

**SINTESIS, PENAMBATAN MOLEKUL, DAN UJI SITOTOKSIK
SENYAWA NANOSUSPENSII ANALOG KURKUMIN
1-BENZIL-3,5-BIS(3,4-DIMETOKSIBENZILIDIN)-4-PIPERIDON
SEBAGAI KANDIDAT ANTIKANKER PAYUDARA**

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INTISARI

Kanker payudara merupakan keganasan akibat pertumbuhan sel abnormal pada jaringan payudara serta menjadi salah satu jenis kanker paling banyak ditemukan dan menempati urutan kedua tertinggi secara global. Akan tetapi, pengobatannya masih memiliki kelemahan. Oleh karena itu, penelitian ini bertujuan untuk menemukan kandidat obat yang potensial dengan mensintesis analog kurkumin dalam bentuk nanosuspensi sebagai kandidat antikanker payudara, kemudian mengevaluasi aktivitas sitotoksik, indeks selektivitas, serta interaksi molekulnya terhadap protein target.

Sintesis senyawa 1-benzil-3,5-bis(3,4-dimetoksibenzilidin)-4-piperidon dilakukan melalui kondensasi Claisen-Schmidt dengan katalis basa. Hasil sintesis dikarakterisasi menggunakan KLT *scanner*, ATR-IR, ^{13}C NMR, dan ^1H NMR. Kurkumin dan analog kurkumin diformulasikan menjadi ukuran nano melalui metode nanosuspensi menggunakan Tween 80, kemudian dikarakterisasi menggunakan PSA dan SEM. Aktivitas sitotoksik terhadap sel MCF-7 dan sel Vero diuji menggunakan metode MTT *assay*. Penambatan molekul dilakukan terhadap protein Bcl-2, PI3K, dan ER α menggunakan Autodock Vina.

Analog kurkumin 1-benzil-3,5-bis(3,4-dimetoksibenzilidin)-4-piperidon berhasil disintesis, menghasilkan persen hasil sebesar 45,36% dan kemurnian 100%. Analog kurkumin berhasil diformulasikan dalam bentuk nanosuspensi yang menghasilkan ukuran partikel 158 nm dengan sistem nano yang lebih homogen dan stabil. Hasil uji sitotoksik terhadap sel MCF-7 menunjukkan nilai IC_{50} analog kurkumin, nanosuspensi analog kurkumin, kurkumin, dan nanosuspensi kurkumin sebesar 34,52; 30,28; 25,93; dan 18,87 $\mu\text{g mL}^{-1}$ dengan IS masing-masing sebesar 1,42; 8,25; 0,50; dan 0,52. Hasil tersebut menunjukkan nanosuspensi analog kurkumin kurang meningkatkan aktivitas sitotoksik tetapi meningkatkan IS dibandingkan dengan kurkumin sehingga berpotensi sebagai kandidat antikanker payudara. Selain itu, hasil penambatan molekul menunjukkan bahwa senyawa analog kurkumin memiliki afinitas ikatan yang lebih rendah dan lebih stabil terhadap protein Bcl-2 dan PI3K dibandingkan dengan kurkumin.

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

**SYNTHESIS, MOLECULAR DOCKING, AND CYTOTOXIC TEST OF
CURCUMIN ANALOG NANOSUSPENSION
1-BENZYL-3,5-BIS(3,4-DIMETHOXYBENZYLIDENE)-4-PIPERIDONE
AS A CANDIDATE FOR BREAST CANCER THERAPY**

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ABSTRACT

Breast cancer is a malignancy caused by the growth of abnormal cells in breast tissue, and it is one of the most commonly diagnosed cancers and ranks second globally. However, its treatment still has limitations. Therefore, this study aims to identify a potential drug candidate by synthesizing a curcumin analog in the form of a nanosuspension for breast cancer treatment and then evaluating its cytotoxic activity, selectivity index, and molecular interactions with target proteins.

The synthesis of the curcumin analog 1-benzyl-3,5-bis(3,4-dimethoxybenzylidene)-4-piperidone was carried out via a Claisen–Schmidt condensation using a base catalyst. The synthesis products were characterized using TLC scanning, ATR-IR, ^{13}C NMR, and ^1H NMR. Curcumin and curcumin analog were formulated into nanoscale particles via the nanosuspension method with Tween 80 and then characterized with PSA and SEM. Cytotoxic activity against MCF-7 and Vero cells was tested using the MTT assay. Molecular docking was performed against the Bcl-2, PI3K, and ER α proteins using AutoDock Vina.

The curcumin analog 1-benzyl-3,5-bis(3,4-dimethoxybenzylidene)-4-piperidone was successfully synthesized with a 45.36% yield and 100% purity. It was then formulated into a nanosuspension with a particle size of 158 nm, resulting in a homogeneous and stable nanosystem. Cytotoxicity test results on MCF-7 cells showed IC₅₀ values for the curcumin analog, curcumin analog nanosuspension, curcumin, and curcumin nanosuspension of 34.52, 30.28, 25.93, and 18.87 $\mu\text{g mL}^{-1}$ with selectivity index values of 1.42, 8.25, 0.50, and 0.52, respectively. These results indicate that the curcumin analog nanosuspension exhibits lower cytotoxic activity but a higher IS value compared to curcumin, making it a potential candidate for breast cancer treatment. Furthermore, the result of molecular docking studies indicates that the curcumin analog exhibits lower binding affinity and stability toward Bcl-2 and PI3K proteins compared to curcumin.

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