QM 042 - SEVERAL LOGP IN A SAME QSAR STUDY? AN EXAMPLE WITH HIV-INTEGRASE INHIBITORS.

EDUARDO B. DE MELO(PG)[1,2]; MÁRCIA M. C. FERREIRA(PQ)[2].

[1] Farmácia/UNIOESTE; [2] IQ/UNICAMP. márcia@iqm.unicamp.br.

Several methods of deriving LogP from molecular structure for using in QSAR/QSPR studies are currently available. How do select the methodology most suitable for a study? Or still, is it possible and admissible to build a model with more than one LogP? A study of LogP applied to a set of thirty-three carboxamides inhibitors of HIV-integrase was carried out using fourteen methodologies. That study was performed employing correlation matrix and Hierarchical Cluster Analysis (HCA). The majority of the LogP values had presented high intercorrelation ($R > 0.8$), meaning that they provide mainly the same information. The three methods that presented the lowest intercorrelation ($R < 0.6$) and were best correlated with the biological activity data (pIC50):

	ACDLogP	CSLogP	IALogP	pIC50	Type
ACDLogP	1	0.550	0.361	0.469	substructure approach based in atom contribution
CSLogP		1	0.541	0.412	whole molecule approach based in topological and E-state índices
IALogP			1	0.448	whole molecule approach based in topological indices and neural networks

Those results indicated that the three methodologies, although having the same physical meaning in a QSAR model, could provide different informations to the model, which is in turn related to the specific information used in each methodology for LogP calculation. Classic QSAR models, applying multiple linear regression method (MLR), were constructed using the BuildQSAR program. Four models were obtained:

Model	LogP	R	S	F
1	ACD; CS; IA	0.755	0.661	11.955
2	ACD; CS	0.746	0.659	17.616
3	ACD; IA	0.736	0.671	16.505
4	CS; IA	0.614	0.781	8.487

Model (2) was chosen as the best one. In conclusion, it has been shown that it is possible the use of more than one type of LogP in a same QSAR model, but attention must be paid to the calculation method, its correlation with others and information extracted from it.

Financial Support: FAPESP/CNPQ.