SINTESIS NANOPARTIKEL ANALOG KURKUMIN BERBAHAN DASAR 3-BENZILOKSIBENZALDEHIDA, AKTIVITAS SITOTOKSIK TERHADAP SEL KANKER PAYUDARA MCF-7 DAN STUDI PENAMBATAN MOLEKUL

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INTISARI

Kanker payudara merupakan penyakit yang paling umum menyerang perempuan secara global dan menyumbang angka kematian yang signifikan setiap tahunnya. Terapi konvensional seperti kemoterapi sering menimbulkan berbagai efek samping, seperti kerusakan sel normal, resistensi obat, serta toksisitas sistemik, sehingga mendorong pengembangan agen antikanker baru yang lebih aman dan selektif. Penelitian ini bertujuan untuk mengembangkan senyawa analog kurkumin yang berpotensi sebagai agen antikanker payudara.

Sintesis analog dilakukan menggunakan reaksi kondensasi aldol silang Claisen-Schmidt antara senyawa 3-benziloksibenzaldehida dan variasi keton N-benzil-4-piperidon, N-metil-4-piperidon, 4-piperidon, dengan bantuan katalis basa. Senyawa hasil sintesis dikarakterisasi menggunakan TLC *scanner*, FTIR, ^{1}H-NMR dan ^{13}C-NMR untuk mengonfirmasi struktur kimia. Kurkumin dan analognya kemudian diformulasikan dalam bentuk nanopartikel melalui metode sonikasi dengan bantuan surfaktan Tween 60, ukuran partikel dianalisis menggunakan *Particle Size Analyzer* (PSA). Aktivitas sitotoksik senyawa terhadap sel kanker payudara MCF-7 dievaluasi menggunakan metode MTT. Untuk menilai selektivitas terhadap sel kanker, uji MTT juga dilakukan terhadap sel normal Vero. Penambatan molekul dilakukan untuk mengidentifikasi potensi interaksi senyawa terhadap target protein kanker serta memahami mekanisme toksisitas secara molekuler.

Formulasi senyawa kurkumin dan analognya dalam bentuk nanopartikel menghasilkan ukuran partikel masing-masing 87,80 nm (AKA-NP), 82,83 nm (AKB-NP), 90,90 nm (AKC-NP) dan 41,80 nm (kurkumin-NP), yang seluruhnya berada pada rentang <100 nm. Uji sitotoksisitas terhadap sel kanker payudara MCF-7 menunjukkan bahwa nilai IC_{50} kurkumin, kurkumin-NP, AKA, AKA-NP, AKB, AKB-NP, AKC dan AKC-NP masing-masing adalah 51,140; 13,878; 164,104; 118,170; 19,969; 7,669; 55,157; 49,626 μg mL^{-1}, dengan nilai IS berturut-turut 0,449; 2,007; 1,153; 1,139; 5,896; 9,227; 1,198; dan 1,340. Hasil ini menunjukkan bahwa formulasi nanopartikel meningkatkan aktivitas sitotoksik dibandingkan bentuk non-nanopartikel, dengan AKB-NP sebagai kandidat paling potensial berdasarkan nilai IC_{50} dan IS. Selain itu, hasil simulasi penambatan molekul mengindikasikan bahwa AKA, AKB dan AKC memiliki afinitas ikatan yang rendah, menandakan pengikatan yang stabil dengan protein target Bcl-2 dan ERα.

Kata kunci: analog kurkumin monoketon, antikanker, kanker payudara, nanopartikel, penambatan molekul

SYNTHESIS OF CURCUMIN ANALOG NANOPARTICLES BASED ON 3-BENZYLOXYBENZALDEHYDE, CYTOTOXIC ACTIVITY AGAINST MCF-7 BREAST CANCER CELLS, AND MOLECULAR DOCKING STUDIES

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ABSTRACT

Breast cancer is the most commonly diagnosed cancer in women worldwide and remains a leading cause of cancer-related mortality. Conventional therapies, such as chemotherapy, often result in adverse effects, including damage to healthy cells, drug resistance, and systemic toxicity. These limitations have prompted the search for new anticancer agents that are safer and more selective. This study aims to develop curcumin analogs with potential as breast anticancer agents through in vitro and in silico approaches.

The analogs were synthesized via Claisen-Schmidt cross-aldol condensation between 3-benzyloxybenzaldehyde and N-benzyl-4-piperidone, N-methyl-4-piperidone, and 4-piperidone ketone derivatives, using a base catalyst. The synthesized compounds were characterized using TLC scanner, FTIR, ^{1}H-NMR, and ^{13}C-NMR to confirm their chemical structures. Curcumin and its analogs were then formulated into nanoparticles by sonication with Tween-60 as a surfactant, and particle size was analyzed using a Particle Size Analyzer (PSA). The cytotoxic activity of the compounds was evaluated against MCF-7 breast cancer cell lines using the MTT assay. The MTT assay was also performed on normal Vero cells. Molecular docking studies were conducted to explore the interaction of curcumin analogs with target proteins involved in breast cancer, providing insights into their potential mechanisms of action. The results of this study are expected to support the development of novel, effective, and selective anticancer drug candidates based on curcumin derivatives.

The formulation of curcumin and its analogs into nanoparticle form yielded particle sizes of 87.80 nm (AKA-NP), 82.83 nm (AKB-NP), 90.90 nm (AKC-NP), and 41.80 nm (curcumin-NP), all of which were within the <100 nm range. Cytotoxicity testing against MCF-7 breast cancer cells showed that the IC_{50} values of curcumin, curcumin-NP, AKA, AKA-NP, AKB, AKB-NP, AKC, and AKC-NP were 51.140; 13.878; 164.104; 118.170; 19.969; 7.669; 55.157; 49.626 μg mL^{-1}, respectively, with IS values of 0.449; 2.007; 1.153; 1.139; 5.896; 9.227; 1.198; 1.340, respectively. These results indicate that the nanoparticle formulations enhanced cytotoxic activity compared to their non-nanoparticle forms, with AKB-NP emerging as the most promising candidate based on IC_{50} and SI values. Furthermore, molecular docking simulations indicated that AKA, AKB, and AKC exhibited low binding affinities, suggesting stable interactions with the target proteins Bcl-2 and ERα.

Keywords: anticancer, breast cancer, curcumin analog monoketone, nanoparticle, molecular docking