THEORETICAL STUDY ON SOME β-LACTAMS AS SUBSTRATES OF THE BACTERIAL MULTIDRUG RESISTANCE ACRB PUMP

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AcrB pump is a part of the most important multidrug efflux system of gram-negative bacteria, which excretes β-lactam antibiotics. This study concerns relationships between molecular descriptors of 16 β-lactams (penicillins and cephalosporins) and their efflux rates (minimal inhibitor concentrations, MICs) caused by three distinct *Salmonella typhimurium* strains. Conformational search, geometry optimization at PM3 and MMFF94 level, and calculation of various molecular descriptors was performed. Partial Least Squares (PLS) regression models were built for prediction of MICs. Docking of selected drugs to the pore recognition site (PRS) of the AcrB pump was also performed. Parsimonius PLS models were obtained (Q^2 > 0.67, R^2 > 0.79) with several lipophilicity, electronic and hydrogen bond descriptors. Conformation changes in docking are minor in pore channel chains and large in β-lactams. Hydrophilic drugs bind stronger to the PRS than lipophilic and amphiphilic drugs, what agrees with the PLS results.