]Escola de Farmácia e Odontologia de Alfenas – Centro Universitário Federal

Introduction: Monoolein, glycerol monooleate (GMO), is a polar lipid that forms gels with a lyotropic liquid crystalline structure in the presence of water. Cubic phases gels of (GMO)/water have been proposed as sustained drug delivery systems, due its particular characteristic in controlling drug release. Objetive: The aim of this work was to study the use of GMO/water cubic phase gels as transdermal delivery system for nicotine. Methods: Cubic phase gels were prepared containing nicotine 1% v/w. Nicotine 1% (v/v) aqueous solution was employed as control. The in vitro release study were performed using a modified Franz type diffusion cell with cellulose acetate membrane. The amount of nicotine released was determined by HPLC. Results: The cubic phase gels sustained nicotine release for 48 hours. The amount of nicotine released through the synthetic membrane was a linear function of the square root of time (flux = 299.04 μg.cm-2.h-1/2), indicative of diffusion controlled release. Conclusions: GMO/water cubic phase gels controlled the nicotine release. The results obtained indicate the potential use of GMO cubic phase gel as a sustained drug release system for transdermal delivery.

Financial Support: PIBIC/CNPq
Supervisor: Profa. Dra. Gislaine Ribeiro Pereira

TF002 - STRUCTURAL STUDY OF LIQUID CRYSTALS AND MICROEMULSIONS USING CREEP EXPERIMENTS AND POLARIZING LIGHT MICROSCOPY

MARIA CRISTINA COCENZA URBAN (PG)[1]; DANIELE SILVEIRA LANDGRAF (IC)[1]; VICTOR HUGO VITORINO SARMENTO (PQ)[2]; LEILA APARECIDA CHIAVACCI (PQ) [2]; MARIA PALMIRA DAFLON GREMIÃO (PQ)[1]

[1]FCF-UNESP, Araraquara-SP-Brazil;[2] IQ–UNESP, Araraquara-SP-Brazil.

Liquid crystals and microemulsions have received increasing attention as drug delivery systems due to advantages related to physical stability and broad solubilization potential. The investigation of their structural properties is important to understand the mechanism of drug release. The aim of this study was to investigate the influence of the components proportion - propoxyl 5OP ethoxyl 20OE cethyl alcohol (surfactant), isopropyl miristate (oil) and water - in the structural evolution of the systems, using the creep-recovery rheological experiments and polarizing light microscopy. The first set of selected samples was prepared with fixed surfactant content and the second one with fixed oil content. The results showed that the components proportion influences structural features and mechanical properties of the systems, promoting the formation of micellar solutions and more ordered structures with lamellar and hexagonal arrangements. The influences of the structural evolution of these systems with the ratio oil/water phase in the drug delivery behavior will be evaluated.

Financial Support: CAPES, FAPESP
Supervisor: Maria Palmira Daflon Gremião

TF003 - DEVELOPMENT AND RHEOLOGICAL CHARACTERISATION OF BIOADHESIVE SEMI-SOLID, THERMOSENSITIVE SYSTEMS FOR THE PERIODONTAL POCKET ADMINISTRATION

MARCOS LUCIANO BRUSCHI (PG)[1]; HEITOR PANZERI (PQ)[2]; OSVALDO DE FREITAS (PQ)[1]; MARIA PALMIRA D. GREMIÃO (PQ)[3]; DAVID S. JONES (PQ)(4); ELZA HELENA G. LARA (PQ)[1]

[1]Programa de Pós-Graduação em Ciências Farmacêuticas - Faculdade de Ciências Farmacêuticas de Ribeirão Preto - USP; [2] Faculdade de Odontologia de Ribeirão Preto USP; [3] Faculdade de Ciências Farmacêuticas de Araraquara UNESP; (4) School of Pharmacy The Queen's University of Belfast UK

Introduction: Bioadhesive semi-solid systems to antimicrobial or anti-inflammatory agent delivery to the periodontal pocket (PP) have been used as adjuncts to mechanical cleaning of the tooth surface in periodontitis. These improve retention within the PP and, hence, the clinical performance of formulations. Objective: The aim of this study was to develop and characterise bioadhesive semi-solid systems, composed of Poloxamer 407 (P407) and Carbopol 934P® (C934P), for the administration of drugs to the PP. Methodology: Forty formulations were prepared containing P407 and C934P. This study examined the gelation temperature (GT), flow (continuous shear analysis), and oscillatory properties of the liquid formulations at 5 C (LQ). Results: The formulations were different in the appearance and consistency. Two of thirteen LQ showed suitable GT and plastic flow behaviour. Increased polymer concentrations and temperature increased G', G", and η', yet decreased the tan δ. LQ were elastic at 25 and 37 °C. Conclusions: The results have shown that these formulations possess suitable characteristics to be administrated into the PP.

Financial support: CAPES
Supervisor: Prof. Dra. Elza Helena G. Lara

TF004 - THERMAL BEHAVIOUR STUDY OF SOME DIURETIC AGENTS FROM TWO DIFFERENT MANUFACTURERS

EDEMILSON CARDOSO DA CONCEIÇÃO (PQ)[1]; VINICIUS BARRETO DA SILVA (IC)[1]; CLÉVIA FERREIRA DUARTE GARROTE (PQ)[1]; OSVALDO DE FREITAS (PQ)[2]

[1]Faculdade de Farmácia da UFG; [2] Faculdade de Ciências Farmacêuticas de Ribeirão Preto–USP.

Diuretic medications are among those most often prescribed in clinical practice because of their efficacy and safety for the treatment of cardiovascular diseases, especially congestive heart failure and arterial hypertension. The thermal behavior of the diuretic agents amiloride hydrochloride, hydrochlorthiazide and spironolactone obtained from Sigma and supplied by the Brazilian pharmaceutical industry were studied comparatively by thermogravimetry (TG), derived thermogravimetry (DTG) and differential exploratory calorimetry (DSC). The results obtained showed differences in the thermal profiles of the amiloride hydrochloride samples indicating polymorphic forms, presence of impurities in one of the spironolactone samples, and no differences in the thermal profiles of the hydrochlorthiazide samples.

Supervisor: Edemilson Cardoso da Conceição

TF005 - MINIMIZATION OF THE CONTENT ON RESIDUAL ORGANIC SOLVENT ON PLGA NANOSPHERES

ANDRÉ ROMERO DA SILVA(PG); ANA MARIA DE OLIVEIRA(PQ); FABIO AUGUSTO(PQ); RENATO ATILIO JORGE(PQ)

Instituto de Química, Universidade Estadual de Campinas, Campinas, SP, Brazil

In-mesotetraphenylporphyrin (InTPP) was encapsulated on poly(lactide-co-glycolide) (PLGA) nanospheres for its application in pre-clinical tests using photodynamic therapy. The emulsion solvent-evaporation method was used to prepare the nanoparticles, with chloroform as a solvent. The solvent is eliminated by evaporation under magnetic agitation, but some residual solvent (RS) may remain, which poses a potential health risk. Experiments arranged according to a fractional factorial design (FFD) were performed to minimize the RS on the nanospheres, by optimizing the values of some operational parameters related to their preparation. Headspace Solid Phase Microextraction (SPME) and GC-ECD were used for quantification of RS on the lyophilized nanoparticles. The residual chloroform level was below 5.0 μg kg^{-1} for all experiments. The FFD showed that increasing the stirring rate for the emulsification as well as the ethanol concentration in the aqueous phase decreases the RS in the PLGA nanospheres. The results indicate that RS concentration in nanospheres is in accordance with the limits prescribed in the USP, allowing its application in future clinical tests.

Financial Support: FAPESP and UNICAMP
Supervisor: Prof. Dr. Renato. A. Jorge

TF006 - INFLUENCE OF CROSSLINKED CHONDROITIN SULFATE ADDITION ON EUDRAGIT® FREE FILMS. A STUDY OF THE SWELLING PROPERTIES AND THE PERMEABILITY.

ÉLCIO JOSÉ BUNHAK (PG)[1]; ELISABETE SCOLIN MENDES[2]; NEHEMIAS CURVELO PEREIRA[2]; OSVALDO ALBUQUERQUE CAVALCANTI[2]

[1]State University of the West of Paraná - UNIOESTE, [2]State University of Maringá - UEM / Paraná/Brazil.

To improve the specificity of drug delivery, some polysaccharides have been modified. Chondrointin sulfate (ChS) is readily water soluble mucopolysaccharide present a potential with excipient for controlled drug delivery systems. Crosslinked ChS would be less hydrophilic and provide a better material as a vehicle in oral delivery formulation. The aim of this study was evaluate free films made of the crosslinked ChS and Eudragit®RS30D Films were manufactured by casting process after appropriate dispersion of knows concentration of ChS crosslinked with trisodium trimetaphosphate and Eudragit®. The obtained materials were characterized by swelling (fluids of gastric or intestinal simulation) and permeability (water vapour transmission) studies, performed on isolated films. The results showed that the swelling behaviour and the transmission of water vapour were influenced to the addition of the crosslinked ChS concentration when compared to the control. That confirms that crosslinked ChS is less hydrophilic and thus would provide a better shield for application on controlled drug delivery systems.

Financial Support: The autors to thank Solabia do Brasil and Almapal (SP) for facilities of chondrointin sulfate, and Eudragit® (Röhm Pharma) and triethyl citrate (Morflex) samples.
Supervisor: Elisabete S. Mendes

TF007 - PREPARATION AND MORPHOLOGY EVALUATION OF IBUPROFEN-LOADED POLYHYDROXYALKANOATES MICROSPHERES

FRANÇOISE CARMIGNAN (PG) [(1)]; ELENARA LEMOS SENNA (PQ) [(1)]

[(1)] Programa de Pós Graduação em Farmácia, Centro de Ciências da Saúde, Universidade Federal de Santa Catarina

Introduction: Polyhydroxyalkanoates are naturally occurring biodegradable polyesters produced as energy storage products by many bacterias. These polymers have been considered promising materials for drug controlled delivery. Objective: The aims of this work were to prepare and to characterize unloaded and ibuprofen (IBF)-loaded microspheres from poly(3-hydroxybutyrate) (PHB) and its copolymer with 3-hydroxyvalerate, P(HBV). Methodology: The w/o solvent/evaporation method was used to prepare the microspheres. The IBF to polymer ratio was 1:2 or 1:4. Particle morphology was evaluated by scanning electron microscopy (SEM). Drug encapsulation efficiency and IBF content were determined by UV spectrophotometry at 265 nm. Results: Spherical particles were visualized by SEM, but the surface porosity was varied as the preparation conditions function. Encapsulation efficiency (%) and IBF content (mg/100mg) varied from 86.04 to 60.03 and 26.68 to 12.01, respectively. However, IBF crystals were visualized by SEM when 1:2 the drug to polymer ratio were employed. Conclusion: Particles morphology and physical state of IBF on the microspheres were affected by the preparation conditions.

Financial Support: CNPq
Supervisor: Elenara Senna

TF008 - DEVELOPMENT AND EVALUATION OF FILMS MADE OF PECTIN, CASEIN AND THE CONJUGATE PECTIN-CASEIN

CAROLINA FRACALOSSI REDIGUIERI (IC)[1]; OSVALDO DE FREITAS (PQ)[1]

[1]Faculdade de Ciências Farmacêuticas de Ribeirão Preto da Universidade de São Paulo

Introduction: Since the fifties the polymeric membranes (films) have been used for the covering of solid pharmaceutical forms to mask their taste, smell or color, for physicochemical protection and for their resistence in the stomach. More recently, depending on the physicochemical characteristics, they have also been used to control drug delivery. Objective: Preparation and avaliation of films made of the conjugate pectin-casein comparing to the pectin and casein films Methodology: The films were prepared by the dispersion of pectin, casein and the conjugate pectin-casein in water in different concentrations. The dispersions were spread into polycarbonate plates and dried in incubator. To evaluate the films it was used DSC, and the following tests: the resistence to desintegration, the permeability of water vapor and tension-deformation properties. Results: The conjugate pectin-casein films presented very diferent characteristics and properties compared to the pectin and to the casein films. Conclusions: The conjugate pectin-casein films have showed to be a potencial pharmaceutical form to control drug delivery.

Financial Support: FAPESP
Supervisor: Dr. Osvaldo de Freitas

TF009 - PREPARATION OF PECTIN/CASEIN MICROPARTICLES CONTAINING METRONIDAZOLE FOR THE TREATMENT OF PERIODONTAL DISEASE

CAMILA FRACALOSSI REDIGUIERI (PG)[1]; OSVALDO DE FREITAS (PQ)[1]

[1]Faculdade de Ciências Farmacêuticas de Ribeirão Preto da Universidade de São Paulo

Introduction: Periodontitis is an inflammatory and infectious disease that results in destruction of tooth support structures and, subsequently, in tooth loss. Antibiotic administration into the periodontal pocket is one of the alternatives for the treatment of the disease Objective: Preparation of pectin/casein microparticles containing metronidazole for sustained release in the periodontal pocket. Methodology: Casein and pectin were dispersed in water under alkaline conditions for 12 hours. Metronidazole was added into the mixture and the pH was lowered until 5.0 either with citric acid or HCl. The dispersion was dried in spray-dryer. Results: Microparticles of pectin/casein conjugate were able to embody metronidazole crystals having no significant difference in their morphology by using either one of the acids. However, when citric acid was used, drug recovery yield from the microparticles was lower than that obtained with HCl. Conclusions: The microparticles of pectin/casein conjugate are able to embody metronidazole crystals providing a potential pharmaceutical form to control the drug delivery.

Financial Support: FAPESP
Supervisor: Dr. Osvaldo de Freitas

TF010 - THERMAL DECOMPOSITION AND DRUG-EXCIPIENT COMPATIBILITY STUDIES OF GLIBENCLAMIDE WITH VARIOUS EXCIPIENTS IN TWO DIFFERENT ATMOSPHERES

MARIELLA ZARONI(PG)[1]; MARCO A. CARVALHO FILHO(PQ)[2]; ITAMAR F. ANDREAZZA(PQ)[1]; MAYUMI E. O. SATO(PQ)[1]; JÚLIO C. DA ROCHA(IC)[2]; FELIPE P. NEVES(IC)[2]

[1]Department of Pharmacy UFPR(PR);[2] Department of Pharmacy Unicenp(PR)

Several investigations have been carried out into the application of thermogravimetry (TG), differential thermal analysis (DTA) and differential scanning calorimetry (DSC) in preliminary preformulation studies for the evaluation of solid state interactions as an aid to excipient selection. This study investigates the interaction between Glibenclamide and a number of pharmaceutical excipients (xanthan gum, guar gum, microcrystalline cellulose, povidone, Eudragit L100®, Opadry®), using two different dynamics atmospheres by mean of TG, DTG and DSC methods. TG, DTG and DSC curves were obtained using DTG-60/TG-DTA and DSC-60 thermal analysis equipment (Shimadzu). Heating rate: 10ºC.min-1; purge gas: air and nitrogen at a flow of 100 mL.min-1; weight of samples: 4-10 mg. Sample hold: alumina for TG/DTA and aluminum for DSC. The TG-DTG and DSC curves provided information on the thermal stability and thermal decomposition of Glibenclamide and the excipients studied. No drug-excipient incompatibility was observed.

Financial Support: CAPES
Supervisor: Mayumi E. O. Sato

TF011 - SURFACE RHEOLOGY OF DTAB/L-CARRAGEENAN AQUEOUS SOLUTIONS

M. ELISABETE D. ZANIQUELLI(PQ)[1],THATYANE MORIMOTO NOBRE (PG)[1], KENNETH WONG(PQ)[2]*

[1] Lab.Físico-Química de Superfícies e Colóides – Dep.Química- FFCLRP – USP-Rib.Preto.
[2] Lab.Físico-Química- Centro de Pesquisas de Paulínia – Rhodia Brasil.
*Present Address: Firmenich Co., Switzerland.

Macromolecules and surfactants are found together in different kinds of formulations. For liquid interfaces, as those found in emulsions and foams, the surface rheology plays an important role. This work deals with a cationic surfactant and carrageenans, a sulphated polysaccharide used as thickener, gelling agent or dispersant.
The aim of this work was to study the interaction between λ-carrageenan and dodecyltrimethyl ammonium bromide (DTAB), by means of surface tension (γ) as well as surface dilatational elasticity (ε) measurements. A dynamic drop tensiometer OCA-20, Dataphysics-GE, makes use of the shape of a pendant drop that can be periodically oscillated. The deformation (relative area variation) and shape of the drop are used to determine γ and e ε as $\varepsilon = d\gamma/d\ln A$.
The results indicate that the presence of the λ-carrag. (concentration 2.5×10^{-3}%) impinges an elasticity to the system that increases with the surfactant concentration. A maximum is observed at the critical aggregation concentration of the system, after wich the system is no longer elastic.

Financial Support: FAPESP, Rhodia and CNPq
Supervisor: M. Elisabete D. Zaniquelli

TF012 - CYTOTOXICITY OF DOXORUBICIN ENCAPSULATED IN SITE-SPECIFIC CON A-CONJUGATED LIPOSOMES

HERCÍLIA M.L. ROLIM SANTOS (PG)[1]; FERNANDO B. QUEIROZ (IC)[2]; MARIANE C.B. LYRA (IC)[1]; ROSA M.S. MAIOR (PQ)[2]; SILENE C. NASCIMENTO (PQ)[3]; NEREIDE S. SANTOS MAGALHÃES (PQ)[1]

[1]LIKA-UFPE; [2]Depto Química Fundamental-UFPE; [3]Depto Antibióticos-UFPE

Doxorubicin (DOX) is an antineoplastic agent, which is associated with a dose-limiting cardiotoxicity. The aim of this study was to encapsulate DOX into liposomes with Concanavalin A lectin conjugated at their surface for drug targeting. Liposomes containing DOX (1 mg/ml) were prepared with soybean phosphatydilcholine, cholesterol, stearylamine and dipalmitoylphosphatidylethanolamine (DPPE) linked to m-maleimidobenzoyl-N-hydroxysuccinimide (MBS). DPPE-MBS liposomes were then conjugated to SATA-Con A derivative. The liposome's cytotoxicity was evaluated on NCI-H292 and HEp-2 cells. The DOX concentration required to inhibit 50% of cell proliferation was 1.25 µg/ml for NCI-H292 cells treated with Con A-liposomes. An inhibition of 70% of HEp-2 cell proliferation was observed 72 hours after incubation (630 ng/ml). In contrast, DOX solution inhibited only 20% cell proliferation for both cell lines. These results suggest a strong interaction of the Con A-liposomes with cells, facilitating thereby the DOX penetration into cells, especially in HEp-2 cells.

Financial support: Rede Nanobiotec-MCT/CNPq
Supervisor: Nereide S. Santos Magalhães

TF013 - EVALUATION ON REOLOGICAL BEHAVIOR FROM DISPERSIONS OF SUPRAMOLECULAR PECTIN/ PROTEIN COMPOUND, HIGH METHOXYL PECTIN AND AMIDATED PECTINS

EDEMILSON C. CONCEIÇÃO (PQ)[1]; FERNANDO SCHIMIDT (PQ)[1]; OSVALDO DE FREITAS(PQ)[2]

[1]FF-UFG; [2]FCFRP–USP

Introduction: The pectins are complex polysaccharides found at cellular wall in citric plants, with important applications in pharmaceutical field. Chemical modifications can change your properties as the gelling and thickening agents. Objective: In the present work we evaluated the rheological behavior of different dispersions of pectins with high methoxyl, pectin with 17% amide group, pectin with 14% amide group in relation to behavior of dispersions of a supramolecular pectin/casein compound. Methodology: The rheological measurements were performed using a rheometer Brookfield (LV-DVIII) at 30° C, varying the shear rate from 10 to 260 s^{-1}. Results and Conclusions: The obtained data showed that the apparent viscosity of pectin dispersions with high methoxyl, pectin with 17% of amide group, pectin with 14% of amide group was superior to those of supramolecular pectin/protein compound for all the equivalent concentrations, existing a direct proportionality between the apparent viscosity, characterized as a Newtonian fluids. These characteristics presented by supramolecular compound can be considered the most important ones that a polymer presents potential use in the pharmaceutical area.

Financial Suport: UFG
Supervisor: Osvaldo de Freitas

TF014 - ACCOMPANIMENT OF MICROBIAL AND PHYSICOCHEMICAL BEHAVIOR OF MEBENDAZOLE SUSPENSION

SIMONE BORTOLAN DOS SANTOS (IC)[1]; ANA J. P. SANTINHO(PQ)[1]

[1]Faculty of Pharmacy and Biochemistry of Presidente Prudente, University of Western São Paulo (UNOESTE) – Brazil.

Introduction: Mebendazole is susceptible to chemical decomposition, its suspension has been available in the University Hospital (UH) of Presidente Prudente though there was not been determined its shelf life. Objective: To accompany the microbial and physicochemical behavior of mebendazole oral suspension prepared for use in the UH. Methodology: Mebendazole suspension was prepared (n=3), packed and stored at 22ºC for 12 month. Samples were submitted at pH determination, UV absorption analysis and microbial limit tests. All tests were performed monthly in accordance to Brazilian Pharmacopoeia. Results: The pH value changed on 0.2 units as long as the quantity, in mg, of mebendazole in the portion of suspension was maintained into pharmacopoeial requires. Microbial tests demonstrated absence of bacterial specimens, however yeast and molds were presented into the pharmacopoeial limit. It should justify the development of unpleasant flavor, indicating some problem with the preservative system. Conclusion: It could suggest that the shelf life was found to be 30 days at 22ºC. Nevertheless, to increase the shelf life it would be necessary to adequate the pH formulation in relation of preservative system.

Supervisor: A.J.P.Santinho

TF015 - PHAMACOKINETICS AND BIOAVAILABILITY OF USNIC ACID-LOADED NANOCAPSULES

NOEMIA PEREIRA DA SILVA SANTOS(PQ)[1],[2]; LETÍCIA GHIGGI(IC)[1]; HELEN CRISTINA PEDRONI(PG)[1]; SILENE CARNEIRO NASCIMENTO(PQ)[3]; TERESA DALLA COSTA(PQ)[1]; NEREIDE STELA SANTOS MAGALHÃES(PQ)[2].

[1]Fac. Farmácia-UFRGS; [2] LIKA-UFPE ; [3]Depto. Antibióticos-UFPE. nssm@ufpe.br

The usnic acid (UA) was nanoencapsulated as to provide a suitable dosage form for in vitro and in vivo studies. The nanoencapsulation of UA produced a decrease in its hepatotoxicity (30%) and an increase of 22% in antitumor activity. The aim of this study was to evaluate the pharmacokinetics and bioavailability of UA. The UA plasma concentration was measured in healthy rats. Animals received a dose of the 15 mg/kg (i.p.) or 2.5 mg/kg (i.v.) of the UA suspension or UA-loaded nanocapsules. The UA content was analyzed in blood samples. Individual plasma profiles were evaluated and pharmacokinetic parameters estimated. Plasma concentrations of UA were higher after administration of the nanoencapsules than the suspension form. The areas under the curves (AUC) were 4.34 ±1.42mg.h/ml and 5.8±1.53 mg.h/ml for UA suspension and UA-loaded nanocapsules, respectively. The same pattern was observed for the peak plasma concentration (Cmax free= 4.75±0.74 mg.h/ml and Cmax encapsulated= 8.23±0.89 mg.h/ml). The encapsulation thus increased the bioavailability of UA in 34% in comparison to the suspension form.

Financial support: Nanobiotec/MCT-CNPq.
Supervisor: Teresa Dalla Costa

TF016 - SKIN PERMEATION IMPROVEMENT OF TMPYP FOR TOPICAL PHOTODYNAMIC THERAPY (PDT)

GUILHERME MARTINS GELFUSO(PG)*; RENATA FONSECA VIANNA LOPEZ(PQ)*

*Departamento de Ciências Farmacêuticas, FCFRP, USP

TMPyP is a cationic porphyrin that interacts with nucleic acids and has been used in PDT of cancer, which is a treatment involving the administration of a photosensitizing agent and its subsequent activation by light. Topical PDT is a therapy in which the photosensitizer is administered to the patient through the skin and accumulates in the tissue. As the passive skin permeation of TMPyP is insufficient for full therapeutic effect, we have been examining the potential of iontophoresis as a method to enhance TMPyP delivery. Passive and iontophoretic delivery of TMPyP from a non-ionic gel were studied using a modified "Franz" diffusion cell and porcine skin. TMPyP iontophoretic transport from the anode compartment was followed over a period of 6h at a constant current of 0.5 mA/cm^2. Furthermore, before these experiments drug delivery of non-ionic and anionic gels was also examined using a hydrophilic membrane. The release rate of TMPyP from non-ionic gel was 17.5 µg/cm^2/h, higher than that of anionic gel (0.8 µg/cm^2/h) and not significantly different from the aqueous solution one. Skin permeation experiments showed that anodic iontophoresis of positive TMPyP caused a considerable (~17 fold) enhancement over the passive flux.

Financial Support: FAPESP
Supervisor: Profa. Renata Fonseca Vianna Lopez

TF017 - THE DOXORUBICIN INCORPORATION IN MICROEMULSIONS AND STUDY OF "IN VITRO" ANTIPROLIFERATIVE ACTIVITY BY CELLS OF CULTURE

THALITA PEDRONI FORMARIZ (PG)[1]; LUCIANA KONECNY KOHN (PG)[2]; ARNÓBIO ANTÔNIO DA SILVA JÚNIOR (PG)[1]; JOÃO ERNESTO DE CARVALHO (PQ)[2]; ANSELMO GOMES DE OLIVEIRA (PQ)[1].

[1] Departamento de Fármacos e Medicamentos – FCFAR/UNESP
[2] CPQBA/UNICAMP

Microemulsions (ME) and submicroemulsions (SEM) systems have a great potential as a drug delivery systems and also have been frequently to be used to increase the solubility of lipophilic drugs in aqueous medium. In this work we have studied the parameters for the development of a suitable EM and ME systems as a drug carrier for a water insoluble antitumorals using Doxorubicin (DOX) was drug model. For this, the interaction of DOX with the ME and EM was studied. Several ratios of Soya Phosphatidylcholine/Eumulgin® HRE40 were used in order to determineted the region of SEM and ME domain into a pseudo-ternary phase diagram. The rate of the incorporated DOX in ME system, the "*in vitro*" release and the antiproliferative activity of DOX-ME and DOX-SEM using cell culture were evaluated. The obtained results show that the DOX-ME is able to obtain therapeutic effect and a prolonged release of the drug. The antiproliferative activity showed that the ME and SEM can be used as a drug carrier system in cancer therapy.

Financial Support: FAPESP
Supervisor: Anselmo Gomes de Oliveira

TF018 - PREPARATION AND PHYSICAL AND CHEMICAL CHARACTERIZATION OF PARTIAL PROTEIN HYDROLYSATES COMPLEXES WITH MINERALS

RENATA FRANZAN (PG)[1]; ZEKI NAAL (PQ)[1]; OSVALDO DE FREITAS (PQ[1]

[1] Faculdade de Ciências Farmacêuticas de Ribeirão Preto – Univ. de São Paulo

Introduction: Minerals, such as Cu, Fe, Mn and Zn are essentials in life maintenance. Their deficiencies contribute mainly to childhood mortality and morbidity. Objective: Preparation and physical and chemical characterization of mineral complexes with partial hydrolysates of soy protein, based on hypothesis that mineral complex has more bioavailability than inorganic minerals. Methodology: Partial hydrolysates of soy protein were prepared according to the procedure described by Freitas (1993) and characterized by FPLC system with Superdex Peptide HR 10/30 column. The mineral-peptide complex was prepared according to the procedure described by Chaud et al (2000). The metal linked quantity was determined by atomic absorption and binding sites determination was made by infrared spectroscopy and near infrared spectroscopy. Results: According to the hydrolysates characterization method there was no differences between 9 to 27 hours and enzymatic concentration between 1.8 to 5.4 % of soluble material yield. Complex reaction occurred according to expected. Conclusions: Partial hydrolysate soy protein has showed to be a potential substrate to prepare mineral complexes.

Financial Support: CAPES
Supervisorr: Dr. Osvaldo de Freitas

TF019 - OPTIMIZATION OF THE CONDITIONS FOR QUERCETIN/B-CYCLODEXTRIN COMPLEXATION USING A FACTORIAL DESIGN

GREICE STEFANI BORGHETTI (PG)[1]; VALQUIRIA LINCK BASSANI (PQ)[2]

[1 2] Programa de Pós-graduação em Ciências Farmacêuticas - Universidade Federal do Rio Grande do Sul

Quercetin is a flavonoid with several biological activities, including the antioxidant one. Its use in pharmaceutical field is, however, limited by its poorly aqueous solubility. Quercetin was found to form inclusion complex with cyclodextrins with improved its solubility (CALABRO *et al*., 2004; PRALHAD, RAJENDRAKUMAR, 2004; ZHENG *et al.*, 2005). In view to choose the better conditions for semi-industrial production of quercetin/b-cyclodextrin complexes, the present work presents a factorial design for studying the influence of operational conditions as the temperature (27 or 37 ºC), agitation period (24 or 48 h) and excess amount of quercetin (3 or 6 mM) on the complexation. Following these conditions, a phase solubility study was carried out, according to the method reported by Higuchi and Connors (1965) in the molar ratios of 1:0,5; 1:1; 1:1.5; 1:2 and 1:2.5. The quercetin was assayed in the supernatant by UV at 372 nm. The results of the factorial design demonstrated that the better complexation condition is obtained at 37 ºC, during 24 h and with 6 mM of quercetin. Solubility studies revealed a linear relationship between the increase in quercetin solubility and the increase in β-cyclodextrin concentration and the curve obtained can be classified as the A_L type. The complexation quercetin/β-cyclodextrin was confirmed characterizing the complexes obtained in the ratio 1:1, dried by spray-drying (Buchi 190®), by using DSC, IR and ^{1}H-NMR techniques.

