

The Efficacy of HIV-1 Protease Inhibitors on HIV-2 Protease

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Protease inhibitors have been a regular part of the HIV infection treatment since 1995. They are still widely used including in HAART therapy. Due to the predominance of HIV-1 in developed Western countries, antiviral drug design has generally focused on the inhibition of HIV-1, whereas only a limited number of studies consider HIV-2. It is important to compare the effectiveness of HIV protease inhibitors in proteases from both the HIV-1 and HIV-2 strain, as HIV-2 is endemic in West Africa, and also occurs in France, Spain, Brazil and Portugal. We used AMBER molecular dynamics and MM-GBSA binding analysis to investigate the relative effectiveness of ten FDA-approved HIV-1 protease inhibitors for the HIV-2 protease. We find that all of the inhibitors are more effective in treating HIV-1, however they show good efficacy for HIV-2 protease. Atazanavir, ritonavir and, tipranavir were the most effective HIV protease inhibitors in HIV-2 protease. This information will allow us to investigate commonalities between the best drugs for HIV-2 protease and design novel inhibitors to deter the transmission of HIV-2.

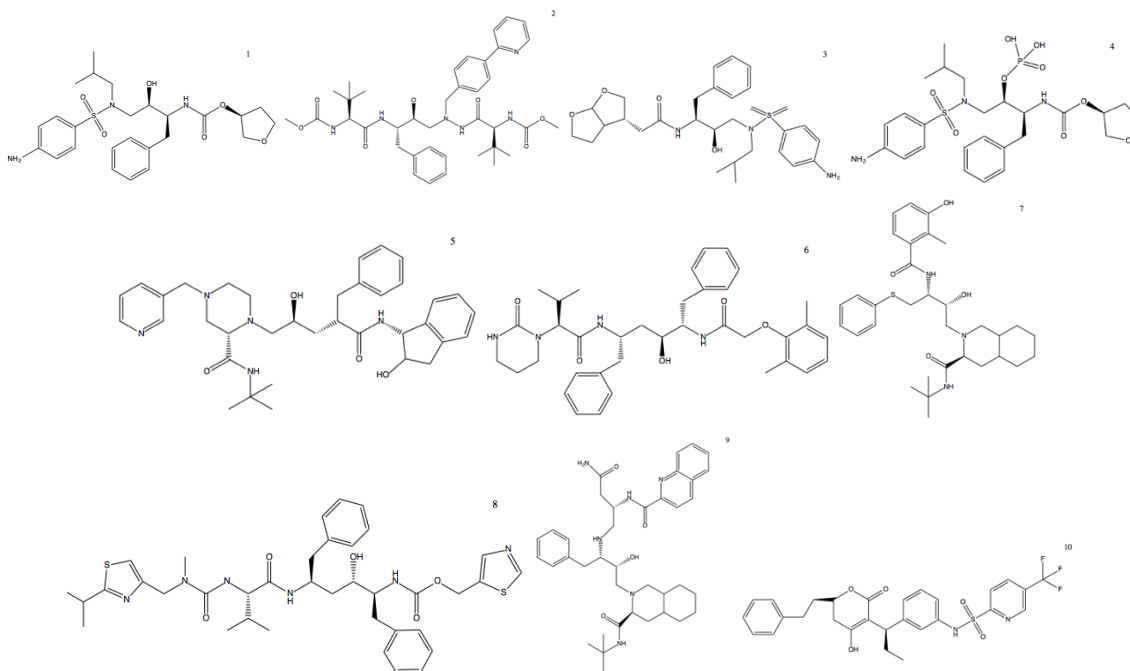


Figure 1 FDA approved protease inhibitors (from the top-left): (1) Amprenavir, (2) Atazanavir, (3) Darunavir, (4) Fosamprenavir, (5) Indinavir, (6) Lopinavir, (7) Nelfinavir, (8) Ritonavir, (9) Saquinavir, (10) Tipranavir