Molecular Docking and QSAR Study of 1,3-disubstituted 2-propanols as β-Secretase-1 inhibitors

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Abstract:
β-Secretase is the enzyme responsible for the Amyloid-β plaques found in Alzheimer’s disease. Inhibition of this enzyme should prove to be very useful in combating Alzheimer’s disease. Current options for treating the cognitive symptoms associated with Alzheimer's are inadequate, giving urgency to the search for novel therapeutic strategies. In this study a set of 1,3-disubstituted 2-propanols with β-Secretase-1 (BACE-1) inhibitory activity, which protects newborn neurons from apoptotic cell death was subjected to quantitative structure–activity relationship (QSAR) analysis to find the structural requirements for ligand binding. A collection of chemometrics methods such as: multiple linear regression (MLR), factor analysis-based multiple linear regression (FA-MLR), were employed to make connections between structural parameters and enzyme inhibition. To better understand the structure–activity relationships (SAR) of them, a docking study procedure has been applied exploiting different conformational and ionic states of BACE-1. The results revealed the predictable model and significant structural dependency on the BACE-1 inhibitory activity of the studied compound.

Keyword: Alzheimer’s disease, BACE-1, Docking, QSAR