Financial Support: Brazilian Government (CNPq). Adviser of the MSc thesis Valquiria Linck Bassani, PhD.
Supervisor: Prof. Dra Valquiria Linck Bassani - valqui@farmacia.ufrgs.br

TF020 - INFLUENCE OF NANOPARTICLES SIZE ON PRAZIQUANTEL RELEASE PROPERTIES

RUBIANA MARA MAINARDES (PG)[1]; PRISCILA OLIVEIRA CINTO (PG)[1]; MARIA PALMIRA DAFLON GREMIÃO (PQ)[1]; RAUL CESAR EVANGELISTA (PQ)[1]

[1]Programa de Pós-graduação em Ciências Farmacêuticas - Faculdade de Ciências Farmacêuticas de Araraquara-UNESP/Brazil

Introduction. The rate of drug release from nanoparticles (NP) is governed by several factors and the particle size is one of the most important. Objective. Verify the influence of NP size on praziquantel drug release kinetics. Methodology. The size of NP were measured by light scattering. The amount of drug entrapped in the NP was determined by HPLC. A diffusion cell containing dissolution medium was used for the in vitro drug release. The NP were put in contact with the medium by means a cellulose acetate membrane. At different time intervals, aliquots of 100 µL were withdrawn and the drug concentration was assessed by HPLC. Results. The release profiles of two NP batches with different sizes but with approximately the same drug content were compared. At the end of the experiment (24h), the cumulative release revealed values that were different for each different size, corresponding to 10% of the initially entrapped drug for the larger particles and to 28% for the smaller particles. It was also observed that the smaller NP show a burst effect bigger than the larger ones. Conclusion. It was observed that the praziquantel release rate from larger NP was slower than small sized NP.

Finnancial support: CAPES
Supervisor: Raul Cesar Evangelista

TF021 - STUDY ON THE CURCUMINOID EXTRACTION FROM CURCUMA LONGA ROOTS.

VIVIANE MAIRA PAULINO PAULUCCI (PG); LUÍS ALEXANDRE PEDRO DE FREITAS (PQ)

Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP

Introduction: Curcuma longa L belonging to Zingiberaceae, is usually encountered in tropical and sub-tropical regions. Recently, many researches have attributed medicinal properties to curcuminoids, such as liver protector, anti-oxidant, anti-inflammatory and anti-tumor. Objective: This work aims to develop a standardized extract from the roots of curcuma and to evaluate its "in vitro" anti-oxidant activity. Methodology: Grounded roots of curcuma were extracted in a Soxhlet apparatus varying the solvent (ethanol 70% and 96%) and extraction time (12 and 24hs) in a full factorial design (2^2). The total curcuminoid content, TCC, was determined by spectrophotometry at 425nm, using curcumin as reference. The anti-oxidant activity, AAA, was determined by the DPPH method. Results: The best extraction result was observed for ethanol 70% during 12hs, yielding 4.46% of TCC in dry extract, and the highest AAA (C_{50}=0.011). The TCC was affected by extraction time at 5% significance level and the AAA was affected by solvent type at 15% significance level. Conclusion: Dry extract properties showed that the Soxhlet is effective for Curcuma extraction and the best result is attained with ethanol 70% for 12 h.

Financial support: CNPq
Advisor: Luís Alexandre Pedro de Freitas.

TF022 - ENCAPSULATION OF MAGNETIC PARTICLES INTO CROSS-LINKED GELATIN MICROCAPSULES

AMANDA K. A. SILVA (PG); ERICA L. SILVA (IC); ELQUIO E. OLIVEIRA (PG); ARTUR S. CARRIÇO (PQ); ERYVALDO S. T. EGITO (PQ)

UFRN-PPGCSA/Laboratório de Sistemas Dispersos (LASID) e DFTE

INTRODUCTION. Magnetic particles have been largely used in biotechnology. OBJECTIVE. The aim of this work was to describe a method to encapsulate magnetic microparticles into gelatin microcapsules in order to improve their properties for in vivo use. METHODOLOGY. Magnetic particles were produced by coprecipitation of iron salts in alkaline medium. The magnetic suspension was added to a gelatin solution. The emulsification process was then carried out in chloroform: ciclohexane solution containing sorbitan triesterate. Interfacial cross-linking reaction took place by adding a terephthaloyl chloride solution. The sample was analyzed by X-ray powder diffraction, optical microscopy and vibrating sample magnetometry. RESULTS. Characterization data demonstrated that magnetic particles were successfully encapsulated in gelatin microcapsules. Such system was found to be superparamagnetic. CONCLUSIONS. Besides agglomeration and oxidation may be prevented, particle encapsulation into gelatin microparticles may also play an important role in increasing particle biocompatibility.

Financial support: CNPq, BNB and Capes- Brazil.
Adviser: Eryvaldo Sócrates Tabosa do Egito

TF023 - USE OF O/W EMULSION TO OBTAIN FLOATING BEADS OF CALCIUM ALGINATE AND COATING BY IN SITU POLYMERIZATION

JOSÉ CLAUDIO GOVANI(IC)[1]; KELI DOS SANTOS PROENÇA(IC)[1]; NEWTON ANDRÉO-FILHO(PQ)[1]

[1]University of Sorocaba

Introduction: Drugs controlled release systems have been used to delivery drugs in specific organs or sites for absorption. Thus, floating beads can be used to maintain the drug release in the stomach for a higher time that conventional dosage forms, collaborating with local actions or enabling the prolonged release in TGI. Objectives: Prepare calcium alginate floating beads using o/w emulsion intrapped in the system and coating them with urea/formaldehyde polymer. Methodology: Beads were obtained by dripping of o/w emulsion, containing calcium alginate 1% w/v in external phase, in $CaCl_2$ 1M, under stirring. The beads formed were coated by deposition of urea/formaldehyde polymer obtained by monomers reaction in acid mean (pH~2). Results: The particles obtained were spherical shape (1.5mm diameter) and floated in simulated gastric fluid (HCl 0.1M) during the entire test. After the coating, the surface of the beads showed explicit polymer deposition, easily observed through optical microscope. The coating did not affect the floating properties. Conclusion: The system purposed was adequate to obtain floating beads and the film coating will be able to controlling the drug release of the beads.

Financial support: University of Sorocaba
Adviser: Newton Andréo-Filho

TF024 - TOPICAL DELIVERY OF VITAMIN K USING A LIQUID CRYSTALLINE DELIVERY SYSTEM

LUCIANA B. LOPES (PG)[1]; FERNANDA F. SPERETTA (IC)[1]; M. VITÓRIA L. B. BENTLEY (PQ)[1]

[1]Faculdade de Ciências Farmacêuticas de Ribeirão Preto – USP, Ribeirão Preto, SP

Introduction: Monoolein is a polar lipid that swells in water giving rise to several liquid crystalline systems, including the reverse hexagonal phase. Objectives: The present study was aimed at investigating the ability of the reverse hexagonal phase to improve topical delivery of vitamin K. Methods: The hexagonal phase was prepared by melting monoolein, followed by addition of vitamin K (VitK) at 3% (w/w) and water at 30% (w/w). The skin penetration and percutaneous permeation of VitK was evaluated using porcine ear skin mounted in a Franz diffusion cell at 3, 6, 9 or 12 h post-application. A VitK solution (3%) in vaseline was used as control formulation. Results: The skin penetration of VitK in both stratum corneum and [epidermis without stratum corneum + dermis] was significantly improved ($p < 0.05$) when the hexagonal phase was used compared to the control solution at all time points studied. The hexagonal phase also significantly ($p < 0.05$) enhanced the percutaneous permeation of VitK. Conclusions: These results suggest the potential of the reverse hexagonal phase of monoolein as a topical delivery system for vitamins.

Finnancial support: CNPq, FAPESP.
Supervisor: Profa. Dra. Maria Vitória L.B. Bentley

TF025 - TECHNOLOGICAL DEVELOPMENT IN CONTEMPORARY PHARMACEUTICAL WAY CONTAINING EXTRACT OF PRÓPOLIS

JEKSON LUIZ DA SILVA(IC)[1];MÔNICA FELTS DE LA ROCA(IC)[1];JOSÉ LAMARTINE SOARES(IC)[1];LÍVIO CÉSAR CUNHA NUNES(PG)[2]; ANTÔNIA MARIA DAS GRAÇAS LOPES CITÓ[2]; PEDRO JOSE ROLIM NETO[1]

[1]LTM/UFPE;[2]NTF/UFPI

Própolis has been demonstrating great therapeutic potential (curative/preventive) in their use in the oral cavity against the bacterial plate and gum inflammations. The chewing gum use stimulates the flow to salivate, potentializing the capacity remineralizante of the saliva.It was aimed at to develop a contemporary pharmaceutical form (chewing gum in the form of chewable tablet). the preparation of the extract própolis etanolic was Standardized (EEP) to the 8% (p/v) for extraction during 30 minutes under constant agitation at 70ºC. The activity antimicrobials in vitro was verified (against *S. mutans and C. albicans*) for the diffusion method in solid middle. It was obtained chewable tablets through direct compression, after a planning excipientes qualitative/ quantitative. The tested microorganisms were shown sensitive to EEP.The obtained tablets (I weigh medium 1.50g and hardness 7.0 Kgf/cm²) they showed good taste and easy obtaining. The characteristics of the obtained product us they take to deduce an increase of the activity against the decay and the microorganisms of the oral cavity, fact that it will be tested alive in later.

Financial Support:CAPES/CNPq
Supervisor: PEDRO ROLIM e A.GRAÇAS CITÓ

TF026 - APPLICATION OF THE RULAND METHOD IN THE DETERMINATION OF RELATIVE CRYSTALLINITY IN PHARMACEUTICAL MATERIALS

PATRIK OENING RODRIGUES (PG)[(1)]; TEÓFILO MAZON CARDOSO(PQ)[(2)]; MARCOS ANTONIO SEGATTO SILVA(PQ)[(3)]

[1] Universidade da Região de Joinville (UNIVILLE), [2] Centro Universitário da Grande Dourados (UNIGRAN), [3] Universidade Federal de Santa Catarina (UFSC)

The Ruland method applies a simple relationship between the areas of the crystalline peaks and the amorphous halo of an X-ray diffraction pattern, being the crystallinity determined through the integration among these areas. The objective of this work was to apply the methodology proposed by Ruland in the determination of the relative crystallinity (X_c^{rel}) of AZT, nimodipine (two material raw) and HPMC. The patterns of powder X-ray diffraction were determined in equipment Philips, using nickel filter, tube with anode of CuKa, in interval from 3 to 50 °C with time of step of 1 second. Equipment of SEM was used for morphologic evaluation of particles. The relative crystallinity of the AZT determined by Ruland method was 75.16 %. The photomicrographs of the drug showed the presence of orthorombic crystals. The nimodipine samples presented low crystallinity, with 26.42 % and 18.86 %, respectively. The photomicrographs of the samples allowed verifying the low crystallinity of this drug. As most of the polymers, HPMC presented low crystallinity, with 12.9 % for K4M and 18.96 % for K15M. The photomicrographs showed the presence of amorphous material, preferentially.

Financial Support: CAPES
Supervisor: Marcos Antonio Segatto Silva

TF027 - STUDY ON THE GASTRIC RESISTANT COATING OF SOFT GELATIN CAPSULES

CAMILA R. KFOURI (PG) [1]; MARIELLA VIEIRA (IC) [1]; PRISCILA D. YUVAMOTO (IC) [1]; ROBERTA ONDEI (IC) [1]; LUÍS A. P. FREITAS (PQ) [1]

[1] Faculdade de Ciências Farmacêuticas de Ribeirão Preto -FCFRP/USP

Introduction: Polymeric coating is widely applied for protecting pharmaceutical dosage forms from gastric fluid and to control the release rate of active ingredients. However, the use of polymeric coatings for soft gelatin capsules is not fully addressed in the scientific literature. Objective: To develop a gastric resistant formulation and evaluate the spouted bed process for coating of soft gelatin capsules. The coating formulation was prepared with the methacrylic acid - ethyl methacrylate copolymer (Eudragit® L30D55), with triethyl citrate as plasticizer. Different formulations and process conditions were evaluated. Temperature and humidity were found to affect the physical-mechanical properties of the coated capsules. The best coatings were submitted to disintegration tests according to the Pharmacopoeia, and showed gastric resistance for 60 minutes in hydrochloride acid solution. In all cases, the polymeric film was released after 10 minutes in phosphate buffer solution (pH=7.5).

Financial Support: Fapesp
Supervisor:Luis Alexandre Pedro de Freitas

TF028 - EVALUATION OF PARABENES INIBITING ACTIVITY SETIVITY RELATED TO DIFFERENT INCORPORATION TECHNIQUES IN A EMULSION

MARCELO S. MENDES(IC)[1]; MARIA ROSA M. PRADO(PQ)[1]; NEIVA LUBI(PQ)[1]; RENATA PALMEIRA(IC)[1].

[1] Centro Universitário Positivo (Unicenp)

Pharmaceutical products and cosmetics classified as non-sterile require a preservative system according to official policies of minimal limits of microbial presence. Paranabenes (propylparabene and methylparabene), are preservative compounds utilized in emulsions and their adding to emulsified systems do not exempt problems related to solubilization, or even the inactivation by tensoactives. Pharmacokinetcis studies and the need of potencializing agents addition must be therefore developed. The aim of this study was to evaluate the inhibitor activity of parabenes in differents incorporation techniques. Emulsions were prepared as follows : E1 without preservatives; E2 propylparabene added in oily phase (OF) and methylparabene in acquous phase (AF) ; E3 propylparabene + methylparabene in AF solubilized with propylene glycol; E4 propylparabene + methylparabene in AF with EDTA, the preservative challenge (PCT) test was carried out, according to USP XXIV in the aforesaid emulsions. The obtained results showed that E1 and E2 were reproved in the PCT. It was concluded that the manipulation technique and the inclusion of potencializing agents can influence in the inhibiting activity of parabenes.

Financial Support: Centro Universitário Positivo (UnicenP)
Supervisor: Msc Maria Rosa Machado Prado and Msc Neiva Cristina Lubi

TF029 - MACROSCOPIC IMAGING STUDY OF HYDROXYPROPYLMETHYLCELLULOSE (HPMC) MATRICES TABLETS

ARIANE PINHEIRO CRUZ (PG) [1];PATRIK OENING RODRIGUES (PQ)[2]; MARCOS ANTONIO SEGATTO SILVA (PQ)[1]

[1] Universidade Federal de Santa Catarina (UFSC);[2] Universidade da Região de Joinville (UNIVILLE);

In macroscopic observation of hydrophilic matrices, the swelling front separates the rubbery region from the glassy region, the erosion front separates the matrix from the solvent and the diffusion front is located between the swelling and erosion fronts. This study monitored the hydration of HPMC matrices tablets containing zidovudine by mapping of properties such as swelling kinetic, hydrophilic matrix erosion and fronts formation. Four formulations (F1, F2, F3 and F4) were prepared by mixing drug and HPMC in different concentrations (25 and 50 % w/w) and viscosities (K4M and K15M). Digital photographs were obtained from matrices colored with gencian violet 10 % (v/v) in different times. Size of glassy region of the matrices decreased while size of rubbery region increased with time. This result is probably linked to speed of water uptake for this system, doing that the swelling front moves more quickly in direction to both center and edge of the matrix. This process is associated to the prolonged release of drugs, once the liberation of the drug located in the glassy region is dependent of the time and swelling speed of matrix.

Financial support: CAPES
Supervisor: Prof. Dr. Marcos Antonio Segatto Silva

TF030 - EVALUATION OF A NEW METHOD FOR THE PREPARATION OF ACETAMINOPHEN TABLETS USING CYCLODEXTRIN DISPERSION

NELSON PEREIRA DA SILVA JUNIOR (PG)[1]; MARIA PALMIRA DAFLON GREMIÃO(PQ)[1] ; ANA DÓRIS DE CASTRO(PQ)[1]

[1]Programa de Pós-graduação em Ciências Farmacêuticas, UNESP – Araraquara - SP

Acetaminophen (APH) is a leader compound to treat pain of several origins in humans. APH is slightly soluble in water and shows poor compressibility. Cyclodextrins (CD) have been reported in a number of studies in the pharmaceutical field to interact with many drugs to form inclusion complexes. These inclusion complexes have been extensively used to improve the solubility, stability and bioavailability of various drugs. The preparation methods of CD-containing tablets include freeze drying or slow solvent evaporation. However, these procedures were time consuming and multistage. In this work a new method for preparing APH tablets using cyclodextrin dispersion was evaluated. Aqueous β-CD/APH dispersions were used as granulating liquid and different excipients, such as starch, lactose and cellulose, were added. The flowability and compressibility proprieties were also evaluated. Better results were achieved with formulations using starch, since it showed better flow and higher hardness. Further studies are in progress in order to investigate the chemical properties of the formulations.

Financial Support:CAPES
Advisor: Prof. Dr. MARIA PALMIRA DAFLON GREMIÃO

TF031 - DEVELOPMENT OF METHOD FOR TREATMENT AND DISCARDING OF SUSPENSIONS OF ANTIPARASITIC AIMING THE REDUCTION OF COSTS AND OF THE POSSIBLE IMPACTS TO THE ENVIRONMENT

LUCIANA C.DE ARAÚJO(PG)[1]; ARNÓBIO ANTÔNIO DA SILVA JR(PG)[2]

[1]NUPLAM-UFRN; [2]UNESP-ARARAQUARA.

Introduction: Due to importance of the treatment of waste, and existence of a great volume of liquid medicines to be incinerated by a pharmaceutical industry, it became necessary to develop viable methods for treatment and discarding of such waste.
Objectives: To depreciate of the harmful effect to the environment, for the reduction of the concentrations of medicines in the filtered of each suspensions, in a way that presents values below of the allowed for elimination in sewerage system. To minimize costs, for the reduction of the weight to be cremate.
Method: Treatment of the suspensions, with aluminum sulphate solution 1%; filtration; elimination of the liquid phase; drying of the solid phase and destination to incineration. The concentration of medicines in the filtered was determined by specter photometric in the UV-VIS.
Results: Reduction the concentration of the Metronidazole 40mg/mL around 100 times and of the Mebendazole 20mg/mL around 150 times. The weight to be incinerated was reduced at about 96%.
Conclusion: The process is viable, permit the reduction of the concentrations of medicines and of the possibles damages to the environment.

Supervisor: Fernanda N.Raffin[1]; Túlio F.A.L.Moura[1]; Hérida R.N.Salgado[2]

TF032 - EVALUATION OF THE INTESTINAL ABSORPTION OF PRAZIQUANTEL-CONTAINING LIPOSOMES THROUGH EVERTED GUT SAC MODEL

PRISCILA O. CINTO(PG)[1]; BEATRIZ ZANCHETTA(IC)[2]; PATRÍCIA SEVERINO(IC)[2]; POLLYANNA TAMASCIA(IC)[2]; RUBIANA M. MAINARDES(PG)[1]; MARCO V. CHAUD(PQ)[2]; MARIA PALMIRA D. GREMIÃO(PQ)[1]

[1]FCFAR/UNESP; [2] FACIS/UNIMEP

Introduction: Praziquantel (PRZ) is the drug currently available for the treatment of schistosomiasis. The limitation of this drug is its low effectiveness in the treatment that has been related to their poorly water solubility and fast metabolism. Aim: Evaluation of the intestinal absorption of PRZ-containing liposomes (L-PRZ) through everted gut sac model. Methods: Liposomes were prepared by sonication. PRZ concentration was determined by HPLC. Results: The amount of drug transported through sac everted from gut was greater for the PRZ in suspension of that L-PRZ. Conclusion: Despite a further increasing observed in PRZ solubility in PC containing-liposomes, some restrictions were imposed by the L-PRZ through the intestinal membrane. This reduction in the transport of the PRZ can cause a located effect on the intestinal membrane, resulting in an increase of the PRZ effect, since the place of the most concentration of the parasites are the mesenteric veins. This can be as a starting point to development alternative formulation and to evaluate the mechanism of transport of liposomes through the intestinal membrane.

Supervisor: Profa. Dra. Maria P. D. Gremião

TF033 - MICROPARTICLES D L-PLA LOADED ESTRADIOL: STUDY IN VITRO RELEASE OF DRUG IN HEK 263 CELLS TRANSFECTED WITH PERE-TA-SEAP.

SILVIA REGINA PENGO MACHADO (PQ)[1]; RAO, G. A. (PQ)[2]; JULIANA MALDONADO MARCHETTI (PQ)[1]; JEFFREY A. HUGHES (PQ)[2].

[1]College of Pharmacy São Paulo University , R. P. Brazil.;[2] College of Pharmacy, Florida University , FL, USA;

Introduction Micro and nanoparticles made from biodegradable polymers have become the most promising dosage forms for controlled release of drugs. The development of *in vitro* reporter gene assays for short-term screening of estrogenic activity has been studied by many researchers recently. Objective to analyze the efficiency of intracellular estradiol delivery using microparticles an *in vitro* reporter gene assay system. Methodology D L-PLA microparticles loaded estradiol were prepared by emulsion/ evaporation solvent method. The HEK 293 cells were transfected using Exgen 500. The estradiol free and encapsulated were added in cells. The SEAP assay was used to measure through chemiluminescent reading. Results Increasing estradiol concentrations lead high SEAP expression and maximal SEAP expression was observed at 500 nM. SEAP expression also increased with time and maximal expression was observed at 48 hours after treatment with drug. Conclusion Many studies should be realized to validate and to padronize this protocol.

Financial Support: Fapesp
Supervisor: Profa Dra Juliana M. Marchetti

TF034 -PREPARATION AND CHARACTERIZATION OF CHITOSAN MICROPARTICLES FOR ENCAPSULATING ALL-TRANS RETINOIC ACID

ANA AMÉLIA M. LIRA (PG); DENISE ANDRIOLI (IC); JULIANA M. MARCHETTI (PQ)

Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, São Paulo, Brasil, 14040-903

Introduction: All-trans retinoic acid has been extensively used in dermatological therapy. Unfortunately, its poor water solubility, photolability and local irritation reactions strongly limit its topical use. In order to overcome these disadvantages the utilization of microparticles has been proposed. Objective: The aim of the present study was to prepare chitosan microparticles for encapsulating retinoic acid. Methodology: Microparticles were prepared according to the modified method earlier described by Ko et al. (2002). The morphology, size, drug content and release behavior of the microparticles were investigated. Results: In general, microparticles presented higher drug content than 90%. They had an irregular surface, although those prepared with TTP solution at low pH values (pH 2.0) had a smoother surface and more sustained release. Different MW of chitosan also changed the release rate of the microparticles tested. Conclusion: The results of our study showed that these microparticles can be a viable alternative as a controlled release device to improve the effectiveness of all-trans retinoic acid for topical use.

Financial Support: CNPq
Supervisor: Prfª Dra. Juliana M. Marchetti

TF035 - EVALUATION OF BENZOYL METRONIDAZOLE RELEASE FROM CHITOSAN HYDROGELS

EDIVANIA LOPES(PG)[1]; WILLEM MESSIAS ANDRADE(IC) [1]; TUIZA GALGANE ALMEIDA PEREIRA(IC)[1]

[1] Universidade Federal do Rio Grande do Norte, rua Gal. Cordeiro de Farias, s/n. Natal RN.

Chitosan is a copolymer obtained with several deacetilation degrees of chitin. The presence of amino groups allows its solubility in pH range corresponding to the pH of organic and inorganic acids, leading to formation of water soluble salts and viscous solutions with properties of physical hydrogels that can be chemically crosslinked forming bioadhesive gels. The objective of this work is to compare the benzoyl metronidazole (bm) release from physical gels and gels crosslinked with formaldheide (in the form of pessaries). Chitosan gels were obtained from a chitosan solution at 3.5% in acetic acid at 1%, where 500mg of bm were additioned. For pessaries formation the hydrogel formulation received 1.5% of formaldheide. The dissolution was carried out in a paddle apparatus. Samples were withdrawn in predetermined times and quantified by espectrophotometry at 313nm. The amount of drug released from physical gels was 60% in the first hour and 75% in 12 hours. The pessaries showed to control drug release, with 10% liberated in the first hour and 25% in 12 hours. Comparing the release profiles of chemical and physical chitosan crosslinkage showed to be efficient in delaying the release of drug.

Supervisor: Fernanda Nervo Raffin(PQ)[1]

TF036 - PROGESTERONE-LOADED BIODEGRADABLE MICROSPHERES: PREPARATION, MORPHOLOGY AND RELEASE PROPERTIES

LECSI MARICELA ROMERO PEÑA[1](PQ); NATÁLIA NETO PEREIRA[2] (IC); MARIA INÊS RÉ[1](PQ)

Instituto de Pesquisas Tecnológicas - IPT[1]; Faculdade de Ciências Farmacêuticas – USP[2]

Progesterone is a lipophilic drug used to control reproductive function and as postmenopausal therapy. The oral delivery is limited since it is not tolerated in higher doses, but its biological half-life is short. One of the possibilities to overcome this limitation can be the association of progesterone with a controlled delivery system, such as microparticles, to ensure a better control of its release rate. Besides oral administration, the drug loaded-microparticles could be incorporated into the body by other administration route such as intramuscular or subcutaneous injections. In this work, different biodegradable polymers were associated to progesterone to investigate their potential to control the drug delivery. Progesterone-loaded PHB-HV, PLA and PLA-PEG microspheres were prepared by an emulsification/evaporation technique and the effect of the type of polymer on the morphological characteristics, encapsulation yield and on the in vitro release kinetics was evaluated. The results suggest that it is possible to obtain high encapsulation yield and controlled drug delivery to achieve therapeutical efficacy by using biodegradable polymers as carrier for progesterone.

Financial support: IPT
Supervisor: Maria Inês Ré

TF037 - DEVELOPMENT AND CARACTERIZATION OF MICROPARTICLES "BEADS" FOR EVALUATION OF MASTICATORY EFFICIENCY

PRISCILA ERNESTO MORESCHI (PG)[1]; WILSON MESTRINER JR(PQ)[2]; OSVALDO DE FREITAS (PQ)[1]

[1] Faculdade de Ciências Farmacêuticas[2] Faculdade de Odontologia de Ribeirão Preto da Universidade de São Paulo

Text: The evaluation of the masticatory efficiency is an important dentistry diagnosis, however at this time there isn´t an efficient method to determine it. Objective: Development of microparticles systems (beads) as evidence in the determination of the masticatory force. Methodology: Beads had been prepared according to the method of ionotropic gelation. Dispersions of the complex pectin-casein containing colorant had been dripped on calcium chloride solution ($CaCl_2$), which remained, for different periods of time, under agitation. After drying, beads were evaluated concerning hardness, spalling and quantification of the colorant under different levels of spalling. Results: There had been demonstrated that more spherical and uniforms beads were obtained using dispersion at 6%, in $CaCl_2$ 1.0%, with time of permanence of 20 minutes. The amount of colorant released is proportional to the extension of the bead spalling. Conclusion: This particle system is a promising device for the evaluation of the masticatory efficiency.

Supervisor: Prof. Dr. Osvaldo de Freitas

TF038 - SPRAY DRYING MICROENCAPSULATION OF SODIUM DICLOFENAC

MAIRA NETO ZAMPIÉR (IC); LETÍCIA POLLO OLIVEIRA (IC); MARINA DE FREITAS SILVA (IC); PAULA BOTTA TARALLO (IC); MARILIA DUARTE GERARDI (IC); CLÁUDIA REGINA FERNANDES SOUZA (PG); RUBIANA FERREIRA BOTT (PG); WANDERLEY PEREIRA DE OLIVEIRA (PQ)

Faculdade de Ciências Farmacêuticas de Ribeirão Preto

Introduction: Manufacturing drugs in a polymeric device is a common technique, where drug release is regulated either by diffusion though the polymer barrier, or by erosion of the polymer matrix. The use of spray drying technique for microencapsulation may offer the advantage of making the process in one step.
Objective: This work involves diclofenac microencapsulation in Eudragit RS and RL polymer solutions.
Methodology: Four formulations were tested, considering the variables of polymer and polymer/drug rate. The microencapsulation processes were done in two temperatures, 100 and 150 °C. Assays such as size distribution, dissolution, humity and microencapsulation efficiency were done with the prepared microcapsules.
Results: According to the preliminary results, obtained in this study, it was selected four formulations to study the dissolution profiles.
Conclusion: By the comparison between 100 and 150°C, it is noticed that the microparticles prepared at 150°C released more drug.

Supervisor: Wanderley Pereira de Oliveira

TF039 - EVALUATION OF DELAMINATION PROCESS OF BENTONITE WITH DIFFERENT MOLECULES FOR DRUG DELIVERY SYSTEMS

HELVÉCIO VINÍCIUS ANTUNES ROCHA(PG)[1]; LÚCIO MENDES CABRAL(PQ)[2]; AILTON SOUZA GOMES(PQ)[1]

[1]IMA–UFRJ; [2]FF-UFRJ

Introduction: Nanotechnology is a good opportunity for the controlled delivery of drugs. Objective: The work pretends the evaluation of new formulations of tablet coatings for colon targeting of mesalamine and topical delivery of dapsone in leprosy therapy. Methodology: Delamination procedure of bentonite with L-tryptophan was made as described in literature with views of determination of the performance of the process. One similar methodology was utilized to intercalate dapsone. The best results were utilized to intercalate with chitosan and ethylcellulose. The formed materials were submited to physical, chemical and mechanical tests before use in the formulation procedure. Main results: The results with bentonite delamination showed an increase of host space of the clay with dapsone and tryptophan. The intercalation with chitosan and ethylcellulose resulted in one bigger host space than with the not-delaminated clay. The mechanical properties of the materials were improved and the dissolution studies gave best results. Conclusions: These new materials seens to be one good way of controlling the delivery of drugs and one way of technological application of chitosan in tablet coating.

Financial Support: CAPES, MCT
Supervisor: Lucio Cabral; Ailton Gomes

TF040 - DEVELOPMENT OF A OIL-IN-WATER EMULSION FORMULATION FOR TOPICAL NAPROXEN DELIVERY

VIVIAN RIGO (IC) [1], LETÍCIA CAMPAGNA WARCKEN (IC) [1], REGINA GENDESLEVSKI KELMANN (PG) [2], DANIELLE ABRAMCHUK (IC) [1], JOCEANA SOARES SPEROTTO (PQ)[1], FABIANA ERNESTINA BARCELLOS DA SILVA (PQ)[1]

[1] Universidade Regional Integrada do Alto Uruguai e das Missões - URI - Campus Erechim
[2] Universidade Federal de santa Catarina

Emulsions are semisolid preparations widely used as vehicle in topical formulations. At industrial level this kind of pharmaceutical formulation requests flow important parameters analysis. Without these parameters it is not possible predict easy bottle withdrawal and easy skin application. Furthermore the formulation physical stability is extremely necessary. Pharmaceutical emulsion development presenting adequate compatibility and stability requires equally adequate formulation components choice in order to get elegant aspects preparations and appropriate bioavailability. The study's objective was to develop and to evaluate Naproxen oil-in-water emulsion. The emulsion containing 5% Naproxen was formulated according to the drug hydrophobic characteristics. Aspects as rheological behavior and physical stability (Emulsion signs, pH, centrifugation test, behavior, tixotropy and viscosity) were analyzed. The developed formulation showed physical stability in such conditions having plastic behavior and tixotropy characteristics.

