KAJIAN PENAMBATAN MOLEKUL DAN SIMULASI DINAMIKA MOLEKUL ANALOG ETORICOXIB SEBAGAI INHIBITOR COX-2

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INTISARI

Kajian penambatan molekul dan simulasi dinamika molekul analog Etoricoxib sebagai inhibitor Enzim *Cyclooxygenase-2* (COX-2) telah dilakukan. Tujuan dari penelitian ini adalah mengidentifikasi aktivitas penghambatan analog Etoricoxib terhadap COX-2 melalui penambatan molekul serta menganalisa kestabilan kompleks dengan hasil penghambatan COX-2 yang terbaik melalui simulasi dinamika molekul.

Struktur molekul Etoricoxib dan analog Etoricoxib digambar menggunakan GaussView 5.0 kemudian minimasi energi dilakukan terhadap struktur tersebut. Struktur enzim COX-2 (PDB ID: 6COX) diunduh dari situs web RCSB PDB kemudian minimasi energi dilakukan terhadap struktur tersebut. Penambatan molekul Etoricoxib dan analognya dilakukan terhadap enzim COX-2 untuk mengetahui aktivitas penghambatan enzim COX-2 dari senyawa-senyawa tersebut. Simulasi dinamika molekul dilakukan terhadap kompleks enzim COX-2 dengan analog yang memiliki aktivitas penghambatan terbaik untuk mengetahui kestabilan kompleks tersebut. Minimasi energi, penambatan molekul, dan simulasi dinamika molekul dilakukan menggunakan YASARA.

Penambatan molekul menunjukkan bahwa semua analog memiliki aktivitas penghambatan enzim COX-2, membentuk ikatan hidrogen konvensional dengan residu asam amino Arg513 sama seperti Etoricoxib. Energi pengikatan analog A (5-kloro-2-(naft-2-il)-3-(4-metilsulfonilfenil)piridin) merupakan yang terrendah di antara Etoricoxib dan semua analog. Simulasi dinamika molekul yang dilakukan selama 20 ns menunjukkan bahwa struktur dinamis kompleks enzim COX-2 dengan analog A stabil berdasarkan grafik RMSD, RMSF, dan Rg. Analog A diperkirakan memiliki aktivitas penghambatan enzim COX-2 yang lebih baik daripada aktivitas milik Etoricoxib.

Kata kunci: antiinflamasi, COX-2, Etoricoxib, penambatan molekul, simulasi dinamika molekul

MOLECULAR DOCKING AND MOLECULAR DYNAMICS SIMULATION STUDY OF ETORICOXIB ANALOGUES AS COX-2 INHIBITORS

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ABSTRACT

Molecular docking and molecular dynamics simulation study of Etoricoxib analogues as Cyclooxygenase-2 (COX-2) Enzyme inhibitors has been conducted. This study was aimed to identify the inhibitory activity of Etoricoxib analogues against COX-2 via molecular docking and to analyse the stability of complex with the best COX-2 inhibition results via molecular dynamics simulation.

The molecular structures of Etoricoxib and Etoricoxib analogues were drawn using GaussView 5.0, energy minimization was then performed on each structure. The COX-2 enzyme structure (PDB ID: 6COX) was downloaded from the RCSB PDB website and energy minimization was then performed on the structure. Molecular docking of Etoricoxib and its analogues was carried out against the COX-2 enzyme to assess the COX-2 inhibitory activity of each compound. Molecular dynamics simulation of COX-2 enzyme complex with analogue that exhibited the best inhibitory activity was performed to assess the stability of the complex. Energy minimization, molecular docking, and molecular dynamics simulation were all performed using YASARA.

Molecular docking showed that all analogues exhibited COX-2 inhibitory activity, by forming conventional hydrogen bonds with the amino acid residue Arg513, similar to Etoricoxib. The binding energy of analogue A (5-chloro-2-(naphth-2-yl)-3-(4-methylsulfonylphenyl)pyridine) was the lowest among Etoricoxib and its analogues. Molecular dynamics simulation conducted for 20 ns showed that the dynamic structure of COX-2 enzyme complex with analogue A was stable based on the RMSD, RMSF, and Rg graphs. Analogue A was predicted to have a greater COX-2 inhibitory activity compared to Etoricoxib.

Keywords: anti-inflammatory, COX-2, Etoricoxib, molecular docking, molecular dynamics simulation