Title: Quantitative Sequence-Activity Modeling of Linear Hexapeptide Antibiotics: An Approach for the Prediction and Description of Antifungal Activity

Abstract: The growing emergence of bacterial/fungal superbugs in clinics has limited effectiveness of current antibiotics. Therefore, design and development of antibiotics with novel mode of actions represent a particular challenge. Antimicrobial peptides (AMPs) which act mostly by damaging bacterial/fungal cell membrane are effective molecules in innate immune system and can provide promising antibiotics for treatment of superbugs-associated infections. However, design of new AMPs with improved therapeutic index is always demanding. Quantitative sequence-activity modeling (QSAM) is an effective chemoinformatic technique employing quantitative structure–activity relationship for biomolecules. In this approach, biosequence activities of therapeutic agents; e.g., peptides, are linked to functional/structural properties. Here, a QSAM study was performed on a series of linear hexa-AMPs with different activity profile against \textit{C. albicans} superbugs using segmented principal component strategy. For this, structures of the amino acids in hexa-AMPs sequences were drawn and optimized by Hyperchem, v.8. Then, different structural information, such as constitutional, charges, and topological descriptors were extracted and classified into groups with similarity in their informational contents. Each group was separately subjected to principal component analysis (PCA). The extracted PCs were used as the descriptors of the model after variable selection. Our results showed that constructed models covered more than 85% of the variance in train and test sets. Also, information on the highlight zone of the hexapeptides (representing a general part of peptide structure with highest impact upon antifungal activity) was obtained. The applied descriptors for this structure–activity model were sensitive to polarity of amino acids in the peptide sequences.

Acknowledgments: Financial support of this project by National Elites Foundation is highly appreciated.

Antimicrobial Peptides, Superbugs, Chemoinformatic, Quantitative Sequence-Activity Modeling, Amino Acid Descriptors

Presentation: Poster