# PENAMBATAN MOLEKUL DAN SIMULASI DINAMIKA MOLEKUL DARI METABOLIT SEKUNDER ALGA HIJAU (*Ulva lactuca*) TERHADAP PROTEIN KINASE B (AKT1) SEBAGAI ANTIKANKER USUS BESAR

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## ABSTRAK

Dalam penelitian ini, telah dilakukan penambatan molekul dan simulasi dinamika molekul dari metabolit sekunder alga hijau *Ulva lactuca* terhadap Protein Kinase B (AKT1) sebagai kandidat antikanker usus besar. Kanker usus besar merupakan penyakit dengan prevalensi tinggi secara global, termasuk pada negara Indonesia. Tingginya kasus resistensi terhadap terapi kanker konvensional mendorong pencarian alternatif. *Ulva lactuca* telah dilaporkan memiliki potensi antikanker terhadap sel HCT-116, yang diketahui mengekspresikan AKT1 tinggi. Penelitian ini bertujuan menganalisis afinitas, stabilitas, dan interaksi metabolit *Ulva lactuca* terhadap AKT1. Metodologi meliputi penyaringan ligan menggunakan Lipinski's Rule of Five, *network pharmacology* untuk identifikasi target sentral AKT1, preparasi protein target 3MVH, validasi penambatan molekul, penambatan molekul senyawa uji dan pembanding, serta simulasi dinamika molekul. Dari 96 senyawa Ulva lactuca, 29 senyawa memenuhi aturan Lipinski. Analisis *network pharmacology* mengkonfirmasi AKT1 sebagai target sentral terkait kanker usus besar. Hasil penambatan molekul menunjukkan S24, S64, dan S92 sebagai ligan uji terbaik dengan nilai ΔG berturut-turut -8,09, -7,79, dan -7,83 kkal/mol, serta Ki berturut-turut 1,18; 1,94; dan 1,83 μM. Nilai ini mendekati ligan alami WFE (ΔG -9,68 kkal/mol; Ki 0,08 μM) dan obat pembanding MK-2206 (ΔG -10,43 kkal/mol; Ki 0,02 μM). Simulasi dinamika molekul selama 100 ns menunjukkan semua kompleks stabil (RMSD < 2.0 Å). Ligan S24 disimpulkan sebagai kandidat paling menjanjikan, dengan nilai energi pengikatan total MM/PBSA -37,63 kkal/mol (mendekati ligan alami -37,6 kkal/mol) dan pola ikatan hidrogen yang stabil dan banyak. Penelitian ini merekomendasikan ligan S24 sebagai kandidat obat baru yang potensial untuk dikembangkan lebih lanjut dalam pengobatan kanker usus besar melalui studi *in vitro* dan *in vivo*.

**Kata Kunci:** *Ulva lactuca*, Protein Kinase B (AKT1), Kanker Usus Besar, Penambatan Molekul, Simulasi Dinamika Molekul.

# MOLECULAR DOCKING AND MOLECULAR DYNAMICS SIMULATION OF GREEN ALGAE SECONDARY METABOLITES (*Ulva lactuca*) ON PROTEIN KINASE B (AKT1) AS COLON ANTICANCER

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## ABSTRACT

In this study, molecular docking and molecular dynamics simulations were conducted on secondary metabolites from the green alga *Ulva lactuca* against Protein Kinase B (AKT1) as a colon cancer candidate. Colon cancer is a highly prevalent disease globally, including in Indonesia. The high rate of resistance to conventional cancer therapies necessitates the search for alternative treatments. *Ulva lactuca* has been reported to possess anticancer potential against HCT-116 cells, which are known to express high levels of AKT1. This research aimed to analyze the affinity, stability, and interaction of *Ulva lactuca* metabolites with AKT1. The methodology encompassed ligand screening using Lipinski's Rule of Five, *network pharmacology* for the identification of AKT1 as a central target, preparation of the 3MVH protein target, validation of the molecular docking procedure, molecular docking of test and comparative compounds, and molecular dynamics simulations. Out of 96 *Ulva lactuca* compounds, 29 met Lipinski's criteria. *Network pharmacology* analysis confirmed AKT1 as a central target related to colon cancer. Molecular docking results identified S24, S64, and S92 as the best test ligands with ΔG values of -8.09, -7.79, and -7.83 kcal/mol, respectively, and Ki values of 1.18, 1.94, and 1.83 μM, respectively. These values approached those of the native ligand WFE (ΔG -9.68 kcal/mol; Ki 0.08 μM) and the comparative drug MK-2206 (ΔG -10.43 kcal/mol; Ki 0.02 μM). Molecular dynamics simulations over 100 ns showed all complexes were stable (RMSD < 2.0 Å). Ligand S24 was concluded to be the most promising candidate, with a total binding energy (MM/PBSA) of -37.63 kcal/mol (approaching the native ligand's -37.6 kcal/mol) and a stable and abundant hydrogen bond pattern. This study recommends ligand S24 as a potential novel drug candidate for further development in colon cancer treatment through *in vitro* and *in vivo* studies.

**Keywords**: *Ulva lactuca*, Protein Kinase B (AKT1), Colon Cancer, Molecular Docking, Molecular Dynamics Simulation.