Abstract

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) have gained a definitive place due to their unique antiviral potency, high specificity and low toxicity in antiretroviral combination therapies used to treat HIV. To design more specific HIV-1 inhibitors, 218 Non-nucleoside reverse transcriptase inhibitors with their EC_{50} values were collected from different literature sources. Then, a different type of fingerprint descriptors were calculated by PaDEl descriptor and afterwards enhanced replacement method (ERM) was used as the variable selection approach to choose more relevant variables. Based on selected descriptors, a classification SVM model was constructed to categorize compounds into two groups of active and inactive. The most potent inhibitor available in the set was used to carry out a similarity search in PubChem server to retrieve compounds similar to the hit compound. The screened compounds with above 85 percent of similarity to the hit compound were used as the input to the SVM model. Likewise, the most active compound in the set has been used as the input to the Pharmit web server to screen the Molport library by constructing structure based pharmacophre models. Shape filters for protein and ligand and also Lipinski rule of five were used to filter the output of virtual screening from resulted pharmacophore models. 334 compounds were reported. Among them, The SVM model rendered 7 active compounds and they were also analyzed by ADMET.

Keyword: Non-nucleoside reverse transcriptase inhibitors; fingerprint; ERM; Virtual screening; pharmacophre

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Discovery of new chemical scaffolds for none-nucleoside reverse transcriptase inhibitors using virtual screening

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