# INTISARI

## Penambatan Molekul, Sintesis dan Uji *In Vitro* Senyawa Analog Kurkumin sebagai Anti-Inflamasi

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Penelitian ini dilakukan untuk mendapatkan senyawa analog kurkumin yang memiliki kemampuan sebagai anti-inflamasi. Pada penelitian ini dilakukan penambatan molekul (*molecular docking*) terhadap makromolekul siklooksigenase-2 (COX-2) yang bertanggung jawab dalam proses inflamasi. Penambatan molekul dilakukan menggunakan Autodock-Vina terhadap 15 senyawa analog kurkumin dan hasil penambatan dievaluasi dengan PyMOL. Pemeringkatan berdasarkan afinitas ikatan, energi ikatan, ikatan hidrogen dan ikatan van der Waals dilakukan untuk evaluasi penambatan molekul. Senyawa analog kurkumin potensial telah disintesis secara eksperimental dengan 2 tahap reaksi. Reaksi kondensasi aldol dilakukan dengan menggunakan *microwave* dengan waktu 3 x 10 detik. Analisis hasil sintesis senyawa analog kurkumin dilakukan dengan HPLC, MS, $^{1}$H dan $^{13}$C-NMR. Aktivitas anti-inflamasi senyawa analog kurkumin dilakukan dengan menggunakan metode penghambatan denaturasi albumin.

Evaluasi penambatan molekul menghasilkan 6 senyawa analog kurkumin yang berpotensi memiliki aktivitas sebagai anti-inflamasi. Sintesis senyawa analog kurkumin dilakukan melalui reaksi kondensasi aldol antara turunan benzalasetone dengan beberapa benzaldehid. Hasil sintesis menunjukkan keenam senyawa analog kurkumin tersebut memiliki kemurnian 100% dengan rendemen untuk senyawa 1-(1,3-benzodioksol-5-il)-5-(4-hidroksi-3-metoksifenil)penta-1,4-dien-3-on yaitu 82,68%, senyawa 1-(1,3-benzodioksol-5-il)-5-(3,4-dimetoksifenil) penta-1,4-dien-3-on yaitu 87,08%, senyawa 1-(1,3-benzodioksol-5-il)-5-(4-metoksifenil)penta-1,4-dien-3-on yaitu 85,23%, senyawa 1-(3,4-dimetoksifenil)-5-(4-hidroksi-3-metoksifenil) penta-1,4-dien-3-on yaitu 88,51%, senyawa 1-(3,4-dimetoksifenil)-5-(4-nitrofenil) penta-1,4-dien-3-on yaitu 86,79% dan senyawa 1-(4-hidroksi-3-metoksifenil)-5-(4-metoksi-fenil)-penta-1,4-dien-3-on yaitu 85,67%. Pengujian aktivitas anti-inflamasi dari senyawa yang disintesis menunjukkan aktivitas yang sangat baik dengan persen penghambatan pada 100, 200, 400 dan 600 µg/ml yang lebih tinggi dibandingkan natrium diklofenak sebagai obat anti-inflamasi nonsteroid (NSAID).

*Kata Kunci* : *analog kurkumin, anti-inflamasi, penambatan molekul, sintesis, in vitro*

# ABSTRACT

## Molecular Docking, Synthesis, and In Vitro Test of Curcumin Analogues as Anti-Inflammatory

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Research has been done to obtain curcumin analogue compounds that have the ability as anti-inflammatory. In this study molecular docking has been performed in silico using the cycloooksigenase-2 (COX-2) protein that responsible for the inflammatory process. Molecular docking using Autodock-Vina was performed on 15 curcumin analogue compounds and the results were evaluated with PyMOL. Scoring based on binding afinity, hydrogen bonding, and van der Waals bonding were performed for molecular docking evaluation. The potential curcumin analogue compounds are experimentally synthesized with 2 stages of the reaction. The aldol condensation reaction is carried out by using microwave with a time of 3 x 10 seconds. Results from curcumin analogue studies were performed with HPLC, MS, $^{1}H$ and $^{13}C$-NMR. Anti-inflammatory activity of curcumin analogue compounds was performed using inhibition of albumin denaturation method.

Molecular docking evaluation recommends 6 curcumin analogue compounds that potentially have activity as anti-inflammatory. The synthesis of curcumin analogue compounds was done by aldol condensation reaction between benzalacetone derivatives with some benzaldehid. Synthesis results show the compounds curcumin analog has 100% purity with yields for the compound 1-(1,3-benzodioxol-5-yl)-5-(4-hydroxy-3-methoxyphenyl) penta-1,4- dien-3-one is 82.68%, compound 1-(1,3- benzodioksol-5-yl)-5-(3,4-dimethoxyphenyl) penta-1,4-dien-3-one is 87.08%, compound 1-(1,3-benzodioksol-5-yl)-5- (4-methoxyphenyl) penta-1,4-dien-3-one is 85.23%, compound 1-(3,4-dimethoxyphenyl)-5-(4-hydroxy-3-methoxyphenyl) penta-1,4-dien-3-one is 88.51%, compound 1-(3,4-dimethoxyphenyl)-5-(4-nitrophenyl) penta-1,4-dien-3- one is 86.79% and the compound 1-(4-hydroxy-3-methoxy-phenyl)-5-(4-methoxy-phenyl)-penta-1,4-dien-3-one is 85.67%. Anti-inflammatory activity of the synthesized compounds showed excellent activity with higher percentage of inhibition at 100, 200, 400 and 600 μg/ml compared to diclofenac sodium as nonsteroidal anti-inflammatory drug (NSAID).

*Keywords: curcumin analogues, anti-inflammatory, molecular docking, synthesis, in vitro*