# Classical and advanced molecular dynamics study on ligand-protein interactions targeted at HCV NS3/4A protease

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Hepatitis C virus (HCV) infection is the global health problem leading to liver inflammation which can develop to hepatocellular carcinoma. Even if the commercial anti-HCV drugs are available, the side effects have shown up and the mutations have caused the drug resistance. Therefore, understanding of the drug-target interactions and searching potent compound against HCV are needed for further drug design and development. Since NS3/4A protease has an essential role in viral replication, it becomes a major drug target. Using the classical molecular dynamics (MD) simulation, the ligand-protein interactions between the known anti-HCV drugs (boceprevir and telaprevir) and inhibitors (danoprevir and BI201335) and NS3/4A protease were explored. These four ligands displayed a strong hydrogen bonding interaction with A157, while the hydrogen bonding interaction with backbone of R155 was decreased in both drugs. This result was supported by the MM-GBSA binding free energies in which the two known inhibitors showed higher efficiency than the two anti-HCV drugs. Meanwhile, the steered MD was employed to screen the potent compounds against NS3/4A out from ZINC database. It was found that 59500093, 59784724, 13527817 and 26660256 compounds come to be the candidates of potent HCV inhibitor and van der Waals interaction is the main contribution in stabilizing the NS3/4A complex.