ABSTRAK

Alzheimer merupakan penyakit neurodegeneratif akibat kurangnya asetilkolin pada otak. Hal ini diakibatkan hidrolisis asetilkolin oleh enzim asetilkolinesterase (AChE). Penghambat AChE merupakan terapi yang digunakan untuk pengobatan Alzheimer. ZINC000253412911 merupakan senyawa bahan alam yang berpotensi memiliki aktivitas penghambatan AChE. Penelitian ini bertujuan untuk mengetahui interaksi dan stabilitas kompleks ZINC000253412911-AChE melalui simulasi penambatan dan dinamika molekul selama 15 ns menggunakan YASARA-Structure. Nilai *Root Mean Square Deviation* (RMSD) penambatan ulang huprine X, RMSD penambatan ZINC000253412911, serta ΔRMSD *backbone* dan ΔRMSD *ligand movement* pada 5 – 10 ns fase produksi diamati pada penelitian ini. Kompleks ZINC000253412911-AChE dinyatakan stabil apabila nilai ΔRMSD ≤ 2,000 Å. Penambatan ulang menghasilkan 100 pose penambatan ulang terbaik dengan nilai RMSD ≤ 2,000 Å sehingga protokol yang digunakan dalam penambatan ulang dapat digunakan dalam penambatan ZINC000253412911. Hasil penambatan molekul sebanyak 100 kali menghasilkan 3 klaster pose konformasi kompleks ZINC000253412911 – AChE. Interaksi yang terbentuk yakni hidrogen, aromatis, dan hidrofobik. Hasil simulasi dinamika molekul menunjukkan dua dari tiga pose stabil dengan nilai ΔRMSD ≤ 2,000 Å. Asam amino yang secara dominan berperan menstabilkan kompleks ZINC000253412911 – AChE yakni Tyr70, Asp72, Trp84, Tyr121, Trp279, Ile287, dan Phe330. Selama dinamika molekul, nilai RMSD *ligand movement* ketiga pose > 2,000 Å yang mengindikasikan konformasi ZINC000253412911 berbeda dengan konformasi awal sebelum dinamika molekul.

Kata Kunci: Alzheimer, Asetilkolinesterase, ZINC000253412911, Penambatan Molekul, Dinamika Molekul

ABSTRACT

Alzheimer's disease is a neurodegenerative disorder caused by a lack of acetylcholine in the brain. This is caused by hydrolysis of acetylcholine by acetylcholinesterase (AChE) enzyme. AChE inhibitors are therapies used for Alzheimer's disease treatments. ZINC000253412911 is a natural compound that has the potency to have AChE inhibitory activity. This study aimed to determine the interaction and stability of the ZINC000253412911-AChE complex through molecular docking and 15-ns dynamics simulations using YASARA-Structure. The Root Mean Square Deviation (RMSD) values of redocking, RMSD of docked ZINC000253412911 resulted from molecular docking, ΔRMSD of the AChE backbone, and ΔRMSD of the ligand movement in 5 – 10 production run were observed in this study. The ZINC000253412911-AChE complex is considerably stable if the ΔRMSD value is ≤ 2,000 Å. Redocking simulations resulted in 100 best-redocked poses with RMSD values of ≤ 2,000 Å, thereby the protocol used in redocking could be used for molecular docking of ZINC000253412911. Molecular docking results produced 3 clusters of ZINC000253412911 - AChE complex conformational poses. The interactions formed were hydrogen, aromatic, and hydrophobic. The results of molecular dynamics simulations showed that two of the three poses were stable with the ΔRMSD values ≤ 2,000 Å. The amino acids that played a dominant role in stabilizing the ZINC000253412911 – AChE complex were Tyr70, Asp72, Trp84, Tyr121, Trp279, Ile287, and Phe330. During the molecular dynamics, the RMSD values of the ligand movement of the three poses were > 2,000 Å, which indicated that the ZINC000253412911 conformation were different from the initial conformation before the molecular dynamics.

Keywords: Alzheimer's disease, acetylcholinesterase, ZINC000253412911, molecular docking, molecular dynamics