Financial Support: URI - Campus Erechim
Supervisor: Fabiana Ernestina Barcellos da Silva

TF041 - WATER VAPOUR TRANSMISSION RATES OF MUCOADHESIVE BILAYERED FILMS INTENDED TO BUCCAL DRUG DELIVERY

FABIANA DA COSTA (IC)[1]; GIOVANNA BONFANTE BORINI (PQ)[1]; JOSE BENTO ALVES (PQ)[1]

[1]Universidade de Uberaba – Uberaba - MG

OBJECTIVE: To study the water vapour transmission rates (WVTR) of bilayered films (BF) composed of a protective layer and a mucoadhesive layer. METHODS: The films were prepared by the casting/solvent evaporation technique. The mucoadhesive layer was composed of HPMC, plasticized with PEG 400. Three different insoluble polymers were used as protective layer. WVTR were determined for BF in two different positions: with the protective layer up and with the protective layer down. WVTR were also determined for each layer separately (as a monolayered film). RESULTS: The WVTR of protective monolayered films were smaller than the WVTR of adhesive monolayered films. The WVTR of BF were similar to WVTR of mucoadhesive monolayer and higher than those of the protective monolayer. The WVTR of BF determined with the protective layer down was smaller than WVTR of BF determined with the protective layer up. CONCLUSION: Although the WVTR of BF and WVTR of mucoadhesive layer were similar, some protective effect was observed when the position of BF was changed. There is an influence from the mucoadhesive layer under the protective layer, leading to an increase of WVTR of BF.

Financial Support: Fapemig, Universidade de Uberaba
Supervisor: Profa. Giovanna Bonfante Borini

TF042 - CAN INFRARED SPECTROSCOPY ADEQUATELY EVALUATE INTERACTIONS BETWEEN GALLIC ACID AND TECHNOLOGICAL EXCIPIENTS?

RENATA LONGHINI (PG)[1]; MARIA RAMOS VOLPATO (IC)[1]; PEDRO ROS PETROVICK (PQ)[1]

[1]Programa de Pós-graduação em Ciências Farmacêuticas, Universidade Federal do Rio Grande do Sul

The success of a pharmaceutical formulation depends also on the careful choice of excipients. In the development of a dosage form the preformulation phase allows knowing the physicochemical properties of the active substance and permits to evaluate its behavior against excipients. Gallic acid (GA), a polyphenol, was select for this phase. Six technological excipients were utilized: colloidal silicon dioxide (CSD), sodium croscarmelose (SCC), crospovidone(XPV), magnesium stearate (MGS), microcrystalline cellulose (MCC) and sodium starch glycolate (STG). Physical mixtures of GA+excipients (1:1 by weight) were prepared, compressed with KBr, and analyzed. The FT-IR spectra data did not show any indication of physical and or chemical interactions of the model substance with CSD, CCM and STG. Conversely, some spectra alterations were found for de mixtures with SCC, XPV and MGS, suggesting physical interactions. Thus the present results could not be accepted as conclusive. Infrared analysis shows to be not able, as only evaluation method, to identify weak interactions, mainly of physical character, needing the help of other non spectrometric techniques.

Financial support: CNPq
Supervisor: Pedro Ros Petrovick

TF043 - INFLUENCE OF EXTRACTIVE PARAMETERS ON PREPARATION OF SOLUTION FROM PSIDIUM GUAJAVA L.

ÍTALO VERÍSSIMO DA SILVA (IC)[1]; POLIANA CARLOS ALVES (IC)[1]; ALMIR GONÇALVES WARDERLEY (PQ)[2], LUIZ ALBERTO LIRA SOARES (PQ)[1]; TATIANE PEREIRA DE SOUZA (PQ)[1]

[1]Department of Pharmacy/UFRN; [2]Department of Pharmacology and Physiology/UFPE

INTRODUCTION: The leaves of Psidium guajava are widely used in the traditional medicine for treating of diarrhea and infectious diseases. Pharmacological and toxicological experiments confirm its therapeutic efficacy, safety and indicate the phenolic compounds as possible responsible for its activity. OBJECTIVE: The aim of this work is evaluate the influence of extractives parameters on tannin content of solutions obtained from leaves of P. guajava. METHOD: The influence of drug proportion (2.5%; 5.0% and 7.5%; w/v) and alcohol concentration (0.0%, 50% and 100%; v/v) on the tannin content was evaluated following a factorial design 32. The extractives solutions were elaborated by decoction on reflux during 15 min. The tannins content was assayed by spectrophotometric method at 271nm using casein as precipitant agent. RESULTS: The ANOVA and response surface demonstrated that only the alcohol concentrations have significant influence on tannins content and follow a quadrate model. CONCLUSION: Independent of the drug proportion, the alcohol concentration that produced solution with higher tannins content was 50%.

Advisor:Tatiane Pereira de Souza

TF044 - EVALUATION OF XYLAN MICROCAPSULES PRODUCED WITH DIFFERENT LIPOPHILIC AGENTS

TOSHIYUKI NAGASHIMA JR. (PG) [1]; ACARÍLIA E. SILVA (IC) [1]; MARCELO G. SILVA (IC) [1]; ELQUIO E. OLIVEIRA (PG) [1], E. SÓCRATES T. EGITO (PQ) [1].

[1]UFRN-CCS, PPGCSA, Laboratório de Sistemas Dispersos (LASID), Natal/RN, Brazil. socrates@ufrnet.br.

INTRODUCTION: Due to its digestion resistance, xylan has been pointed out as a promising polymer to produce colon-specific microcapsules. OBJECTIVES: The aim of this study was to produce xylan microcapsules by using different lipophilic phases in the emulsification step and evaluate their influence on the microcapsule features. METHODOLOGY: The xylan microcapsules were produced by interfacial cross-linking process. Chloroform:cyclohexane, Miglyol® 810N, and soybean oil were employed as lipophilic agents in each experiment. RESULTS: All the samples presented distinct visual features. They were relatively homogeneous and their pH values did not show significant variation. Their morphology was found to vary depending on the experimental set-up. Two preparations showed a quite spherical shape and a similar mean size. However, for another one it was observed to be larger and oblong in shape. CONCLUSIONS: The produced systems may represent a new carrier for colon-specific drug delivery with reduced toxicity since chloroform and cyclohexane could be easily replaced by Miglyol® 810N or soybean oil.

Financial support: CNPq, BNB and CAPES.
Supervisor: E. Sócrates T. Egito.

TF045 - IN VITRO RELEASE OF 5-FLUOROURACIL FROM MAGNETIC NANOSPHERES FOR THE CANCER TREATMENT

ALVARO ANTONIO ALENCAR DE QUEIROZ (PQ); ESDRAS DUARTE DOS PASSOS (PG)

Departamento de Física e Química/Instituto de Ciências Exatas, Universidade Federal de Itajubá, C.P. 50, 37.500-903, Itajubá/MG, Brasil. E-mail: alencar@unifei.edu.br

Hyperthermia is a promising approach for the cancer treatment that uses oscillating magnetic fields to heat target areas (cancer tissue) containing magnetizable particles. The possibility of a combined therapy, which would include the release of encapsulated chemotherapeutic agents that will act on the injured cells after hypertermia treatment, may increases the efficiency of the cancer treatment. The present study was aimed at developing and exploring the use of encapsulated $Y_3Fe_{5-x}Al_xO_{12}$ magnetic nanoparticles for cancer therapy based on the delivery of fluorouracil to tumor sites for use in the hyperthermia treatment. Poly (2-hydroxyethyl methacrylate) (PHEMA) nanospheres containing $Y_3Fe_{5-x}Al_xO_{12}$ ($0<x<2$) and 5-fluorouracil were prepared by suspension polymerization. In vitro studies indicated that nanospheres were found suitable for prolonged drug delivery during hyperthermia treatment. The magnetic PHEMA nanospheres seems to be a promising carrier for the release of antitumor drugs during the hyperthermia treatment.

Financial Support: Fapemig, Capes.
Supervisor: Dr. Alvaro Antonio Alencar de Queiroz.

TF046 - SIMVASTATIN BIOCOMPATIBLE MICROEMULSION FOR PHARMACEUTICAL USE

VICTOR A. DOMINICI(IC)[1], BOLÍVAR P. G. L. DAMASCENO(PG)[1] AND E. SÓCRATES T. EGITO(PQ)[1]

[1] UFRN-CCS-Programa de Pós-graduação em Ciências da Saúde (PPGCSa) – Laboratório de Sistemas Dispersos (LASID) – Natal-RN-Brazil .

INTRODUCTION: Simvastatin is a cholesterol-lowering agent practically insoluble in water and poorly absorbed by the gastro-intestinal tract. Because of that several studies have suggested formulating Simvastatin in lipid carriers like microemulsions (ME) OBJECTIVE: The aim of this study was to prepare and evaluate a Simvastatin microemulsion METHODOLOGY: The free system was prepared by mixing 68%$_{(p/v)}$ of water, pH 7.4 , 11%$_{(p/v)}$ of Mygliol 812N®, 6.3%$_{(p/v)}$ of Phospholipon 90G® and 14.7%$_{(p/v)}$ of Tween 80®. The Simvastatin was incorporated at around 10mg/mL into the ME under slight magnetic stirring and was quantified by a spectrophotometry assay. The pH and macroscopic appearance were evaluated in both systems. RESULTS: The free system showed a limpid and translucent aspect like a true microemulsion, the pH and the refractive index were around 7.91 and 1,374 respectively. No significantly changes were observed after incorporation of Simvastatin. CONCLUSIONS: These results suggest that ME may be a eligible delivery system to carry Simvastatin, which has potential applications.

Financial Support: PIBIC, BNB and CNPq 47836/01-7-NV
Supervisor: E. Sócrates T. Egito

TF047 - IN VITRO EVALUATION OF PECTIN/HYDROXYPROPYLMETHYLCELLULOSE (HPMC) MATRIX SYSTEMS CONTAINING QUERCETIN DESIGNED FOR COLONIC DELIVERY

LIS M MONTEIRO (IC)[1]; LEANDRO A CALIXTO (IC)[1]; LUCIANA C GRADE (IC)[1]; MARIA JV FONSECA (PQ)[2]; OSVALDO DE FREITAS (PQ)[2]; RÚBIA CASAGRANDE (PQ)[1]; MARCELA M BARACAT (PQ)[1]

[1]Department of Food and Drugs Technology, CCA-UEL
[2]Department of Pharmaceutical Science, FCFRP–USP

INTRODUCTION Local or systemic Inflammatory Bowel Disease (IBD) may be treated by colon targeted drug delivery. In this regard, studies demonstrated that antioxidants as quercetin present beneficial anti-inflammatory effects in experimental IBD. However, quercetin has a low hydrosolubility and a slow dissolution rate from solid oral forms, which restrict the development of sustained-release formulations. OBJECTIVE This study evaluated quercetin delivery systems from matrix tablets consisting of different pectin/HPMC mixtures. METHODOLOGY The in vitro dissolution profiles of the different drug/polymer systems were compared. RESULTS The results showed the in vitro time lag of 2 h, and the drug dissolution rate pectin/HPMC system was faster than the HPMC containing lactose system. CONCLUSION These results suggest that the novel pectin/HPMC quercetin delivery system would successfully increase quercetin release into the colon.

Advisors: Rúbia Casagrande and Marcela M Baracat

TF048 - IN VIVO RELEASE PROFILE FROM PLGA IMPLANTS WITH 17β-ESTRADIOL

DAISY JANICE AGUILAR NETZ (PG)[1]; JULIANA MALDONADO MARCHETTI (PQ))[1]; JANETE APARECIDA ANSELMO-FRANCI (PQ)[2]

[1] Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP
[2] Faculdade de Odontologia de Ribeirão Preto-USP

Introduction: Subcutaneous implants have been recognized as a useful drug delivery system that provides greater assurance of patient compliance and a better therapeutic outcome than conventional drug therapies, particularly for chronic medication. The benefits of long-term hormone replacement therapy (HRT) in postmenopausal women - relief of vasomotor symptoms, prevention of urogenital atrophy and treatment of osteoporosis - have been well established in long-term studies. Objective: the objective of the present study was to evaluate the release profile of 17-β estradiol (E2) with two implants types, made from PLGA ratio molar 50:50 (A) and 75:25 (B) in animal model. Methodology: thirty female Wistar rats, surgically ovariectomized were used. All animal were recovered of the surgery for at 2 weeks before the initiation of studies. The implant insertion was carried out under aseptic conditions. The implants was introduced in the dorsal region of the rats and for this, one incision of 1,5 cm was performed. Plasma levels were determined whit RIA of double body. Results and conclusion: comparing the plasma profiles of E2 in two groups, the implant B appeared to best profile release once demonstrated to be able to maintain a sustained release of E2 through the period of subcutaneous implantation.

Financial Support: Capes
Supervisor: Juliana Maldonado Marchetti

TF049 - PREFORMULATION PARAMETERS IN CARBAMAZEPINE PELLETS RELEASE BY EXTRUSION/ SPHERONIZATION

DIVA SONAGLIO(PQ)[1]; BERNARD BATAILLE(PQ)[2]

[1]Depto Ciências Farmacêuticas/UFSC, Brazil; [2]Université. Montpellier I, France

Carbamazepine (CBZ) is a first-choice anticonvulsant drug. Intermittent side effects have been correlated to fluctuations in plasma concentrations that suggest the study of modified release formulations as a powerful approach to improve its therapeutic use. In this study, we investigate the technological feasibility of CBZ/microcrystalline cellulose (MCC) pellets by the E/S process. The variables investigated were particle size of CBZ, content of a soluble excipient and water content. The extrusion/spheronization (E/S) conditions were fixed. Dissolution tests were conducted according USP monograph to CBZ extended-release. Results indicated that CBZ pellets can be obtained by E/S. We verified that the decrease of particle size of CBZ caused a slowdown of the dissolution rate. This is probably caused by the decrease of beads porosity. The addition of lactose in the formulations improved the dissolution rate. This suggests an improving dissolution and diffusion process of CBZ. The low-water solubility of CBZ, which is a factor of dissolution rate limited absorption of the tablets, can be increased by a higher surface area of the pellets and the inclusion of soluble excipient such as lactose.

Financial Support: CNPq.
Supervisor: Bernard Bataille.

TF050 - BIODEGRADABLE MICROSPHERES TO OCULAR CIPROFLOXACIN CONTROLLED RELEASE

ARNÓBIO ANTÔNIO DA SILVA JÚNIOR(PG)[1]; THALLITA PEDRONI FORMARIZ(PG)[1]; FERNANDO PAGANELI(PQ)[2]; JOSE AUGUSTO CARDILLO(PG)[2]; ANSELMO GOMES DE OLIVEIRA(PG)[1]

[1]Faculdade de Ciências Farmacêuticas de Araraquara-UNESP;[2]Hospital de Olhos de Araraquara.

The ciprofloxacin (CP) is a quinolone and the polylactic-co-glycolic acid (PLGA) is a biodegradable copolymer. The purpose of this work was to determine aplicability of the CP loaded PLGA microspheres as ocular controlled release system. For this, microspheres with relationship CP/PLGA 1:1w/w and 1:2 w/w were obtained by spray drying and were charactherized. In vitro release study, amounts of microspheres equivalent to 1mg of CP was incubated in phosphate buffer and serial CP measurements was determined by UV spectrophotometric analysis. The release time was of 4 and 24 hours to CP loaded PLGA microspheres 1:1 and 1:2 respectively. In vivo study, amouts of microspheres equivalent to 1mg/0.1mL of CP were injected in the sub–Tenon's capsule space of 30 albino rabbits and the overtime released CP concentration in the aqueous and vitreous humor was determined by high performance liquid chromatography analysis.The CP/PLGA 1:2 microspheres system reached therapeutic levels within 12 hours in aqueous and vitreus humor and remained in this range up to 7 days.

Finantial support: CAPES, CNPQ, FAPESP, PADC-UNESP.
Supervisor: Anselmo Gomes de Oliveira

TF051 - DIFFERENTIAL SCANNING CALORIMETRY (DSC) OF PRAZIQUANTEL (PZQ) IN SOLID DISPERSIONS (SDS) IN SODIUM STARCH GLYCOLATE (GSA)

ANDRÉA C. LIMA (PG)[1]; ALINE BORELLI ALONSO (IC)[2]; POLLYANNA TAMASCIA (IC)[2]

1) Universidade Estadual Paulista Júlio de Mesquita Filho (UNESP); 2) Universidade Metodista de Piracicaba (UNIMEP)

PZQ is a drug with low solubility used for the schistosomiasis treatment. SDs preparation, whose main purpose is to increase poorly-water soluble drug rate dissolution in water through the solid state modification. DSC is adapted to possible interactions evidence in drug physical structure and in DSs carrier. SDs were prepared according dissolution method. Ethanol and distilled water were used as the solvent. Desiccation was in a vacuum oven until a constant weight. The sample thermograms were recorded on a Shimadzu DSC-50 at a 10 ºC/min heating rate. The thermal behavior was studied by investigation over 20-250ºC the temperature range. PZQ curve shows an endothermic peak at 138 ºC. PZQ heat was -105.48 J/g. A DSC of DSs displays endothermic peak in the same drug melting point range, with PZQ -20.90 J/g heat. About 80% of PZQ crystalline mass passed for amorphous state. This solid state is modification is enough to increase PZQ dissolution rate in water.

Financial Support: CNPq
Supervision: Maria P. D. Gremião[1] and Marco V. Chaud [2]

TF052 - MICROEMULSIONS FOR TOPICAL DELIVERY OF ASIATIC ACID PRESENT IN CENTELLA ASIATICA

RAFAEL TASSIRO CACHIBA (IC)[1], RENATA FONSECA VIANNA LOPEZ (PQ)[1]

[1]Departamento de Ciências Farmacêuticas, FCFRP, USP

Asiatic acid is a pentacyclic triterpene found in the Centella asiatic. Studies show that this substance induces apoptose in cells of human melanoma, increasing reactive species of oxygen, and the activation of the Caspases. The present work obtained and characterized microemulsions containing a fraction of total triterpenes of Centella asiatica (with 20% of asiatic acid) for further skin application of these systems. A pseudo-ternary phase diagram was constructed by titration of a series of olive oil/nonionic surfactant mixture (Span 80®/Tween 80® 2:1) with water. Selected mixtures defined in the diagrams were examined for their psychochemical characteristics, such as stability, optical properties, refractive index, pH, density, droplet size, conductivity and reology. These systems showed to be isotropic, translucent and stable, with droplet sizes varying from 27 to 138 nm, and a pseudoplastic behavior. Condutivity and refractive index measurement showed that microemulsions obtained seems to be water-in-oil (w/o) systems, which could improve skin retention of asiatic acid applied topically.

Financial support: CNPQ/PIBIC
Supervisor: Profa. Dra. Renata Fonseca Vianna Lopez

TF053 - INVESTIGATION OF HYDROTROPIC AGENTS EFFECT ON IMIQUIMOD WATER SOLUBILITY

CAROLINA AZENHA MARTINS (IC)[1]; DANIEL DE PAULA (PG)[1]; MARIA VITÓRIA LOPES BADRA BENTLEY (PQ)[1]

[1] Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP

Introduction: Imiquimod (Imq) is an immune response modifier used in the treatment of a variety of skin diseases; however, the low water solubility limits its use. Hydrotropes are substances that, at high concentrations, may enhance the solubility of hydrophobic compounds in water. Objective: The aim of this work was to investigate the effect of hydrotropic agents (benzoic acid, salycilic acid and urea) on Imq water solubility. Methodology: Drug solubilization experiments were conduced in aqueous solutions at various pHs (2.0 to 9.0) and in the presence of different hydrotropes concentrations (0 to 2.0 M) at pHs 5.0 and 7.4, which were added by excess of drug, mixed at 30 rpm for 24 hours at 25ºC, and then, analysed by UV-HPLC. pKa and porcentage of drug and hydrotropes ionized were also determined in potenciometric studies. Results: The results displayed that Imq water solubility increased in the presence of hydrotropes, depending on pH solution and hydrotrope ionization. Better improvement at pH 7.4 than at 5.0 was observed in bezoic acid solutions. Conclusions: Hydrotropes are effective on enhancing Imq water solubility and the solubilization is pH-dependent.

Financial Support: FAPESP
Supervisor: Profa. Dra. Maria Vitória Lopes Badra Bentley

TF054 - DEVELOPMENT OF PHARMACEUTICAL DOSAGE OF TOPICAL APPLICATION FOR TREATMENT OF ONYCHOMYCOSIS

FLAVIANE CRISTINA DE BRITO GUZZO(IC)[1]; ALEXANDRE BRONHARO FIORATTI(IC)[1]; JOYCE RUIZ REZENDE(IC)[1]; KARIMI SATER GEBARA(IC)[1]; MARCEL PADOVANI GIOLO(IC)[1]; SELMA LUCY FRANCO(PQ)[1]

[1] State University of Maringá

Introduction: Studies that proved the action of propolis extract against yeasts that cause onychomycosis have shown the necessity of developing a topical pharmaceutical dosage using propolis. Objective: To obtain an antifungal medication with large spectrum and low cost. Methodology: Extraction of propolis proceeded by turboextraction. The content of flavonoids in the extract was verified. A research was done for choosing the adequate dosage and its excipients. 12 formulations were obtained and their macroscopic evaluation was verified, as well as their pH and viscosity values. The technique for quantification of active substances in the formulations is being developed. Results: It was concluded that the development of an O/W emulsion would be the most appropriate. Emulsions 4 to 8 were reproved in macroscopic evaluation. The pH of emulsions, as content of waxes and humidity of propolis and content of flavonoids in extract were in the allowed values. Conclusions: For the obtaining of an effective and safe medication is necessary the selection of its excipients and its quality control. The results pointed the emulsion 11 as the most adequate for onychomycosis treatment

Advisor: Selma Lucy Franco

TF055 - DEVELOPMENT AND RHEOLOGICAL BEHAVIOR OF MICROEMULSION SYSTEM CONTAINING PROCETYL AWS® AS SURFACTANT

DANIELA PAULA LONGO (PG)[1]; MARIA VIRGÍNIA SCARPA* (PQ)[1]; ANSELMO GOMES DE OLIVEIRA (PQ)[1]

[1] FCFar-UNESP – * scarpamv@fcfar.unesp.br

Introduction: Microemulsions (ME) present great potential as drug delivery vehicles. ME isotropic and thermodynamically stable dispersion of either "water in oil or oil in water" systems stabilized buy pure or mixed amphiphiles. Objetive: Development and rheological behavior of microemulsion systems. Methodology: A ternary phase diagrams were made using Procetyl® (propoxyl 5OP ethoxyl 20 OP cethyl alcohol) as surfactant, dibutyl adipate as oil phase and water using the titulation method. The rheological behavior of four microemulsions was carried out to at 25ºC and 37ºC using a rotational reometer of parallel plates. Results and Conclusions: The obtained systems were classified in liquid and viscous microemulsion, emulsion, semitransparent system and separation of phases. The reograms of three formulations presented different ascending and descending curve characterizing thixotropy. For the most liquid formulation a newtonian behavior was observed where the stress shear is directly proportional to shear rate. At 37ºC the rheological behavior of the formulations was similar to 25ºC but they support smaller stress and needing a larger time for the restructuring.

Financial Support: FAPESP and CAPES
Supervisor: Profa. Dra. Maria Virgínia Scarpa

TF056 - THE EFFECT OF THE EXCIPIENTS ON THE DISSOLUTION PROFILES OF FLUOXETINE HYDROCHLORIDE HARD CAPSULES FORMULATIONS

IRENE CLEMES KÜLKAMP[1] (PQ); MELISSA ZÉTOLA (PQ)[1]; BIANCA RAMOS PEZZINI[1](PQ); GIOVANA CAROLINA BAZZO[1] (PQ).

[1]Departamento de Farmácia. Universidade da Região de Joinville. Campus Universitário, 89201-972, Joinville – SC.

Hard capsules are solid pharmaceutical dosage forms widely used. The dissolution profile of a drug is affected by several factors, including the excipients used in the preparation of the formulations. These excipients may compromise the dissolution of the drug and its therapeutic effect. The goal of the present study was to prepare hard capsules formulations containing fluoxetine hydrochloride and to evaluate the influence of the excipients used in the dissolution profile of the drug. Eight formulations were proposed using a factorial plan, varying the type and content of the diluents (microcrystalline cellulose and/or starch) and the presence of the glidant Aerosil[â]. The weight average, drug content and dissolution profiles were determined. Seven formulations were in agreement with pharmacopeial specifications for weight average and all the formulations presented the fluoxetine content specified in the USP monograph. The dissolution of the drug was fast for all the formulations. More than 90 % of the drug was dissolved in 10 minutes indicating that was no significant influence of the excipients in the release profile of fluoxetine.

TF057 - OBTENTION AND CHARACTERIZATION OF MICROEMULSIONS FOR TOPICAL DELIVERY.

LUCIANA M. P. CAMPOS (PG)[1]; RENATA F. V. LOPEZ (PQ)[1]*

[1] FCFRP - USP

In photodynamic therapy (PDT), 5- aminulevulinic acid (ALA) applied topically is converted into protoporphyrin IX, a photosensitizer which upon excitation with light can induce tumor destruction. Due to its hydrophilic characteristics, ALA has limited penetration into the skin. The aim of this work is to obtain and characterize a variety of microemulsion systems for futher incorporation of ALA for topical PDT. Five pseudo-ternary phase diagrams were constructed by titration of a series of ethyl oleate/nonionic surfactants mixtures (Labrasol®/Plurol Oleique® and Span 80®/Tween 80®, in different ratios) with water at ambient temperature. Select mixtures defined in the diagrams were examined for their psychochemical characteristics, such as stability, optical properties, refractive index, pH, density, droplet size, conductivity and reology. All diagrams presented regions that showed to be isotropic and stable, with droplet sizes in the order of mm and refractive index and pH decreasing with water weight ratio increase. The reologycal studies for the most of these systems indicated a pseudo plastic behavior. For Labrasol/Plurol systems the type and structure were examined by measured electric conductivity and viscosity and confirmed the presence of o/a, a/o and bicontinuous structure by percolation transitionv

Financial Support: FAPESP
*Supervisor

The authors did not follow the Scientific Committee's suggestion for an English language review

TF058 - TOOTHPASTE DEVELOPMENT FOR CHLOREXIDINE IN THE CHEMICAL CONTROL OF THE BACTERIAL PLAQUE

ROBERTO PONTAROLO(PQ)[1];MAYUMI SATO(PQ)[1];Mª LUIZA FÁVERO(PQ)[1]

[1]Department of Pharmacy,UFPR

The chlorhexidine, the biguanidines group, shows a wide antibacterial spectra, being used in odontology to inhibit the formation of plaque, caries and gingivitis. The objective that work is develop a dentifrice as a vehicle for the chlorhexidine to control chemically the bacterial plaque. The dentifrice was submitted to the preliminary study of stability and the pH, density, consistency, viscosity, organoleptic characteristics, rheology (pseudoplastic and thixotropic) and dosing parameters were monitored in zero, one, two and three months. The antimicrobial activity before the *Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus mutans and Candida albicans* was evaluated in the times zero and three months. After that, an extraction and dosing method by HPLC in the toothpaste was developed and validated. During monitored time, alterations were not observed in the values of pH, density, consistency, viscosity and rheologic characteristics. There was a decrease in the chlorhexidine content from the third month on, with the formation of a possible degradation product. The antimicrobial activity has not altered during the tests, not even when there was a decrease in the chlorhexidine content. The developed method has shown linearity, specificity, accuracy and precision.

TF059 - DETERMINATION OF ZETA POTENTIAL AND SIZE DISTRIBUTION VALUES: INFLUENCE EVALUATION OF POLYMERS ON NANO-EMULSION STABILITY

[1] JACQUELINE MOREIRA DE MORAIS(PG), [1] KAUÊ P. BOOCK(PG), [1] ORLANDO D. H. SANTOS (PG), [1] PEDRO A. ROCHA FILHO(PQ)

[1] Departamento de Ciências Farmacêuticas - Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo

Emulsion stability is controlled by the properties of the adsorbed layer of its globules. The structure of this layer depends on the composition and concentration of the surfactants and/or the polymers added. The aim of this study was to evaluate the stability of oil-water nano-emulsion, analyzing the effects of polymers on its physicochemical parameters: zeta potential and size distribution values. Samples were yielded by emulsion phase inversion method. Canola oil, distilled water, nonionic surfactants and different polymers were used as raw materials. Zeta potential and size distribution were performed using Coulter Counter DELSA 440SX. The outcomes confirmed high negative zeta potential values and nanometer size droplets even after polymers addition. Moreover, samples did not show any sign of instability. The results suggested an increment of electrostatic component beyond the expected increase of the steric contribution to stability mechanism of this system initially stabilized only by nonionic surfactants. This study is currently being extended to a storage period of 30 days.

Financial support: Capes
Supervisor: Pedro Rocha Filho

TF060 - EVALUATION OF PHYSICAL PROPERTIES OF TOPICAL EMULSIONS (O/W) CONTAINING ANIONIC AND NON-IONIC EMULSIFIERS

DIEGO MONEGATTO SANTORO (PG)[12]; CRISTINA HELENA DOS REIS SERRA (PQ)[2]

[1] Laboratórios Stiefel Ltda; [2] Faculdade de Ciências Farmacêuticas da Universidade de São Paulo

Introduction: The physical stability of emulsions can be evaluated through droplets distribution evaluation, rheological properties, thermal analysis, microscopy and others.
Objective: Evaluate the physical stability of emulsions containg different concentrations of anionic (A – potassium cetyl phosphate 3, 5 e 7%) and non-ionic emulsifiers (N – glyceril monostearate, 3, 5 e 7%), and the influence of the scale-up process.
Methodology: Evaluate the droplets distribution with laser diffraction, rheology analysis, microscopy and thermogravimetry (TG).
Results and Conclusion: The values of 90% of the droplets were below 92.66 µm, 50.28µm and 38.80µm, respectively for 3, 5 and 7% of N emulsifier. For system A, 90% of the droplets were below 3.85µm, 4.89µm and 63.57µm, for 3, 5 and 7%. The scale-up process influenced both systems, with an increase in the viscosity on system A from 6.614 Pa.s to 81.55 Pa.s and from 3.366 Pa.s to 7.153 Pa.s for system N. In the TG analysis, only bulk water could be detected in system N and, in the system A, both interlamellar and bulk water were detected (initial and stability).

