ABSTRAK

Penyakit Alzheimer merupakan gangguan neurodegeneratif progresif yang ditandai oleh penurunan fungsi kognitif dan memori, serta peningkatan aktivitas enzim *asetilkolinesterase* (AChE), yang menyebabkan degradasi neurotransmiter asetilkolin. Flavonoid dipilih dalam penelitian ini karena telah dilaporkan memiliki berbagai aktivitas biologis yang relevan dengan mekanisme patofisiologi penyakit Alzheimer, termasuk sebagai antioksidan, antiinflamasi, dan agen neuroprotektif. Penelitian ini bertujuan untuk menganalisis potensi senyawa turunan flavonoid sebagai penghambat enzim AChE melalui pendekatan *in silico* dengan dua target protein yaitu AChE dari spesies *Tetronarce californica* (PDB ID: 1EVE) dan *Homo sapiens* (PDB ID: 4EY7). Tahapan penelitian meliputi preparasi ligan dan reseptor, validasi metode *docking*, penambatan molekuler menggunakan *AutoDock Vina*, serta analisis interaksi residu menggunakan *Discovery Studio Visualizer*. Hasil *docking* menunjukkan bahwa senyawa karanjin, luteolin, dan luteolin-7-O-glukosida memiliki nilai afinitas ikatan yang mendekati ligan alami pada kedua protein (-10,6 hingga -11,2 kkal/mol) dan menunjukkan interaksi dengan residu penting di sisi aktif AChE. Ketiga senyawa tersebut juga memenuhi kriteria *Lipinski's Rule of Five* yang mendukung kelayakan farmakokinetiknya. Berdasarkan temuan ini, senyawa turunan flavonoid (karanjin, luteolin, dan luteolin-7-O-glukosida) berpotensi dikembangkan sebagai agen terapeutik alternatif untuk Alzheimer melalui mekanisme penghambatan enzim AChE.

Kata kunci: Alzheimer, asetilkolinesterase, flavonoid, *in silico*, *molecular docking*, 1EVE, 4EY7

ABSTRACT

Alzheimer's disease is a progressive neurodegenerative disorder characterized by cognitive and memory decline, along with increased activity of the enzyme acetylcholinesterase (AChE), which leads to the degradation of the neurotransmitter acetylcholine. Flavonoids were selected in this study due to their reported biological activities relevant to the pathophysiological mechanisms of Alzheimer's disease, including antioxidant, anti-inflammatory, and neuroprotective properties. This research aims to analyze the potential of flavonoid derivatives as AChE inhibitors using an in silico approach with two protein targets: AChE from Tetronarce californica (PDB ID: 1EVE) and Homo sapiens (PDB ID: 4EY7). The research stages included ligand and receptor preparation, docking method validation, molecular docking using AutoDock Vina, and residue interaction analysis via Discovery Studio Visualizer. Docking results indicated that the compounds karanjin, luteolin, and luteolin-7-O-glucoside exhibited binding affinities comparable to those of the native ligands on both proteins (-10.6 to -11.2 kcal/mol) and showed interactions with key active site residues of AChE. These three compounds also met the criteria of Lipinski's Rule of Five, supporting their pharmacokinetic feasibility. Based on these findings, the flavonoid derivatives karanjin, luteolin, and luteolin-7-O-glucoside show potential as alternative therapeutic agents for Alzheimer's disease through AChE inhibition.

Keywords: Alzheimer's disease, acetylcholinesterase, flavonoids, in silico, molecular docking, 1EVE, 4EY7