

**SINTESIS, STUDI PENAMBATAN MOLEKUL, DAN UJI
SITOTOKSISITAS NANOSUSPENSI ANALOG KURKUMIN
1-BENZIL-3,5-BIS(3-FENILALILIDEN)-4-PIPERIDON TERHADAP SEL
KANKER PAYUDARA MCF-7**

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INTISARI

Pengembangan analog kurkumin monokarbonil dilakukan untuk memperoleh senyawa antikanker yang lebih stabil dan meningkatkan aktivitas biologisnya. Penelitian ini bertujuan untuk mensintesis analog kurkumin monokarbonil 1-benzil-3,5-bis(3-fenilaliliden)-4-piperidon kemudian diformulasikan dalam bentuk nanosuspensi. Karakterisasi senyawa hasil sintesis dikonfirmasi menggunakan ATR-IR, $^1\text{H-NMR}$, dan $^{13}\text{C-NMR}$, sedangkan karakteristik sediaan nanosuspensi dievaluasi dengan PSA-DLS dan SEM. Aktivitas sitotoksik dievaluasi terhadap sel MCF-7 dan sel Vero untuk memperoleh IC_{50} dan indeks selektivitas. Studi penambatan molekul dilakukan untuk menganalisis interaksi molekul dan afinitas ikatan senyawa terhadap protein target Bcl-2, PI3K, dan $\text{ER}\alpha$.

Hasil penelitian menunjukkan bahwa analog kurkumin monokarbonil berhasil disintesis sebagai padatan kuning dengan rendemen 39,6% dan kemurnian 92%. Formulasi nanosuspensi berhasil menurunkan ukuran partikel dari 883 nm menjadi 176 nm, menurunkan PDI dari 0,69 menjadi 0,19, serta mengubah zeta potensial dari $-24,59 \text{ mV}$ menjadi $-38,32 \text{ mV}$. Nilai IC_{50} terhadap sel MCF-7 menurun dari $148,03 \mu\text{g mL}^{-1}$ menjadi $36,46 \mu\text{g mL}^{-1}$ setelah diformulasikan menjadi nanosuspensi, sedangkan indeks selektivitas meningkat dari 0,70 menjadi 3,52. Hasil tersebut menunjukkan bahwa nanosuspensi analog kurkumin memiliki aktivitas sitotoksik dan selektivitas dengan kategori sedang terhadap sel MCF-7 dibandingkan sel Vero. Hasil penambatan molekul menunjukkan bahwa analog kurkumin memiliki afinitas ikatan yang lebih negatif dibandingkan kurkumin terhadap protein target, sehingga diprediksi memiliki interaksi yang lebih stabil. Berdasarkan hasil tersebut, analog kurkumin 1-benzil-3,5-bis(3-fenilaliliden)-4-piperidon berpotensi untuk dikembangkan sebagai kandidat senyawa antikanker payudara dalam bentuk nanosuspensi.

Kata kunci: analog kurkumin, kanker payudara, nanosuspensi, penambatan molekul, sitotoksitas

***SYNTHESIS, MOLECULAR DOCKING STUDIES, AND CYTOTOXICITY
EVALUATION OF 1-BENZYL-3,5-BIS(3-PHENYLALLYLIDENE)-
PIPERIDIN-4-ONE CURCUMIN ANALOGUE NANOSUSPENSION
AGAINST MCF-7 BREAST CANCER CELLS***

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ABSTRACT

The development of monocarbonyl curcumin analogs is carried out to obtain more stable anticancer compounds with improved biological activities. This study aimed to synthesize the monocarbonyl curcumin analog 1-benzyl-3,5-bis(3-phenylallylidene)-piperidin-4-one and formulated as a nanosuspension. Characterization of the synthesized compound was confirmed using ATR-IR, ^1H -NMR, dan ^{13}C -NMR spectroscopy, while the characteristics of the nanosuspension formulation was evaluated using PSA-DLS and SEM. The cytotoxic activity was evaluated against MCF-7 breast cancer cells and Vero cells to determine the IC_{50} values and selectivity index. Molecular docking studies were performed to analyze the molecular interactions and binding affinities of the compound against Bcl-2, PI3K, and $\text{ER}\alpha$ target proteins.

The results of the study show that a monocarbonyl curcumin analog was successfully synthesized as a yellow solid with a yield of 39.6% yield and 92% purity. Nanosuspension formulation successfully reduces the particle size from 883 nm to 176 nm, decreased the polydispersity index from 0.69 to 0.19, and changed the zeta potential from -24.59 mV to -38.32 mV. The IC_{50} value against MCF-7 cells significantly decreased from $148.03 \mu\text{g mL}^{-1}$ to $36.46 \mu\text{g mL}^{-1}$ after nanosuspension formulation, while the selectivity index increased from 0.70 to 3.52. These results indicate that the curcumin analog nanosuspension possesses moderate cytotoxic activity and moderate selectivity toward MCF-7 cells compared to Vero cells. Molecular docking results showed that the curcumin analog had more negative binding affinities than curcumin toward the target proteins, indicating a more stable predicted interaction with three target proteins. Based on these findings, the monocarbonyl curcumin analog 1-benzyl-3,5-bis(3-phenylallylidene)-piperidin-4-one has potential to be developed as a breast anticancer candidate in a nanosuspension formulation.

Keywords: breast cancer, curcumin analog, cytotoxic, molecular docking, nanosuspension