ABSTRACT

Human Immunodeficiency Virus (HIV) is a virus that attacks the human immune system and can lead to Acquired Immunodeficiency Syndrome (AIDS). The number of HIV infections continues to rise worldwide, including in Indonesia, thus requiring new therapeutic alternatives to overcome resistance to conventional antiretroviral therapy. This study explores the potential of bioactive ellagitannin compounds from pomegranate (Punica granatum), such as ellagic acid, punicalin, and punicalagin, as candidate inhibitors of HIV-1 integrase in complex with LEDGF/p75. The research employed molecular dynamics simulations using the GROMACS program on a Linux/Ubuntu-based system. Analyses included radius of gyration, RMSD, RMSF, enzyme–ligand interaction energy, and conformational changes in the enzyme's active site. Visualization was performed using Chimera 1.11.2 to identify key residues involved in ligand binding and to observe conformational changes in the catalytic domain of the enzyme. The results demonstrated that punicalagin exhibited the most significant inhibitory potential against the HIV-1 integrase–LEDGF/p75 complex, followed by punicalin, ellagic acid, and pirmitegravir. The strongest interaction energies were found in pirmitegravir (-168.5673) and ellagic acid (-148.0386), while the largest conformational changes in the catalytic site were observed with punicalagin (0.2227) and punicalin (-0.2069). The inhibition mechanism involves interactions of -C=O, -OH, and -CH3 groups with the key residues Phe-181 and Ile-182, leading to an induced-fit inhibition. This conformational alteration in the Catalytic Core Domain (CCD) of HIV-1 integrase prevents the integration of viral DNA into the host chromosomal DNA. Therefore, ellagitannins from pomegranate have the potential to be developed as novel drug candidates for HIV therapy.

Keyword: HIV-1 integrase, LEDGF/p75, ellagitannin, punicalagin, molecular dynamics, induced fit