World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:18, No:12, 2024

Towards Designing of a Potential New HIV-1 Protease Inhibitor Using Quantitative Structure-Activity Relationship Study in Combination with Molecular Docking and Molecular Dynamics Simulations

Authors : Mouna Baassi, Mohamed Moussaoui, Hatim Soufi, Sanchaita RajkhowaI, Ashwani Sharma, Subrata Sinha, Said Belaaouad

Abstract : Human Immunodeficiency Virus type 1 protease (HIV-1 PR) is one of the most challenging targets of antiretroviral therapy used in the treatment of AIDS-infected people. The performance of protease inhibitors (PIs) is limited by the development of protease mutations that can promote resistance to the treatment. The current study was carried out using statistics and bioinformatics tools. A series of thirty-three compounds with known enzymatic inhibitory activities against HIV-1 protease was used in this paper to build a mathematical model relating the structure to the biological activity. These compounds were designed by software; their descriptors were computed using various tools, such as Gaussian, Chem3D, ChemSketch and MarvinSketch. Computational methods generated the best model based on its statistical parameters. The model's applicability domain (AD) was elaborated. Furthermore, one compound has been proposed as efficient against HIV-1 protease with comparable biological activity to the existing ones; this drug candidate was evaluated using ADMET properties and Lipinski's rule. Molecular Docking performed on Wild Type and Mutant Type HIV-1 proteases allowed the investigation of the interaction types displayed between the proteases and the ligands, Darunavir (DRV) and the new drug (ND). Molecular dynamics simulation was also used in order to investigate the complexes' stability, allowing a comparative study of the performance of both ligands (DRV & ND). Our study suggested that the new molecule showed comparable results to that of Darunavir and may be used for further experimental studies. Our study may also be used as a pipeline to search and design new potential inhibitors of HIV-1 proteases.

Keywords : QSAR, ADMET properties, molecular docking, molecular dynamics simulation.
Conference Title : ICBBB 2024 : International Conference on Bioscience, Biotechnology, and Biochemistry
Conference Location : New York, United States
Conference Dates : December 09-10, 2024