Financial Support: Laboratórios Stiefel Ltda
Supervisor: Profa. Dra. Cristina Helena dos Reis Serra

TF061 - EVALUATING OF DERMATHOLOGICAL FORMULATIONS WITH ASCORBIC ACID ADQUIRED IN PHARMACIES IN SOROCABA-SP

GRACIELE PEREIRA CARRAPEIRO(IC)[1]; NEWTON ANDRÉO-FILHO(PQ)[1]

[1]University of Sorocaba

Introduction: Ascorbic acid is largely used in dermatological formulations to the most different aims. Its instability in presence of oxygen room, light or alkaline mean is known. Objectives: Evaluate the pH of formulations of o/w non-ionic creams containing ascorbic acid 5%, its market conditions and packing materials. Methodology: Ten samples were compounding and acquired in pharmacies set on downtown of Sorocaba city, being assessed about pH (in natura and dilutions 1:10 and 1:100) using potencyometric equipment and universal indicator paper. The consistence was evaluated visually. All information on label of the flask and eventual orientations were recorded. Results: The results showed that just one formulation (sample 2) presented adequate pH to stability and absorption of the ascorbic acid, pH lower than 3,5. Further, the shelf-live for the samples were variables (extremes: sample 10, 2 months and sample 1, 6 months). Some formulations had the instructions to maintain in refrigerator while other not. All the samples were supplied in white and opaque polypropylene/polyethylene plastic. Conclusion: The formulations tested were out of pH range, able to bring higher stability and absorption, evidencing absence of care with the stability of compounding medicines or cosmetics. Another problem was the absence of standardization for the shelf-life of these products.

Financial Support: University of Sorocaba
Supervisor: Newton Andréo-Filho

The authors did not follow the Scientific Committee's suggestion for an English language review

TF062 - INTERACTIONS BETWEEN STAIN ALUMINUM LAKE FD&C NO. 6 (18% ALUMINUM LAKE) AND COMBINED POLYMERS OF METHACRYLIC ACID AND ETHYL ACRYLATE

HALINE FERNANDA SANTANA CASTANHO (PQ)[1], WALLACE LOPES (PQ)[1]., GIDEL SOARES (PQ)[2], LUIS HENRIQUE GARCIA-AMOEDO(PQ)[1], TEREZINHA DE JESUS ANDREOLI PINTO(PQ)[3]

[1] Fundação Instituto de Pesquisas Farmacêuticas – FIPFARMA;[2] Fundação para o Remédio Popular – FURP;[3] FCF/USP

Introduction: The forms of enteric dosages coated with methacrylic acid polymers and ethyl acrylate are used with purpose of gastric protection. Possible interactions between the polymers and excipientes forming a covering film can affect the product biodisponibility. Objective: The aim was to verify interactions between stain aluminum lake FD&C no. 6 (18% aluminum lake) and combined polymers of methacrylic acid and ethyl acrylate, and its consequences to pharmaceutical form. Methods: Placebo tablets were compressed and divided in two groups: A and B. Both groups had been coated with same covering formularization, being group A with stain aluminum lake and group B without stain aluminum lake. Samples had been storaged 22 days in climatic chamber 50º/90% UR and daily disintegration tests according to USP 28 methodology had been carried. The covering solutions of both groups were applied in surface solid and submitted to drying and storage in ambient temperature and at 50º/90%UR for posterior analysis in InfraRed. Results: Group A presented increase and group B reduction, in the disintegration time. Samples submitted to IR analysis presented no differences. Conclusion: The results suggest that exist a possible interaction between the components in study, hindering the enteric disintegration of the final pharmaceutical form.

TF063 - PRE-FORMULATION STUDY OF PROPRANOLOL TABLETS

E.S.B.N. MACHADO (PG)[1]; L.S.S.JÚNIOR (IC)[1]; M.G.CARVALHO (IC)[1]; I.D. SILVA (IC)[1]; T.F.A. MOURA (PQ)[1]; F.N.RAFFIN (PQ)[1]

[1]Pharmacy Departament/CCS/UFRN Natal-RN Brasil.

Propranolol, a non-selective ß-adrenergic blocking agent, has been widely used in the treatment of hypertension, mainly by its physiological characteristics, such as: fast and complete absorption, low toxicity and fast therapeutical response. The development of a formulation must take into account physical-chemical aspects as possible incompatibilities between the components, as well as technological and biopharmaceutical aspects. The pre-formulation study of a tablet was the aim of this work, where fillers as microcrystalline cellulose (CM), lactose (LAC) and starch (AM) were tested. Binary mixtures were prepared at 1:1, 1:3 and 3:1 drug/excipient ratios and tests of bulk and tapped volumes, DSC, drug content and dissolution were carried out. The thermograms showed that the mixtures had thermal stability at all the ratios, except the mixture with CM at 1:1, where the melting point of the drug dropped to 148 °C. The amounts of propranolol dissolved in the recently prepared samples are in accordance with the Brazilian Pharmacopoeia, not less than 75% in 30 minutes. In the samples kept 18 months at ambient temperature, a reduction in the dissolution rate was observed with LAC mixtures (about 50%), although they showed the best flow and compressibility.

TF064 - INFLUENCE OF THE SOLID DISPERSION IN THE AQUEOUS SOLUBILITY OF DRY EXTRACT OF CISSUS SULCICAULIS OBTAINED WITH DICLHOROMETHANE.

CAROLINA RIBEIRO CAMERIN(IC)[1]; CAROLINE HARADA OKUDA(IC)[1]; LUCIANE CRUZ LOPES(PQ)[1]

[1]Universidade Metodista de Piracicaba

Introduction: One of the main difficulties in medicinal properties evaluation of vegetable extracts obtained with apolar solvent is the low solubility of the same in physiologically compatible vehicles. Objectives: To evaluate the influence of solid dispersion (SD) in the solubility of vegetable extracts obtained with diclhoromethane (DCM). Methodology: The extract Cissus sulcicaulis Baker in DCM was obtained by maceration. SD was prepared by co-precipitation method in the proportion of 1:1 of the extract and dissolved Polyvinylpyrrolidone K30, respectively, in DCM and ethanol 30%. The solvents were evaporated and SD maintained in desiccator until constant weight. The solubility of the extract in SD was evaluated by terpenes dissolution in water. The dissolved terpene amount was qualitatively evaluated, by CTL. Results: SD has significantly improved the terpene solubility in the extract obtained with apolar solvent. Conclusion: DS increases the solubility of constituents with low solubility coefficient in water present in vegetable extracts obtained with apolar solvent. This finding makes easy the use of these extracts in studies in vivo for pharmacology activity evaluation.

Advisor: Prof. Dr. Marco Vinícius Chaud (PQ)[1]

TF065 - DISSOLUTION PROFILE OF PREDNISOLONE CAPSULES FROM COMPOUNDING PHARMACIES.

ELIANE V. CAIXETA[1](PG); PATRÍCIA RIBAS[1] (PG); MIRIAM ATTUX[1] (PG); HENRIQUE PASCOA[1] (IC); ANA LÚCIA T. C. ZAMPIERI[1] (PG); DANIELLE G. A. DINIZ[1] (PG); ELIANA M LIMA[1] (PQ)

[1]Universidade Federal de Goiás

Introduction: Pharmaceutical formulations must provide satisfactory stability and bioavailability for any drug delivery system. Slightly water-soluble drugs, such as prednisolone, suffer remarkable influences from de formulation constituents on the physical-chemical properties of the final product. Compounding pharmacies play an important role in the pharmaceutical market, and detailed studies about these products are required. Objectives: Evaluate in vitro release profile of prednisolone from different excipient mixtures, in hard gelatin capsules from compounding pharmacies. Methods: Prednisolone capsules (5 mg) were prepared with excipients A (Aerosil, Lactose, microcrystalline cellulose) and B (Aerosil, lactose, PEG 4000, sodium lauril sulfate). Samples were submitted to in vitro dissolution assay, according to the USP 28, and compared to the standard reference tablet. Results: Release rates varied from 20% (formula B) after 30 minutes to 60-80% (formula A). Conclusions: Pharmaceutical excipient combinations used by compounding pharmacies must be evaluated for their ability in promoting adequate drug release.

Financial Support: FINEP; FUNAPE; CNPq.
Advisor: Profa. Dra. Eliana Martins Lima.

TF066 - EVALUATION OF LIPOSOME-SURFACTANT INTERACTION BY DYNAMIC LIGHT SCATTERING

FABRÍCIA S. FERREIRA[1] (IC) ; CARINA P. I. ALVES[1] (PG); ELIANA M. LIMA[1] (PQ)

[1]Universidade Federal de Goiás

Introduction: Solubilization of lipid bilayers induced by surfactants promotes structural lamellar alterations followed by morphological changes and the appearance of mixed micelles. Different intermediate structures can be formed depending on several conditions, including type and concentration of the surfactant. Objectives: To demonstrate liposome-surfactant interactions when surfactants of different properties are used. Methods: Phosphatidylcholine unilamellar liposomes were prepared by chloroform injection method. Ionic and non-ionic surfactants were added at concentrations ranging from 1 to 100 mM. After each surfactant addition, samples were submitted to dynamic light scattering. Results: Size measurements of liposomes showed significant changes in the lipid bilayers when different surfactants were added. Anionic and cationic products lead to similar responses, with mostly mixed micelles at the concentration ratios evaluated. On the other hand, non-ionic surfactants were incorporated into lipid membranes up until 50 mM, when disruption and micelles were observed. Conclusion: Liposome dispersions exhibit distinct behaviors when in contact with different surfactant products in the aqueous media.

Financial Support: FINEP; FUNAPE; CNPq.
Advisor: Profa. Dra. Eliana Martins Lima

TF067 - LONG-TERM STABILITY EVALUATION OF EMULSIONS BY DROPLET SIZE ANALYSIS

FABIO ROCHA FORMIGA(PG)[1]; JANUS PABLO F. MACEDO(PG)[1]; ILANA ANDRÉA A. FONSECA(IC)[2]; KLARISSA BEZERRA DE SOUZA(IC)[2]; LUÍS ALBERTO L. SOARES(PQ)[2], E. SÓCRATES T. EGITO(PQ)[1]

[1]UFRN-CCS, PPGCSA, Laboratório de Sistemas Dispersos (LASID), socrates@ufrnet.br; [2]UFRN-CCS, Departamento de Farmácia, Laboratório de Sistemas Dispersos (LASID), Natal/RN, Brasil.

INTRODUCTION: O/W emulsion systems are thermodynamically unstable dispersions. Therefore, stability studies must be carried out. OBJECTIVE: The aim of this work was to evaluate the droplet size of emulsions in the long-term stability studies. METHODOLOGY: Two procedures were used to prepare the emulsions: the Phase Inversion Temperature (PIT) and the Spontaneous Emulsification Process (SEP), according to a standard formula. An optical microscope equipped with a calibrated eyepiece micrometer (1 unit = ≈ 1.6 μm at 400x) was used to estimate the mean size. RESULTS: At 24 h after preparation, the mean sizes were 3.621 ± 0,144 μm and 6.719 ± 0,671 μm for PIT and SEP, respectively. The same protocol was repeated 18 months later. It was found that the droplet sizes for PIT and SEP were 5.802 ± 0.698 μm and 6,421 ± 0.803 μm, respectively. CONCLUSIONS: These data suggest that SEP induces small variations in the droplet size, and emulsions prepared by PIT are more coalescence susceptible.

Financial Support: CNPq, BNB, Capes-Brazil
Advisor: Eryvaldo Sócrates Tabosa do Egito

TF068 - FORMALDEHYDE INDUCED GASTRIC-RESISTANCE IN HARD GELATIN CAPSULES CONTAINING NAPROXEN

ANA LÚCIA T. C. ZAMPIERI (PG)[1]; ELIANA M. LIMA (PQ)[1]

[1]Universidade Federal de Goiás

Introduction: Enteric-coating is a method used for the preparation of drug dosage forms that resist disintegration during the passage through the stomach, but disintegrate in the intestinal fluid. Objectives: To develop a simple and reproducible method to produce enteric release gelatin capsules based on the cross-linking reaction induced by formaldehyde. Methods: Naproxen hard gelatin capsules were immersed in hydroalcoholic (70 – 90%) solutions containing several concentrations of formaldehyde (0,2 - 0,6 $mMol.L^{-1}$) and then submitted to an in vitro release test to evaluate enteric release performance. Results: Drug release profile was remarkably influenced by formaldehyde and alcohol concentration in the solutions used to treat the capsules. Although all capsules resulted in less than 10% release after 2 hours in gastric fluid, only the capsules produced with 0,2 $mMol.L^{-1}$ formaldehyde and 90% alcohol were able to release not less than 85% of the drug in the intestinal fluid, as stated by the United States Pharmacopeia. Aldehyde residue was measured by HPLC. Conclusion: Gelatin cross-linking induced by formaldehyde can be used as an alternative method to produce enteric release capsules under strict conditions.

Financial Support: FINEP; FUNAPE; CNPq.
Advisor: Profa. Dra. Eliana Martins Lima.

TF069 - EVALUATION OF ENALAPRIL RELEASE PROFILE FROM INDIVIDUALLY COATED COMPRESSED GRANULES AND TABLETS

RODINELLI BORGES DE OLIVEIRA (PG)[1]; ELIANA M. LIMA (PQ)[1]

[1]Universidade Federal de Goiás

Introduction: Enalapril is a prodrug whose metabolic hydrolysis product is enalaprilate, a competitive Angiotensin Converting Enzyme Inhibitor, used for the treatment of rennin-dependent hypertension. Tablet formulations must protect enalapril from a solid-state degradation process, leading to diketopiperazine formation. Objectives: Develop tablet formulations of enalapril based on polymer coating procedures capable of maintaining drug stability with a desirable release profile. Methods: Enalapril granules were coated with hydroxypropyl methylcellulose (HPMC) 2.5% in a Mycrolab fluidized bed system. Coated (CGr) and uncoated granules (UGr) were compressed into 7mm round tablets. Tablets made from UGr were also coated. Samples were submitted to in vitro dissolution tests. Results: Fluidized bed method was able to provide homogeneous coating both on tablets and granules. Coated granules exhibited a slower release profile during the first 15 minutes of the test; however both formulations were able to provide a minimum of 80% release at 30 minutes. Conclusion: HPMC did not interfere with the 30 minute point of the dissolution test. Stability tests are being conducted to determine the most suitable formulation.

Financial Support: FINEP; FUNAPE; CNPq.
Advisor: Profa. Dra. Eliana Martins Lima

The authors did not follow the Scientific Committee's suggestion for an English language review

TF070 - CHARACTERIZATION AND ENCAPSULATION PROFILE OF ISOTRETINOIN IN SMALL UNILAMELLAR LIPOSOMES

CARINA P. I. ALVES [1] (PG); ELIANA M. LIMA (PQ)[1]

[1]Universidade Federal de Goiás

Introduction: Among several other applications, Isotretinoin's effect on cell differentiation makes this drug an important alternative for the treatment of acute myeloid leukemia. Encapsulating retinoids in liposomes is a promising improved isotretinoin delivery system, leading to a better stability, solubility and specificity profile. Objectives: Encapsulating isotretinoin in unilamellar liposomes, comparing encapsulation efficiency obtained by two different methods, followed by the determination of liposomes' properties. Methods: Liposomes were prepared either by lipid film hydration or chloroform injection methods, followed by titanium probe sonication. Size exclusion chromatography was used to separate encapsulated and free drug, quantitative determination was performed by HPLC and UV spectrophotometry. Liposomes were also characterized by dynamic light scattering and electron spin resonance. Results: Encapsulation efficiency varied depending on liposome composition and preparation method, although EPR assays did not show significant changes in drug-vesicle interactions. Conclusions: Isotretinoin can be satisfactory encapsulated into phosphatidylcholine liposomes, positioning itself in the lipid membrane.

Financial support: CNPq, FINEP, FUNAPE
Advisor: Profa. Dra. Eliana Martins Lima.

TF071 - PREPARATION AND CHARACTERIZATION OF POLY (DL-LACTIDE) AND POLY (DL-LACTIDE-CO-GLYCOLIDE) MICROPARTICLES ENCAPSULATING ALL-TRANS RETINOIC ACID

PALOMA CORDO (PG); ANA AMÉLIA M. LIRA (PG); DENISE ANDRIOLI (IC); JULIANA M. MARCHETTI (PQ)

Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, São Paulo, Brasil, 14040-903

Introduction: All-trans retinoic acid, an analog of vitamin A, has been a first-line treatment for the topical management of inflammatory and non-inflammatory acne. Unfortunately, some drawbacks such as poor water solubility, photolability and local irritation reactions strongly limit its topical use. Objective: the aim of the present study was to prepare all-trans retinoic acid microparticles using poly-DL-lactide (PLA) and poly-DL-lactide-co-glycolide (PLGA) to overcome these disadvantages and to improve its effectiveness. Methodology: PLA and PLGA microparticles were prepared for conventional o/w emulsion-solvent evaporation method. Morphology, size, drug content and release behavior were investigated. Results: In general, microparticles presented drug content was higher than 90% and smoother and spherical shape. The release behavior of PLA and PLGA microparticles were different. Conclusions: The results of our study showed that these microparticles can be promising alternative as controlled release system for all-trans retinoic acid for topical use

Financial Support: CNPq
Advisor: Profª. Drª. Juliana M. Marchetti

TF072 - SOLID DISPERSION INFLUENCE IN THE RATE OF BUPROPION DISSOLUTION

POLLYANNA TAMASCIA(IC)[1], ANDREA C. LIMA(PG)[1], BEATRIZ ZANCHETTA(IC)[1], CAROLINE H. OKUDA(IC)[1], PATRICIA SEVERINO(IC)[1]

[1] Universidade Metodista de Piracicaba

Introduction: Solid dispersions (SD) are characterized by the presence of one or more dispersed drugs in one carrier, biologically inert in the solid state and has been used to improve the solubility of a poorly water soluble drugs. Objective: The objective of this study was to evaluate the influence of SD in the rate of bupropion (BUP) dissolution. Methodology: SD, in the preparation of 1:2, was prepared through co-precipitation of ethanol solution of BUP with an aqueous solution of polioxyethylene alkyl ethers (AE-POE). Dissolution study was conduced at 50 rpm speed in aqueous medium at 37º C. BUP dissolved at 2, 5, 10, 20, 30 and 45 min times was determined by UV spectrophotometry (252nm). Physical mixtures (PM) of BUP with AE-POE were prepared in the same proportion. Result: In the relative proportion of 1:2, SD of BUP: AE-POE hasn't improved the rate of BUP dissolution. The results found were inferior to those obtained for PM. Conclusion: The relative proportion between drug and carrier is critical in the increase of dissolution rate. The carrier concentration twice larger may have led to clusters formation and possibly a complex BUP: AE-POE with a new chemical entity.

Financial support:FAPIC
Supervisor: Prof.Dr. Marco Vinícius Chaud

TF073 - PHASE BEHAVIOR STUDIES OF SYSTEMS COMPOSED BY NONIONIC SURFACTANTS, CANOLA OIL AND PG/WATER

FÁBIA CRISTINA ROSSETTI (PG)[1]; ANTÔNIO CLÁUDIO TEDESCO (PQ)[2]; M. VITÓRIA L. B. BENTLEY (PQ)[1].

[1] Faculdade de Ciências Farmacêuticas de Ribeirão Preto – USP
[2] Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto – USP

Introduction: Recently, microemulsions have been included in the investigated spectrum of potential dermal therapeutics in order to obtain enhanced skin penetration.
Objectives: Selection and characterization of microemulsion systems from phase diagrams composed by Span®/Tween®, canola oil and propylene glycol (PG)/water. Methodology: Phase diagrams were constructed by titration of canola oil/surfactant mixtures with PG/water. Surfactant mixtures were 3:1 (volume of Span® and Tween®) and PG/water mixtures were 1:1, 2:1, 3:1. Characterization was made by visual inspection, polarization microscopy and conductivity.
Results: Phase diagrams (1:1; 2:1, 3:1) showed 4, 8 and 13 isotropic systems, respectively. The maximum amount of water incorporated in the systems was 10%, 20% and 30%, respectively. Low conductivity indicated the systems are W/O. Conclusions: It is not possible to obtain high water incorporation in the absence of short-chain alcohols, it is possible to obtain more isotropic systems by lowering the polarity of the aqueous phase and titration of the surfactants mixtures lead to the formation of systems W/O.

Financial Support: Fapesp
Supervisor: M. Vitória L. B. Bentley

TF074 - DEVELOPMENT OF A HYDROXYETHYLCELLULOSE GEL FORMULATION FOR TOPICAL DELIVERY OF NAPROXEN

REGINA G. KELMANN (PG)[1]; FABIANA E.B. SILVA (PQ) [2]

[1] Universidade Federal de Santa Catarina ; 2 Universidade Regional Integrada do Alto Uruguai e das Missões

Naproxen is a non-steroidal anti-inflammatory drug compound with analgesic and antipyretic effects, used for treatment of rheumatoid arthritis, osteoarthritis and some others muscle disorders. In oral dosages it has been associated with gastrointestinal side effects. The development of a topical presentation for this drug could solve these side effects due to a low systemic absorption. The study's objectives are develop a Naproxen hydroxyethylcellulose gel and a analytical methodology to determine the drug content. The gel was formulated according to the drug hydrophobic characteristics, containing 5% of Naproxen. To determine the drug content, sample of the final formulation was diluted in ethyl alcohol in order to give a final concentration of 20 µg/mL. The resulting solution was measured in UV spectrophotometer at 272 nm against a reagent blank. The method was validated according to ICH guidelines for validation of analytical procedures. The results show that the gel basis is compatible with the used excipients, and the addiction order of them influences the formulation stability. The proposed method was found to be simple, linear, rapid, precise, accurate and sensitive.

Financial Support: PIIC/URI
Supervisor: Fabiana E. B. Silva

TF075 - PREPARATION OF PLGA MICROSPHERES BY EMULSIFICATION/ SOLVENT EVAPORATION PROCESS EMPLOYING MICROFLUIDIC STRUCTURES

ROSEANE MARIA RIBEIRO COSTA (PG)[1]; MARIA INÊS RÉ (PQ)[1]; MÁRIO RICARDO GONGORA-RUBIO (PQ)[2]; MÁRCIO RODRIGUES DA CUNHA (PG)[2]

INSTITUTE FOR TECHNOLOGICAL RESEARCH OF THE STATE OF SÃO PAULO, P.O. BOX 0141, 05508-901 - SÃO PAULO, BRAZIL [1]LABORATORY OF PARTICLE TECHNOLOGY, MIRE@IPT.BR; [2]MICROFLUIDICS LABORATORY, GONGORAM@IPT.BR

The scope of this work is to report the potential of several micromixers manufactured in LTCC (Low Temperature Co-fired Ceramics) for the production of biodegradable microspheres by an emulsification/solvent evaporation process from a w/o/w double emulsion. PLGA microspheres were obtained with micromixers arranged in several geometrical configurations and the influence of some process and formulation parameters, such as the total liquid flow rate and the type of solvent, on the characteristics of the microspheres was examined with special focus on the particle size distribution. Microspheres with monomodal size distributions having mean diameters ranging from 6-37µm were produced with excellent reproducibility. Because of its simple set-up and its suitability for continuous production, the results suggest that an emulsification/solvent evaporation process employing microfluidic structures is suitable for the automated and aseptic production of polymeric microspheres for drug controlled release.

Supported by IPT
Supervisor: Maria Inês Ré

TF076 - EFFECT OF PLASTICIZERS ON THE PROPERTIES OF CHITOSAN AND N-CARBOXYMETHYLCHITOSAN FILMS

ROBERTA LAMIM(PG) [(1)]; RILTON ALVES DE FREITAS(PQ) [(1)]; ELIMAR IVAN RUDEK(PQ) [(2)]; HELENA MARIA WILHELM(PQ) [(3)]; TANIA MARI BELLÉ BRESOLIN(PQ) [(1)]

[(1)] Programa Mestrado Ciências Farmacêuticas - UNIVALI, Itajaí (SC), Brazil, [(2)] Curso de Odontologia - UNIVALI, [(3)]LACTEC-UFPR, Departamento de Química Aplicada, Curitiba-PR, Brazil

Chitosan (Ch) is a cationic natural polysaccharide and the N-carboxymethylchitosan (N-CMCh) is a water soluble derivative that retain various chemical, physical and biological properties of Ch. In this work were develop films of Ch and N-CMCh (1% w/w), unplasticized and plascticized with PEG 400 or Glycerol (15% w/w on polymer). The free films obtained by casting method were evaluated to thickness, mechanical properties, water vapor transmission (WVRT) and film dissolution in water, acid and alkali solution. The type of biopolymer and plasticizers affected significantly the mechanical and WVTR films properties. The most suitable plasticizer was PEG 400, that didn't change the WVRT and allowed elastic films. The N-CMCh films showed 67%, 10% and 82% of solubility in water, HCl 0,1 M and pH 7.4 buffer, respectively, while the Ch films were totally soluble in the 2 first medium and remained practically insoluble in the latter medium. These plasticized films are suitable to specific clinical and pharmaceutical applications as film coating or membranes for drug release.

Financial support: PRoPPEC e PIPG-UNIVALI
Adviser: Dr. Tania Mari Bellé Bresolin

TF077 - INFLUENCE OF DIFFERENT FACTORS ON TEMPERATURE PHASE TRANSITIONS OF MO:OA AQUEOUS SYSTEMS

VANESSA PAULA DA MATTA (IC); DANIEL DE PAULA (PG); MARIA VITÓRIA LOPES BADRA BENTLEY (PQ)

Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP

Introduction: It has been hypothesized that guest molecules incorporated into liquid crystalline phases formed by Monoolein (MO):Oleic Acid (OA) can be released due to phase transitions, which are an interesting skill in the development of new drug delivery systems. Objective: To investigate the influence of pH, ionic strength (IS) on the temperature phase transitions of MO:OA systems in water, using Cyclosporine A (CsA) as peptide model drug. Methods: MO:OA at various percentages were mixed in excess of aqueous solutions at different pHs and ISs and analyzed by polarized light microscopy at different temperatures. Samples were dispersed in water and characterized by light scattering and turbidimetric analyzes. Results: OA and IS induced the transition of cubic (Fc) to hexagonal (Fh) phase at pH 4.5. Besides, at pH 7.4, the addition of OA(1-4%) reduced the Fc-Fh phase transition to low levels of temperature (40-50ºC). Conclusion: Phase transitions temperatures of MO:OA systems can be tuned by pH and IS variation.

Supported by FAPESP
Supervisor: Maria Vitória Lopes Badra Bentley

TF078 - STUDY ON PEUMUS BOLDUS EXHAUSTIVE EXTRACTION IN SOXHLET APPARATUS

CRISTIANE CARDOSO CORREIA (PG); LUÍS ALEXANDRE PEDRO DE FREITAS (PQ)

Faculdade de Ciências Farmacêuticas de Ribeirão Preto – USP

Introduction: Peumus boldus (Pb) is a plant of wide use due to its varied therapeutical effects, such as antipirectic, anti-inflammatory, antioxidant and hypoglycemic. Objective: This work seeks to study the factors related to the Soxhlet extraction process using a factorial planning (32). Methodology: The factors studied were the solvent (acetic acid, ethanol 70% and ethanol 96%) and extraction time (12, 24 and 36hs). The solids and flavonoid contend, as well as the antioxidant activity, AA (DPPH) of the extracts were evaluated by the analysis of variance. Results: The ANOVA showed that AA was affect by extraction time, solvent and the interaction between these factors at 1 %, 0,1% and 1 % respectively. Also, the solids content, SC, was affect significantly by the factors studied. Analysis of the experimental data showed that the best extraction condition was the one using ethanol 70% and the shorter extraction time, 12 hs. Based on the results, further experiments with extraction times of 3 and 6 hs were carried out. The AA and SC increase with extraction time until 12 hs and thereafter they tend to decrease. Conclusion: The best extraction condition for Pb in a Soxhlet is accomplished with ethanol 70% for 12 hs.

Financial Support: Capes
Advisor: Luis Alexandre Pedro de Freitas

The authors did not follow the Scientific Committee's suggestion for an English language review

TF079 - 4-NEROLYDILCATECOL INCLUSION COMPLEX IN HYDROXYPROPYL- β- CYCLODEXTRIN

LEAL, A. F.V. B (IC); VALERIANO, V. S.(IC); REZENDE, K. R.(PQ)

Faculdade de Farmácia, Universidade Federal de Goiás

Introduction: 4-nerolydilcatechol is a prenilated catechol very abundant in Pothomorphe umbellate scrub. Its antioxidant activity is about 40X higher than α-tocopherol. However, low aqueous solubility drugs do not yield feasible pharmaceutical formulations. β-cyclodextrins, are cyclic oligosaccharides composed of 1-4-linked D-glucopiranose units which has a lipophilic central cavity. In aqueous solutions, they are able to form complexes with non polar molecules, by taking up a drug molecule or some lipophilic moiety into the central cavity. Therefore, they act as technological alternatives to enhance solubility, dissolution rate and oral bioavailability. Aim: To study 4NC inclusion complexation on hydroxypropyl- β-cyclodextrin (HP- β- CD) by the aqueous phase solubility method (HIGUCHI & CONNORS, 1965). Methods: Daily standard curves (3,0-100,0 µg/mL) and inclusion complex analysis were done by HPLC-UV method using Methanol:water 9:1, C18 column (150x4.6 mm) and 1.0 mL/min flow rate. The stoichiometric quantities of 4NC and HP- β- CD were dissolved in Milli-Q water up to 1:1; 1:5; 1:10 and 1:20, respectively. All measurements were performed under ultrasonic bath and after each 5 min interval and also at the end of 55 min. Results: The 4NC detected amount was, at the average, 76.9; 80.6; 58.3 and 29.7% of total amount added. Therefore, phase solubility diagram of inclusion complex was tentatively inferred as B1 type, according to HIGUCHI & CONNORS.

