Abstract

The 3D-QSAR study of non-peptidic inhibitors of protein tyrosine phosphatase (STEP) as anti-Alzheimer's drugs was performed by comparative molecular field analysis (CoMFA), and comparative molecular similarity indices analysis (CoMSIA) methods to determine the factors required for the activity of these compounds. An alignment rule for the compounds was defined using Distill in SYBYL 7.3. The predictive ability of CoMFA and CoMSIA were determined using a test set giving predictive correlation coefficients of 0.770, and 0.746 respectively indicating good predictive power. Based upon the information derived from CoMFA and CoMSIA, identified some key features that may be used to design new inhibitors for STEP. Molecular docking studies were also employed to study the molecular mechanisms of inhibitors. To propose new active compounds, the resulting CoMFA contour maps were used. Finally, in silico ADMET studies was performed on new design compounds to compare the computed ADMET descriptor values with the accepted ranges.

Keywords: 3D-QSAR, STEP, CoMFA, CoMSIA, Molecular docking and ADMET.

University of Zabol
Graduate school
Faculty of Science
Department of Chemistry

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Supervisors:

Dr. Ali Reza Samzadeh Kermani

Dr. Fereshteh Shiri

By:

Hadi Saleh Poudineh

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