In silico analysis of drug resistance in HIV-reverse transcriptase inhibitors

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Abstract: Globally, 36.7 million people were living with HIV at the end of 2016. An estimated 0.8% of adults aged 15–49 years worldwide are living with HIV "[1]". The human immunodeficiency virus type 1 (HIV-1) reverse transcriptase (RT) is a very critical target enzyme for drug development. HIV-1 RT catalyzes production of double-stranded proviral DNA(dsDNA) using single-stranded viral RNA(ssRNA) as template "[2]". The role of Reverse Transcriptase (RT) enzyme is vital in the life cycle of HIV virus. Drug resistance is the major clinical problem for the treatment of virus-infected individuals "[3]". In this work, the role of single point mutations of reverse transcriptase on drug resistance has been studied based in silico methods. At the first stage in this study, the most important single point mutations of reverse transcriptase enzyme have been simulated. Consequently, cross-docking simulations were used to compare binding energies of native and mutated RT enzymes with some known inhibitors. The purpose of the study was to find some structural features which are responsible for drug resistance against this target. The findings of this study suggest that presence of phosphate groups increase the chance of drug resistance. Another important finding was that hydrazine carboxamide substructure was beneficial to decrease less drug resistanc

Key words: AIDS; HIV-I; Cross-docking simulations; reverse transcriptase; drug resistance

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