STUDI *IN SILICO* AKTIVITAS PENGHAMBAT *ACETYLCHOLINESTERASE* DAN *BETA-SECRETASE* SENYAWA ANDROGRAFOLID SERTA TURUNANNYA SEBAGAI KANDIDAT TERAPI ALZHEIMER

SKRIPSI

SARAH AL RISALLAH TSALITSAH
A242024

SEKOLAH TINGGI FARMASI INDONESIA
YAYASAN HAZANAH
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Sebagai salah satu syarat untuk memperoleh gelar Sarjana Farmasi

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Oktober 2025

Disetujui oleh :

Pembimbing	**Pembimbing**
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ABSTRAK

Alzheimer merupakan penyakit neurodegeneratif progresif yang ditandai penurunan kognitif akibat akumulasi β-amiloid dan defisit asetilkolin. Terapi multitarget melalui penghambatan *acetylcholinesterase* (AChE) dan *beta-secretase* (BACE1) dianggap lebih efektif. Andrografolid, senyawa utama *Andrographis paniculata*, diketahui memiliki efek neuroprotektif sehingga berpotensi sebagai agen terapi Alzheimer. Penelitian ini bertujuan mengevaluasi potensi andrografolid dan turunannya sebagai inhibitor AChE dan BACE1 melalui studi *in silico*. Metode mencakup prediksi farmakokinetik (ADME), toksisitas, potensi aktivitas biologis, serta penambatan molekuler dengan *AutoDock* Vina. Hasil menunjukkan seluruh senyawa memenuhi kriteria *Lipinski Rule of Five* dengan tingkat toksisitas relatif aman (kelas IV–VI) meski berpotensi toksik terhadap sistem imun. Prediksi potensi aktivitas berdasarkan *Structure Activity Relationship* (SAR) mengindikasikan kemampuan sebagai *dementia treatment* yang berpotensi menjadi agen terapi Alzheimer. Analisis penambatan molekuler memperlihatkan andrografolid dan turunannya memiliki energi ikatan kompetitif terhadap reseptor AChE (PDB ID: 4EY7) dan BACE1 (PDB ID: 6OD6) mendekati ligan pembanding donepezil dan verubecestat. Interaksi terjadi melalui ikatan hidrogen dan hidrofobik dengan residu asam amino kunci pada sisi aktif, menghasilkan kompleks yang stabil, sehingga dapat disimpulkan andrografolid dan turunannya berpotensi sebagai inhibitor multitarget terapi Alzheimer dan layak dipertimbangkan dalam pengembangan obat tahap lanjut.

Kata kunci : Alzheimer, andrografolid, *in silico*, *acetylcholinesterase*, *beta-secretase*

ABSTRACT

Alzheimer's disease is a progressive neurodegenerative disorder characterized by cognitive decline due to β-amyloid accumulation and acetylcholine deficit. A multitarget therapy approach through inhibition of acetylcholinesterase (AChE) and beta-secretase (BACE1) is considered more effective. Andrographolide, the major compound of Andrographis paniculata, is known to exhibit neuroprotective effects, thus showing potential as an Alzheimer's treatment agent. This study aimed to evaluate the potential of andrographolide and its derivatives as AChE and BACE1 inhibitors through an in silico approach. Methods included pharmacokinetic (ADME) prediction, toxicity evaluation, biological activity prediction, and molecular docking using AutoDock Vina. Results demonstrated that all compounds met the Lipinski Rule of Five with relatively safe toxicity levels (class IV–VI), although showing possible immunotoxicity that requires further investigation. Activity prediction based on Structure Activity Relationship (SAR) indicated potential as dementia treatment. Molecular docking analysis revealed that andrographolide and its derivatives exhibited competitive binding energies toward AChE (PDB ID: 4EY7) and BACE1 (PDB ID: 6OD6), comparable to the reference ligands donepezil and verubecestat. Stable interactions were formed through hydrogen bonding and hydrophobic contacts with key amino acid residues at the active sites. In conclusion, andrographolide and its derivatives possess promising potential as multitarget inhibitors for Alzheimer's disease and merit further development in drug discovery.

Keywords*: Alzheimer's disease, andrographolide, in silico, acetylcholinesterase, beta-secretase*

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