Comparative QSAR modeling of 2-phenylindol derivatives for predicting the anticancer activity using genetic algorithm multiple linear regression and back-propagation-artificial neural network techniques

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Abstract

Quantitative structure-activity relationship (QSAR) studies on a series of 2-phenylindole derivatives as anticancer drugs were performed to choice the important molecular descriptor which is responsible for their anticancer activity (expressed as pIC50)). The geometry optimizations were performed on the structures using Gaussian 09W software with the density functional B3LYP and 6-311G(d,p) basis sets . Dragon 5.4 software was used to calculate molecular descriptors, and the genetic algorithm (GA) procedure and backward regression were used to proper selection of the most relevant descriptors. Different chemometric tools including the backward multiple linear regression (BW- MLR) and backpropagation-artificial artificial neural network (BP-ANN) were carried out to design QSAR models. The squared correlation coefficient (R2) and the Root Mean Squared Error (RMSE) values of the GA-MLR model were calculated to be 0.2843 and 0.7001 respectively. The BP-ANN model was the most powerful, with the square of predictive correlation coefficient R2pred, root mean square error (RMSE), and absolute average deviation (AAD) which was equal to 0.9416, 0.0238, and 0.0099, respectively. The external validation criteria (Q2F1, Q2F2, Q2F3, and concordance correlation coefficient were applied to assay predictive efficiency of QSAR model derived by BP-ANN method. The results derived from the BP-ANN indicated that the anticancer activity of 2-phenylindole derivatives depends strongly on 3D descriptors namely Radial Distribution Function (RDF) descriptors and 3D-molecular geometry of the studied compounds play an important role for these activities. Thus, it could be useful in the design of new 2-phenylindole derivatives having anticancer potency.

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