ABSTRAK

Alternatif pengobatan Alzheimer dengan target enzim asetilkolinesterase (AChE) menggunakan senyawa bahan alam sedang berkembang pesat hingga saat ini. Daidzein, senyawa bahan alam yang sering ditemukan di produk kacang kedelai, telah diteliti memiliki sifat neuroprotektif. Penelitian ini bertujuan untuk memprediksi interaksi dan mengetahui stabilitas kompleks daidzein dengan AChE. Penambatan ulang dan molekul dilakukan sebanyak 100 kali. Di sisi lain, dinamika molekul dilakukan sebanyak lima replikasi selama 15 ns dengan lima ns pertama sebagai fase ekuilibrasi dan sepuluh ns berikutnya sebagai fase produksi. Penambatan ulang donepezil pada sisi aktif AChE menghasilkan nilai RMSD ≤ 2,000 Å sehingga dapat digunakan untuk memprediksi pose daidzein. Simulasi penambatan molekul memprediksi dua klaster pose daidzein yang kemudian diklasifikasikan sebagai daidzein pose dominan (DPD) dan daidzein pose non dominan (DPND). Kedua pose memperoleh nilai RMSD *backbone* ≤ 2,000 Å dengan DPND replikasi satu memiliki nilai RMSD *backbone* > 2,000 Å pada beberapa *snapshot*. Kelima replikasi DPD mempunyai RMSD *ligand movement* > 2,000 Å. Meskipun demikian, DPD masih berada dalam sisi aktif AChE dengan membentuk interaksi aromatik pada Trp286. Di sisi lain, DPND replikasi dua, empat, dan lima memperoleh nilai RMSD *ligand movement* ≤ 2,000 Å karena mampu mempertahankan interaksi aromatik dengan Trp286 dan Tyr341 serta interaksi hidrogen dengan Tyr72, Asp74, Tyr124, Tyr337, His287, dan Tyr341. Berdasarkan hal tersebut dapat disimpulkan bahwa daidzein dapat stabil dengan membentuk interaksi aromatik dan hidrogen pada sisi aktif AChE.

Kata Kunci : Alzheimer, asetilkolinesterase, daidzein, *in silico*

ABSTRACT

Utilization of natural compounds targeting acetylcholinesterase (AChE) as alternative treatments for Alzheimer's disease has significantly increased. Daidzein, natural compound found in soybean-derived products, may enhance cognitive function. This study aimed to predict interactions and evaluate stability of daidzein-AChE complex. Redocking and molecular docking were conducted with 100 replications while molecular dynamics were conducted with five replications for 15 ns included five ns equilibration phase followed by ten ns production phase. Molecular docking of donepezil resulted RMSD of ≤ 2,000 Å. Therefore, this method could predict daidzein binding poses. Molecular docking of daidzein revealed two distinct clusters then classified as dominant daidzein pose (DDP) and non-dominant daidzein poses (NDDP). All replicates of DDP and NDDP exhibited a backbone RMSD of ≤ 2,000 Å although the first replicate of NDDP resulted in backbone RMSD exceeding 2,000 Å in several snapshots. However, daidzein was capable of maintaining the stability of its backbone conformation. All DDP showed ligand movement RMSD of > 2,000 Å. However, DDP remained within the AChE active site due to aromatic interactions with Trp286. In contrast, the second, fourth, and fifth replications of NDDP showed ligand movement RMSD of ≤ 2,000 Å. NDDP remained stable due to aromatic interactions with Trp286 and Tyr341, also forming hydrogen bonds with Tyr72, Asp74, Tyr124, Tyr 337, His287, and Tyr341. This research revealed that daidzein is capable of staying within the AChE active site while interacting through hydrogen and aromatic interactions.

Keyword : Alzheimer, acetylcholinesterase, daidzein, *in silico*