Abstrak

STUDI POTENSI SENYAWA FLAVONOID TERPRENILASI TERHADAP RESEPTOR EGFR DAN C-MET MELALUI PENDEKATAN *MOLECULAR DOCKING*

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Latar Belakang: reseptor tirosin kinase yaitu *ephitalial growth factor receptor* (EGFR) dan *cellular mesenchymal to epithelial transition factor* (C-MET) dapat mengalami mutasi yang berperan dalam pertumbuhan *non small cell lung cancer* (NSCLC). Mutasi tersebut dapat menyebabkan resistensi terhadap terapi NSCLC. Salah satu senyawa yang memiliki potensi untuk terapi NSCLC, yaitu flavonoid terprenilasi. Beberapa Flavonoid terprenilasi dilaporkan menghambat sel NSCLC secara *in vitro*. Namun belum diketahui adanya potensi interaksi spesifik antara flavonoid terprenilasi dengan EGFR dan C-MET sehingga diperlukan metode untuk memprediksi afinitas keduanya. Penelitian ini bertujuan untuk mengetahui potensi interaksi senyawa flavonoid terprenilasi terhadap target protein EGFR dan C-MET melalui *molecular docking*.

Metodologi: penelitian ini dilakukan dengan mengevaluasi parameter Lipinski dan toksisitas senyawa flavonoid terprenilasi menggunakan ADMETlab. Penambatan senyawa flavonoid terprenilasi pada protein dilakukan dengan menggunakan PyMOL, PyRx, dan BIOVIA Discovery Studio. Potensi senyawa flavonoid terprenilasi dianalisis berdasarkan nilai *binding affinity* dan interaksi dengan residu penting.

Hasil Penelitian: pada protein EGFR, dua senyawa uji yaitu senyawa -TB2 (642) dan -TB3 (643) memiliki *binding affinity* yang lebih negatif (-8,5 kkal/mol dan -8,6 kkal/mol) daripada kontrol positif (-8,4 kkal/mol) dan jumlah interaksi residu penting yang sama banyaknya dengan kontrol positif, yaitu sebanyak 4 ikatan. Pada protein C-MET, senyawa uji memiliki *binding affinity* dan jumlah interaksi dengan residu penting yang tidak lebih baik dari kontrol positifnya.

Kesimpulan: senyawa flavonoid terprenilasi berpotensi sebagai kandidat protein EGFR namun kurang berpotensi sebagai kandidat protein C-MET.

Kata Kunci: EGFR, C-MET, flavonoid terprenilasi, *molecular docking*

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Abstract

STUDY OF THE POTENTIAL OF PRENYLATED FLAVONOID COMPOUNDS AGAINST EGFR AND C-MET RECEPTORS THROUGH A MOLECULAR DOCKING APPROACH

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Background: receptor tyrosine kinases, such as the epidermal growth factor receptor (EGFR) and the cellular mesenchymal to epithelial transition factor (C-MET), can acquire mutations that contribute to the development of non-small cell lung cancer (NSCLC). These mutations may result in resistance to current NSCLC treatment. Prenylated flavonoids are a group of compounds with potential for NSCLC treatment. In vitro studies have reported that several prenylated flavonoids inhibit NSCLC cell growth. However, the specific interaction potential between prenylated flavonoids and EGFR or C-MET remains unknown, necessitating the use of methods to predict their affinities. This study aimed to characterize the potential interactions of prenylated flavonoid compounds with the target proteins EGFR and C-MET through molecular docking.

Methodology: this study evaluated the drug-likeness and toxicity profiles of the compounds using ADMETlab. Compounds docking against protein targets were performed using PyMOL, PyRx, and BIOVIA Discovery Studio. The potential of the compounds were analyzed based on their binding affinity values and interactions with critical residues.

Result: compounds -TB2 (642) and -TB3 (643) exhibited more favorable binding affinities (−8,5 kcal/mol and −8,6 kcal/mol) than the positive control (−8,4 kcal/mol) and formed an equivalent number of interactions with critical residues, namely four bonds in the EGFR protein. However, the test compounds demonstrated neither stronger binding affinities nor more interactions than the positive control in the C-MET protein.

Conclusion: prenylated flavonoids possess promising potential as EGFR protein candidates but exhibit comparatively limited potential as C-MET protein candidates.

Keywords: EGFR, C-MET, prenylated flavonoid, molecular docking

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