Financial support: SECTEC-GO/CNPq
Supervisor: Kênnia Rocha Rezende

TF080 - POLYMERIC MATRIX OF PECTINS AND AMINOACID FOR DRUG RELEASE

VÂNIA GIROTTO DE MOURA (IC)[1]; MÔNICA FREIMAN S. RAMOS (PG)[1]; OSVALDO DE FREITAS (PQ)[1]

[1]Fac. Ciências Farmacêuticas de Ribeirão Preto, USP, Avenida do Café s/ no Monte Alegre - RP, SP, Brazil.

Introduction: The development of new systems for releasing drugs allows increasing their efficacy and minimizing their adverse reactions, as well as controlling their specific absorption in the gastro-intestinal tract. The critical factor for the success of oral administrated drugs is the short permanence in gastro-intestinal superior tract. Such a difficulty could be overcome by using matrix polymers as pectins to direct the releasing of the drug specifically into the colon.Objective: This work aimed to evaluate the liberation rate of drugs supported in pectin matrices and different concentrations of glycine, using paracetamol as the drug model. Methodology: Three types of high methoxylation degree pectins was used (USP, JMH6, 7128). Tablets were obtained by direct compression of the mixture with the polymer on a hydraulic press (4000 lb). The in vitro dissolution tests were performed at pH 1.5 and 6.0 in SOTAX AT7 equipment, at 50 rpm. Aliquots were taken from 15, 30, 60, 120, 180, 240 and 300 min and their absorbances were measured at 242 nm. Results and Conclusion: The tablets prepared with three pectin showed to release paracetamol slower in the acidic than the buffered medium. The glycine presence doesn't modify the paracetamol liberation significantly in the systems with pectin 7128 or JMH6. However, decreasing glycine concentrations led to a decrease in the free paracetamol in both dissolution systems for the USP pectin.

Financial Support: CNPq, FAPESP
Supervisor: Osvaldo de Freitas

TF081 - CHARACTERIZATIONOF TABLETS COATED WITH GLYCERYL MONOSTEARATE BY FLUIDIZED HOT-MELT COATING

RODRIGO GONÇALVES MARTINS(PQ)[1], GIOVANNA BONFANTE BORINI(PG)[1,2] LUIS ALEXANDRE PEDRO DE FREITAS(PQ)[1]

[1]Faculdade de Ciências Farmacêuticas de Ribeirão Preto – Universidade de São Paulo; [2]docente do curso de Farmácia Industrial – Universidade de Uberaba-Uberaba-MG

Introduction: Wax materials can be used to coat tablets with the same purposes of polymer coatings, but eliminating the use of solvents. Objective: To study the physical characteristics of tablets coated with glyceryl monostearate. Methods: Coated tablets were prepared by hot-melt using a top-spray fluidized bed. Eight experiments were performed, varying wax rate, nozzle distance and atomizing air pressure. Glyceryl monostearate was melted 10ºC above its melting point and atomized on the bed of tablets. The physical properties evaluated were: disintegration time, weight increase and uniformity, shape uniformity, shape factor change and percentage of agglomeration. Results: The disintegration time, weight increase and uniformity, shape uniformity, shape factor change and percentage of agglomeration were affected by the coating conditions. Tablets coated with a uniform wax layer showed good physical properties. Conclusion: The results demonstrate that fluidized hot melt coating is an efficient and reliable process to obtain coated tablets.

Financial Suport: CNPq
Supervisor: Luis Alexandre Pedro de Freitas

TF082 - EFFECT OF SOLVENTS AND CYCLODEXTRINS ON THE ACETAMINOPHEN SOLUBILITY

AMANDA GOMES MARCELINO(IC)[1]; ANA DÓRIS DE CASTRO (PQ)[2]; MARIA PALMIRA DAFLON GREMIÃO (PQ)[2]

[1]Depto de Fármacos e medicamentos, FCF-UNESP – Araraquara - SP
[2]Programa de Pós-graduação em Ciências Farmacêuticas, UNESP

Acetaminophen (APH) is poorly soluble in water and this study aims to investigate the effect of different solvents on the solubility of this drug. The solubility assays were conducted according to the methodology described by HIGUCHI and CONNORS (1965). The drug solubility was investigated in water, in cyclodextrins (CD) aqueous solutions and in water/polyethyleneglycol 400 (PEG 400) mixture at different ratios. The absorbance at 243 nm was read on spectrophotometer. The poor solubility of this drug in water was confirmed. The 9 mM CD aqueous solution showed to be 30% more efficient than water in dissolving APH, but the solvent system containing PEG with dielectric constant of 25.3 demonstrated to be the best solvent, although a pink color developed faster than with the others solvents, which can indicate a hydrolytic reaction in a higher degree. The results confirmed that water is not a good solvent for APH, the aqueous solution of CD has only slightly improved the drug solubility, but the mixture water/PEG lead to a very significant improvement on the APH solubility, about 130% higher than in water.

Financial Support: PADC-FCF – UNESP
Supervisor: ANA DÓRIS DE CASTRO; MARIA PALMIRA DAFLON GREMIÃO

TF083 - DAUNORUBICIN DERIVATIVE ASSOCIATION WITH A LIPIDIC MICROEMULSION (LDE): PHYSICO-CHEMICAL STUDIES

RAQUEL DA SILVA TEIXEIRA(PG)[1,2]; CLAUDETE JUSTINA VALDUGA(PQ)[2]; RAUL CAVALCANTE MARANHÃO(PQ)[1-3]

[1] FMUSP. [2]Instituto do Coração, FMUSP. [3]FCF,USP.

Introduction: A lipid microemulsion (LDE) that binds to LDL receptors (LDLr) can be used as a vehicle for antitumoral drugs since some neoplastic cells have LDLr overexpression. Daunorubicin (DNR), an acute myeloid leukemia treatment drug is of limited use because of its high toxicity. Its association with LDE gives a low 0.7% yield due to low lipophilicity. Objectives: To chemically modify DNR to increase its lipophilicity, and the LDE association rate. Methodology: An oleyl moiety was attached to DNR in the presence of N,N'dicyclohexylcarbodiimide e 4-dimethylaminopyridine. The derivative was purified and analysed by NMR, HPLC and mass spectroscopy, then associated with LDE in a 1:5 and 1:10 proportions in mass drug/lipid. The association rate, particle diameter and stability were evaluated by spectrophotometry and laser scattering. Results: The N-oleil daunorubicin was obtained in quantitative yield and the mean association rate with LDE was 68 ±7.5 and 85±5% in the proportions 1:5(n=12) and 1:10 (n=5) respectively. Particle diameter was 75 and 99nm respectively for 1:5 and 1:10 proportions. LDE diameter was 42 nm. Conclusions: DNR higher lipophilicity increased the LDE association rate thus favoring possible future clinical applications.

Financial Support:FAPESP.
Supervisor: Raul C. Maranhão

TF084 - EQUIVALENCE STUDY OF HIDROCHLOROTIAZIDE TABLETS

MELINA G. CARVALHO(IC)[1]; RENATA A. CRUZ(IC)[1]; ANDREZA A. DE MEDEIROS(PG)[1]; EDIVÂNIA LOPES(IC)[1]; FERNANDA N. RAFFIN(PQ)[1]; MARCO V. M. NAVARRO(PQ)[1]

[1]Universidade Federal do Rio Grande do Norte- Gen. Gustavo Cordeiro de Faria St; s/n. Petrópolis - Natal/RN - 59010-180

INTRODUCTION: Two pharmaceutical products are equivalent when they contain the same drug at the same concentration and dosage form. They can contain identical excipients or not, but they must fit the official compendia and present similar characteristics. OBJECTIVE: In this work, an equivalence study was carried out to compare the tablets developed by NUPLAM and the reference product (Clorana™). METHODOLOGY: Parameters such as hardness, dissolution profile, disintegration, assay, average weight and friability were evaluated. RESULTS: The developed product presented all the results in the required limits: 100.12% (assay), 76.91% dissolved in 30 minutes, hardness of 8.55 kgf, friability of 0.12% and total disintegration in 3 minutes. The dissolution test evidenced the same profile for both products since there was superposition of the curves obtained for the reference medicine and the new product. CONCLUSION: As the developed tablets presented considerable quality and the comparison with Clorana™ did not show significant difference, they can be considered equivalent products and be regularly produced.

Financial support: FAPAM-UFRN
Directed by: Túlio F. A. de L. e Moura

TF085 - IN VITRO RELEASE STUDY OF CIS-[RU(NO_2)$(BPY)_2$(4-PIC)]$^{1+}$ THROUGH DIFFERENT SATURATED FORMULATIONS

DANIELLE C. A. E SILVA (PG)[1]; THAÍS T. PUPO (IC)[1]; ROBERTO S. DA SILVA (PQ)[1]; RENATA F. V. LOPEZ[1]*

[1]FCFRP-USP

In the last years, the use of compounds capable of releasing NO *in vivo* has become a very active area of research. The complex *cis*-[Ru(NO_2)$(bpy)_2$(4-pic)]$^{1+}$ is a NO-donor agent that presents some promising characteristics, as thermal stability of the Ru^{II}-NO_2^+ bond, and under light or electrochemical stimulation can release NO. Aiming topical application with controlled release of *cis*-[Ru(NO_2)$(bpy)_2$(4-pic)]$^{1+}$, *in vitro* release of this complex through saturated formulations ((i) PBS pH 5, (ii) dehydrated chitosan hydrogel and (iii) chemically crosslinked chitosan gel (glutaraldehyde 0.05%)) was investigated using Franz diffusion cell and cellulose acetate membrane. Complex release from the formulations was monitored over a period of 12 h to determined its release profile. Results showed that chitosan hydrogel release rate was 3-fold higher than the one of saturated PBS, indicating that hydrogel water deficiency probably facilitate water diffusion across the matrix increasing, consequently, drug delivery. On the other hand, crosslinked the gel lowered 5-fold the diffusivity of the complex across the matrix. In conclusion, this work demonstrated that simple modifications in the formulation can significantly altered and controlled *cis*-[Ru(NO_2)$(bpy)_2$(4-pic)]$^{1+}$ release.

Support by CNPq, FAPESP
Supervisor: RENATA F. V. LOPEZ

TF086 - EVALUATION OF BUPROPION DISSOLUTION RATE IN SOLID DISPERSION WITH POLIETHYLENE GLYCOL

BEATRIZ ZANCHETTA(IC)[1]; CAROLINE HARADA OKUDA(IC)[1]; PATRICIA SEVERINO(IC)[1]; POLLYANNA TAMASCIA(IC)[1] and MARCO VINÍCIUS CHAUD(PQ)[1].

[1]Faculdade de Ciências da Saúde – Universidade Metodista de Piracicaba (UNIMEP)

Introduction: Bupropion (BUP) is an antidepressant therapeutically used in smoking cessation. The bio-availability of this pharmaco is limited by low solubility in water. The solid dispersions (SD) have been used to increase solubility and dissolution rate of poorly water solubility drugs. Objective: To evaluate dissolution rate of BUP in SD with polyethylene glycol (PEG6000). Methodology: SD obtained by co-evaporation contained one part of BUP for one part of PEG6000. Dissolution rate of BUP in SD was developed using apparatus II of dissolution equipment. BUP dissolved in 2,5,10,20,30 and 45 min. was analyzed in a UV spectrophotometer (252nm). Dissolution rate of BUP in SD was compared to the dissolution of free BUP and in the physical mixture (PM). Results: SD has increased about 10% dissolution rate of BUP and has modified the liberation profile. Conclusion: The increase of dissolution rate is due to the increase of the surface area and of the moistness of BUP. The modification of dissolution profile happens, probably, to the formation of clusters of PEG which modifies the liberation of BUP in SD.

Financial Support: FAPIC-UNIMEP
Supervisor: Marco Vinícius Chaud

TF 087 - EVALUATION OF PREPARATION METHOD IN LIBERATION AND DISSOLUTION IBUPROFEN IN HARD GELATINOUS CAPSULES

PATRÍCIA SEVERINO(IC)[1]; ALINE ALONSO(IC)[1]; BEATRIZ ZANCHETTA(IC)[1]; FERNANDA FOLTRAN(IC)[1]; GISLAINE R. LEONARDI(PQ)[1] AND MARCO VINÍCIUS CHAUD(PQ)[1]

[1]Universidade Metodista de Piracicaba(UNIMEP)

Introduction: Bioavailability of drugs in hard gelatinous capsules are influenced by the formulation components and by the preparation method of the pharmaceutical dosage forms. Objective: Evaluate the influence of mixture and filling up processes in Ibuprofen(IBF) dissolution profile. Methodology: IBF was used as drug model of BCS group II. The formulation the formulation excipients chosen was IBF micromeritic. Powder mixture was conducted through geometric dilution of the components or agitation in closed cylinder. Capsule filling up was made by the bulk density calculation or forced to the powder mixture to the interior of the capsule. Content uniformity, disintegration time and dissolution profile were settled. Results:A significant variation of the dissolved drug amount is shown. The content uniformity was irregular, with variations over 10%. Disintegration time was not changed. And, among the appraised parameters, the dissolution profiles were most influenced by the techinique adopted. Conclusion: In the preparation of hard gelatinous capsules the mixture and filling up process of the capsules may alter the liberation and dissolution.

Financial Supports:UNIMEP
Supervisor:Marco Vinícius Chaud

TF088 - IMPROVEMENT OF ISONIAZID AND RIFAMPICIN TECHNOLOGICAL PROPERTIES BY WET GRANULATION

THAÍS J. DE A. FERREIRA(IC)[1]; INARA D. DA SILVA(IC)[1]; LÍLIAN T. DE A. TEIXEIRA(IC)[1]

[1]Universidade Federal do Rio Grande do Norte

Rifampicin (R) and Isoniazid (I) are tuberculostatic drugs that show unfavorable physical characteristics as flowability and filling of capsules. The aim of this work was obtaining granules evaluating the influence of drug/excipient rates in the flow and density. The wet granulation method was used. The drugs were mixed separately with starch and wetted with ethanol (R) and distilled water (I) to obtain distinct granules in order to observe the influence of each drug on the cited properties. Tapped and apparent densities as well as repose angle were determined according to European Pharmacopeia. Particle size distribution was obtained by the sieving method. Dissolution was carried out in HCl 0,1N (R) and distilled water (I). Drug concentration was determined by spectrophotometry at 475 (R) and 263nm (I). The granules prepared with minor quantity of excipient (5:1) showed that the densities increased, flowability was improved and the dissolution fitted the compendia requirements [86, 92% (I) and 74, 33% (R)] comparing to granules at 1:1 ratio. In conclusion, granulation corrected the technological properties, improving the rifampicin and isoniazid encapsulation.

Financial Support: FAPAM-UFRN
Supervisor: FERNANDA RAFFIN(PQ)(1)

TF089 - IN VITRO CUTANEOUS PENETRATION OF KETOCONAZOLE THROUGH PORCINE SKIN FROM SEMISOLID FORMULATIONS

ZAIDA MARIA FARIA DE FREITAS (PG) [1]; ELISABETE PEREIRA DOS SANTOS (PQ)[1]; SILVIA STORPIRTIS (PQ) [2]; NÁDIA MARIA VOLPATO (PQ)[1].

[1]Faculdade de Farmácia – UFRJ;[2] Faculdade de Ciências Farmacêuticas - USP.

Introduction: Porcine skin is a well-accepted model for the human barrier and is often used to assess pharmaceutical formulations mainly in vitro. Objective: A system of vertical difusion and excised skin from the porcine ear have been used to evaluate the KTZ's penetration in the skin of the commercial products (A, B) and the developed one (F0:2). Methodology: The total excised porcine skin has been set up over the cell of diffusion with the stratum corneum facing the donor compartment. The receptor chamber was filled with buffer solution. The presence of the drug in the receptor medium has been monitored up to 8 hours. The samples were then submitted to HPLC analysis. Results: The obtained data show that the formulations A, B and F0:2 do not present a statistically different profile of cutaneous penetration on the epidermis and dermis, by the level of 5% ($p = 0.609$ and $p = 0.269$, respectively). Conclusions: The amount of KTZ decreased with the depth, in other words, in the dermis a lower value has been detected for the drug after the application of the formulations A, B and F0:2.

Financial Support: LabCQ (FF/UFRJ).
Supervisor: Silvia Storpirtis, Nádia M. Volpato.

TF090 - EVALUATION OF SODIUM BENTONITE-BASED SYSTEMS AS DISSOLUTION ENHANCERS FOR WET GRANULATED AND DIRECT COMPRESSED TABLETS

LUIZ MARCELO LIRA(PG)[1]; DIANA S.G. NUNES (IC)[1];LÚCIO MENDES CABRAL(PQ)[1,2]

[1] Faculdade de. Farmácia – UFRJ; [2] INCQS – FIOCRUZ

Introduction: The use of sodium bentonite-based systems for class II drugs as dissolution enhancer was investigated. Objective: Evaluate sodium bentonite and a derivate intercalated as dissolution enhancer of class II Chlorpropamide and Ketoconazole drugs. Methodology: Bentonite intercalation with choline was made as described in literature. Kneadings, granulations and physical mixtures were prepared with different ratios drug:carrier (1:0,1 to 1:2 w/w). The wet granulated and direct compressed tablets were made with similar ratios. The analitical techniques used in study were Differential Scanning Calorimetry, X-rays diffraction, Infrared Spectometry and dissolution studies. Main results: Bentonite intercalation showed an increase of lammelar space of clay with choline. The best release of Chlorpropamide tablets were with 1:0,25 w/w ratio (both wet granulation and direct compressed). All results for direct compressed tablets were higher than for wet granulation. No dissolution enhancenment was noted with Ketoconazole tablets. Conclusions: The proposed mechanism for enhancer dissolution was a plus of swelling behaviour, tablet manufacturing and surface charge interaction with bentonite and drugs

Supervisor: Lucio Mendes Cabral

TF091 - IN VITRO IONTOPHORETIC DELIVERY OF DMAE P-ACETAMIDOBENOATE FROM NON-IONIC GEL

TAÍS GRATIERI (IC)*; RENATA FONSECA VIANNA LOPEZ(PQ)*

*Departamento de Ciências Farmacêuticas, FCFRP, USP

2-Dimetylaminoethanol (DMAE) is a competitive inhibitor of choline uptake and also inhibits coline kinase and coline oxidase. DMAE has been investigated as a skin tensor due to its ability on increasing skin firmness with improvement in underlying facial muscle tone. As iontophoresis has been a promising method to improve the penetration of drugs, into or through the skin, the aim of this study was to investigate the iontophoretic delivery of DMAE from a non-ionic gel, once the topical administration of a gel formulation is easier than an aqueous solution. Passive and iontophoretic delivery of DMAE from a non-ionic gel and aqueous solution were studied using a modified "Franz" diffusion cell and porcine skin. DMAE iontophoretic transport from the anode compartment was followed over a period of 6h at a constant current of 0.5 mA/cm^2. The iontophoretic flux of DMAE from non-ionic gel was 1.88 µg/cm^2/h, higher than that of passive permeation (0.37 µg/cm^2/h) and not higher than the iontophoretic flux from the aqueous solution (4.78 µg/cm^2/h). Skin permeation experiments showed that anodic iontophoresis of DMAE from non-ionic gel caused a considerable (~ 5 fold) enhancement over the passive flux.

Financial Support: FAPESP
Supervisor: Profa. Renata Fonseca Vianna Lopez

TF092 - PRE-FORMULATION STUDY ON THE DEVELOPMENT OF A HIDROCHLOROTIAZIDE PHARMACEUTICAL EQUIVALENT

RENATA A. CRUZ(IC)[1], MELINA G. CARVALHO(IC)[1], ROSSANA M. VERAS(IC)[1], ANDREZA A. DE MEDEIROS(PG)[1], FERNANDA N. RAFFIN(PQ)[1], MARCO V. M. NAVARRO(PQ)[1]

[1]Universidade Federal do Rio Grande do Norte

Pre-formulation is the first part of the rational development of a dosage form. It consists on the study of the physical-chemical properties of a drug, isolated and combined to other substances. The purpose of this work is to obtain information to support the development of a hidrochlorotiazide pharmaceutical equivalent. A study concerning the rheological behavior, based on European Pharmacopoeia tests, and compatibility with excipients, using Differential Scanning Calorimetry (DSC), was carried out. Binary mixtures were prepared with some pharmaceutical excipients such as lactose super tab, cellulose MC101, aerosil 200, sodium croscarmellose, talc and magnesium stearate, which were sieved and grinded during 10 minutes until complete homogenization with hidrochlorotiazide. The mixture of drug and lactose super tab presented the best rheological characteristics, however, when analyzed by DSC it was observed an incompatibility (Maillard's reaction), which indicates that a formulation with this excipient can have the stability decreased. Through this pre-formulation study, it was possible to develop a hidrochlorotiazide tablet.

Financial support: FAPAM-UFRN
Supervisor: TULIO MOURA(PQ)1

TF093 - THE APPLICATION OF AN ELLECTRICAL CURRENT FOR DOXORUBICIN TOPICAL DELIVERY

STEPHANIA F. TAVEIRA (PG)[1] ; RENATA F. V. LOPEZ (PQ)1*

[1]FCFRP/USP

Doxorubicin (DXR) quickly became one of the most potent commonly used anticancer agent after its discovery in 1969. Unfortunately, its nonselective cytotoxicity limits the use of higher doses in most conventional chemotherapeutic drug regimens. Topical chemotherapy of this drug could be an interesting alternative to treat skin cancer with reduced systemic toxicity. Iontophoresis, i.e., the application of a mild electric current to drive molecules into the skin, may be a way to improve DXR skin penetration. The aim of this work was to evaluate the in vitro topical penetration of passive and iontophoretic saline solutions containing DXR. All experiments were performed using iontophoretic vertical diffusion cells, pig ear skin and Ag/AgCl electrodes. DXR transport from the anode compartment was followed over a period of 8h at a constant current of 0.5 mA/cm². Studies of passive permeation showed that the drug doesn't cross the skin in detected amounts. On the other hand, iontophoresis of DXR increased significantly not only the permeation but also the skin retention of the drug.

Support by FAPESP
Supervisor: Renata Fonseca Vianna Lopez

TF094 - ENCAPSULATION OF CIPROFAXACIN HYDROCHLORIDE IN LOADED POLY (LACTIC-CO-GLYCOLIC ACID) LIPOSOME

LUANA CARDOSO DE OLIVEIRA(PG)[1]; ARNÓBIO ANTÔNIO DA SILVA JÚNIOR(PG)[1]; ANSELMO GOMES DE OLIVEIRA(PQ)[1]

[1] Programa de Pós-graduação em Ciências Farmacêuticas – UNESP – Araraquara, oliveiag@fcfar.unesp.br

Fluoroquinolones are broad spectrum of antibiotics widely used to treat ocular infections. Conventional dosage forms have poor drug bioavailability mainly due to ocular physiological constraints. Liposomes have been used as an alternative to prolong drug effect at site of action. The aim of this study was to design liposomes-encapsulated ciprofloxacin hydrochloride and to evaluate the effect of poly (lactic-co-glycolic acid) (PLGA) on the drug encapsulation. For this, liposomes were prepared with hydrogenated soy phosphatidylcholine, with and without PLGA, and ciprofloxacin in different concentrations. The liposomes were obtained by sonication, and the non-encapsulated drug was separated from load-liposome by size exclusion chromatography using a Sephadex G-50 column. The fractions containing the load liposomes were freeze dried and quantitatively dissolved in methanol for determination of the encapsulation efficiency. The results show that the exclusion by chromatography efficiently separated the non-encapsulated drug and that the PLGA addition increased the ciprofloxacin hydrochloride encapsulation.

Financial Support: CAPES, CNPQ, FAPESP
Advisor: Prof.Dr.Anselmo Gomes de Oliveira

TF095 - DEVELOPMENT OF MICROEMULSIONS SYSTEMS CONTAINING SOYA PHOSPHATIDYLCHOLINE AND TWEEN 20: HLB INFLUENCE.

CRISTINA MARIA FRANZINI(PG)[1]; THALITA PEDRONI FORMARIZ (PG)[1]; ANSELMO GOMES DE OLIVEIRA(PQ)[1]

[1]Faculdade de Ciências Farmacêuticas, Universidade Estadual Paulista Júlio de Mesquita Filho, UNESP, Araraquara, oliveiag@fcfar.unesp.br

Microemulsions are a clear, isotropic, and thermodynamic stable systems, containing usually surfactant, co-surfactant, oil and water components. The aim of this study was the development of microemulsion system containing cholesterol/propyleneglycol caprylate/dicaprylate as oil phase, polyoxiethylene sorbitan monolaurate/soya phosphatylcholine as surfactant and aqueous phase. The HLB influence as well as the rheological behavior and the physical stability were also studied. The composition of the surfactant mixture varied in order to obtain HLB values in the range of 9.08-11.8. The stability of the systems was determined by turbidimetry at 410 nm daily for fifteen days. The rheological study was performed using a Carri Med CSL rheometer showing a Newtonian behavior for all systems. The results showed that the microemulsion/emulsion obtained were more stable at HLB 11. The better proportion of soya phosphatidylcholine/polyoxiethylene sorbitan monolaurate to stabilize the systems was 44.9:55.1%.

Financial Support: CAPES, CNPQ, FAPESP
Advisor: Prof.Dr.Anselmo Gomes de Oliveira

TF096 - CHITOSAN:PECTIN:HIDROXIPROPILMETHYLCELLULOSE PHATALATE MULTIPARTICULATE SYSTEM FOR COLONIC DELIVERY USING TRIANCINOLONE AS MODEL DRUG

GISELLE FARIA OLIVEIRA (PG)[1]; LÍVIA QUEIROZ CARVALHO (IC)[1]; RAUL CESAR EVANGELISTA (PQ)[1]

[1]Programa de Pós-Graduação em Ciências Farmacêuticas - F.C.F- UNESP – Araraquara – SP

A multiparticulate system with the potential for site-specific delivery to the colon has been investigated. Among the different approaches to achieve colon-selective drug delivery, the use of polymers, specifically those biodegradable by colonic bacteria, holds great promise. In this work, a system combining specific biodegradability and pH-dependent release is presented. Complex coacervation was applied to prepare multiparticulate combinations of chitosan (CS) and Ca^{2}+ as cationic components and pectin (PC) as anionic. The inert particles have been prepared at 3:1 ratio of PC:QS, containing 2% of calcium and 0.5% of enteric polymer, hidroxypropylmethyl cellulose phthalate (HPMCP). Particles containing 100 mg of triancinolona (TC) have been also produced resulting an entrapment efficiency of about 85%. System characterization included granulometric, morphological and swelling behavior analyses in media that simulates gastrointestinal tract. Results from swelling experiment under simulated gastric condition have shown that CS:PC combinations with HPMCP lead to the decrease swelling ratio of the particles.

Financial Support: CAPESAdvisor: Prof. Dr. RAUL CESAR EVANGELISTA

TF097 - PHYSICAL CHARACTERIZATION OF THREE TABLET DISINTEGRANTS

LENILTON S. DA S. JÚNIOR(IC)[(1)]; ANTÔNIO C. DE L. NETO(IC)[(1)]; ANDREZA A. MEDEIROS(PG)[(1)]

[1]Universidade Federal do Rio Grande do Norte -Gen. Gustavo Cordeiro de Faria St; s/n. Petrópolis -Natal/RN-59010-180

Disintegrants are excipients that improve the breakdown of tablets and granules in smaller particles. A fast disintegration can promote a fast dissolution, which increases the drug absorption. The aim of this work is to estimate, through physical characterization, the quality of three disintegrants widely used in the pharmaceutical industry: Croscarmellose Sodium (CS), Sodium Starch Glicolate (SG) and Crospovidone (CP). The rheological tests done according to the European Pharmacopoeia were: angle of repose, flow rate, bulk and tapped densities, from which the following parameters were obtained: Hausner ratio, Carr index, porosity and vacuum. The granulometry was determined through optical microscopy based on the Ferret diameter (objective 10x). Distinct batches from each raw material (3 for CP, 3 for SG and 9 for CS) were analyzed and the results were submitted to ANOVA. SG showed significant differences (P=0,05) among the batches for angle of repose and CP, for bulk and tapped densities, which indicates different flowability and compatibility. Studies to determine the influence of these variations on formulations will be carried out.

Financial Support: FAPAM-UFRN
Supervisor: Fernanda Raffin ; Túlio Moura

TF098 - STANDARDIZATION OF HYDROALCOHOLIC EXTRACTS OF *ACMELA BRASILIENSIS* (WEDELIA PALUDOSA) (ASTERACEAE)

THAISA BACCARIN (IC)[1]; ALEXANDRA I. CZEPULLA (PG)[1]; RENE A. FERREIRA (PQ)[1]; TANIA M. B. BRESOLIN (PQ)[1]; VALDIR CECHINEL FILHO (PQ)[1].

[1] UNIVALI, CCS, Programa de Mestrado em Ciências Farmacêuticas/NIQFAR
Rua Uruguai, 458 – Itajaí/SC – 88303-202 e-mail: thaisa27@yahoo.com.br

The development of phytotherapics drugs requests the execution of series of stages in order to obtain an effective, safe and with quality drug. This study had for objective to standardize the process of obtaining hydroalcoholic extracts of A. brasiliensis. The vegetable drug was characterized by macro- and microscopic analysis and teor extractive. The extraction process was optimized through modifications in the method (maceration and turbo-extraction) and time of extraction, alcoholic degree and granulometria of drug. The obtained fluid extracts were analysed by chromatographic profile, pH, alcoholic degree, densisity and extractable fraction determination. The extracts were concentrated for thin extracts obtaintion. The particle size between 0.150 and 0.5mm presented larger yield in relation to the extractable fraction. The turbo-extraction was the most effective method. It was verified that in the time of 20 min and being used ethanol 60% as liquid extractor, it has the largest proportion of dry residue. The extracts were concentrated to 90-95% of weight loss for obtaining the thin extracts. Through this study were found the best conditions to obtain the hydroalcoholic extracts of A. brasiliensis as well as the obtaintion of its thin extract.

