Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
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Computer-aided design of novel antibacterial3-hydroxypyridine-4-ones: Application of QSAR methods based on the MOLMAP approach

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Background and Aims: Although the number of medicinal agents is increasing every year, but there is still a tremendous need to design new drugs to combat human diseases. QSAR models allow medicinal chemists to predict the biological activities of untested and even not prepared compounds. Using traditional techniques, it may take months to synthesize a new compound for biological assays. Application of computational techniques for designing biologically active novel compounds reduces experimental research cost and saves a lot time. Search for new antimicrobial agents with novel modes of action represents a major target in anti infective chemotherapy. 3-Hydroxypyridine-4-one derivatives have shown good inhibitory activity against bacterial strains. In this work it was reported the application of MOLMAP descriptors based on empirical physicochemical properties with GA-PLS and CP-ANN methods to propose some novel 3-hydroxypyridine-4-one derivatives with improved antibacterial activity against Staphylococcus aureus.
Methods: A large collection of 302 novel derivatives of this chemical scaffold was selected for this purpose. The activity classes of these compounds were determined using the two QSAR models. To evaluate the predictability and accuracy of the obtained models, nineteen compounds belonging to all three activity classes were prepared and the activity of them was determined against Staphylococcus aureus.
Results: Comparing the experimental results and the predicted activity classes revealed the accuracy of the obtained models. Seventeen of the nineteen synthesized molecules were correctly predicted by GA-PLS model according to the antimicrobial evaluation method. The CP-ANN based prediction was correct for sixteen out of the nineteen synthesized molecules.
Conclusions: Since the results approve the predict capability of the two QSAR models, compounds belonging to the active class of the predicted molecules will be good candidates to be synthesized and evaluated in the future researches. Thus it can saved time, cost and money.

Keywords: CP-ANN; 3-Hydroxypyridin-4-one; MOLMAP; QSAR; Antibacterial activity