SINTESIS DAN PENAMBATAN MOLEKUL SENYAWA ANALOG KURKUMIN DARI SINAMALDEHIDA DENGAN 1-BENZIL-4 PIPERIDON SERTA AKTIVITAS SITOTOKSIKNYA TERHADAP SEL KANKER PAYUDARA T47D

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INTISARI

Senyawa analog kurkumin monoketon diketahui memiliki potensi pada berbagai aktivitas biologis salah satunya sebagai antikanker, oleh karena itu pada penelitian ini dilakukan sintesis senyawa analog kurkumin monoketon dengan bahan dasar sinamaldehida dan 1-benzil-4-piperidon. Penelitian terdiri dari tahap sintesis analog kurkumin melalui reaksi kondensasi Claisen-Schmidt dengan metode sonikasi, elusidasi struktur senyawa hasil sintesis dilakukan menggunakan spektrometer ATR-IR, ^{1}H- dan ^{13}C-NMR. Penambatan molekul menggunakan AutoDock Vina dilakukan terhadap protein target *Epidermal Growth Factor Receptor* (EGFR), *B-cell lymphoma* (Bcl-2), dan p53 mutan untuk mengetahui afinitas ikatan serta interaksi yang terbentuk antara senyawa analog kurkumin dan kurkumin dengan protein target. Senyawa analog kurkumin selanjutnya diuji sitotoksisitasnya yang dilakukan secara *in vitro* terhadap sel kanker payudara T47D dan sel normal Vero.

Sintesis analog kurkumin menghasilkan senyawa (3*E*,5*E*)-1-benzil-3,5-bis((*E*)-3-fenilaliliden)-4-piperidon dengan kemurnian sebesar 91 % dan persen hasil 40 %. Evaluasi penambatan molekul analog kurkumin dan terhadap protein EGFR, Bcl-2, dan p53 diperoleh hasil senyawa analog kurkumin memiliki nilai afinitas ikatan yang lebih negatif dibandingkan dengan senyawa kurkumin dan ligan alami protein target EGFR serta p53 mutan. Penambatan molekul terhadap protein Bcl-2 menunjukkan senyawa analog kurkumin menghasilkan nilai afinitas yang lebih negatif dibandingkan senyawa kurkumin tetapi lebih positif dibandingkan dengan ligan alami. Hasil uji sitotoksisitas menunjukkan bahwa senyawa analog kurkumin memiliki aktivitas sitotoksik yang rendah sedangkan kurkumin memiliki aktivitas sitotoksik yang tinggi terhadap sel kanker payudara T47D dengan nilai IC50 153.240,92 dan 10,62 μg/mL. Selain itu, keduanya memiliki selektivitas rendah terhadap sel normal Vero dengan nilai sebesar 0,95 dan 1,53.

Kata kunci: analog kurkumin, Claisen-Schmidt, penambatan molekul, sinamaldehida, aktivitas sitotoksik.

SYNTHESIS AND MOLECULAR DOCKING OF CURCUMIN ANALOG FROM CINNAMALDEHYDE WITH 1-BENZYL-4-PIPERIDONE AND ITS CYTOTOXIC ACTIVITY AGAINST T47D BREAST CANCER CELL

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ABSTRACT

Curcumin monoketone analog compounds are known to have potential in various biological activities, one of which is as an anticancer, therefore in this study, the synthesis of curcumin monoketone analog compound was carried out using cinnamaldehyde and 1-benzyl-4-piperidone as the basic materials. The study consisted of the stages of curcumin analog synthesis through the Claisen-Schmidt condensation reaction with the sonication method, elucidation of the structure of the synthesized compound was carried out using ATR-IR, ^{1}H- and ^{13}C-NMR spectrometers. Molecular docking using AutoDock Vina was carried out on the target proteins Epidermal Growth Factor Receptor (EGFR), B-cell lymphoma (Bcl-2) and mutant p53 to determine the binding affinity and interaction formed between curcumin analog compound and curcumin with target proteins. The curcumin analog compound was then tested for their cytotoxicity which was carried out in vitro against T47D breast cancer cell and normal Vero cell.

Synthesis of curcumin analog produced compound (3E,5E)-1-benzyl-3,5-bis((E)-3-phenylallylidene)-4-piperidone with a purity of 91.13 % and yields 40%. Evaluation of the molecular docking of curcumin analog to EGFR, Bcl-2 and mutant p53 proteins obtained the results of curcumin analog compound having a more negative binding affinity value compared to curcumin compound and native ligand of EGFR and mutant p53 target proteins. Molecular docking to Bcl-2 protein showed that curcumin analog compound produced a more negative affinity value than curcumin compound but more positive compared to native ligand. The results of the cytotoxicity test showed that curcumin analog compound had low cytotoxic activity while curcumin had high cytotoxic activity against T47D breast cancer cell with IC50 values of 153,240.92 and 10.62 μg/mL. In addition, both had low selectivity against normal Vero cell with value 0.95 dan 1.53.

Keywords: curcumin analog, Claisen-Schmidt, molecular docking, cytotoxicity activity.