Implementation of the In Silico Method in Studying the Potential of Ligand Pairings from Bioactive Compounds of Rambutan (*Nephelium lappaceum L.*) Epicarp as an Inhibitor for the Treatment of Alzheimer's Disease

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ABSTRACT

Alzheimer's disease is a chronic, progressive, and incurable condition causing brain shrinkage over time. While the main cause is unknown, protein dysfunction, including amyloid plaques and tau aggregation, play significant roles. Through in-silico molecular docking, this research enhances binding efficiency by linking ligands as pairs to target two proteins simultaneously, accelerating potential treatment.

This study explores *Nephelium lappaceum L.* epicarp, Indonesia's highly available native fruit, as a potential treatment due to its antioxidant, anti-inflammatory, or anti-amyloidogenic bioactive compounds. Using in-silico molecular docking, this research aims to identify the ligand pair with the highest potential as Alzheimer's disease inhibitor, contributing to safer and more effective treatments.

In Molecular Docking Stage 1, 7 of 14 bioactive compounds were selected through Toxicity and Drug-likeness prediction and docked with 20 Alzheimer's target proteins. The 3 strongest complexes (IL10, BACE1, and AKT1 bound with Ethyl acetate, Acetone, and DMSO) were redocked in Molecular Docking Stage 2 alongside APBB1 and TauMAPT. The complexes were docked in Autodock Vina. Binding energies and residues validity, interaction distances (VdW & Coulomb), H-bonds, salt bridges, pi-pi stacking, and hydrophobic interactions were analysed.

Among all ligand pairs, Ethyl acetate-Acetone had the strongest binding energy (-6.5 kcal/mol), while DMSO-Ethyl acetate (-6.0 kcal/mol) and Acetone-DMSO (-5.9 kcal/mol) also showed strong affinity. However, DMSO-Ethyl acetate demonstrated the highest stability needed in effective protein dysfunction inhibition, with only 2 interaction values outside the ideal ranges, making it the ligand pair with the highest potential as an inhibitor in Alzheimer's treatment.

Keywords:

1. Alzheimer’s disease
2. *Nephelium lappaceum L.*
3. Ligand pairs
4. Molecular Docking