Financial Support: PIPG/UNIVALI
Supervisor: Ruth Meri Lucinda-Silva

TF099 - OBTAINTION AND CHARACTERIZATION OF SMALL UNILAMELAR LIPOSOMES CONTAINING CAFFEINE

MARLUS CHORILLI (PG)(1); THEREANA CRISTINA RIMÉRIO (IC)1; ANSELMO GOMES DE OLIVEIRA (PQ)1; MARIA VIRGÍNIA SCARPA (PQ)1.c

[1] FCFar – UNESP

Introduction: Due to great difficulty of diffusion of actives substances through skin different systems as well as the liposomes, have been studied in order to increase the cutaneous penetration. Objective: The aims of this work were to obtain and to characterize liposomes prepared by sonication containing caffeine (CAF). Methods: Liposomes containing soy phosphatidylcholine – PS (40mM), hydrogenated PS (40 mM), cholesterol – CHOL (6 mM) and CAF (30mg/mL) were characterized by size distribution, encapsulation efficiency and refractive index. Results and Conclusions: Results of refraticve index were very similar to the water values. Uniform size distributions with low polidispersity were obtained. The diameters observed for PS/CHOL about 64 nm, for PS 80 nm, PSH/CHOL 85 nm, PS/CAF 145 nm, PS/CHOL/CAF 147 nm, PSH/CHOL/CAF 152 nm, PSH 166 nm e PSH/CAF 481 nm. Encapsulation efficiency of 10.8% was obtained for PSH/CHOL/CAF, followed of PS/CHOL (6.6%), PSH/CAF (3.1%) and PS/CAF (1.5%).

Financial Support: FAPESP and CAPES
Supervisor: Profa. Dra. Maria Virgínia Scarpa.

TF100 - PREPARATION OF ZNPC LOADED PLGA NANOPARTICLES FOR PDT

EDUARDO RICCI JÚNIOR (PG) ; JULIANA MALDONADO MARCHETTI (PQ)

*Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Av. do Café, s/n, 14040-903, Ribeirão Preto, SP, Brazil.

Zinc phthalocyanine (ZnPc) is a hydrophobic photosensitizer and may be loaded onto poly-(D,L lactide-co-glycolide) acid (PLGA) nanoparticles (Np). This releasing system increases the selectivity of tumor targeting by increasing photosensitizer uptake in tumor tissue. The objective of this study was to produce ZnPc loaded PLGA Np using a solvent emulsion evaporation method. The yield, size, size distribution, morphological characterization, encapsulation efficiency, and in vitro releasing studies were evaluated. PLGA Np were prepared with success, presenting yield of 80%, encapsulation efficiency of 65%. The morphology of the Np was examined by SEM and particles have spherical shape and smooth surface. Np have a size distribution between 228 and 390 nm with mean of 285 ± 5.1 nm. The small polydispersity index, 0.17, suggests that the size distribution is homogeneous. The in vitro releasing profile has a burst of 15%, following a low releasing rate. Initial burst occurred probably molecules in the outer layer of the Np. Drug releasing from PLGA Np is governed by diffusion and polymer erosion. PLGA Np is a promising sustained releasing system for PDT.

Financial support: FAPESP
Supervisor: Juliana Maldonado Marchetti

TF101 - STUDY OF LIPOSOMES STABILITY CONTAINING SOY PHOSPHATIDYLCHOLINE (PC) AND HYDROGENATED PC (PCH) WITH AND WITHOUT CHOLESTEROL BY TURBIDITY METHOD

THEREANA CRISTINA RIMÉRIO (IC)[1]; MARLUS CHORILLI (PG)[1]; ANSELMO GOMES DE OLIVEIRA (PQ)[1]; MARIA VIRGINIA SCARPA * (PQ)[1]

[1]FCFar-UNESP – scarpamv@fcfar.unesp.br

Introduction: Liposomes are structures composed by phospholipids as PC and PCH. Amongst the used methods to the liposomes stability, turbidity method is widely used. Objetive: The objective of this work was to study the liposomes stability containing PC or PCH with and without cholesterol by turbidity method. Methods: Liposomes had been stored at 30ºC during 90 days and periodically the readings of the absorbance by spectrophotometry in 410nm for verification of the possible turbidity alterations. Results and Conclusions: Increases in the turbidly with time occurred for PC liposomes. In the presence of CHOL righer turbidty was obtained probably reflecting the increase in the sixe of liposomas. For PCH liposomas the presence of CHOL did not affect the turbidity suggesting physical stability of the structures.

Financial Support: FAPESP and CAPES
Supervisor: Profa. Dra. Maria Virgínia Scarpa

TF102 - MACROSCOPICAL AND LEAF ANATOMY STUDY OF EUGENIA UNIFLORA L.

LUZIANA DE AZEVEDO FIRMINO(IC)[1]; ALAIZE DE P. MARTINS(PQ)[1]; MARIA CÉLIA R. D. DE AGUIAR(PQ)[1]; MARIA CLEIDE R. D. DE CARVALHO(PQ)[1].

[1] Universidade Federal do Rio grande do Norte.

Eugenia uniflora L. is a plant from the Myrtaceae family, commonly used for diarrheas treatment in the Northeast of Brazil. The purpose of this work was to study the morphology and anatomy of the leaves in routine analyses. Leaves were collected in Natal, RN. For the macroscopic study it was used magnifying glass. The microscopical one was carried out using the powder and through thin cuts of fresh leaves in the paradermic and cross sections, followed by photomicrographs in the optic microscope. The leaves showed oval and elliptic limb from 2 to 7.5 cm of length by 1 to 3.5 of width, acuminated apex, re-entrant basis, shining and glabrous ventral face, presenting translucent points and peninerve ribbing. Short petiole with 1 to 3mm of length. Lower and upper epidermis showed cells with irregular contour, hypoestomatic leaves with numberless paracytic stomata and non-glandular trichomes. Subepidermic glands and ring collenchyma. Numerous prismatic crystals and druses in the parenchyma. Medium ribbing with vascular bicollateral bundles. These characteristics are important to the correct pharmacognostical identification of this medicinal plant.

Supervisor: Alaize de P. Martins

TF103 - POLY-3-HYDROXYBUTYRATE (PHB) AND PHB/EUDRAGIT® E MICROPARTICLES CONTAINING PIROXICAM: PREPARATION AND IN VITRO DRUG RELEASE

GIOVANA CAROLINA BAZZO [1] (PG); ELENARA LEMOS-SENNA[2] (PQ); ALFREDO TIBÚRCIO NUNES PIRES [1](PQ).

[1] Grupo de Estudos em Materiais Poliméricos (POLIMAT), Departamento de Química.
[2] Laboratório de Farmacotécnica, Departamento de Ciências Farmacêuticas.
Universidade Federal de Santa Catarina, Florianópolis – SC.

PHB is a biocompatible polymer which has been used as a matrix to control the drug releasing in specific conditions. The aim of this work was to obtain microparticles of PHB or PHB/Eudragit® E blends containing piroxicam (PXC) and to evaluate the drug release. The microparticles were prepared by w/o emulsion solvent evaporation technique. Pure PHB or 80/20, 70/30 and 50/50 PHB/Eudragit E ratio blends were used to prepare the microparticles. The releasing studies were carried out in pH 1,2 medium at 37 °C. Spherical particles presenting a mean diameter around 40 μm were obtained for all formulations. The surface of PHB microparticles was rougher and more porous than those prepared from PHB/Eudragit E blends. The PXC encapsulation efficiency was 10% for PHB, but it was significantly increased as Eudragit ratio was increased in the blend. The PXC release was 100% from microparticles prepared from blends. The PHB microparticles released 70% and 90% of the drug after 60 and 240 min, respectively. These results could be explained by the porous structure of the microparticles and the solubility of Eudragit® E in acidic medium.

Supervisor: Prof. Dr. Alfredo Tibúrcio Nunes Pires

TF104 - VALIDATION OF A HPLC METHOD FOR RU-NO COMPLEXES RELEASED FROM TOPICAL FORMULATIONS

THAÍS TALLARICO PUPO (IC)*, DANIELLE C. ALMEIDA (PG)*, MARÍLIA G. SAUAIA (PG)**, ROBERTO S. DA SILVA (PQ) **, RENATA F. V. LOPEZ (PQ)*

* DCF, FCFRP/USP; ** DFQ, FCFRP/USP

The research in nitric oxide (NO) field has been considerable expanded, specially that involving the application of new NO drugs as a medicine. Ru-NO complexes are NO-donors agents that present promising characteristics. They could be applied topically to avoid some side effects that can occur when NO is used as a therapeutic agent. The object of this work was the validation of an HPLC method for simultaneous quantitative determination of *cis*-$[Ru(NO_2)(bpy)_2(4\text{-pic})]^{1+}$ and its aqueous complex (formed when NO is released) for further determination of the drug into and through the skin. Preliminary drug release experiment was also carried out using the developed method. Separation and quantitative determination was achieved using a Shim-pack CLC-ODS column 250mm x 4.6mm (5μm), a mobile phase constituted of methanol/phosphate buffer 0,01M pH7,0/TFA (37:63:0.5v/v) at a flow-rate of 1.0mL/min and UV detection at 290 nm. The method showed precision, accuracy, sensitivity and selectivity for all the analyses performed. A linear calibration curve was obtained over the concentration range of 0.05-25.0 μg/mL. The release rate of Ru-NO complex from hydroxyethilcellulose gel was high (19.48 $\mu g/cm^2/h$).

Financial support: FAPESP*
Supervisor: Profa. Dra. Renata F. V. Lopez

TF105 - CHARACTERIZATION OF DIFFERENT SAMPLES OF QUERCETIN IN SOLID-STATE

MARIANA PETRY(IC)[1]; GREICE STEFANI BORGHETTI(PG)[2]; IGUATINÂ DE MELLO COSTA(PG)[2]; PEDRO ROS PETROVICK(PQ)[2]; VALQUIRIA LINCK BASSANI(PQ)[2]

[1] Faculdade de Farmácia–Universidade Federal do Rio Grande do Sul;[2] Programa de Pós-Graduação em Ciências Farmacêuticas-Universidade Federal do Rio Grande do Sul.

The present work was designed to compare two commercial samples of quercetin, one presenting pharmaceutical grade (QPG) and the other one pro-analise grade (QPA) by means of different techniques. The HPLC results showed a very similar retention time, although the peak area of QPG was smaller than QPA. Both samples presented UV and IV spectra data in accordance with the spectra related in the literature. Distinct onset temperature and variation of enthalpy associated to the loss of water and melting point were observed in the DSC response. The aqueous solubility value obtained to QPA sample was lower than QPG. Both samples presented the same XRPD pattern, but different particle morphology could explain these different characteristics. In conclusion, this first report on physical and chromatographic characterization of quercetin shows a variation of its properties following its origin.

Financial Support: Brazilian Government (CAPES/CNPq/FAPERGS)
Supervisor: Profa. Dra Valquiria Linck Bassani – valqui@farmacia.ufrgs.br
Prof. Dr. Pedro Ros Petrovick - prpetrovick@farmacia.ufrgs.br

TF106 - HYDROXYAPATITE ENCAPSULATION IN CHITOSAN SPHERES

KELLE CRISTINA GARCIA (PG)[1];MÔNICA MELO [2],ELIANA RIGO[2];ANSELMO ORTEGA BOSCHI [2];RAUL CÉSAR EVANGELISTA[1]

[1] Faculdade de Ciências Farmacêuticas–UNESP–Araraquara–SP
[2] DEMA/Biolab, Universidade Federal de São Carlos-UFSCar

Natural bone is composed by calcium phosphates, mainly hydroxyapatite (HA) and colagen fibers. So that, combination of properties of different materials may present a great potencial to biomedical application. The calcium phosphate use, expecially HA, as biomaterial is very diffused, moreover, natural polymers have been researched due to its abundance in nature as well as its facility of obtention. Among these polymers, chitosan presents great potencial to application as biomaterial. Combination of chitosan with hydroxyapatite in biodegradable spheres structure seems to be an interessant rout to promote local bone regeneration. In the present work spheres of chitosan and HA were prepared and characterized by scanning eletronic microscopy (SEM) and infrared spectroscopy (IV). HA particles were well soaked and uniformly distributed in chitosan spheres.

Adiviser - Raul César Evangelista

TF107 - INFLUENCE OF PROCESS PARAMETERS ON GRANULE SIZE PREPARED BY HOT-MELT COATING USING THE FACTORIAL DESIGN TOOL

GIOVANNA BONFANTE BORINI (PG)[1,2]; TONI CARVALHO (PQ)[1]; LUIS ALEXANDRE PEDRO DE FREITAS (PQ)[1]

[1]Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP; [2]docente do curso de Farmácia Industrial-Universidade de Uberaba-MG

Objective: To study the influence of process parameters on granule size prepared by hot-melt coating using a factorial design tool. Methodology: Hot-melt coating experiments were performed using a top-spray fluidized bed equipment. The substrate was particles ranging from 0.7 to 1.0mm in size. The chosen factors were nozzle distance, wax rate and atomizing air pressure. After each coating experiment, particle size distribution was determined. To characterize granule size the mean diameter, the percentage of particles between 2 and 2.8mm and the percentage of particles higher than 2.8mm were calculated. Results: During the coating experiments particle agglomeration has occurred. Statistical analysis showed that only the wax rate and atomizing air pressure effects were significant on granule size. Conclusions: Factorial design tool was useful to understand the influence of chosen parameters on granule size. Particles agglomeration has occurred despite of particle coating showing that to coat small particles and reduce agglomeration it is necessary specific conditions.

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Adviser: Prof. Dr. Luis Alexandre Pedro de Freitas

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Toxicologia / *Toxicology* (TO)

TO001-THE INFLUENCE OF TOBACCO ON METHEMOGLOBIN VALUES

THIAGO M. CAMARGO(IC)[1]; VIRGÍNIA S. NAZATO(PQ)[1]; DOUGLAS F. SILVA (PQ)[1], EDILMA M. A. VASCONCELOS(PQ)[1]; RENATA DE LIMA(PQ)[1] ; SARA J. OLIVEIRA(PQ)[1]; YOKO OSHIMA-FRANCO(PQ)[1]

[(1)]University of Sorocaba (UNISO), Sorocaba, SP, Brazil.

Introduction: Methemoglobin is formed when iron of the heme moiety in the hemoglobin molecule becomes oxidized from the ferrous to the ferric state. Exposure to some chemicals can increase methemoglobin levels and the smokers are continually exposed to pollutant as result from cigarette combustion. Objective: To compare the methemoglobinemie in UNISO' students, smokers (test) with non smokers (control), after approval by Committee for Ethics in Clinical Research (UNISO) and obtained the Informed Consent. Methodology: EDTA-blood (5 mL) was taken from each of 36 volunteers and methemoglobin (Hegesh method) was immediately quantified. The results (% of total hemoglobin) ± S.E.M. with $p < 0.05$ (*t*-Student test) were considered significant. Results: Control group (n= 22) had 2.5 % ± 0.4, whereas test (n=14) had 6.8 % ± 1.2, significantly different one each other. Discussion and Conclusion: Considering that reference value is 1.5% an increased value was found for control that can reflect an indirect exposure to tobacco. However, smokers clearly had accumulated methemoglobin. Further studies will show whether these results are or not transitory.

Supported by PROBIC
Advisor´s name: Yoko Oshima-Franco

TO002-DETERMINATION OF OLIGOELEMENTS IN HYDRO-ETHANOLIC PROPOLIS EXTRACTS USING ATOMIC ABSORPTION SPECTROPHOTOMETRY (AAS) AND GRAPHITE FURNACE (AAS).

EFIGÊNIA QUEIROZ DE SANTANA[1](PQ); ALAOR APARECIDO ALMEIDA[2](PQ); WILMA DE GRAVA KEMPINAS[1](PQ); CHUNG MAN CHIN[3](PQ).

[1]Universidade do Sagrado Coração, Bauru; [2]UNESP, Botucatu; [3]UNESP, Araraquara

INTRODUCTION: Propolis is a resinous substance collected by honeybees from leaf buds and cracks in the bark of various plants. It is composed of 50% resin, 30% wax, 10% essential oils, 5% pollen and 5% various organic compounds. Most propolis preparations are based on ethanol extracts. In this sense, propolis has been used extensively in medicine for many years, and there is substantial evidence indicating that propolis has antiseptic, antifungal, antibacterial, antiviral, anti-inflammatory and antioxidant properties. OBJECTIVE: The objective of this work was to determine the concentration of oligoelements (Mn, Cu, Zn and Cr) in 17 samples of hydro-ethanol extracts of propolis. METHODS: The mineralization of the extracts was performed in a special microwave and the concentrations of oligoelements in the extracts were determined using atomic absorption spectrophotometry (AAS) and graphite furnace AAS. RESULTS AND CONCLUSION: Zinc was detected in all the samples and chromium in 82% of the samples. It can be concluded that the presence of oligoelements in these extracts corroborates its use in alternative medicine.

Financial Support: CEATOX

TO003-STEREOSELECTIVE DETERMINATION OF THE MAJOR IBUPROFEN METABOLITES IN HUMAN URINE BY SPME AND HPLC: OPTIMIZATION OF THE EXTRACTION CONDITIONS

ANDERSON RODRIGO MORAES DE OLIVEIRA(PG)[1]; FERNANDO JOSÉ MALAGUEÑO DE SANTANA(PG)[1]; PIERINA SUELI BONATO(PQ)[1]

[(1)]Universidade de São Paulo, FCFRP-USP, Brazil

Solid-phase microextraction (SPME) is an extraction technique which integrates the steps of sampling, extraction and concentration of the analyte. The aim of this work is to show that off-line SPME and HPLC is a useful tool for the direct, rapid and simultaneous stereoselective determination of the two major ibuprofen metabolites in human urine. In this work, several parameters were investigated such as fiber coating, extraction time and temperature, pH, ionic strength, desorption time and carryover. Analyses were conducted using a Shimadzu liquid chromatograph. Data were collected using a Chromatopak integrator. The resolution of the 2-OHIbu enantiomers and COOHIbu stereoisomers was performed at 22 ºC on a Chiralpak AS column using hexane-isopropanol (95:5, v/v) + 0.05% TFA as mobile phase, at a flow-rate of 1.2 mL/min. The extraction optimization showed that the best condition for the extraction was: extraction for 30 min after the addition of 20% NaCl and 1 mL 1 M phosphate buffer, pH 3.8 at 25ºC, using a CW-TPR fiber. Methanol was used as desorption solvent for 3 min. No carryover was observed between the extractions.

Financial Support: CNPq, Fapesp
Supervisor: Pierina Sueli Bonato

TO004-METHOD DEVELOPMENT AND VALIDATION FOR THE DETERMINATION OF TETRACYCLINES BY CAPILLARY ELECTROPHORESIS.

MÓNICA CECILIA VARGAS MAMANI[1]; SUSANNE RATH[1]; GUSTAVO TAYAR PERES[2]; JAIME AMAYA FARFÁN[2]; FELIX GUILLERMO REYES REYES[2].

[(1)]Institute of Chemistry, Department of Analytical Chemistry, State University of Campinas, SP, Brazil. [(2)]Department of Food Science, State University of Campinas, SP, Brazil.

Introduction: Tetracycline (TC), chlortetracycline (CTC), oxytetracycline (OTC) and doxycycline (DXC) are widely used in human and animals and vegetables.
Objective: an optimized CE method for the analysis of TC, CTC, OTC and DXC was developed.
Methods: A fractional factorial design (2^{4-1}) was carried out to distinguish the significant parameters (pH, buffer concentration and temperature) affecting the TC separation.
Results: The optimal separation conditions were achieved using: fused-silica capillary: *l*(e.l) = 52cm, L(t.l)= 60.6cm, 50mm I.D.; $Na_2 CO_3$ 50mM - EDTA 1mM, pH 10; 13 kV and 23°C. The method was *in-house* validated for TC in drugs by the following parameters: linear range (25 – 500 mg mL^{-1}), linearity (0.999), sensitivity (0,6032±0,00432), intra-assay precision (RSD< 3%). The accuracy of the method was evaluated through comparison of results obtained by the US pharmacopoeia official HPLC-method.
Conclusion: the proposed method shown adequate for use the analysis for the determination of TC, CTC, OTC and DXC.

Financial support: CNPq, Fapesp.
Supervisor: Susanne Rath.

TO005-EVALUATION OF THE GENOTOXIC POTENTIAL OF ACUTE, SUBACUTE AND SUBCHRONIC TREATMENT WITH A GEL CONTAINING PROPOLIS FOR BURNS

ALINE RAFAELA DA SILVA RODRIGUES(IC)[1], JULIANA MARQUES SENEDESE(PG)[1], ANDRESA A. BERRETTA(PG)[2,3], JULIANA MALDONATO MARCHETTI(PQ)[3], DENISE CRISPIM TAVARES(PQ)[1]

[1]Universidade de Franca, SP, [2]Apis Flora Industrial e Comercial Ltda., Ribeirão Preto, SP, [3]FCFRP-USP, Ribeirão Preto, SP.

INTRODUCTION: Propolis is elaborated by bees from plant resins and exudates, and has a large scarring activity. OBJECTIVE: The present study evaluated the genotoxic potential of a propolis gel for burns based on the analysis of micronuclei in Wistar rat peripheral blood. METHODOLOGY: The animals were injured on the back and then submitted to acute, subacute and subchronic treatment consisting of daily dermal applications of gels containing different concentrations of propolis (1.2, 2.4 and 3.6%). Peripheral blood smears were obtained 24 h, 7 days and 30 days after application of the gels to the dorsal lesions. RESULTS: The results showed no increase in the frequency of micronuclei in animals treated with gel containing different concentrations of propolis compared to the negative control for the three treatment times. CONCLUSION: At the experimentals condition, it has become possible to suggest that the gel with propolis did not show a clastogenic effect.

Financial Support: FAPESP, UNIFRAN & APIS FLORA COMERCIAL E INDUSTRIAL Ltda.
Advisor´s Name: Profa. Dra. Denise Crispim Tavares

TO006-OPTIMIZATION OF TWO-PHASE LIQUID-PHASE MICROEXTRACTION OF MIRTAZAPINE FROM HUMAN PLASMA

FERNANDO JOSÉ MALAGUEÑO DE SANTANA (PG)[1]; ANDERSON RODRIGO MORAES DE OLIVEIRA (PG)[1]; PIERINA SUELI BONATO (PQ)[1]

[1]Universidade de São Paulo, FCFRP-SP, Brazil

LPME (liquid phase microextraction) is a simple, inexpensive and efficient preconcentration and clean-up method based on porous polypropylene hollow fibre membrane. It has been used for sample pre-treatment prior chromatography and electrophoresis analyses. In this work, LPME was developed for the extraction of the antidepressant mirtazapine from human plasma. The effects of different parameters influencing the efficiency of extraction were described and optimized (extraction solvent, extraction time, acceptor-to-donor volume ration, sample dilution, organic modifier, extraction pH, salt effect, multiple extractions). Under optimized conditions, mirtazapine was extracted with 22 μL toluene from 0.7 ml of plasma previously diluted with 3.1 ml deionized water and alkalinized with 0.15 ml 10 M NaOH. Mefloquine was used as internal standard. The chromatographic analysis was carried out through chiral HPLC using a Chiralpak AD column and hexane-ethanol (98:2, v/v) plus 0.1% diethylamine as mobile phase, at a flow rate of 1.5 ml/min. Detection was carried out at 292 nm. LPME demonstrated a lower organic solvent consume, as well as, higher selectivity and sensibility for mirtazapine extraction.

Financial Support: CNPq, Fapesp
Supervisor: Pierina Sueli Bonato

TO007- SUBCRONIC PRE-CLINICAL TOXICITY OF *FOENICULUM VULGARE* MILL. IN SACHETS.

ALESSANDRA CAMILO DA SILVEIRA CASTELO BRANCO (PG)[1]; JOSUÉ DO AMARAL RAMALHO (IC)[1]; JADSON GOMES DANTAS (IC)[1]; THAYSE VIANA PALAMARO (IC)[1]; NELSON LACERDA JÚNIOR (IC)[1]; HOSANA BANDEIRA SANTOS (PG)[1]; MARGARETH DE FÁTIMA FORMIGA MELO DINIZ (PQ)[1].

[1]Universidade Federal da Paraíba

Introduction: Sachets correspond to 80% of the teas sold in the world. Objective: Evaluate the toxicity of *Foeniculum vulgare* Mill in sachets, according to Oga (2003). Methodology: We tested the macerated and dried ethanol extract. In the subchronic test (28 days), wistar mice were divided in 4 groups (n=20), being a control and the others received doses of 8,5 mg/kg (usual), 25,5 mg/kg (3 times) and 76,5 mg/kg (9 times), orally. The parameters assessment were water/ration consumption, temperature, glucose, ponderal evolution, behaviour alterations, besides biochemicals and hematologycals. Results and conclusion: In the treated animals with the highest dose, leucocytosis was observed in males, related to inflammatory processes; and in the females, the neutrophilia could be attributed to necroses, inflammations and metabolic disturbances. The increase of the lactic desidrogenase, a hepatic enzyme, observed in both sexes for all the doses, may be related to hepatotoxicity. Histopatologics studies are in development for better conclusions.

Financial Support: CNPq
Supervisor: Margareth F. F. Melo Diniz

TO008-EFFECTS ON THE DAPSONE INDUCED METHEMOGLOBINEMIA BY N-ACETYLCYSTEINE

MAURICIO H MELLO(PG)[1], NATÁLIA V MORAES(IC)[1], WILSON R MALFARÁ(PQ)[1], REGINA H C QUEIROZ (PQ)[1].

[(1)]FCFRP–USP

Introduction: Dapsone (DDS) is useful in various pathological conditions as infectious diseases or inflammatory conditions. The main adverse effect associated to DDS exposure is a high level methemoglobinemia (MHb). Two hydroxylamine (NOH) metabolites are responsible by this effect, which occurs by an oxidation of the hemoglobin's iron. N-Acetylcysteine (NAC) is a mucolitic agent, used in paracetamol intoxication, for its capacity of generate glutathione (GSH), a powerful antioxidant.
Objective: Evaluate the effects of NAC on the DDS induced MHb.
Methodology: 6 groups (n=8) of Wistar male rats were submitted to an intraperitoneal treatment of: DDS 40mg/kg, NAC 75mg/kg, DDS+NAC together, DDS+NAC 1h before, DMSO and saline. MHb was evaluated by cianomethemoglobin method and GSH concentration was confirmed by spectrophotometer.
Results: NAC increased to double or triple the levels of DDS induced MHb, and turned to normal the GSH level.
Conclusions: When sulphonamides are metabolized, beyond the NOH, N-oxides derivatives are formed also, which can be reduced by GSH to the NOH metabolite. When GSH is provided to the cells that are under the action of DDS, the levels of the metabolites NOH can be increased, leading to a rise of MHb levels.

Financial Support: FAPESP
Supervisor: Regina Helena Costa Queiroz

TO009- ISOLATION AND BIOCHEMICAL CARACTERIZATION OF A TOXIN FROM *TITYUS SERRULATUS* SCORPION VENOM WITH ACTION ON THE COMPLEMENT SYSTEM

DANIELA T. BERTAZZI (PG)[1]; ANTONIO F. Q. MARONGIO (PG)[1]; SUELY V. SAMPAIO (PQ)[2]; ANA E. C. S. AZZOLINI (PQ)[1]; ANA ISABEL DE ASSIS-PANDOCHI (PQ)[1]; ELIANE C. ARANTES (PQ)[1]

(1) Depto de Física e Química; (2) Depto Análises Clínicas, Toxicológicas e Bromatológicas - FCFRP– USP.

I*ntroduction:* The complement system (CS) activation by animal venoms has been described and resulted in important discoveries. The aim this present study was to isolate the toxin from *T. serrulatus* venom (TsV) with action on the CS and to evaluate its effects using *in vitro* assays. *Methods:* The toxin was purified from TsV by chromatography on CM-cellulose-52 followed by RP-HPLC of lyophilized fraction I. The effect of toxin on CS was evaluated using *in vitro* haemolytic assays, immunoelectrophoresis and neutrophil migration. *Results:* The isolated toxin is a single polypeptide chain, corresponding to an approximate *Mr* of 10,000. This protein induced a concentration-dependent reduction in lytic activity of the classical and alternative pathways of CS, neutrophil chemotaxis and alterations in C3 and factor B electrophoretic mobility.*Conclusion:* Our results show that the toxin activates the CS, leading to factor B and C3 cleavage, reduction of serum lytic activity and generation of complement chemotactic factors.

Supported: FAPESP
Supervisor: Dra.Eliane C. Arantes

TO010- COMPARATIVE CYTOTOXICITY OF DITERPENES ISOLATED FROM *XYLOPIA LANGSDORFFIANA* ON HUMAN LEUKAEMIA CELLS

MARIANNA VIEIRA BARRETO SILVA(PG)[1]; MARISTELLA CONTE ANAZETTI(PG)[2]; JOSEAN FECHINE TAVARES(PG)[1]; MARCELO SOBRAL DA SILVA(PQ)[1]; MARGARETH DE FÁTIMA FORMIGA MELO DINIZ(PQ)[1]; PATRÍCIA SILVA MELO(PQ)[2]; MARCELA HAUN(PQ)[2]

(1)Universidade Federal da Paraíba; (2)Universidade Estadual de Campinas

Introduction: *Xylopia langsdorffiana* (Annonaceae) is commonly known as "pimenteira-da-terra". A phytochemical study with the stem bark of *X. langsdorffiana* led to the isolation of labda 8 (17),12*E*,14-trien-18-oic acid, 7-ß-acetoxytrachyloban-18-oic acid and ent-atisane-7-ß,16-α diol. Other diterpenes of type labdane, atisane and trachylobane, isolated of different species showed cytotoxic and antitumoral effect in several cell lines. Objective: Evaluate the antitumoral activity of these diterpenes on leukaemia cell lines (HL60, U937, K562). Methodology: Two endpoints were used for evaluate the cytotoxic activity of compounds in study: MTT dye reduction and phosphatase activity. Results and conclusion: Atisane was the most toxic compound in all cells (IC_{50} values ranging from 40μM on K562 for MTT reduction to 175 μM on HL60 cells) and trachylobane showed an intermediate cytotoxity (IC_{50} values of 110μM, 160μM and 200μM on HL60, U937 and K562 cells, respectivelly). Thus these diterpenes merit further studies as antitumoral agents.

