Application of Monte Carlo Algorithm to Explore Simplified Molecular-Input Line-Entry System based Molecular Descriptors of BACE1 inhibitors for Therapeutic Application in Alzheimer’s Disease

International Journal of Computer Applications
Foundation of Computer Science (FCS), NY, USA

Volume 182
Number 11

Year of Publication: 2018

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10.5120/ijca2018917745

Abstract

Application of computer science and algorithms are now become an integral part of the drug discovery research. In the current work, well known Monte Carlo (MC) algorithm was used to develop quantitative structure-activity relationship (QSAR) models with molecular descriptors derived from simplified molecular-input line-entry system (SMILES) representation of beta-site APP cleaving enzyme1 (BACE1) inhibitors. A set of BACE1 inhibitors was obtained from the binding database and subsequently divided into training, test, calibration and external sets. The QSAR models were developed from the training set compounds while other sets used to assess the quality of developed models. With- and without-influence of cyclic rings on inhibitory activity were considered to develop the QSAR models. Best QSAR models were selected based on statistical parameters of final models. High correlation and low standard error values of training, test, calibration and external sets undoubtedly suggested that the selected models were robust and efficient enough to predict the inhibitory activity of the molecules. On evaluation of statistical parameters it was revealed that cyclic rings of molecular scaffold significantly contributed to the inhibition of BACE1. The molecular fragments were found to be crucial to increase or decrease
the inhibitory activity of the molecules which indicated that models have mechanistic interpretation. Therefore, important molecular fragments explained by the QSAR models can be used to design new and novel BACE1 inhibitors for therapeutic application in Alzheimer's disease.

References


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**Index Terms**

Computer Science  
Algorithms

**Keywords**

Alzheimer's disease; BACE1 inhibitors; QSAR; Monte Carlo algorithm; SMILES