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Kajian In Silico Mekanisme Aktivitas Galaktagog Kombinasi Katuk (Sauropus androgynus), Kelor (Moringa oleifera), Dan Temulawak (Curcuma xanthorrhiza): Studi Network Pharmacology, Prediksi Farmakokinetik, Molecular Docking, dan Molecular Dynamics.
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INTISARI

Latar Belakang: Hipogalaktia merupakan salah satu penyebab utama rendahnya keberhasilan pemberian Air Susu Ibu (ASI). Daun katuk (*Sauropus androgynus*), daun kelor (*Moringa oleifera*), dan rimpang temulawak (*Curcuma xanthorrhiza*) masing-masing telah dilaporkan memiliki potensi sebagai galaktagog secara individual. Namun mekanisme molekuler yang mendasari kombinasi poliherbal ketiga tanaman tersebut belum pernah dikaji secara komprehensif.

Tujuan: Mengeksplorasi dan memprediksi mekanisme molekuler aktivitas galaktagog melalui pendekatan in silico berbasis integrasi profil fitokimia, *network pharmacology*, prediksi ADMET, *molecular docking*, dan *molecular dynamics*.

Metode: Penelitian diawali dengan *untargeted metabolomic profiling* menggunakan LC–HRMS untuk mengidentifikasi senyawa dalam sediaan poliherbal galaktagog. Senyawa yang memenuhi kriteria *drug-likeness* dan ADMET serta *marker compound* dianalisis menggunakan *network pharmacology* untuk mengidentifikasi target protein, *hub* protein, dan jalur biologis terkait laktasi. Target prioritas kemudian divalidasi melalui *molecular docking* dan simulasi *molecular dynamics* selama 100 ns.

Hasil: Profiling LC–HRMS mengidentifikasi 53 metabolit terkurasi. Skrining ADMET menghasilkan sembilan senyawa prioritas untuk analisis lanjutan. Analisis *network pharmacology* menghasilkan 95 protein irisan dengan hub protein utama meliputi AKT1, EGFR, STAT3, JUN, dan NFKB1, serta menunjukkan pengayaan signifikan pada *prolactin signaling pathway*. *Molecular docking* menunjukkan kompleks Xerantholide–AKT1 memiliki afinitas pengikatan tertinggi, sedangkan apigenin dan isorhamnetin menunjukkan afinitas tinggi terhadap EGFR. Simulasi *molecular dynamics* menunjukkan bahwa kompleks Xerantholide–AKT1 dan Apigenin–EGFR mempertahankan pose pengikatan yang stabil, interaksi dengan residu-residu kunci, serta kestabilan struktural sepanjang simulasi 100 ns.

Kesimpulan: Integrasi pendekatan komputasional menunjukkan bahwa aktivitas galaktagog kombinasi poliherbal diprediksi dimediasi melalui mekanisme multitarget yang terutama berpusat pada AKT1 dan EGFR, dengan STAT3 sebagai regulator pendukung. Temuan ini menghasilkan model mekanistik komputasional yang dapat menjadi dasar rasional bagi penelitian eksperimental lanjutan untuk memvalidasi aktivitas galaktagog sediaan poliherbal.

Kata kunci: galaktagog; *Sauropus androgynus*; *Moringa oleifera*; *Curcuma xanthorrhiza*; *network pharmacology*; *molecular docking*; *molecular dynamics*

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ABSTRACT

Background: Hypogalactia is one of the causes of unsuccessful breastfeeding. Although *Sauropus androgynus*, *Moringa oleifera*, and *Curcuma xanthorrhiza* have each been reported to possess galactagogue properties, the molecular mechanisms underlying their combined polyherbal formulation remain poorly understood.

Objectives: To explore the molecular mechanisms underlying the galactagogue activity of a polyherbal formulation through an integrated in silico approach combining phytochemical profiling, network pharmacology, ADMET prediction, molecular docking, and molecular dynamics simulation.

Methods: Untargeted metabolomic profiling using liquid chromatography–high-resolution mass spectrometry (LC–HRMS) was performed to characterize the phytochemical composition. Compounds that fulfilled the drug-likeness and ADMET criteria, together with predefined marker compounds, were subsequently analyzed using network pharmacology to identify candidate protein targets, hub proteins, and lactation-related biological pathways. Priority targets were further evaluated by molecular docking, followed by 100-ns molecular dynamics simulations to assess the stability of ligand–protein interactions.

Results: LC–HRMS analysis identified 53 curated metabolites. ADMET screening prioritized nine compounds for downstream analyses. Network pharmacology revealed 95 overlapping protein targets, with AKT1, EGFR, STAT3, JUN, and NFKB1 emerging as the principal hub proteins, together with significant enrichment of the prolactin signaling pathway. Molecular docking identified the Xerantholide–AKT1 complex as exhibiting the strongest predicted binding affinity, whereas apigenin and isorhamnetin showed high binding affinities toward EGFR. Molecular dynamics simulations further demonstrated that both the Xerantholide–AKT1 and Apigenin–EGFR complexes maintained stable binding conformations, persistent interactions with key binding-site residues, and overall structural stability throughout the 100-ns simulations.

Conclusions: Integrated computational analyses suggest that the galactagogue activity of the polyherbal formulation is mediated through a multitarget mechanism centered primarily on AKT1 and EGFR, with STAT3 serving as a supporting regulatory node. These findings provide a mechanistic hypothesis and a rational framework for future experimental studies to validate the galactagogue activity of this polyherbal formulation.

Keywords: galactagogue; Sauropus androgynus; Moringa oleifera; Curcuma xanthorrhiza; network pharmacology; molecular docking; molecular dynamics.