Bioactivity Prediction of Phytochemicals Against Aminoglycoside Resistance Using QSAR Modelling

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Aminoglycoside (AG) resistance in bacteria is an international crisis that is estimated to have 10 million infections annually by the year 2050. With the widespread of multidrug resistance bacteria, AGs are becoming useless along with the novel drugs. Many studies have determined that the fastest route to identify treatment for AG resistance is restoring the effectiveness of existing AGs by combining them with compounds with antimicrobial properties. The main purpose of this study was to identify such compounds by predicting their bioactivity against the AG resistance in bacteria using a Quantitative Structure Activity Relationship (QSAR) model. Bioactivity data of 24 AGs and 2000 phytochemicals were retrieved from ChEMBL site. Several software was used: QSARINS; to build the model, PaDEL- Descriptor for the generation of molecular descriptors. The best QSAR model obtained using Genetic Algorithm (GA) with correlation coefficient (R^2) of 0.6969 and root mean-squared error (RMSE) of 0.7795. Based on that model, the QSAR equation used to predict the pIC50 values of the phytochemicals can be given as: pIC50 =-27.7308+[50.8350*(AATS5p)] +[-14.7553*(GATS5e)]+ [3.8896*(minssCH 2)]+[-1.5777*(maxwHBa)]. Total 14 phytochemicals had predicted bioactivity against AG resistance. They are Alpha-pinene, Miltefosine, Tilarginine, Kojic acid, Isoniazid, Gallic acid, Deacetylasperuloside, Citrifolinin B, 4-Aminobenzamidine, 2-(dodecylamino)butan-1-ol , 2-Diisopropylamino-Ethanol, 2-Diisopropylamino-Ethanol, and 1-ethyl-3-pyridin-2-ylurea. As many of them are known for their antimicrobial activity against different species, they can be considered in combining with AGs to increase the antibiotic effect. With the developed model, a large volume of phytochemicals can be screened prior to the laboratory experiments and reduce the sample number, resources, cost and time taken.

Keywords: Aminoglycosides, Antibiotic resistance, QSAR, Ligand based, Drug discovery