The molecular level energy calculation and Molecular dynamics studies on structurally similar HTLV and HIV protease enzymes using HIV-PR inhibitors

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Abstract

The HIV-1 and HTLV-I are retroviral proteases which share 31% sequence identity and high structural similarities. Yet, their substrate specificities and inhibition profiles are differing from each other and due to these reasons; most of the HIV-PR inhibitors fail to interact with HTLV-PR. Here we examined the approved drugs of HIV-PR inhibitors towards both retroviral protease and examined the difference between both proteases through the binding energy, interaction energy and molecular dynamics studies. Even though there is 31% sequence similarity between these two retroviral proteases, there is 78% similarity in amino acids present in binding cavity. This active site correlation gives more positive intensions towards working principle "How HIV-PR inhibitors can work with HTLV-PR". To understand the HIV-PR inhibitors mechanism in HTLV-PR, we performed molecular dynamics (MD) simulations for both retroviral protease enzymes in their Apo state and in complex state in order to compare their dynamic behaviors. These studies enhance our indulgent of correlation between sequence, structure, and dynamics in this protein family. We found extensive similarities in both protein dynamics, as well as in the energetics of their interactions with ligand substrates. The Darunavir, Nelfinavir, Saquinavir and Tipranavir shows better interaction

energies with atoms present in the HTLV-PR and this is due to the presence of common amino acids in both the protease binding sites. When treating with all approved compounds of HIV-PR with both proteases only Darunavir, Nelfinavir, Saquinavir and Tipranavir shows better interactions, sufficient energy level and dynamic activeness with HTLV-PR. Both the retroviral protease having the similar binding region and due to these common binding modes, the Darunavir, Nelfinavir, Saquinavir and Tipranavir is having the activeness towards the HTLV-PR. In future, the chemical libraries of these compounds will arise as better inhibitors against HTLV-PR.

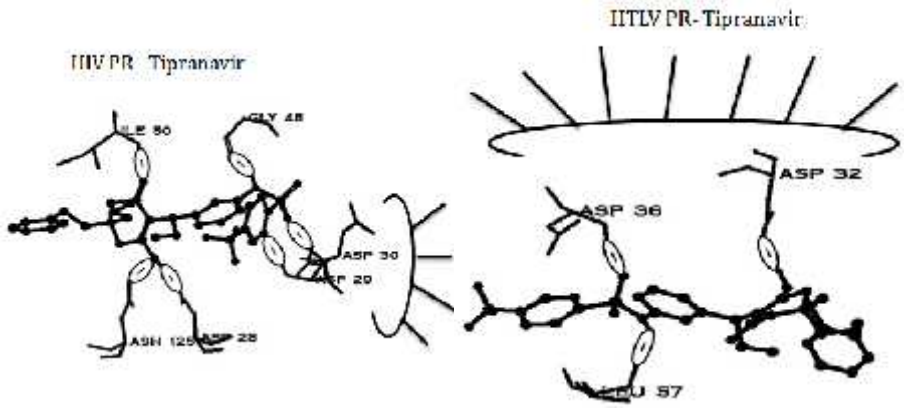

Figure 1. Tipranavir action between HIV and HTLV proteases, shows common amino acid involve in the interactions

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