MOLECULAR DOCKING AND MOLECULAR DYNAMIC SIMULATION OF KAEMPFEROL DERIVATIVES AS ANTI-ACNE CANDIDATES AGAINST CUTIBACTERIUM ACNES PaNA

Catharina Beata Nugraha
21/478102/PA/20732

ABSTRACT

The research aims are to identify the inhibitory activity of Kaempferol derivatives against *C. acnes* through molecular docking studies and analyze the stability of the *C. acnes* complex with the best Kaempferol derivative through molecular dynamics simulation studies.

The research was started with the ligand preparation by drawing the kaempferol and its derivative using GaussView, which then the energy of each compound was minimized. The procedure was continued with protein preparation by downloading the pdb file of the PaNA enzyme from PDB RCSB website, and then the energy minimization of the protein was performed. Molecular docking of kaempferol and its derivative was carried out against PaNA enzyme to check the inhibitory activity of each compound. Molecular dynamic simulation of the PaNA enzyme with the best-docked complex was performed to check the stability of the complex. Energy minimization, molecular docking, and molecular dynamics were carried out using YASARA.

The 8 derivatives showed PaNA enzyme inhibitory activity based on molecular docking by forming conventional hydrogen bonds with the amino acid residue Tyr423 as kaempferol. The binding energy of derivative C, -8.046 kcal/mol, was the lowest among kaempferol and the 8 derivatives. Molecular dynamics simulation was conducted for 100 ns showed that PaNA enzyme complex with derivative C was stable based on the RMSD, RMSF, and Rg graphs. Derivative C, kaempferol-2'-O-rhamnoside, 3,5,7-trihydroxy-2-(4-hydroxy-2-(((2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)phenyl)-4H-chromen-4-one, was predicted to have a more significant PaNA inhibitory activity than kaempferol.

Keywords: anti-acne, kaempferol, molecular docking, molecular dynamic simulation, *propionium acnes*

PENAMBATAN MOLEKUL DAN SIMULASI DINAMIKA MOLEKUL DARI TURUNAN KAEMPFEROL SEBAGAI KANDIDAT ANTI-ACNE TERHADAP CUTIBACTERIUM ACNES PaNA

Catharina Beata Nugraha
21/478102/PA/20732

INTISARI

Penelitian ini bertujuan untuk mengidentifikasi aktivitas penghambatan derivatif Kaempferol terhadap *C. acnes* melalui studi molecular docking dan menganalisis stabilitas kompleks *C. acnes* dengan derivatif Kaempferol terbaik melalui studi simulasi dinamika molekuler. Penelitian diawali dengan preparasi ligan dengan menggambar kaempferol dan derivatifnya menggunakan GaussView, yang kemudian energi masing-masing senyawa diminimalkan. Prosedur dilanjutkan dengan preparasi protein dengan mengunduh file pdb enzim PaNA dari situs PDB RCSB, kemudian dilakukan minimisasi energi protein. Molecular docking kaempferol dan derivatifnya dilakukan terhadap enzim PaNA untuk memeriksa aktivitas penghambatan masing-masing senyawa. Simulasi dinamis molekuler enzim PaNA dengan kompleks terdocking terbaik dilakukan untuk memeriksa stabilitas kompleks. Minimalisasi energi, docking molekuler, dan dinamika molekuler dilakukan menggunakan YASARA.

8 derivatif menunjukkan aktivitas penghambatan enzim PaNA berdasarkan docking molekuler dengan membentuk ikatan hidrogen konvensional dengan residu asam amino Tyr423 sebagai kaempferol. Energi pengikatan derivatif C, -8.046 kkal/mol, merupakan yang terendah di antara kaempferol dan 8 derivatif. Simulasi dinamika molekuler dilakukan selama 100 ns yang menunjukkan bahwa kompleks enzim PANa dengan derivatif 3 stabil berdasarkan grafik RMSD, RMSF, dan Rg. Derivatif C, kaempferol-2'-O-rhamnoside, 3,5,7-trihydroxy-2-(4-hydroxy-2-(((2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)phenyl)-4H-chromen-4-one, diprediksi memiliki aktivitas penghambatan PaNA yang lebih signifikan daripada kaempferol.

Kata kunci: anti-jerawat, kaempferol, penambatan molekul, *propionium acne*, simulasi dinamika molekule