PENAMBATAN MOLEKUL, ADMET, SINTESIS ANALOG KURKUMIN MONOKETON BERBAHAN DASAR *N*-METIL-4-PIPERIDON DAN AKTIVITAS SITOTOKSIK TERHADAP T47D *CELL LINE*

Frika Rahmawari
21/484527/PPA/06190

INTISARI

Telah dilakukan studi penambatan molekul, ADMET, sintesis dan uji aktivitas sitotoksik terhadap T47D *cell line* senyawa analog kurkumin monoketon (AKM) yang bertujuan untuk menemukan kandidat obat antikanker yang potensial. Pada penelitian ini dilakukan studi penambatan molekul kurkumin dan enam senyawa 3,5-bis[(3-hidroksifenil)metilidena]-1-metilpiperidin-4-on (AKM A), 3,5-bis[(4-hidroksifenil)metilidena]-1-metilpiperidin-4-on (AKM B), 3,5-bis[(4-hidroksi-3-metoksifenil) metilidena]-1-metilpiperidin-4-on (AKM C), 3,5-bis[(4-metoksifenil)metilidena]-1-metilpiperidin-4-on (AKM D), 3,5-bis[(3,4-dimetoksifenil)metilidena]-1-metilpiperidin-4-on (AKM E), dan 3,5-bis[(3,4,5-trimetoksifenil) metilidena]-1-metilpiperidin-4-on (AKM F), dengan protein target p53, EGFR, dan Bcl-2 menggunakan Autodock Vina serta prediksi farmakokinetika (ADMET) melalui pendekatan *in silico* berbasis web. Sintesis dilakukan terhadap tiga senyawa dengan nilai afinitas ikatan terendah, interaksi asam amino spesifik, dan profil farmakokinetika yang baik melalui reaksi kondensasi Claisen-Schmidt. Elusidasi struktur dilakukan menggunakan FTIR, ^{1}H-NMR, dan ^{13}C-NMR. Uji aktivitas sitotoksik senyawa AKM dilakukan secara *in vitro* terhadap sel kanker payudara (T47D) dan sel normal (Vero) dengan metode *Microculture Tetrazolium Technique* (MTT).

Berdasarkan hasil analisis *in silico* penambatan molekul dan prediksi ADMET diketahui bahwa senyawa AKM A, B, dan C memiliki prediksi aktivitas antikanker terbaik terhadap p53, EGFR, dan Bcl-2. Hasil sintesis antara *N*-metil-4-piperidon dengan 3-hidroksibenzaldehida, 4-hidroksibenzaldehida, 4-hidroksi-3-metoksibelzaldehida menghasilkan senyawa AKM A, B, dan C dengan persen hasil masing-masing sebesar 51,402%; 85,670%; dan 60,544%. Hasil uji aktivitas sitotoksisitas terhadap T47D *cell line* menunjukkan bahwa AKM A dan AKM B menunjukkan aktivitas tinggi dengan nilai IC_{50} masing-masing sebesar 3,651 dan 7,299 μg/mL, sedangkan AKM C menunjukkan aktivitas sedang dengan nilai IC_{50} sebesar 80,248 μg/mL. Perhitungan nilai indeks selektivitas menunjukkan AKM A, B, dan C memiliki nilai masing-masing sebesar 6,555; 206,059; 31,936 yang menunjukkan bahwa ketiga senyawa analog kurkumin monoketon tersebut memiliki potensial sebagai agen antikanker payudara.

Kata kunci: analog kurkumin, *N*-metil-4-piperidon, penambatan molekul, uji sitotoksik

MOLECULAR DOCKING, ADMET, SYNTHESIS OF N-METHYL-4-PIPERIDONE-BASED CURCUMIN MONOKETONE ANALOGUE AND CYTOTOXIC ACTIVITY OF T47D CELL LINE

Frika Rahmawari
21/484527/PPA/06190

ABSTRACT

A study on molecular docking, ADMET, synthesis, and cytotoxic activity assay against T47D cell line of analog compounds of curcumin monocetone (AKM) has been conducted with the aim of discovering potential anticancer drug candidates. In this research, molecular docking studies of curcumin and six compounds 3,5-bis[(3-hydroxyphenyl)methylene]-1-methylpiperidin-4-one (AKM A), 3,5-bis[(4-hydroxyphenyl)methylene]-1-methylpiperidin-4-one (AKM B), 3,5-bis[(4-hydroxy-3-methoxyphenyl)methylene]-1-methylpiperidin-4-one (AKM C), 3,5-bis[(4-methoxyphenyl)methylene]-1-methylpiperidin-4-one (AKM D), 3,5-bis[(3,4-dimethoxyphenyl)methylene]-1-methylpiperidin-4-one (AKM E), 3,5-bis[(3,4,5-trimethoxyphenyl)methylene]-1-methylpiperidin-4-one (AKM F), with protein targets p53, EGFR, and Bcl-2 using Autodock Vina and pharmacokinetic prediction (ADMET) through web-based in silico approach has been carried out. Synthesis was performed on three compounds with the lowest binding affinity values, specific amino acid interactions, and good pharmacokinetic profiles through Claisen-Schmidt condensation reaction. Structural elucidation was done using FTIR, ^{1}H-NMR, and ^{13}C-NMR. Cytotoxic activity assay of AKM compounds was conducted in vitro against breast cancer cells (T47D) and normal cells (Vero) using the Microculture Tetrazolium Technique (MTT) method.

Based on the results of in silico molecular docking analysis and ADMET prediction, it is known that compounds AKM A, B, and C have the best predicted anticancer activity against p53, EGFR, and Bcl-2. The synthesis results between N-methyl-4-piperidone with 3-hydroxybenzaldehyde, 4-hydroxybenzaldehyde, 4-hydroxy-3-methoxybenzaldehyde produced compounds AKM A, B, and C with percentages of yields of 51.402%, 85.670%, and 60.544%, respectively. The results of cytotoxic activity testing against T47D cell line showed that AKM A and AKM B exhibited high activity with IC_{50} values of 3.651 and 7.299 μg/mL, respectively, while AKM C showed moderate activity with an IC_{50} value of 80.248 μg/mL. Calculation of the selectivity index values showed that AKM A, B, and C have values of 6.555, 206.059, 31.936 respectively, indicating that these three analog compounds of curcumin monoketone have potential as breast cancer agents.

Keywords: curcumin analog, *N*-methyl-4-piperidone, molecular docking, cytotoxicity assay