

Abstrak

STUDI POTENSI SENYAWA AMENTOFLAVON DARI DAUN *Calophyllum soulattri* SEBAGAI INHIBITOR TIROSIN KINASE

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Latar Belakang : *Calophyllum soulattri* merupakan tumbuhan yang mengandung amentoflavon. Amentoflavon mampu menghambat angiogenesis dengan menghambat fungsi VEGFR-2. Pada penelitian ini dilakukan skrining aktivitas penghambatan amentoflavon terhadap 8 enzim tirosin kinase secara *in vitro* dan dilanjutkan dengan penambatan molekul dari enzim yang paling dihambat.

Metodologi : Amentoflavon diperoleh dengan mengisolasi fraksi etil asetat daun *C. soulattri* dengan teknik kromatografi vakum cair, kromatografi kolom, dan kromatotron. Amentoflavon diuji aktivitasnya sebagai inhibitor enzim tirosin kinase secara *in vitro* menggunakan metode *ADP-Glo kinase assay*. Dilakukan juga penambatan amentoflavon terhadap enzim yang paling baik penghambatannya berdasarkan hasil uji *in vitro* dengan AutoDock Vina dan Biovia untuk mengetahui energi ikatan dan interaksi yang terjadi.

Hasil Penelitian : Amentoflavon berhasil diisolasi dari daun *C. soulattri* sebanyak 6,8 mg. Uji *in vitro* menunjukkan aktivitas penghambatan terbaik terhadap enzim KDR/VEGFR-2 (3%). Berdasarkan penambatan molekul terhadap VEGFR-2, nilai energi ikatan amentoflavon yang dihasilkan sebesar -3,1 kkal/mol. Visualisasi penambatan menunjukkan terjadi interaksi hidrogen, interaksi hidrofobik, interaksi elektrostatik, dan interaksi *unvafourable* dengan melibatkan asam amino CYS919 sebagai lokasi pengikatan ATP.

Kesimpulan : Amentoflavon dari *C. soulattri* berpotensi menjadi penghambat enzim tirosin kinase berdasarkan hasil *in vitro* dan *in silico*. Diperlukan pengujian dinamika molekular terhadap VEGFR-2, IGF1R, InsR, PDGFR- α dan PDGFR- β .

Kata Kunci : Amentoflavon, KDR/VEGFR-2, *Calophyllum soulattri*, Tirosin kinase

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Abstract

STUDY POTENCY of AMENTOFLAVONE from *Calophyllum soulattri* LEAVES as TYROSINE KINASE INHIBITORS

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Background : *Calophyllum soulattri* is a plant that contains amentoflavone. Amentoflavone are able to inhibit angiogenesis by inhibiting the VEGFR-2. In this study, screening of the inhibitory activity of amentoflavones against 8 tyrosine kinase enzymes was carried out in vitro and continued with molecular docking of the most inhibited enzyme.

Methods : Amentoflavone were obtained by isolating the ethyl acetate fraction of *C. soulattri* leaves using vacuum liquid chromatography, column chromatography, and chromatotrone. Amentoflavone was tested for its activity as an inhibitor of the tyrosine kinase enzyme in vitro using the ADP-Glo kinase assay method. Amentoflavone were also bound to the enzyme with the best inhibition based on the results of in vitro tests with AutoDock Vina and Biovia to determine the binding energy and interactions that occur.

Results : Amentoflavones were isolated from *C. soulattri* leaves as much as 6.8 mg. The in vitro test showed the best inhibitory activity against the KDR/VEGFR-2 enzyme (3%). Based on the binding of the molecule to VEGFR-2, the bond energy value of the amentoflavones produced was -3.1 kcal/mol. The docking visualization showed hydrogen interactions, hydrophobic interactions, electrostatic interactions, and unfaavourable interactions involving the CYS919 amino acid as the binding site for ATP.

Conclusion : Amentoflavones from *C. soulattri* have the potential to be inhibitors of the tyrosine kinase enzyme based on in vitro and in silico results. Molecular dynamics testing of VEGFR-2, IGF1R, InsR, PDGFR- α and PDGFR- β is required.

Key word : Amentoflavone, KDR/VEGFR-2, *Calophyllum soulattri*, Tyrosine kinase

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