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Quantitative Structure-Activity Relationship Analysis of Binding Affinity of a Series of Anti-Prion Compounds to Human Prion Protein

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Abstract : The present study is based on the quantitative structure-activity relationship (QSAR) analysis of eighteen compounds with anti-prion activity. The structures and anti-prion activities (expressed in response units, RU%) of the analyzed compounds are taken from CHEMBL database. In the first step of analysis 85 molecular descriptors were calculated and based on them the hierarchical cluster analysis (HCA) and principal component analysis (PCA) were carried out in order to detect potential significant similarities or dissimilarities among the studied compounds. The calculated molecular descriptors were physicochemical, lipophilicity and ADMET (absorption, distribution, metabolism, excretion and toxicity) descriptors. The first stage of the QSAR analysis was simple linear regression modeling. It resulted in one acceptable model that correlates Henry's law constant with RU% units. The obtained 2D-QSAR model was validated by cross-validation as an internal validation method. The validation procedure confirmed the model's quality and therefore it can be used for prediction of anti-prion activity. The next stage of the analysis of anti-prion activity will include 3D-QSAR and molecular docking approaches in order to select the most promising compounds in treatment of prion diseases. These results are the part of the project No. 114-451-268/2016-02 financially supported by the Provincial Secretariat for Science and Technological Development of AP Vojvodina.

Keywords : anti-prion activity, chemometrics, molecular modeling, QSAR
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