SINTESIS ANALOG KURKUMIN MONOKARBONIL ASIMETRIS DARI BENZALDEHIDA SERTA UJI AKTIVITASNYA SEBAGAI ANTIMALARIA MELALUI ANALISIS PENAMBATAN MOLEKUL

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INTISARI

Sintesis analog kurkumin monokarbonil asimetris (**AKMA**) dari benzaldehida serta uji aktivitasnya sebagai antimalaria melalui analisis penambatan molekul telah dilakukan. Penambatan molekul dilakukan pada 2 senyawa AKMA dengan substituen para berbeda, yaitu hidroksi (**AKMA A**) dan metoksi (**AKMA B**). Uji aktivitasnya sebagai senyawa antimalaria dilakukan secara *in silico* terhadap protein *Pf*-DHFT-TS dan dilakukan analisis ADMET untuk memprediksi potensinya sebagai obat oral. Kedua senyawa tersebut disintesis menggunakan reaksi Claisen-Schmidt melalui 2 tahap reaksi yaitu sintesis benzalaseton dari benzaldehida dan aseton dilanjutkan kondensasi benzalaseton dengan 4-hidroksibenzaldehida dan 4-metoksibenzaldehida membentuk berturut-turut senyawa **AKMA A** dan **AKMA B**. Hasil sintesis dielusidasi dengan spektrometer FTIR, GC-MS, dan ^{1}H-NMR.

Analisis dengan penambatan molekul menunjukkan bahwa senyawa **AKMA A** dan **AKMA B** memiliki afinitas ikatan berturut-turut sebesar -7,58 dan -6,70 kkal/mol. Nilai energi ikatan ini lebih rendah dibanding energi ikatan ligan asli dan kurkumin sebagai kontrol. **AKMA A** dan **AKMA B** diprediksi memiliki aktivitas antimalaria yang lebih baik daripada kurkumin. Hasil prediksi ADMET menunjukkan senyawa **AKMA A** dan **B** tidak toksik dan memenuhi standar *Lipinski's rule* sebagai obat oral. Sintesis benzalaseton sebagai senyawa intermediet diperoleh dengan rendemen 75,1% sedangkan **AKMA A** dan **AKMA B** dengan rendemen berturut-turut 30,1% dan 30,8%.

Kata kunci: ADMET, AKMA, antimalaria, penambatan molekul

SYNTHESIS OF ASYMMETRICAL MONOCARBONYL CURCUMIN ANALOGUES FROM BENZALDEHYDE AND THEIR ANTIMALARIAL ACTIVITY USING MOLECULAR DOCKING ANALYSIS

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ABSTRACT

Synthesis of the asymmetric monocarbonyl curcumin analogues **(AMCA)** from benzaldehyde and their antimalarial activity tests using molecular docking analysis had been carried out. Molecular docking was conducted on 2 different **AMCA** compounds with different para substituents, specifically hydroxy **(AMCA A)** and methoxy **(AMCA B)**. Their activities as an antimalarial compounds were tested using *in silico* method on Pf-DHFT-TS protein and ADMET analysis to predict their potency as oral drugs. Both compounds were synthesized using the Claisen-Schmidt reaction through 2 steps, i.e., the synthesis of benzalacetone from benzaldehyde and acetone followed by the condensation of benzalacetone with 4-hydroxybenzaldehyde and 4-methoxybenzaldehyde to produce **AMCA A** dan **AMCA B,** respectively. Structural elucidations of the synthesized product were carried out using FTIR, GC-MS, and ^{1}H-NMR spectrometers.

Analysis by molecular docking showed that **AMCA A** and **AMCA B** compounds had bond affinities of -7.58 and -6.70 kcal/mol, respectively. These bond energy values were lower than that original ligand and curcumin as a control. **AMCA A** and **AMCA B** were predicted to have good antimalaria activity than curcumin. ADMET prediction results showed that **AMCA A** and **AMCA B** are not toxic and followed the Lipinski's rule as oral drugs. Synthesis of benzalacetone as an intermediate compound resulted in product with apercentage yield of 75.1%, while **AMCA A** and **AMCA B** had 30.1% and 30.8%, respectively.

Keywords: ADMET, AMCA, *antimalarial, molecular docking*