ABSTRAK

STUDI POTENSI SENYAWA AKTIF DARI BAHAN ALAM SEBAGAI INHIBITOR *PLATELET DERIVED GROWTH FACTOR RECEPTOR-ALFA*

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Latar Belakang: Ekspresi berlebih suatu enzim seperti *platelet derived growth factor receptor alfa* (PDGFRα) dapat menyebabkan perkembangan kanker. Beberapa senyawa alam yang secara empiris digunakan sebagai pengobatan dan diketahui memiliki aktivitas terhadap sel kanker diantaranya *α-mangostin, andrographolide, galangin, gamma mangostin, pinostrobin, pinocembrin, Ethyl p-methoxycinnamate* (EPMC), *xanthorrhizol, curcumin, cinamaldehyde,* dan *alashanoid B.* Penelitian ini bertujuan untuk mengetahui senyawa yang paling berpotensi sebagai inhibitor PDGFRα berdasarkan hasil penambatan molekuler dan aturan Lipinski, sehingga dapat menjadi dasar pengembangan obat baru.

Metodologi: Penambatan molekuler yang dilakukan dengan mengunduh struktur PDGFRα dari PDB, preparasi struktur protein menggunakan AutoDock Tools, penambatan kembali dengan ligan natif menggunakan AutoDock Vina, perhitungan RMSD menggunakan PyMOL, penambatan molekuler senyawa uji, dan visualisasi hasil penambatan pada BIOVIA Discovery Studio. Selanjutnya uji aturan Lipinski dilakukan pada web SCFBio

Hasil Penelitian: Hasil penambatan molekuler 11 senyawa menunjukan *pinocembrin, galangin dan pinostrobin* (golongan flavonoid) sebagai senyawa uji yang memiliki energi ikatan terendah sebesar -9,6 kkal/mol, -9,4 kkal/mol dan -9,3 kkal/mol, sementara senyawa kontrol sunitinib sebesar -8,9 kkal/mol dan ligan natif imatinib sebesar -14,5 kkal/mol. Pada visualisasi penambatan ketiga senyawa flavonoid terdapat residu asam amino yang mengikat situs aktif PDGFRα yaitu GLU644, LYS627, ASP836, CYS677, THR674 dan VAL607. Semua senyawa uji memenuhi syarat aturan lipinski dengan berat molekul < 500 dalton, jumlah hidrogen donor < 5, jumlah akseptor hidrogen < 10, nilai log P <5, dan refraktivitas molar diantara 40-130.

Kesimpulan: Senyawa flavonoid berpotensi sebagai inhibitor PDGFRα dan memiliki prediksi sifat fisikokimia yang baik berdasarkan hasil uji lipinski.

Kata Kunci: PDGFRα, flavonoid, penambatan molekul, lipinski

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ABSTRACT

STUDY OF THE POTENTIAL OF ACTIVE COMPOUNDS FROM NATURAL MATERIALS AS PLATELET DERIVED GROWTH FACTOR RECEPTOR INHIBITORS

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Background: Overexpression of an enzyme such as platelet derived growth factor receptor alpha (PDGFRα) can cause cancer development. Several natural compounds that are empirically used as treatment and are known to have activity against cancer cells include α-mangostin, andrographolide, galangin, gamma mangostin, pinostrobin, pinocembrin, Ethyl p-methoxycinnamate (EPMC), xanthorrhizol, curcumin, cinamaldehyde, and alashanoid B. This study aims to determine the compounds that have the most potential as PDGFRα inhibitors based on the results of molecular docking and Lipinski rules so that they can be the basis for developing new drugs.

Methods: Molecular docking was carried out by downloading the PDGFRα structure from PDB, preparation of protein structures using AutoDock Tools, redocking with native ligands using AutoDock Vina, RMSD calculations using PyMOL, molecular docking of test compounds, and visualization of docking results at BIOVIA Discovery Studio. Furthermore, the Lipinski's rules test was carried out on the SCFBio website.

Result: The results of the molecular docking of 11 compounds showed that pinocembrin, galangin and pinostrobin (flavonoids group) as the test compounds that had the lowest bond energies of -9.6 kcal/mol, -9.4 kcal/mol and -9.3 kcal/mol, while the control compound sunitinib was -8.9 kcal/mol and the native imatinib ligand was -14.5 kcal/mol. On the visualization of the three flavonoid compounds there are amino acid residues that bind to the active site of PDGFRα, that is GLU644, LYS627, ASP836, CYS677, THR674 and VAL607. All test compounds met the requirements of Lipinski's rules with molecular weight < 500 daltons, hydrogen donors < 5, hydrogen acceptors < 10, log P value < 5, and molar refractivity between 40-130.

Conclusion: The flavonoids compound has the potential as a PDGFRα inhibitor and good predictions of physicochemical based on the results of the Lipinski test.

Keywords: PDGFRα, flavonoids, molecular docking, Lipinski

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