

## QSAR study of some 1,3,8-substituted-9-deazaxanthine derivatives as potent and selective A2BAR antagonists by various linear and nonlinear multivariate chemometrics methods

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**Background and Aims:** In this research, we tried to describe the QSAR study between molecular structure and A2B adenosine receptor (A2BAR) pKi of 74 of the 1,3,8-substituted-9-deazaxanthines derivatives as potent and selective A2BAR antagonists. Thereby, the aim of this work is to find a model for the search of novel A2BAR antagonist compounds. Also, the purpose of this study is testing capabilities of various descriptors in prediction of pKi of some new synthesized A2B antagonist by various linear and nonlinear multivariate chemometrics methods.

**Methods:** Stepwise multiple linear regression (SMLR), partial least squares (PLS) and general regression neural networks (GRNNs) approaches were employed for building of regression models. Then, continue the validation of this method in describing binding affinity and comparison methodologies, in order to demonstrate its value as a good QSAR model. The performances of developed model were tested by several validation methods such as external and internal tests and also criteria recommended by Tropsha and Roy.

**Results:** The results revealed the significant role of topological and geometrical descriptors in the binding of the studied compounds against A2BAR. Two methods PLS and GRNN have good statistical qualities. Meanwhile, the PLS model used higher number of descriptors and, consequently, resulted in better performance than SMLR and GRNN. The resulted PLS model had a high statistical quality ( $R^2 = 0.895$  and  $R^2_{LOO} = 0.860$ ) for predicting the activity of the compounds.

**Conclusions:** The results confirmed the superiority of the results obtained by PLS relative to SMLR and GRNN. PLS can be preferred with respect to correlation coefficients of cross-validation, external prediction and on the basis of criteria proposed by Tropsha et al. and Roy and Roy, too. Furthermore, the domain of applicability which indicates the area of reliable predictions is defined. The prediction results are in good agreement with the experimental value.

**Keywords:** Quantitative structure activity relationship; Multivariate linear regression; Partial least square; General regression neural network; A2BAR antagonists