# Penapisan Senyawa Kandidat Inhibitor Protein NS3 Protease-Helikase dengan Fragment-Based Drug Discovery (FBDD) untuk Pengobatan Penyakit Demam Berdarah secara In Silico = Screening of NS3 Helicase DENV Protein Inhibitor with Fragment-Based Drug Discovery (FBDD) for Dengue Fever Treatment with In Silico Method

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Abstrak

Penyakit Demam Berdarah banyak ditemukan di daerah dengan iklim tropis dan subtropis dimana penyakit ini disebabkan oleh virus dengue (DENV) yang ditransmisikan kepada manusia melalui nyamuk. DENV terdiri dari 3 (tiga) protein struktural (capsid (C), premembrane (prM) dan envelope (E)) dan 7 (tujuh) protein non-struktural (NS1, NS2A, NS2B, NS3, NS4A, NS4B dan NS5). Protein NS3 Protease-Helikase pada DENV berperan penting dalam pengolahan poliprotein dan replikasi virus sehingga berpotensi sebagai target dalam proses inhibisi. Dalam penelitian ini, digunakan metode Fragment-Based Drug Discovery (FBDD) untuk penemuan inhibitor DENV NS3 Protease-Helikase yang merupakan senyawa Biogenic yang diperoleh dari database ZINC15. Metode fragment growing untuk modifikasi dilakukan dengan menggunakan Osiris DataWarrior. Simulasi Penambatan Molekul dilakukan dengan menggunakan Molecular Operating Simulator (MOE) pada struktur 3D protein yang diperoleh dari Protein Data Bank (PDB). Melalui simulasi yang dilakukan, diperoleh lima ligan terbaik yang dipilih berdasarkan nilai RMSD, , pKi serta kestabilan interaksi yang terbentuk dengan protein. Uji karakterisitik ADME (Adsorpsi, Distribusi, Metabolisme, Ekskresi), toksisitas dan medicinial chemistry dilakukan pada kandidat obat menggunakan SwissADME, admetSAR, pKCSM, Osiris DataWarrior serta Toxtree. Hasil uji berdasarkan beberapa parameter menunjukkan compound 175 dan compound 72 hasil fragment growing memiliki karakteristik farmakologi yang baik dan sesuai standar pengembangan kandidat obat.
.....Dengue fever commonly found in areas with tropical and subtropical climates where it cause by the dengue virus (DENV) which transmitted to humans through mosquitoes. DENV consists of 3 (three) structural proteins (capsid (C), premembrane (prM) and envelope (E)) and 7 (seven) non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5). Since NS3 Protease-Helicase protein of DENV plays an important role in polyproteins development and viral replication, it is considered as the target of inhibition process. In this study, Fragment-Based Drug Discovery (FBDD) method was used for the discovery of DENV NS3 Protease-Helicase inhibitor where Biogenic compound obtained from ZINC15 database. Fragment growing method for modification was perfomed by using Osiris DataWarrior. Molecular docking process use Molecular Operating Simulator (MOE) on a 3D protein structure which obtained from Protein Data Bank (PDB). Through the simulations, five best ligand were screened based on RMSD, , pKi value and protein-ligan interaction stability. ADME characteristic tests (Adsorption, Distribution, Metabolism, Excretion), toxicity and medicinal chemistry were carried out on drug candidates using SwissADME, admetSAR, pKCSM, Osiris DataWarrior and Toxtree. The test results based on several parameters showed that compound 175 and compound 72 have good pharmacological characteristics in accordance with drugs development standards.