Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
Isfahan University of Medical Sciences

Qsar study of N-acyl-3,5-bis(arylidene)-4-piperidones as cytotoxic agents

M. Parish[1,*], B. Hemmateenejad[2], R. Miri[1], N. Edraki[1], M. Elyasi[1], M. Khoshneviszadeh[1], J. Dimmock[3]

[1]Medicinal and Natural Products Chemistry Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Medicinal and Natural Products Chemistry Research Center, Shiraz University of Medical Sciences / Chemistry Department, Shiraz University, Shiraz, Iran
[3]College of Pharmacy and Nutrition, University of Saskatchewan, 110 Science Crescent, Saskatoon, Saskatchewan, Canada

Background and Aims: Quantitative structure–activity relationship (QSAR) research field has been widely developed because of its powerful ability to predict drug activity. In this aspect, QSAR analysis of 1-[4-(2-alkylaminoethoxy) phenylcarbonyl]-3,5-bis(arylidene)-4- piperidonesas cytotoxic agents based on reported data on three cell lines including Molt 4/C8 cells, CEM cells and L1210 cells was performed by different chemometric tools.

Methods: The biological data used in this study are cytotoxic activity data of a series of 3,5-bis(arylidene)-4-piperidinones were synthesized by Das et. al. and evaluated against Molt 4/C8 cells, CEM T-lymphocytes and murine L1210 cells. The data set (n = 25) was divided randomly into two groups: calibration set (n = 19) and prediction set (n=6) In model development step, leave-one-out cross-validation was used to optimize the models. The final models were validated using a set of 6 molecules in the test set, which did not contribute to the model development.For the development of QSAR equations, two different methods were used: (i) stepwise multiple linear regression (MLR), (ii) principle component regression (PCR) and (iii) genetic algorithm–partial least squares (GA-PLS).

Result and discussion: The results indicate that GA-PLS analysis is more accurate for predicting the cytotoxic potential of N-acyl-3,5-bis(arylidene)-4-piperidones in all three cell lines. The value of cross-validation statistics suggests the higher prediction ability of the GA-PLS model. The results demonstrate that (electro) topological indices(balaban index (PW3) and spherocity(SIC2) and sum of Electrotopological state indices of aromatic-CH and methyl groups) and spatial parameters (Molecular density) is influential structural descriptors that mainly affect the cytotoxic potential of compounds in all three studied cell lines. The results demonstrate that similar structural descriptors affects the cytotoxic potential of N-acyl-3,5-bis(arylidene)-4-piperidones in three different studied cell lines. This result indicates that similar molecular mechanism is involved in cytotoxic activity of studied compounds in these cell lines.

Keywords: QSAR; GA-PLS; MLR; N-acyl-3,5-bis(arylidene)-4-piperidones; Cytotoxic