Finnancial Support: CNPq
Supervisor: Margareth F. F. Melo Diniz

TO011- ROSMARINIC ACID (RA) FROM *C. VERBENACEA* ON FUNCIONAL ACTIONS OF *B. JARARACUSSU* ENZYMES

LORANE I. S. HAGE(PG)[1]; FÁBIO K. TICLI(PG)[1]; PAULO S. PEREIRA(PQ)[2]; ÂNGELO J. MAGRO(PG)[3]; MARCOS R. M. FONTES(PQ)[3]; MAURÍCIO V. MAZZI(PG)[1]; CAROLINA D. SANT'ANA(PG)[1]; ADÉLIA C. O. CINTRA(PQ)[1]; JOÃO J. FRANCO(PQ)[1]1; ANDREIMAR M. SOARES(PQ)[1]; SUELY V. SAMPAIO(PQ)[1]

[1]Dep. An. Clínicas, Toxicológicas e Bromatológicas, FCFRP, USP, Rib. Preto-SP; [2]UNAERP, Rib. Preto-SP; [3]UNESP, Botucatu-SP

Many plants are used in traditional medicine against various effects induced by snakebite. The objective of this project is study RA biological properties in enzymes from *B. jararacussu* venom. RA and enzymes were isolated by chromatography. RA inhibited the edema and myotoxic activity induced by the basic PLA_2 bothropstoxin I e II (BthTX). It was less efficient to inhibit the PLA_2 activity of BthTX-II and, still less, the PLA_2 and edema-inducing activities of the acidic BthA-I-PLA_2, showing a higher inhibitory activity upon basic PLA_2s. RA was less efficient to inhibit the hemorrhagic and fibrinogenolytic activities of BjussuMP-I metalloprotease, and coagulation activity of BjussuSP-I trombin-like. A model for the interaction of RA with BthTX-I was proposed. It is interesting to speculate that RA, or a derivate, may prove useful in the treatment of snake bite victims and in the treatment of many human diseases in which PLA_2 enzymes have been implicated.

Financial Support: FAPESP and CNPq
Supervisor: Suely V. Sampaio

TO012- STUDY OF POSSIBLE INTERACTIONS OF A *GINKGO BILOBA* EXTRACT: BIOAVAILABILITY OF A RADIOPHARMACEUTICAL AND MORPHOMETRY OF ORGANS FROM THE RATS

SILVANA RAMOS MORENO (PG)[12] JORGE JOSE CARVALHO (PQ)[2]; ANA LÚCIA NASCIMENTO (PG)[2]; EMELY ROCHA (PQ)[2]; MARIO BERNARDO-FILHO (PQ)[2]; LUIZ QUERINO CALDAS (PQ)[1]

[1]Universidade Federal Fluminense, Niterói, RJ. [2]Universidade do Estado do Rio de Janeiro, RJ, Brasil.

Introduction: The health sciences have the radiopharmaceuticals as important compounds used for the diagnosis and treatment. Many substances have been reported to affect the bioavailability of radiopharmaceuticals. *Ginkgo Biloba* extract (EGb) is a phytoterapic that has several effects as, vasodilator and anti-coagulant actions. Objective: We evaluated the effect of an EGb on the bioavailability of the sodium pertechnetate ($^{99m}TcO^-_4Na$) and on the morphometry of the organs from rats. Methods: The animals were treated with EGb and the $^{99m}TcO^-_4Na$ was injected. The organs were counted and the percentages of radioactivity per gram of tissue calculated. Results: The EGb altered the bioavailability of the $^{99m}TcO^-_4Na$ in the kidneys, liver and duodenum ($P<0.05$). Morphometrical alterations on kidney, liver and duodenum due to treatment were significant ($P<0.05$). Conclusion: The EGb could generate metabolites capable to promote changes in the organs and to alter the biodistribution of the $^{99m}TcO^-_4Na$ in the animals.

Financial Support: CAPES, UFF, UERJ
Supervisor: Luiz Querino de Araújo Caldas

TO013-HPLC METHOD FOR DETERMINATION OF ISONIAZID AND ITS METABOLITES IN SERUM: APPLICATION TO PHARMACOKINETICS STUDIES

ROSÂNGELA GONÇALVES PECCININI MACHADO(PQ)[1] ;HELEN MARIANA BALDAN(PG)[1]; HELENE JORGE DE ROSA(PG)[1];VALDECIR FARIAS XIMENES(PQ)[1];IGUATEMY LOURENÇO BRUNETTI(PQ)[1]

(1)Faculdade de Ciências Farmacêuticas/UNESP-Araraquara

We present a method for the analysis of isoniazid(INH) and its metabolites acetylisoniazid(AcINH), acetylhidrazine(AcHz) and hydrazine(Hz) in serum by HPLC.The method was applied for the investigation of kinetic disposition of oral multiple doses of isoniazid(100mg/Kg/day) administered to rats(Wistar,n=50) by 21 days.Serial blood samples were collected in the 24h interval.The biological samples were desproteinized with trichloroacetic acid(10%) and the acetyl metabolites were hydrolised with HCl for 1h.INH and Hz were derivatized with cinnamaldehyde(1% in methanol).The supernatant was analyzed by HPLC using a RP-18 column and a UV detector set at 340nm.The limits of quantitation were 40ng/mL and 50ng/mL for Hz and INH, respectively.The intra and inter-assay precision(CV) were less than 10%.The pharmacokinetics parameters found for INH were:Cmax–79,4ug/ml;tmax-0.5h;$t_{1/2}$-4h;AUC^{0-24}-207ug/ml.h;Cl/f-483ml/h.Kg;Vd/f-2,7L/Kg.The AUC^{0-24} for AcINH,AcHz and Hz were:152,3ug/ml.h;36,5ug/ml.h;2,9ug/ml.h,respectively.The method can be used for quantify INH and its metabolites in serum and suitable for pharmacokinetic studies.

Financial support:CAPES/CNPQ

TO014-METAL QUANTIFICATION IN WISTAR RATS PLASMA TREATED WITH NICOTINE BY SRTXRF

GUILHERME DE MAURO FAVERÃO[1] (IC); ANNA LAURA BECHARA JACOB[1] (IC); MARIA CAROLINA SEMPRINI[1] (IC); GABRIEL H. SATO[1] (IC); BRUNO L. P.BATISTA[1] (IC).

[1] FCFRP – USP.

Introduction: According to WHO about 30% of adults male world population smoke and this custom is the reason for 10% of deaths worldwide. Many studies prove the connection of illnesses with nicotine or its metabolites. Objective: Determination of inorganic elements concentration in rat plasma treated with doxiciclin, followed by nicotine. Methods: Wistar rats were treated with doxiciclin by gavage administration and urethane, intraperitoneal way. Nicotine was injected through femoral vein in dosages 0, 0.6 e 2.0 mmol/kg. Heart frequency and average blood pressure were controlled. Results: Calcium, potassium, vanadium, titanium and iron concentrations presented differences regarding the control group. Discussion: The method sensibility was appropriate for the elements analysis. Potassium plasma concentration was directly proportional to nicotine's dose injected; calcium concentration varies under this influence through the cardiovascular system; titanium concentration varies because it belongs to nicotine's metabolic process; iron concentration is variable according to the smoker's ventilation. Conclusion: Iron, vanadium and titanium presented significant difference regarding the control group.

Supervisor: Orghêda Zucchi

TO015- EFFECT OF FRACTION II-III FROM *TITYUS SERRULATUS* SCORPION VENOM ON LYTIC ACTIVITY OF THE COMPLEMENT SYSTEM (CS)

KELLY DE PAULA SOUZA (IC) [1]; DANIELA TRINCA BERTAZZI (PG)[1], ANA ISABEL DE ASSIS-PANDOCHI (PQ) [1]; SUELY VILELA SAMPAIO (PQ)[2]; ELIANE CANDIANI ARANTES (PQ) [1]

(1) Depto de Física e Química and (2) Depto de Análises Clínicas, Toxicológicas e Bromatológicas [2] - Faculdade de Ciências Farmacêuticas de Ribeirão Preto – USP, Ribeirão Preto- SP, Brazil.

Introduction: The scorpion *Tityus serrulatus* is considered one of the most dangerous species in Brazil. Its venom evokes an inflammatory response but the exact mechanism of this effect is still unknown. *Objetive:* The aim of the present work is to investigate the action of fraction II-III from *Tityus serrulatus* venom (TsV) on the CS, using *in vitro* assay. *Methods:* TsV was extracted and chromatographed as previously described (Toxicon 27, 907-916). Complement consumption by the fraction II-III was evaluated using *in vitro* haemolytic assays. *Results: In vitro* fraction II-III induces a concentration and time-dependent reduction in hemolytic activity of the classical/lectin pathway of complement, with a IC_{50} (sample concentration inhibiting 50% of the lytic activity) of 44,05 µg. *Conclusion:* Our preliminary results show that the fraction II-III has an anticomplemtary effect on the CS indicating that has an important role in the inflammatore response observed in scorpion envenomation.

Supervisor: Dra. Eliane C. Arantes

TO016- *SYNADENIUM UMBELLATUM* INDUCES GENOTOXICITY IN MICE

NÚBIA CRISTIANA DE CASTRO(IC); MARIZE CAMPOS VALADARES(PQ)

Faculdade de Farmácia; Universidade Federal de Goiás

Introduction: *Synadenium umbellatum*, (SU) a euphorbiacea, has been widely used in Brazil as an anitumoral agent. Paradoxically, works in the literature have been attributed to euphorbiaceas an effect modulator of carcinogenesis.
Objective: this work was designed to investigate the genotoxic potential of the SU extract.
Methods: the mice were assigned in 5 groups: control mice (non-exposed); exposed mice to 10, 20 or 50 mg/kg of the ethanolic extract of the SU, for 24 h p.o.; and a group of mice exposed to the cyclophosphamide (CY, as a + control). 24 h after the treatments, the mice were sacrificed for the bone marrow cell micronucleus assay.
Results:CY induced an increase in micronuclei frequency. Mice exposed to the SU also showed an increase in the micronucleus in a dose-dependent manner. The mice exposed to 20 and 50 mg/kg of SU increased 110% and 120% the incidence of micronuclei, respectively, when compared to control. These values were similar to those found with the CY group.
Conclusion: chromosomal mutation is an important event in carcinogenesis. The micronucleus assays have emerged as one of the preferred methods for assessing chromosome damage. In our study SU was found to induce chromosomal damage in mice in a dose-dependent manner suggesting its potential as a mutagenic agent.

Supervisor: Marize Campos Valadares

TO017-ASSAY OF PHENOTHIAZINES COMPOUNDS IN URINE WITH MODIFIED CHEN'S TEST.

AMANDA VANSAN MARANGON (IC)[1]; RENATA CABRERA DE OLIVEIRA(IC)[1] ; MIGUEL MACHINSKI JUNIOR(PQ)[1]

[1] Universidade Estadual de Maringá UEM. DAC. Maringá – PR.

Introduction Phenothiazines are a major class of drugs used as neuroleptics in the treatment of schizophrenia and other psychotic illness; they are also used as sedatives, antihistaminics, antiemetics and anaesthetics. Massive overdose of phenothiazines may cause coma, miosis, and respiratory depression, among other disorders. Objective The objective is to utilized a simple and viable methodology with acceptable specificity and sensibility for the identification of phenothiazines in urine. Methodology In a drop of urine was added a drop of hydrochloric acid followed by a drop of 5 % copper sulphate ($CuSO_4 \cdot 5H_2O$). Color alterations denote presence of phenothiazines compounds. In the specificity tests were used 71 different drugs in search of possible cross-reactivity. Results The detection limits for Promethazine, Levomepromazine, and Chlorpromazine were 0,150 mg/mL, 0,100 mg/mL and 0,075 mg/mL. A brown, green and orange color indicates the presence of a Promethazine, Levomepromazine and Chlorpromazine, respectively. There were no cross reactivity with others drugs. Conclusion This procedure can be used with screening test in lab routine due to the simplicity, specificity and sensibility.

Supervisor: Miguel Machinski Junior

TO018-EVALUATION OF BOTRYOSPHAERAN MUTAGENICITY AND ANTIMUTAGENICITY USING MOUSE BONE MARROW CELLS

JULIANA M. SERPELONI (IC); CAROLINA C. B. O. MIRANDA (PG); ILCE MARA. S. CÓLUS (PQ); EVELINE A. I. FONSECA (IC); ROBERT F.H. DEKKER (PQ); ANELI M. BARBOSA (PQ);

Universidade Estadual de Londrina

Botryosphaeran, a new described fungal exopolysaccharide (EPS) was isolated from the extracellular culture fluid of *Botryosphaeria rhodina,* and evaluated by the micronucleous test for mutagenic and antimutagenic activities. For the mutagenic test 4 groups of mice received *via gavage* once a day, during 15 days, 0.3 ml of saline (negative control) or botryosphaeran solutions (0.75, 1.5 and 3.0 g/L). For the antimutagenicity test one group received 0.3 ml of saline, while another 0.3 ml of 0.75 g/L botryosphaeran solution during 15 days. In parallel with the last treatment, all animals received 0.3 ml of cyclophosphamide via intraperitoneal injection, and were slaughtered 30 hours later. The marrow bone cells were obtained from the femurs, and 2,000 cells were analysed from each animal. The results were submitted to ANOVA and Tukey statistical analysis, and indicated that the concentrations of botryosphaeran evaluated did not show mutagenic activity. Botryosphaeran solution (0.75g/L) decreased the frequency of micronucleous, which are encouraging for others tests that may promote new applications for this EPS in the pharmaceutical area.

Financial support: Fundação Araucária/UEL
Supervisor: Ilce Mara S. Cóllus

TO019-DNA DAMAGE IN BLOOD AND BRAIN CELLS OF BETA-CARBOLINE ALKALOIDS IN MICE

DAIANE LOSS VIEIRA[1] (IC); CAMILE RORIG[1] (IC); MARÍLIA PAULA DAL ALBA[1] (IC); DINARA JAQUELINE MOURA[2] (PG); JOÃO ANTONIO PÊGAS HENRIQUES[2] (PQ); JANE MARLEI BOEIRA[13] (PQ)

(1) URI, Erechim, RS; (2) UFRGS, RS.

The beta-carboline alkaloids are presents in plants and have been of interest due to their psychotropic properties. Their pharmacological activities have been attributed to the ability intercalate DNA. The aim of this study was investigate the DNA damage in blood and brain cells of mice treated with harman, harmine, harmaline and harmol. For this, we used the Comet assay. Mice were treated with a single i.p. dose of vehicle, MMS (positive control) or alkaloids 2,5 and 5,0mg/Kg doses. Animals were sacrificed by decapitation 3 or 24 h after treatment and blood and brain samples were collected from each animal to slides preparation. After electrophoresis the comets were scored and the data were evaluated by Student's t-test. Only harmine showed significant damage index (DI) and frequency (DF) after 3 and 24 h treatment in blood cells. Harmaline and harmol showed this only 24h, while harman increased them just 3hs test. In the brain, harman, harmine and harmaline showed DNA damage increased when compared with harmol, in both tests. These results suggested that harmine showed more capacity in to induce DNA damage in blood, while only harmol did not show this in the brain. Supported: FAPERGS; URI

Supervisor: Jane Marlei Boeira

TO020-EFFECT OF ORALLY ADMINISTRATED RESVERATROL ON THE RENAL FUNCTION OF RATS TREATED WITH CISPLATIN

CÁTIA LIRA DO AMARAL(PG)[1], HELOÍSA DELLA COLETTA FRANCESCATO(PG)[2]; JOANA D'ARC CASTANIA DARIN(PQ)[1]; MARIA DE LOURDES PIRES BIANCHI(PQ)[1]

(1)Faculdade de Ciências Farmacêuticas de Ribeirão Preto – USP; (2) Faculdade de Medicina de Ribeirão Preto – USP

Cisplatin (cDDP) is used on treatment of malignant tumor, but it frequently induces nephrotoxicity. Reactive oxygen specimens are associated with renal failure caused by cDDP that can be preventing by the administration of antioxidants. Resveratrol (Res), which is found in grapes and red wine, could function as antioxidant and reduce renal injure of cDDP. The aim of this work were analyzed whether Res (25, 50 and 100 mg/Kg, single gavage) has protective effect on cDDP-induced nephrotoxicity in male Wistar rats. After 5 days, they were sacrificed and the group that received only cDDP (5mg/Kg, single i.p.) showed renal failure observed by increased serum creatinine and decreased clearance creatinine ($p < 0.05$). The rise of urinary volume and lost of body weight were also observed in this group. However, the groups treated with Res plus cDDP did not differ of cDDP group on parameters cited above. These data show that resveratrol, when administrated by single gavage, could not prevent the kidney damage induced by administration of cisplatin *in vivo*.

Financial support: CNPq
Supervisor: Maria de Lourdes Pires Bianchi

TO021- ACUTE TOXICITY ASSAY OF THE COMPLEX ION $[RU(NH3)4(C_2O_4)]^+$

CARLOS EDUARDO SILVA BARBOSA[1] (PG); SANDRA F. CALIXTO[2] (IC); YARA L. M. CILONI[2] (IC); LUIZ A. PAVANIN[2] (PQ); ELISÂNGELA DE PAULA SILVEIRA-LACERDA[1]*(PQ)

[1]Universidade Federal de Goiás. [2]Universidade Federal de Uberlândia, Uberlândia.

The derived substances of the Ruthenium have been presenting as hopeful chemotherapies against cancer, acting for the reduction of Ru(III) for Ru(II) through the conditions of the tumoral cells cytoplasm; thus Ru(II) would link to DNA. The objective of this research was to evaluate the cis-tetraaminoxalatorutênio(III) acute toxicity. We tested 4 different substances concentrations in Swiss mice males adults. The mice were divided in 5 groups of 6 individuals and inoculated through intraperitonial with the following ruthenium concentrations: 3, 10, 30 and 300 mg/Kg/animal. The registration of behavior and deaths were made during the following 24 hours after the inoculation of the substance. After this time we sacrificed the mice and we analyzed the internal organs. The value of found DL_{50} was 300 mg/Kg/animal. The obtained results allow concluding that in discharges doses the cis-tetraaminoxalatorutênio(III) induces behaviour alterations that suggest depressive activity of the central nervous system, but it doesn't carry serious effects in lower doses.

Financial Support: CNPq, FUNAPE.
Supervisor: Elisângela de Paula Silveira-Lacerda.
Acknowledgments: Christiane de Amorim

TO022-LC-MS-MS DETERMINATION OF AMETRYN IN FRESWATER BIVALVE

ANALU EGYDIO JACOMINI(PG)(1); PIERINA SUELI BONATO(PQ)(2); PLÍNIO BARBOSA DE CAMARGO(PQ)(1)

(1)Departamento de Biologia, FFCLRP/USP; (2)Departamento de Física e Química, FCFRP/USP

The present study describes a method for the analysis of ametryn, an important herbicide employed in sugarcane cultures, in freshwater bivalve *Corbicula fluminea*. The soft parts of 40 animals were homogeneized in a glass potter resulting a unique mass for analysis. Aliquots of 1g wet weight mass were submitted to extraction with HCl 1mol L^{-1} and after alkalinization, the samples were partitioned with dichloromethane. The organic phases were recovered, transferred to conical tubes and the solvent was evaporated to dryness. The residues were dissolved in the mobile phase and analyzed on a C18 column, at a flow-rate of 1mL/min. The detection was performed with a triple quadrupole mass spectrometer, in the MRM mode and positive ESI. The method was validated showing mean ametryn recovery of 59 % (RSD=15%) and quantitation limit of 0.5 ng/g (RSD=13% and accuracy of 1.6%). The linearity of the method extended up to 50 ng/g, with r = 0.9978. The precision and accuracy of the method were measured for the concentrations of 2, 10 and 20 ng/g, showing RSD and accuracy values lower than 15%. In this way, the method can be used for the determination of ametryne in freshwater bivalve.

Finacial support: FAPESP
Supervisor: Pierina Sueli Bonato

TO023-INVESTIGATION OF STEVENS-JOHNSON SYNDROME DUE TO CARBAMAZEPINE

CLARA MENDES BAPTISTA (IC)[1]; AMANDA VANSAN MARANGON (IC)1; FLÁVIA MACHRY SANCHES (IC)[2]; ALEXANDRO JOSÉ JORGE (IC)[3]; PAULO ROBERTO DONADIO (PQ)4; PAULA NISHIYAMA (PQ)5.

1 Pharmacy Course of the UEM; 2 Course of Nursing of the UEM; 3 Course of Medicine of the UEM; 4 Department of Medicine of the UEM; 5 Department of Clinical Analyses of the UEM. State University of Maringá, Maringá - Paraná.

INTRODUCTION: Carbamazepine (CBZ) is a potent anticonvulsivant used in the treatment of complex (psychomotor) and tonic-clonic seizures, as well as trigeminal neuralgia and bipolar affective disorders. Among the side effects of the CBZ most common reported are sleep disorders, anorexia, irritability, ataxia, and diplopia. OBJECTIVE: The aim of this work is to investigate the possibility of the occurrence of Stevens-Johnson Syndrome (SJS) due to carbamazepine. METHODOLOGY: This case happened at the University Hospital of Maringá. Due to the existence of the few informations about the dose that the patient had received and the begining of the effects related it was done a literature review about SJS carbamazepine-induced to elucidate the case. RESULTS AND CONCLUSION: Some papers reports the development of SJS by the association with antiepileptics drugs which suggest, for this case, that SJS was induced by carbamazepine.

Supervisor: Profa. Dra. Paula Nishiyama

TO024-ENANTIOSELECTIVE ANALYSIS OF CYCLOPHOSPHAMIDE IN HUMAN PLASMA FOR PHARMACOKINETIC STUDIES

BRUNO DUMET FERNANDES (PG)[1]; CAROLINA MIRANDA SILVA (PG)[1]; VERA LUCIA LANCHOTE (PQ)[1]

[(1)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto–USP

Introduction: Cyclophosphamide (CPA) is an alkylating agent used as racemic mixture of (+)-(R) and (-)-(S) enantiomers in the treatment of cancer and autoimmune disease. Objective: A high-performance liquid chromatographic assay for enantioselective pharmacokinetic studies of CPA in plasma samples is described. Methods: After extraction with methyl tert-butyl ether, CPA enantiomers and the internal standard (5-ethyl-5-tolylbarbituric acid) were resolved in a Chiral-AGP column using the mobile phase acetonitrile-phosphate buffer (0.025 *M*; pH 4.65) (2:98, v/v) and were monitored by ultraviolet detector (195 nm). Results: This method proved to be suitable for pharmacokinetics studies based on a low quantification limit (2.0 µg/mL for each enantiomer) and a broad linear range (2.0–100.0 µg/mL for each enantiomer). Low values of the coefficients of variation (<15%) were demonstrated for both within-day and between day assays. Conclusion: The method proved to be sensitive, selective and precise for applications to pharmacokinetics studies of the enantioselective disposition of CPA in humans.

Supervisor: Vera Lucia Lanchote

TO025-CARAMBOXIN: THE PUTATIVE NEUROTOXIN OF STAR FRUIT INTOXICATION

RUITHER O. G. CAROLINO(PG)[1]; RENÊ O. BELEBONI(PQ)([1],5); ANDREA B. PIZZO(PQ)[2]; FLAVIO DEL VECCHIO(PQ)[3]; NORBERTO GARCIA-CAIRASCO(PQ)[3]; MIGUEL MOYSES-NETO(PQ)(4); LEONARDO GOBBO-NETO(PG)(6); NORBERTO P. LOPES(PQ)(6); WAGNER F. DOS SANTOS(PQ)[2]; JOAQUIM COUTINHO-NETTO(PQ)[1]

(1) Department of Biochemistry, FMRP, USP; (2) Department of Biology, FFCLRP, USP; (3) Department of Physiology, FMRP, USP; (4) Internal Medicine Department; FMRP, USP; (5) Department of Biotecnology, UNAERP; (6) Department of Physics and Chemistry, FCFRP, USP.

Introduction: The intoxication following consumption of star fruit by patients with renal failure present symptoms such as persistent hiccups, psychomotor agitation and seizures. Oxalic acid has been proposed as the star fruit neurotoxin.
Objectives: Isolate the star fruit toxin; start its chemical elucidation; and study its biological effects.
Methodology and Results: Caramboxin was purified by four chromatographic steps, and its molecular weight was determined by ESI-MS (*m/z* 255.06). In addiction, it was able to induce convulsion and to displace [^{3}H]-GABA from its receptors in synaptic membranes (IC_{50}= 142.6 ± 1.76 nM).
Conclusions: Caramboxin was isolated from star fruit and can be related to the star fruit intoxication. Further studies are on its way to better explain the intoxication symptoms and the complete chemical structure.

Financial Support: CAPES.
Supervisor: Joaquim Coutinho Netto

TO026-AN OVERVIEW ON DAPSONE METABOLISM AND ITS TOXICITY MECHANISMS

MAURICIO HOMEM DE MELLO(PG)[1], NATÁLIA VALADARES DE MORAES(IC)[1], WILSON ROBERTO MALFARÁ(PG)[1], SUELY VILELA SAMPAIO (PQ)[1], ANA MARIA DE SOUZA (PQ)[1], REGINA HELENA COSTA QUEIROZ (PQ)[1]

(1)FCFRP–USP

Introduction: When dapsone (DDS) undergoes hepatic metabolism, it can be acetylated by n-acetyl transferases or receiving an N-hydroxylamine (NOH) group by CYP450-3A4. These NOH metabolites are considered responsible for DDS hemotoxicity. A redox cycle has been suggested by previous *in vitro* studies, involving N-oxides metabolites products. Glutathione (GSH) would be involved in this process, reducing the N-oxides to the previous toxic hydroxylamine metabolites.
Objective: Analyze the effects of GSH supply on DDS-NOH toxic effects, *in vivo*.
Methodology: N-acetylcysteine was given to Wistar male rats as a precursor of GSH. The drug was given alone and together to DDS, and hemotoxicity was evaluated.
Results: GSH supply increased the levels of DDS induced hemotoxicity.
Conclusions: It is now possible to affirm that the association between NAC (GSH) and DDS should be avoided, to prevent the redox cycle of DDS-NOH an N-oxide. GSH supply to the animals under DDS metabolism increased the hemotoxic effects of its metabolites, leading to confirmation of the redox cycle theory. As a concluding study, DDS metabolism is now completely confirmed.

Financial Support: FAPESP
Supervisor: Regina Helena Costa Queiroz

TO027- USE THE BORIC ACID IN THE CONTROL OF THE *CAMPONOTUS VITATTUS* (HYMENOPTERA, FORMICINAE)

LUCIANA DE OLIVEIRA ALMEIDA (PG)[1]; CYNARA DE MELO RODOVALHO (PG)[1]; ANA CAROLINA SIQUIEROLI (PG)[1]; FLÁVIA ASSUMPÇÃO SANTANA (PG)[1]; DANIELA BERALDO BARBOSA (IC)[1]; CAMILA TAKENO COLOGNA (IC)[1].

(1) Universidade Federal de Uberlândia – Instituto de Genética e Bioquímica

Urban ants have been causing inconvenience and economic damages to humans for infesting electronic appliances and also transporting pathogens in hospital environments. Different insecticidal groups are used for the control of these ants, however the results are not satisfactory and what is verified the election of resistant individuals. Boric acid has fungicidal and insecticidal action. It affects the insects protoplasm when ingested and is abrasive to the insects exoskeleton. The objective of this work was to analyze the effects of boric acid in treated colonies of *C. vitattus* aiming to obtain an efficient way of control. Aqueous baits were obtained by the dilution of boric acid 0,1M in sucrose solution 10%. The baits were offered to 5 colonies composed by 15 workers and 15 soldiers each. One colony was used as a control. The results showed that all individuals died before the period of 30 days, while soldiers survived for a longer time, probably because of their bigger size and less quantity of foraging. This study suggests that the use of the boric acid 0,1M in aqueous baits is efficient in the control of the ants.

Financial support: CNPq; UFU
Supervisor: Ana Maria Bonetti

TO028-EFFECT PRE-AND POSTIMPLANTATION OF THE MEGLUMINE ANTIMONATE IN MICE

ALEXANDRA NAVA (IC)[1]; NATIELE CARINE COFFERRI (IC)[1]; CAMILA MICHELE SABEDOT REIK (IC)[1]; CARINA FILIPPINI (IC)[1]; FABIANA ERNESTINA BARCELLOS DA SILVA (PQ)[1]; SILVANE SOUZA ROMAN (PQ)[1]

[1]Universidade Regional Integrada do Alto Uruguai e das Missões – Campus de Erechim, RS.

The meglumine antimonate (MA) is the drug used for the treatment of leishmaniasis. The present study was evaluated the teratogenic potential of the MA that is widely used in human. Swiss mice were divided in 3 groups: day 1 to 6 of pregnancy (GD) (n=5), 7 to 12 GD (n=5), 13 to 18 GD (n=5) and a control group (n=15) received distilled water. It was given subcutaneous injection of 100mg/kg/day of MA, during six days. At the gestational day 18, dams were sacrificed and the number of corpora lutea, implantation sites, resorped, dead and live fetuses and pre-and postimplantation losses were counted. The 1 to 6 GD group showed significantly increased in the indices of loss postimplantation ($\underline{x}$ =11,97±9,37; $\underline{x}$ =2,78±2,94) and reduced of the implantation efficiency ($\underline{x}$ =88,02±8,38; $\underline{x}$ =97,12±3,95), respectively, than the control group. The 7 to 12 GD and 13 to 18 GD had fetal dead ($\underline{x}$ =0,6±0,54) compared with the control group ($p<0,05$). There was a significant increase in the postimplantation loss values (13 to 18 GD group: 9,90%; control group: 0%). Although MA has not intervened in the implantation (1 to 6 GD) it revealed toxic in the organogenesis and fetal period (7 to 18 GD), culminating with the fetal dead.

Financial support: PIIC/URI
Supervisor: Silvane Souza Roman

TO029- ANTIBOTHROPIC SOROTHERAPY AND SALICYLATE USE: A CASE REPORT

GLÁUCIA A. S. GUELSIN (IC)[1]; MAGDA LÚCIA FÉLIX (PQ)[1]

[1]Maringá State University

Introduction The bothropic venon´s action mechanism results from proteolytic, clotting and hemorrhagic physiopathological activities, and the anti-venon sorotherapy is the specific treatment. Objective This work has as its objective to report a clinical case of a bothropic acident victim who continuously made use of Acetyl Salicylic Acid (ASA). Methodology Study performed at the University Hospital (HUM) Poisoning Control Center (CCI-HUM), with data collected from the epidemiological records of Toxicological Occurrence. Clinical Case J.M.S., male, 57, with systemic hypertension and mellitus diabetes, making regular use of Aspirin®. He was bitten by a snake and seen at HUM with edema, blister and equimosis on the hallux and intense local pain. As soon as the bothropic accident has been confirmed, biological material was collected for analysis, coming up abnormal. Eight vials of anti-bothropic serum were infused. After 8 hours there was active bleeding in the lesion local, and the TC was abnormal, thus sorotherapy supplement was given. The TC became normal in 24 hours from the second infusion. The patient was cured released from the hospital. Conclusion The use of Aspirin® seems to have interfered in the response to sorotherapy, emphasizing the importance of pharmacological anamnesis.

