Conformational Analysis of HIV-1 Protease Inhibitors

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HIV-1 Protease Inhibitors are a class of drugs that target one of the enzymes responsible for the reproduction of the virus that causes AIDS. Small molecule drugs that inhibit the HIV-1 protease enzyme have been the focus of significant research in the last 20 years; however, rapid viral mutations lead to decreased drug efficacy. This computational research has investigated the molecular flexibility of current FDA approved HIV-1 Protease Inhibitors using the recently released OPLS 2005 force field in conjunction with the GB/SA solvent model for water, and compared these results with results obtained previously with the AMBER* and OPLS-AA force fields. The 50:50 Low Mode and Monte Carlo conformational search method was used to thoroughly sample the potential energy surfaces and to generate an ensemble of low energy structures. Details concerning the set-up of the conformational sampling will be presented, along with information obtained regarding the overall flexibility and shape of the HIV-1 protease inhibitors Atazanavir, Ritonavir, Indinavir, Amprenavir, Lopinavir, Nelfinavir and Saquinavir.