SINTESIS SENYAWA ANALOG KURKUMIN MONOKETON BERBAHAN DASAR SINAMALDEHIDA DAN TURUNAN BENZALDEHIDA TERENKAPSULASI LIPOSOM DAN UJI SITOTOKSISITAS TERHADAP SEL HELA

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INTISARI

Penelitian ini bertujuan untuk menemukan senyawa analog kurkumin dari bahan sinamaldehida dan turunan benzaldehida sebagai kandidat antikanker yang potensial. Penelitian ini diawali dengan *molecular docking* terhadap tujuh kandidat senyawa analog kurkumin monoketon, yaitu: (1*E*, 4*E*)-1,5-*bis*(4-benziloksi)-3-metoksifenil)penta-1,4-dien-3-on (AKM 1), (2*E*, 5*E*)-2,5-*bis*(4-benziloksi)-3-metoksibenzilidin)siklopentanon (AKM 2), (1*E*, 4*E*)-1,5-*bis*(4-benziloksifenil)-1,4-pentadien-3-on (AKM 3), (2*E*, 5*E*)-2,5-*bis*(4-benziloksibenzilidin)-siklopentanon (AKM 4), (1*E*, 4*E*)-1,5-*bis*(4-(dimetilamino)fenil)penta-1,4-dien-3-on (AKM 5), (2*E*, 5*E*)-2,5-*bis*(4-(dimetilamino)fenil)siklopentanon (AKM 6**)**, dan (3*E*, 5*E*)-1-benzil-3,5-*bis*((*E*)-3-fenilpropenilidin)piperidin-4-on (AKM 7**)** dengan protein TGF-β, CDK2, dan PAK4. Selanjutnya disintesis tiga senyawa dengan afinitas ikatan terendah dan interaksi spesifik disintesis hasil *molecular docking* melalui reaksi kondensasi Claisen-Schmidt dengan metode sonikasi menggunakan katalis basa KOH. Senyawa hasil sintesis dikarakterisasi menggunakan ATR-IR, ^{1}H-NMR, dan ^{13}C-NMR. Setelah itu, senyawa-senyawa tersebut, beserta kurkumin, dienkapsulasi dengan liposom dan dikarakterisasi menggunakan TEM. Senyawa beserta liposomnya diuji sitotoksisitasnya terhadap sel HeLa dengan metode MTT.

Senyawa AKM 7, AKM 3, dan AKM 1 menunjukkan interaksi spesifik pada sisi aktif protein TGF-β, CDK2, dan PAK4, serta memiliki afinitas ikatan yang lebih rendah dibandingkan senyawa lainnya (AKM 2, 4, 5, 6, dan kurkumin). Ketiga senyawa tersebut berhasil disintesis dengan persen hasil masing-masing sebesar 51,61; 59,75; dan 51,95%. Uji sitotoksisitas terhadap sel HeLa menunjukkan nilai IC_{50} yang lebih rendah pada liposom senyawa AKM dibandingkan dengan kurkumin murni, dengan nilai IC_{50} berturut-turut untuk kurkumin, AKM 7, AKM 3, AKM 1, liposom kurkumin, liposom AKM 7, liposom AKM 3, dan liposom AKM 1 adalah 112,217; 13,224; 99,210; 61,143; 21,021; 40,917; 30,149; dan 40,219 μg/mL. Hasil ini menunjukkan bahwa AKM 7 memiliki potensi sebagai kandidat senyawa antikanker yang lebih kuat dibandingkan kurkumin.

Kata kunci: analog kurkumin monoketon, liposom, *molecular docking*, sel HeLa.

SYNTHESIS OF CURCUMIN MONOKETONE ANALOG COMPOUNDS FROM CINNAMALDEHYDE AND BENZALDEHYDE DERIVATIVES ENCAPSULATED IN LIPOSOME AND CYTOTOXICITY TEST AGAINST HELA CELL

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ABSTRACT

This study aims to discover curcumin analog compounds derived from cinnamaldehyde and benzaldehyde derivatives as potential anticancer candidates. The study begins with molecular docking of seven monoketone curcumin analog candidates, namely: (1*E*, 4*E*)-1,5-*bis*(4-benzyloxy)-3-methoxyphenyl)penta-1,4-dien-3-one (AKM 1); (2*E*, 5*E*)-2,5-*bis*(4-benzyloxy)-3-methoxybenzylidene)cyclopentanone (AKM 2); (1*E*, 4*E*)-1,5-*bis*(4-benzyloxyphenyl)-1,4-pentadien-3-one (AKM 3); (2*E*, 5*E*)-2,5-*bis*(4-benzyloxybenzylidene)-cyclopentanone (AKM 4); (1*E*, 4*E*)-1,5-*bis*(4-(dimethylamino)phenyl)penta-1,4-dien-3-one (AKM 5); (2*E*, 5*E*)-2,5-*bis*(4-(dimethylamino)phenyl)cyclopentanone (AKM 6); and (3*E*, 5*E*)-1-benzyl-3,5-*bis*((*E*)-3-phenylpropenylidene)piperidin-4-one (AKM 7). Subsequently, three compounds with the lowest binding affinity and specific interactions from the molecular docking results were synthesized via Claisen-Schmidt condensation reactions with sonication using base catalyst. The synthesized compounds were characterized using ATR-IR, ^{1}H-NMR, and ^{13}C-NMR. After that, these compounds, along with curcumin, were encapsulated with liposomes and characterized using TEM. The compounds and their liposomes were tested for cytotoxic activity against HeLa cells using the MTT method.

Compounds AKM 7, AKM 3, and AKM 1 showing specific interactions at the active sites of the TGF-β, CDK2, and PAK4 proteins, with lower binding affinity compared to AKM 2, 4, 5, 6, and curcumin. These three compounds were successfully synthesized with yields of 51.61, 59.75, and 51.95%, respectively. Cytotoxicity assays on HeLa cells revealed lower IC_{50} values for the liposomal formulations compared to pure curcumin. The IC_{50} values of curcumin, AKM 7, AKM 3, AKM 1, curcumin liposomes, AKM 7 liposomes, AKM 3 liposomes, and AKM 1 liposomes were 112.217; 13.224; 99.210; 61.143; 21.021; 40.917; 30.149; and 40.219 μg/mL, respectively, against HeLa cells. These findings suggest that AKM 7 has a higher potential as an anticancer candidate compared to curcumin.

Keywords: monoketone curcumin analog, liposome, molecular docking, HeLa cell.