# Analisis penambatan molekul senyawa turunan kurkumin pirazol mannich terhadap 5-lipoksigenase dan siklooksigenase menggunakan autodock dan autodock vina = Molecular docking analysis of mannich pyrazole curcuminoid derivatives into 5-lipoxygenase and cyclooxygenase using autodock and autodock vina

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Abstrak

Inflamasi adalah respon dari sistem imun tubuh terhadap hal yang dapat membahayakan tubuh, seperti patogen, sel yang rusak, zat beracun, atau radiasi. Proses inflamasi yang berlebihan dapat menimbulkan beberapa penyakit<span lang="IN" style="mso-ansi-language:
IN"> kronis, seperti inflammatory
bowel disease, diabetes<span lang="IN" style="mso-ansi-language:
EN-US"> melitus tipe I, artritis, <span lang="IN" style="mso-ansi-language:
IN">dan kanker. Beberapa terapi inflamasi menargetkan untuk menghambat metabolisme asam arakidonat jalur siklooksigenase (COX-1 dan COX-2) dan 5-lipoksigenase (5-LOX). Kurkumin merupakan senyawa alami yang memiliki beberapa aktivitas antiinflamasi dan antiproliferasi. Namun, kurkumin memiliki kestabilan dan kelarutan yang buruk. Untuk memperbaiki kekurangan tersebut beberapa modifikasi struktur telah dilakukan, antara lain siklisasi gugus 1,3-dikarbonil membentuk cincin pirazol dan substitusi gugus basa Mannich. Pada penelitian ini dilakukan pengujian in silico dengan penambatan molekuler senyawa turunan kurkumin pirazol Mannich terhadap COX-1, COX-2, dan 5-LOX untuk memprediksi potensi aktivitas antiinflamasi senyawa tersebut. Proses validasi dilakukan dengan program AutoDock dan AutoDock Vina. Hasil validasi menunjukkan bahwa program AutoDock mempunyai nilai Root Mean Square Deviation (RMSD) yang lebih baik dibandingkan dengan AutoDock Vina. Hasil penambatan molekuler menunjukan bahwa seluruh senyawa turunan kurkumin pirazol Mannich memiliki selektivitas terhadap COX-2 dibandingkan terhadap COX-1. Senyawa yang memiliki energi bebas ikatan terendah berturut-turut pada COX-1, COX-2, dan 5-LOX adalah kurkumin pirazol tersubstitusi basa Mannich metilpiperazinÃÂ  (-7,47 kkal/mol), dimetilmorfolin (-11,01 kkal/mol), dan morfolin (-6,55 kkal/mol). Senyawa yang memiliki nilai selektivitas tertinggi adalah kurkumin pirazol tersubstitusi basa Mannich dibutilamin dan morfolin dengan nilai S 0,0001. Maka dari itu, dapat disimpulkan bahwa senyawa kurkumin pirazol Mannich diprediksi memiliki potensi anti-inflamasi melalui penghambatan COX-2 selektif.

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Inflammation is the response of the body's immune system to things that can harm the body, such as pathogens, damaged cells, toxic substances, or radiation. Excessive inflammatory processes can cause several chronic diseases, such as inflammatory bowel disease, type I diabetes mellitus, arthritis, and cancer. Some inflammatory therapies target to inhibit the arachidonic acid metabolism of the cyclooxygenase pathway (COX-1 and COX-2) and 5-lipoxygenase (5-LOX). Curcumin is a natural compound having several biological activities such as anti-inflammatory and antiproliferation. However, curcumin has poor stability and solubility. To improve these deficiencies several structural modifications have been done, such as cyclization of the 1,3-dicarbonyl moiety to form pyrazole ring and the substitution of Mannich base group. In this study, an <i style="mso-bidi-font-style:
normal">in silico </i>test was carried out by molecular docking of curcumin pyrazole Mannich derivatives against COX-1, COX-2, and 5-LOX to predict the anti-inflammatory activity potential of the compounds. The validation process was performed using the AutoDock and AutoDock Vina programs. The validation results indicated that the AutoDock program showed a better value of Root Mean Square Deviation (RMSD) compared to AutoDock Vina. The results of the molecular docking study showed that all pyrazole curcumin Mannich derivatives have selectivity to COX-2 compared to COX-1. Compounds having the lowest free binding energy against COX-1, COX-2, and 5-LOX respectively were curcumin pyrazole substituted Mannich base of methylpiperazine (-7.47 kcal/mol), dimethylmorpholine (-11.01 kcal/mol), and morpholine (-6.55 kcal/mol). The compounds having the highest selectivity value are curcumin pyrazole substituted Mannich base of dibutylamine and morpholine with a value of S 0.0001. Therefore, it can be concluded that curcumin pyrazole Mannich derivatives were predicted to have anti-inflammatory potential by selective inhibitory to COX-2.