



POTENSI EKSTRAK DAUN BELIMBING (*Averrhoa carambola* L.) TERHADAP KANKER LAMBUNG

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INTISARI

Kanker lambung menjadi tantangan kesehatan global karena tingkat morbiditas dan mortalitas yang sangat tinggi disertai prognosis yang buruk. Tingginya prevalensi infeksi *Helicobacter pylori* tidak hanya berkontribusi dalam patogenesis kanker, tetapi juga meningkatkan insidensi kanker lambung di berbagai populasi. Patogenesis kanker tersebut dipicu oleh aktivasi jalur persinyalan PI3K/AKT yang khas dan berkontribusi dalam regulasi proliferasi, angiogenesis, metastasis, dan mempertahankan kelangsungan hidup sel kanker. Aktivitas jalur ini umumnya dipicu oleh amplifikasi dan overekspresi reseptor tirosin kinase (RTK), seperti EGFR dan MET, serta mutasi gen pengatur GTPase terutama RAS. Keterbatasan efektivitas terapi konvensional akibat resistensi mendorong pencarian alternatif berbasis tanaman obat. Daun belimbing (*A. carambola*) diketahui mengandung metabolit sekunder, namun potensi sebagai antikanker lambung belum dieksplorasi. Penelitian ini bertujuan untuk mengevaluasi potensi senyawa daun *A. carambola* melalui analisis *in silico*. Pada penelitian ini, dilakukan identifikasi senyawa dari data GC-MS dan LC-HRMS, prediksi *drug-likeness* (SwissADME), prediksi aktivitas biologis (PASS Online), prediksi protein target (GeneCards, SwissTargetPrediction, STRING), serta analisis *molecular docking*. Empat senyawa potensial berhasil diidentifikasi, yaitu Apigenin, Tangeretin, Nobiletin, dan Torosaflavone A. Senyawa-senyawa ini diprediksi menghambat ekspresi HIF-1 α dan MMP-9, serta meningkatkan aktivasi caspase-8 dan jalur apoptosis. Hasil *molecular docking* menunjukkan Torosaflavone A memiliki afinitas terbaik terhadap EGFR sebesar -8,1 kcal/mol dan AKT1 sebesar -7,2 kcal/mol, sedangkan Apigenin menunjukkan afinitas tinggi terhadap MET sebesar -8,9 kcal/mol. Penelitian ini menjadi kajian pertama yang secara komprehensif mengevaluasi potensi *A. carambola* sebagai kandidat antikanker lambung melalui analisis *in silico*. Hasil penelitian ini diharapkan menjadi dasar bagi pengembangan studi lanjutan secara *in vitro* maupun *in vivo* untuk memvalidasi aktivitas biologis dan mekanisme kerjanya secara eksperimental.

Kata Kunci: *Averrhoa carambola* L., Jalur Persinyalan PI3K/AKT, Kanker Lambung, *In Silico*, Senyawa biokatif



POTENTIAL of STARFRUIT (*Averrhoa carambola* L.) LEAF EXTRACT AGAINST GASTRIC CANCER

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ABSTRACT

*Gastric cancer remains a major global health challenge due to its high morbidity and mortality rates, accompanied by a poor prognosis. The high prevalence of *Helicobacter pylori* infection not only contributes to the pathogenesis of gastric cancer but also increases its incidence across various populations. The disease pathogenesis is primarily driven by the activation of the PI3K/AKT signaling pathway, which plays a crucial role in regulating cellular proliferation, angiogenesis, metastasis, and cancer cell survival. This pathway is typically triggered by the amplification and overexpression of receptor tyrosine kinases (RTKs), such as EGFR and MET, as well as mutations in regulatory genes encoding GTPases, particularly RAS. The limited effectiveness of conventional therapies due to resistance has encouraged the search for alternative treatments based on medicinal plants. The leaves of starfruit (*A. carambola*) are known to contain secondary metabolites, yet their potential as anti-gastric cancer agents remains unexplored. This study aimed to evaluate the potential of *A. carambola* leaf compounds through in silico analysis. The workflow included compound identification using GC-MS and LC-HRMS data, prediction of drug-likeness (SwissADME), biological activity (PASS Online), protein target prediction (GeneCards, SwissTargetPrediction, STRING), and molecular docking analysis. Four potential compounds were identified Apigenin, Tangeretin, Nobiletin, and Torosaflavone A. These compounds were predicted to inhibit the expression of HIF-1 α and MMP-9, while enhancing caspase-8 activation and apoptotic pathways. Molecular docking results revealed that Torosaflavone A showed the highest binding affinity toward EGFR (-8.1 kcal/mol) and AKT1 (-7.2 kcal/mol), whereas Apigenin demonstrated a strong affinity for MET (-8.9 kcal/mol). This study represents the first comprehensive in silico investigation of *A. carambola* leaves as a potential anti-gastric cancer candidate. The findings are expected to provide a foundation for future in vitro and in vivo studies to validate the biological activity and elucidate the underlying mechanisms experimentally.*

Keywords: *Averrhoa carambola* L., PI3K/AKT signaling pathway, Gastric cancer, In Silico, Bioactive compound