Financial Support: ANVISA – Brazil
Advisor: Magda Lúcia Felix

TO030-INTERACTIONS DRUGS OF HIGH RISK WITH ANTIDEPRESSANTS

RENATA SANTANA MUNHOZ BONNI[1]; BRUNA DALLAQUA[1]; TARSILA GRIGOLIN BONATELLI[1]; HENRIQUE CESAR MIELI PAREDE[1]; EFIGÊNIA QUEIROZ DE SANTANA[1](PQ)

[1]Universidade do Sagrado Coração

INTRODUCTION: About 400 million people in the whole world they suffer from depression. One is about a pathology that reaches individuals with diverse physical riots in general, being therefore, necessary other drugs treatments. In aged the concomitant medication use it is bigger due to proper physiology. OBJECTIVE: Thus, it is essential studies surrounding the possible existing drugs interactions between antidepressants and other medicines. METHODOLOGY: Proceeded this revision in scientific articles, books and sites. RESULTS and CONCLUSION: The interaction between triciclics antidepressants (TA) and ant arrhythmics, produces a fall in the speed of conduction in the nervous system, resulting depression of the myocardium, with serious consequences to the patient. TA interacting with narcotic analgesics (meperidine), reducing the metabolism of this, causing respiratory depression. The selective inhibitors of the recaptation of serotonin (SIRS) managed with metoclopramide can result in serotoninergic syndrome and serious extrapyramidals effect. The inhibitors of monoaminoxidase (IMAOs) interacting with the simpatomimetics producing acute adrenergic syndrome; with the meperidine, presenting serious hypertension, hyperthermia, hyperreflexia, coma and death.

TO031- ISOLATION AND PARTIAL BIOCHEMICAL CHARACTERIZATION OF A PROTEASE FROM *TITYUS SERRULATUS* SCORPION VENOM (TSV)

DANIELA T. BERTAZZI (PG)[1]; JULIANA M. FERREIRA (IC)[1]; MAURÍCIO V. MAZZI (PG)[2]; SUELY V. SAMPAIO (PQ)[2]; ELIANE C. ARANTES (PQ)[1]

[(1)]Depto de Física e Química; [(2)] Depto Análises Clínicas, Toxicológicas e Bromatológicas - FCFRP– USP.

Introduction: TsV consists of low molecular weight basic protein neurotoxins, mucus and organic compounds. Scorpion venoms possess only very low levels of enzyme activity, but TsV shows hyaluronidase and proteolytic activities. The aim this work is the isolation and partial characterization of a protease from TsV. *Methods:* The protease was isolated from TsV by a combination of ion-exchange on CM-cellulose-52 and Phenyl-Sepharose CL-4B chromatography (0.01 M Tris-HCl buffer, pH 7.6, containing 4M NaCl, followed by a concentration gradient from 4 to 0 M NaCl, at 25°C). *Results:* The protease is a 10 kDa protein and shows gelatinolytic (time dependent - 0 to 24 hs) and fibrinogenolytic activities (0.1 µg hydrolyzed a-chain of fibrinogen). Fibrinogenolytic activity was completely inhibited by phenantroline and partially inhibited by EDTA, EGTA, b-mercaptoethanol, aprotinin e leupeptin. This is the first report on the isolation and enzymatic characterization of a low molecular weight protease from TsV, which may play a relevant role in local and systemic damage induced by the venom.

Support: FAPESP
Supervisor: Eliane C. Arantes

TO032-ENANTIOSELECTIVE PHARMACOKINETICS OF MEXILETINE IN RATS

ANA LEONOR PARDO CAMPOS GODOY (PG)[1]; CAIO CESAR PARISI (IC)[1]; MARIA PAULA MARQUES (PQ)[1]; VERA LUCIA LANCHOTE (PQ)[1].

[(1)] Universidade de São Paulo. Faculdade de Ciências Farmacêuticas de Ribeirão Preto.

Mexiletine (MEX) is a chiral drug used for the treatment of ventricular arrhythmias. The study reports on the stereoselective pharmacokinetics of mexiletine (MEX), a racemic mixture of (-)-(R) and (+)-(S) enantiomers, in rats. Wistar rats (n=6/time point) received by oral gavage or intravenous racemic MEX (10 mg/kg), and blood samples were collected until 12 h. The enantiomers were analysed by chiral LC-MS/MS. The pharmacokinetic parameters for (-)-(R) and (+)-(S) enantiomers following i.v. MEX are reported as means (95% CI), Wilcoxon test, $p>0.05$: $AUC^{0-\infty}$ 812.9 (487.0-1138.8) *vs* 1001.4 (650.6-1352.2) ng.h/mL; Cl 6.9 (4.3-9.6) *vs* 5.8 (2.6-9.1) L/h/kg; Vd 8.0 (5.0-11.1) *vs* 7.9 (2.5-11.7) L/kg; t1/2b 1.6 (1.4-1.7) vs 1.5 (1.3-1.7) h. The pharmacokinetic parameters for (-)-(R) and (+)-(S) enantiomers following oral gavage MEX are reported as means (95% CI), Wilcoxon test, $p>0.05$: $AUC^{0-\infty}$ 187.6 (35.2-339.9) *vs* 431.7 (49.4-814.0) ng.h/mL; Cmax 85.6 (28.7-200.0) *vs* 202.5 (27.7-377.22) ng/mL and F 22.4 (12.1-32.6) *vs* 38.83 (22.0-55.7)%. Pharmacokinetics of MEX is not enantioselective in rats treated with oral or i.v. racemic MEX.

Supervisor: Vera Lucia Lanchote.

TO033- HEMOLYTIC ACTIVITY OF *DINOPONERA AUSTRALIS* VENOM (HYMENOPTERA, PONERINAE)

CAMILA TAKENO COLOGNA (IC)[1]; DANIELA BERALDO BARBOSA (IC)[1]; FLÁVIA ASSUMPÇÃO SANTANA (PG)[1]; CYNARA DE MELO RODOVALHO (PG)[1]; LUCIANA DE OLIVEIRA ALMEIDA (PG)[1].

(1) INGEB-UFU

The studies of Hymenoptera venoms composition and its properties are still very limited. Ponerinae subfamily is one of the most primitive ants of tropical region. Those ants are usually predators with functional sting. *Dinoponera*, one of the largest ants in the word, pertains to that group. This genus is typically South American and it is represented by just 6 species. This study investigated the hemolytic activity of *Dinoponera australis* venoms. Human blood agar (27 mL) were placed on level dishes and 5mm holes were made in order to apply growing concentration of venom diluted in PBS buffer (1,5; 3; 6; 12 and 30 µg proteins/mL). The control consisted of PBS buffer. After the sample application, the dishes were incubated at 37 °C overnight. The assessment was made measuring the diameter of the lyses zone. The results showed that in all concentrations tested the venom has hemolytic activity. Statistics analyses confirmed the correlation between growing concentrations of venom and the diameter of the lyses zone. This study suggests that in predator ants, the venom may serve to help them on the capture of the prey and may exhibit a defensive hole.

Financial support: CNPq;UFU
Supervisor: Malcon A. M. Brandeburgo

TO034-FENVALERATE RESIDUES IN THE TESTIS AND EPIDIDYMIS OF ADULT AND PREPUBERTAL RATS

ARIELLE CRISTINA ARENA (PG); AZIZE CRISTINA CAPELLI NASSR (PG); DENISE ZUCCARI BISSACOT (PQ); WILMA DE GRAVA KEMPINAS (PQ).

Instituto de Biocências, UNESP, Botucatu, SP, Brasil.

Introduction: Fenvalerate (Fen) is a synthetic pyrethroid insecticide. Previous works showed Fen elicited reproductive toxicity in male rats. Objective: To determine Fen residues in different organs of rats. Methodology: Fen (96.8% purity, 40 mg/Kg/day) dissolved in corn oil was administrated by oral gavage for 30 days to adult male rats. A group of pregnant females received Fen from the 12th day of gestation until the end of lactation. Male pups were sacrificed on the following postnatal days: 40th (prepuberty), 60th (puberty) and 90th (sexual maturity). Control rats received corn oil. Fen residues were determined using High-Performance Liquid Chromatography (HPLC) in the following organs: liver, testis and epididymis. Results: In the rats exposed perinatally Fen residues were not detected at postnatal days 60th and 90th. Although present in the liver of the other rats, the highest concentrations of Fen were found in the epididymis and testis. Conclusion: Residues of Fen accumulates in reproductive-organ of male rats and this can be correlated with reproductive toxic effects.

Financial support: FAPESP, CNPq
Advisor: Wilma De Grava Kempinas

TO035-MALE REPRODUCTIVE TOXICITY OF DIURON IN ADULT RATS

GLAURA SCANTAMBURLO ALVES FERNANDES (PG)[1]; ARIELLE CRISTINA ARENA (PG)[1]; CARLA DAL BIANCO FERNANDEZ (PG)[1]; EUNICE OBA (PQ)[2]; WILMA DE GRAVA KEMPINAS (PQ)[2].

[(1)] Departamento de Biologia Celular, Instituto de Biologia, UNICAMP; [(2)] Departamento de Morfologia, Instituto de Biociências, UNESP – Botucatu.

Introduction: There are few studies on the toxic effects of diuron, a ureic herbicide, especially on the reproductive system. Objective: To evaluate the toxicity of diuron on the reproductive system of adult male rats. Methodology: Adult animals were treated, for 30 days, with 125 and 250 mg/Kg of diuron (Sigma, 98% purity) dissolved in corn oil, by oral gavage. Control rats received only the vehicle. Body and reproductive-organ weights, testosterone concentration, germ-cell counts in the testis and epididymis, sperm morphology, sexual behavior and fertility were analyzed. Results: There were no significant differences in the daily sperm production, sperm counts in the epididymis, sperm morphology, testosterone concentration and in sexual behavior. On the other hand, in the fertility test there was a reduction in the number of fetuses produced by the females that were inseminated by rats treated with 125 mg/Kg diuron. Conclusion: In these experimental conditions, diuron was toxic to the reproduction of male rats, at the dose of 125 mg/Kg.

Financial Support: CNPq.
Advisor: Dr. Wilma De Grava Kempinas.

TO036- PARTIAL ISOLATION AND CHARACTERIZATION OF A TOXIN FROM *BUFO PARACNEMIS* POISON (BPP) WITH ACTION ON THE COMPLEMENT SYSTEM (CS)

ANTONIO F. Q. MARONGIO (PG)[1];DANIELA T. BERTAZZI (PG)[1]; ANA ISABEL DE ASSIS-PANDOCHI (PQ)[1]; ANA E. C. S. AZZOLINI (PQ)[1]; ELIANE C. ARANTES (PQ) [1]

[(1)] Depto de Física e Química - FCFRP– USP.

Introduction: In toads, the skin glands are found on the back as large paratoid glands that contains biogenic amines, indolalkylamines (bufotenin and bufotenidin), steroids (bufotoxin), peptides and proteins that exhibit a large array of effects. Previous study showed that BpP affects the lytic activity of the CS. *Objective:* The aim of this study is to isolate the toxin from BpP with action on the CS. *Methods:* BpP was fractionated on a CM-Cellulose column. The effects of BpP and fractions were evaluated by hemolytic assay of the classical/lectin complement pathways(CP/LP). SDS-PAGE/Gelatin assays were used in order to identify proteolytic activity in BpP. *Results:* 8 fractions, named FI to FVIII, were obtained after chromatography and FI induced decrease in hemolytic activity of CP/LP. SDS-PAGE showed high MW proteins in the partially purified FI. BpV does not present proteolytic activity. *Conclusions*: The decrease in the lytic activity of CS induced by BpP or FI seems to be not dependent of direct proteolysis and the isolation of the toxin needs additional purification steps.

Financial Support: CAPES
Supervisor: Eliane C. Arantes

TO037-STEREOSPECIFIC PHARMACODYMAMICS/PHARMACOKINETICS OF METOPROLOL IN RATS

VANESSA BERGAMIN BORALLI(PG)[1]; TAMARA J. VAN STEEG(PQ)[2]; ELYSABETH C.M. DE LANGE(PQ)[2]; OSCAR E. DELLA PASQUA(PQ)[2]; EDUARDO BARBOSA COELHO(PQ)[3];VERA LUCIA LANCHOTE(PQ)[1]

[(1)]Fac. Ciências Farmacêuticas de Ribeirão Preto, USP; [(2)]Leiden/Amsterdam Center for Drug Research, University of Leiden; [(3)]Fac. Medicina de Ribeirão Preto, USP.

Introduction: Metoprolol (MET) is a b_1-adrenoceptor selective antagonist used in the racemic form for the treatment of hypertension and ischemic heart disease. The S-(-)-MET has >25-fold greater β_1-adrenergic receptor affinity. Objective: To predict the influence of stereoselectivity on *in vivo* effects Pharmacokinetic–Pharmacodynamic (PK-PD) models were developed, and they take into account competitive effects between enantiomers. Methodology: Male Wistar Rats (n=7) were cannulated for the administration by infusion of S-(-)-MET or Rac-MET; for Isoprenaline infusion; for the measurement of heart rate and blood pressure and blood sampling. In the experiment, after 30min, the rats received isoprenaline infusion (rate-5µg/kg/h); at time 60min, the rats received a 15min infusion of Rac-MET (5mg/kg) or S-(-)-MET (2.5mg/kg). Results and Conclusions: The models were able to describe how the racemate affect the effect in heart rate of the pure enantiomer alone, as a function of the blood-concentrations.

Finnancial support: CAPES
Supervisor: Profa. Dra. Vera Lucia Lanchote

TO038-DOES CALCIUM AFFECT THE NEUROTOXICITY CAUSED BY LEAD IN RATS?

TARSILA GRIGOLIN BONATELLI (IC)[1]; PATRICIA DA COSTA P. MARTINS (IC)[1]; ANTÔNIO F. GODINHO (PQ) [2]

[(1)] Universidade do Sagrado Coração; [(2)] UNESP – Botucatu.

INTRODUCTION: The high lead concentration on environment causes one of the most important ambient diseases: lead intoxication. Calcium has a known essential biological function as a regulator of cells. In the human and animal organisms, lead and calcium competes in the same receptors of tissues, specially the bony ones. When they are administered to lab animals can cause neurobehavioral effects. OBJECTIVE: Studying, in rats, the effects on administration of calcium gluconate in the behavior's changes caused by lead. METHODOLOGY: Wistar rats, males, young, received lead (10mg/Kg/day I.P. over 7 days) and lead plus calcium gluconate (0,1; 0,5 e 1,0% on drinking water, over 7 days). On the 8th day of treatment the animals were evaluated in Open field (grooming, ambulation, rearing and freezing) and Elevated plus maze (number of entries and spending time in open and closed arms). RESULTS: In Open field calcium did not intervence on lead effects as grooming and freezing times, but on Elevated plus maze calcium decreased the anxiety effects of lead intoxication. CONCLUSION: Calcium may be able to influence lead neurotoxicity in rats, when this one is evaluated by neurobehavioral methods.

Financial support: CEATOX
Supervisor: Antônio F. Godinho

TO039- ISOLATION OF HYALURONIDASE FROM *CROTALUS DURISSUS TERRIFICUS* SNAKE VENOM (CDTV)

ARTUR T. CORDEIRO (PQ)[1]; MARCOS M. TOLINI (IC) [1]; DANIELA T. BERTAZZI (PG)[1]; ELIANE C. ARANTES (PQ)[1]

(1) Depto Física e Química - FCFRP– USP

Introduction: Hyaluronidase is an enzyme found in venom of several species of animals such as snakes, scorpions, etc. Despite the fact that hyaluronidase itself is not toxic, it can contribute with the local and systemic envenomation since it increases the absorption and diffusion rates of the venom through the victim tissues by catalysing hydrolysis of the glycosaminoglycans in connective tissues. The aim of this study is the isolation and characterization of hyaluronidase from CdtV. *Methods:* CdtV was extracted and fractionated on a CM-Sepharose column eluted with 0.05M sodium acetate buffer, pH 5.5. Fractions 67 to 76 were pooled and filtered on a Sephadex G-75 column eluted with 0.05M sodium acetate, pH5.5, containing 0.15M NaCl. The enzymatic activity was determined according to Pukrittayakamee et al. (*Toxicon,* v.26, p.639, 1988). *Results:* hyaluronidase activity was found on fractions 6 to 10 obtained by gel filtration on Sephadex G-75. The isolated hyaluronidase is a single polypeptide chain, corresponding to an approximate *Mr* of 80,000. *Conclusion*: Despite the fact that the procedure above for hyaluronidase purification is relatively simple, it was able to afford a highly purified enzyme.

Supported: CNPq, FAPESP
Supervisor: Eliane C. Arantes

TO040-EFFECT OF THE EXPOSITION TO POLICYCLIC AROMATIC HYDROCARBONS IN THE SUGARCANE SOOT

LUCIANA AUGUSTO REZENDE(PQ)[1]; CARMEN LOPES(PQ)[1]; VERA SOARES(PQ)[1]; MÁRCIA AFONSO(PQ)[1]; CAIO COSTA(PQ)[1]; MÁRCIO TRIMAILOVAS(IC)[1]; JULIANA PERUCHI(IC)[1]; PAULA OLIVEIRA(IC)[1]

(1)UNAERP

The PAHs are by-products of the incomplete combustion of organic materials, considered mutagenics or carcinogenics.
Mice were submitted to doses of anthracene, naphthalene, benzo(e)pyrene and dibenzo(a,h)anthracene, checking the toxic action of these compounds in the organism.
Samples of sugarcane soot were extracted with dichloromethane and analyzed by gas chromatography. Micronucleus tests were realized with mice, divided in 3 groups (n=5): i) Positive control treated with cyclophosphamide, ii) Negative control treated with dimethylsufoxide, iii) Treated with 8,5; 17 and 34 mg/(kg of corporeal weight) of the 4 HPAs cited.
The analysis of the sugarcane soot extract detected the presence of the 4 PAHs. The micronucleus test for the 3 assayed doses, quantified the presence of the peripheral blood reticulocitos and the micronucleus (MNRETs/1000 cells) disclosing that the anthracene and the naphthalene had not produced alterations, but the benzo(e)pyrene (10.3±2.08) and dibenzo(a,h)anthracene (9.7±1.53) had shown a similar clastogenic action to the positive control (9.0±1.00), suggesting that the exposition of the workers and the population to the HPAs can result in genetic alterations.

Financial Support: UNAERP
Supervisor: Luciana Rezende

TO041-EFFECTS OF DIURON ON TOXICOLOGICAL PARAMETERS IN MALE WISTAR RAT

CIBELE AP. TARARAM(IC)*[12]; TONY F. GRASSI(PG)[2]; ANA L.T. SPINARDI-BARBISAN(PQ)[2]; MARIA A. DOMINGUES(PQ)[2]; JOÃO L.V. DE CAMARGO(PQ)[2]; LUÍS F. BARBISAN(PQ)[12]

[(1)]Dept Morphology-IB; [(2)]Dept Pathology-FM, UNESP Botucatu.

Introduction: Diuron is a widely used substituted urea herbicide. Objective: To analyze the hazard potential of diuron exposure, toxicological (body weight, water and food consumption and organs weight) and hematological (examination of blood) parameters and histology of lymphoid organs were evaluated. Metodology: Male Wistar rats were submitted to a chemical hepatocarcinogenesis model and divided in five groups: G1 to G5 groups were given a single dose of diethylnitrosamine (DEN,200mg/kg b.w.) and G2 to G5 received 125, 500, 1250 and 2500ppm of Diuron through diet, from 2nd to 8th week of experiment. At sacrifice, lymphoid organs, liver and kidneys were removed for histological analysis. Results: Diuron treatment reduced the body weight gain and food consumption at 1250 and 2500ppm. Spleen relative weight was significantly higher at concentrations of 1250 and 2500ppm with increase of red pulp cellularity and hemosiderosis. In bone marrow there was a reduction in maturation at myeloid lineage in 1250 and 2500ppm. Conclusions: The treatment with Diuron during 6 weeks at 1250 and 2500ppm resulted in general toxic effects.

Financial support: CAPES, *PIBIC
Supervisor: Spinardi-Barbisan A.L.T.

TO042- CHRONIC TOXICITY OF *ASTER SQUAMATUS* (SPRENG.) HIERON IN MICE

ROBERTA REGINATO (IC)[1];ANDRÉ JONAS BERVIAN (IC)[1];BERNARDO BALDISSEROTTO (PQ)[2]; JOCEANA SOARES SPEROTTO (PQ)[1]; SILVANE SOUZA ROMAN(PQ)[1]

[1]Universidade Regional Integrada do Alto Uruguai e das Missões -Campus de Erechim, RS
[2]Universidade Federal de Santa Maria, UFSM, RS

Aster squamatus is a plant popularly known as *zé-da-silva* and used as antidiarrhoeic. Crude hidroalcoholic extracts (CHE) were used for to determinate chronic toxicity. For this, were used 150, 300, 600 or 1200 mg/kg, w.o., of extracts in mice (n=10) during 90 days. One control group received only water. We observed some physiological parameters, corporal weight, water consumption and ration. After decapitation of the animals, liver and kidneys samples were obtained. The results were analyzed by ANOVA following Kruskal-Wallis and Mann-Whitney test, and considered significant when $p<0,05$. The results showed that at dose 600 and 1200mg/kg the weight of the animals were decrease and a reduction in the consumption of ration were observed only at 1200 mg/kg. Moreover, were observed in the liver centrolobular coagulative hepatocellular necrosis and kidney alterations, characterized for increase of the filtration space. These data suggest that *A. squamatus* extracts can present toxic effects in mice, in this conditions.

Financial Support: PIIC/URI
Adviser: Silvane Souza Roman

TO043-PROFILE OF PATIENTS WITH INTOXICATION DIAGNOSTIC ATTENDED IN HOSPITALAR CONJOINED OF SOROCABA

RAFAEL MENCK DE ALMEIDA[(1)], YARA POPST ARMANDO[(1)], CÍNTIA ROBERTA DA SILVA[(2)], SHEILA CHRISTINE DE JESUS[(2)], SILVIA PIERRE IRAZUSTA[(3)], SILVIO BARBERATO-FILHO[(4)], MARIA INÊS DE TOLEDO[(4)]

[(1)] Acadêmicos do Curso de Farmácia, Universidade de Sorocaba-Uniso.
[(2)] Farmacêuticas pela Universidade de Sorocaba-Uniso.
[(3)] Diretora Técnica de Patologia Clínica do CHS/ Docente da FATC-Sorocaba
[(4)] Farmacêuticos, Docentes da Universidade de Sorocaba-Uniso, Curso de Farmácia.

Introdution: The notification of intoxication is not compulsory in Brazil and this data is underestimated, although it is recognizedly a public health problem. Objectivo: We analysed medical bulletins of poisoned patients admitted in Hospital Conjoined of Sorocaba (HCS) between september 2002 to september 2003. Methodology: We collected the following datas from medical bulletins: date, age, gender and toxic agent. Results: There were 2992 poisoning cases: the predominant age range was 36-50 years; gender: male prevalence (2754 cases; 92%); toxic agent: abusive drugs (2721 cases; 90,9%) with alcoholic prevalence (2383 cases; 87,6%), use of medicine together with abusive drugs (59 cases; 2%) and medicine (71 cases; 2,4%) with female prevalence. Conclusion: The profile of poisoned patients of HSC and the related aspect of poison agents are discussed in this work.
Key words: emergencial assistance; toxic agent, drugs of abuse, intoxication.

Supervisor: Prof.ª Dra. Yoko Oshima-Franco

TO044- TOXICOLOGICAL EVALUATION AND DETERMINATION OF LD_{50} OF *EUPHORBIA TIRUCALLI* L

ALDO CÉSAR PASSILONGO DA SILVA (PG)[1]; ELISÂNGELA C. B. DA SILVA(PG)[1]; IGOR ARTUR DE FARIAS (PQ)[1]; VERA MARIA PETERS (PQ)[2]; MARTHA DE OLIVEIRA GUERRA (PQ)[2];IVONE ANTÔNIA DE SOUZA(PQ)[1]

[1]UFPE Pharmacy Department [2] UFJF Center of Biology of the Reproduction

Introduction: The *Euphorbia tirucalli* Linn (Euphorbiaceae) is a plant lactescent and sub ligneous. The latex is used in the popular medicine as aiding in the combat to the cancer and in the treatment of warts. Objective: To accomplish the toxicological study of the latex of the *E. tirucalli* and the determination of its DL50 orally. Methodology: For this rehearsal, groups of mice were selected albinos *Mus muscullus* Swiss, males. DL50 was determined by the method Karber and Behrens. The toxicological effects, adverse and behavior reactions were observed during the period of 48 hours. Results: increase of the breathing frequency, agitation and abdominal contortions (it doses of 347,06 mg/kg); escape reaction, lowering of the subsequent train and spasms (dose 539,87 mg/kg); rude tremors, clonical convulsion and widespread, cyanosis and exhaustion (dose 809,8 mg/kg). Conclusion: The effects were more accentuated with the increase of the doses, happening rude tremors, loss of the motive coordination, exhaustion and cyanosis. We verified that the latex of the *E. tirucalli* induces reactions on SNC and peripheral system. Certain DL50 was of 502,45mg/kg.

Supervisor: Ivone Antônia de Souza

TO045-DIRECT ENANTIOSEPARATION OF MEFLOQUINE AND ITS MAIN METABOLITE CARBOXYMEFLOQUINE BY CHIRAL HPLC

IGOR RAFAEL DOS SANTOS MAGALHÃES (PG)[1]; PIERINA SUELI BONATO (PQ)[1]

[(1)]Faculdade de Ciências Farmacêuticas de Ribeirão Preto – USP

Mefloquine, a racemic drug used for the treatment and prophylaxis of malaria, shows stereoselective pharmacodynamic and pharmacokinetic properties in humans. Several direct or indirect methods have been reported previously for the determination of mefloquine enantiomers, but none of them provides the separation of its main achiral metabolite carboxymefloquine. Based on this, the aim of this work was to develop a direct chiral HPLC method to resolve mefloquine enantiomers and carboxymefloquine. Some chiral HPLC columns based on polysaccharide derivatives (Chiralpak AS, Chirapak AD, Chiralcel OJ-R and Chiralcel OD-H) were evaluated under polar-organic or normal mode. Resolution was achieved by the optimization of the type and the ratio of mobile phase modifiers and additives. The modifiers included alcohols and the additives were trifluoroacetic acid (TFA) and diethylamine (DEA). Enantiomeric elution order was evaluated by analyzing pure enantiomers using a procedure described in Qiu (1992). Successful separation was obtained with a cellulose-based chiral column (Chiralcel OD-H, 150 x 4.6 mm, 5 µm particle size) and hexane/ethanol/DEA/TFA (95:5:0.1:0.05 v/v%) as the mobile phase.

Financial Support: CNPq, FAPESP
Supervisor: Profa. Dra. Pierina Sueli Bonato

TO046- EFFECTS OF CLOMAZONE HERBICIDE ON PARAMETERS OF PROTEIN AND CARBOHYDRATE METABOLISM OF SILVER CATFISH *RHAMDIA QUELEN*

CHARLENE CAVALHEIRO DE MENEZES (IC)[1]; MÁRCIA CRESTANI (PG)[1]; MILENE B. FONSECA (IC)[1]; BIBIANA MORAES (IC)[1]; ALEXANDRA PRETTO (IC)[1]; DAIANE S. SOARES (IC)[1]; VÂNIA L. P.VIEIRA(PQ)[1]

[(1)]Federal University of Santa Maria

Introduction: Herbicides are considered to be essential for agricultural development however they may have serious environmental impact.
Objetive: Evaluated parameters of protein and carbohydrate metabolism of *Rhamdia quelen* after exposure to clomazone herbicide.
Methods:The effects of clomazone (0.5 and 1.0 mg/L) on protein and carbohydrate metabolism were evaluated in *Rhamdia quelen* after 12, 24, 48, 96 and 192 hours of exposure with a recovery period.
Results: Liver glycogen increased in all periods and concentrations tested. Muscle glycogen reduced after 24, 48, 96 and 192 h for both clomazone concentrations. Elevated plasma glucose values were observed and variation in glucose in the liver and muscle of exposed fish. Muscle lactate levels increased after 12, 24 and 48 hours of clomazone exposure , but reduced in the liver. Protein levels were enhanced in the liver and muscle, except at 96 and 192 h of exposure.
Conclusion: Clomazone concentrations used appears safe to fish *Rhamdia quelen*, because overall parameters can be recovery after 96 and 192 h in clean water.

Financial Support: CNPq
Supervisor: Vânia L. P. Vieira

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ÍNDICE DE AUTORES/AUTHOR INDEX

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Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

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Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

RBCF

Revista Brasileira de Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

ÍNDICE DE AUTORES/AUTHOR INDEX

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Ciências Farmacêuticas

Revista Brasileira de Ciências Farmacêuticas
Brazilian Journal of Pharmaceutical Sciences

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Unitermos: devem representar o conteúdo do artigo, evitando-se os de natureza genérica. Observar o limite máximo de 6(seis) unitermos.

Introdução: deve estabelecer com clareza o objetivo do trabalho e sua relação com outros trabalhos no mesmo campo. Extensas revisões de literatura devem ser substituídas por referências aos trabalhos bibliográficos mais recentes, nos quais tais revisões tenham sido apresentadas.

Material e Métodos: a descrição dos métodos usados deve ser breve, porém suficientemente clara para possibilitar a perfeita compreensão e repetição do trabalho. Processos e Técnicas já publicados, a menos que tenham sido extensamente modificados, devem ser apenas referidos por citação. Estudos em humanos e em animais devem fazer referência à aprovação do Comitê de Ética correspondente.

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Conclusões: Quando pertinentes, devem ser fundamentadas no texto.

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