SINTESIS, PENAMBATAN MOLEKULER DAN AKTIVITAS ANTIMALARIA SENYAWA ANALOG KURKUMIN DARI 4-HIDROKSIBENZALDEHID DAN KETON

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INTISARI

Telah dilakukan sintesis analog kurkumin dari 4-hidroksibenzaldehida dengan keton, studi interaksinya terhadap protein PfATP6, dan uji aktivitas antimalaria. Penelitian ini bertujuan untuk melakukan sintesis senyawa analog kurkumin dari bahan dasar 4-hidroksibenzaldehida dengan aseton dan siklopentanon melalui reaksi kondensasi Claisen-Schmidt, melakukan penambatan molekuler hasil sintesis dengan protein PfATP6, serta menguji secara *in vitro* terhadap *P.falciparum strain* 3D7 menggunakan senyawa analog kurkumin hasil sintesis.

Senyawa 4-hidroksibenzaldehida dalam etanol ditambahkan aseton dan siklopentanon dengan katalis HCl. Campuran diaduk dan dikontrol menggunakan KLT, kemudian didiamkan selama 24 jam pada suhu ruang. Hasil pengadukan dicuci menggunakan akuades dan metanol. Padatan yang terbentuk direkristalisasi menggunakan metanol. Produk yang diperoleh diidentifikasi menggunakan spektrometer FT-IR, spektrometer MS, serta spektrometer ^{1}H-NMR. Penambatan molekul dilakukan untuk mempelajari interaksi yang terjadi antara kurkumin dan analog kurkumin hasil sintesis dengan protein PfATP6 menggunakan *software* Autodock4. Uji aktivitas antiplasmodium dilakukan secara *in vitro* terhadap parasit *P.falciparum strain* 3D7.

Hasil penelitian diperoleh senyawa analog *1,5-bis(4-hydroxyphenyl)-1,4-pentadiene-3-one* (**a**) dan *2,5-bis(4-hydroxybenzylidene)cyclopentanone* (**b**) berhasil disintesis dengan hasil rendemen 72,13% dan 64,31%. Studi interaksi kurkumin, analog kurkumin **a** dan **b** terhadap protein PfATP6 diperoleh energi bebas Gibbs sebesar -3,89; -4,51; dan -5,78 kkal mol^{-1}. Uji *in vitro* kurkumin, analog kurkumin **a** dan **b** terhadap *P.falciparum strain* 3D7 menghasilkan nilai IC_{50} sebesar 10,03; 3,72; dan 2,68 μM. Berdasarkan hasil tersebut, analog kurkumin **a** dan **b** sebagai antimalaria yang baik serta memiliki penghambatan terhadap parasit *P.falciparum strain* 3D7 yang lebih baik dari kurkumin.

Kata Kunci : kurkumin, analog kurkumin, antimalaria, *P. faciparum*

SYNTHESIS, MOLECULAR DOCKING AND ANTIMALARIAL ACTIVITY OF CURCUMIN ANALOGUES FROM 4-HYDROXYBENZALDEHYDE AND KETONE

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ABSTRACT

Synthesis of curcumin analogues from 4-hydroxybenzaldehyde with ketones, study of its interaction with PfATP6 protein, and assay of antimalarial activity have been carried out. The aims of this study were to synthesize curcumin analogue compounds from 4-hydroxybenzaldehyde with acetone and cyclopentanone by the Claisen-Schmidt reaction, perform molecular anchoring of the synthesized protein with PfATP6, and in vitro test against *P.falciparum* strain 3D7 using the synthetic analogue compound.

The compound 4-hydroxybenzaldehyde in ethanol is added by acetone and cyclopentanone with HCl catalyst. The mixture was stirred and controlled using TLC, then allowed to stand for 24 hours at room temperature. The stirring results were washed using distilled water and methanol. The solid formed was recrystallized using methanol. The products obtained were identified using FT-IR spectrometer, MS spectrometer, and ^{1}H-NMR spectrometer. Molecular docking was carried out to study the interaction between curcumin and the synthesized curcumin analogue with PfATP6 protein using Autodock4 software. Antiplasmodium activity test was carried out in vitro against the *P.falciparum* parasite strain 3D7.

The results showed that the analogues of 1,5-bis(4-hydroxyphenyl)-1,4-pentadiene-3-one (**a**) and 2,5-bis(4-hydroxybenzylidene)cyclopentanone (**b**) were synthesized with the yield of 72.13% and 64.31%. The study of the interaction of curcumin, curcumin analogues **a** and **b** on PfATP6 protein, obtained Gibbs free energy of -3.89; -4.51; and -5.78 kcal mol^{-1}. In vitro tests of curcumin, curcumin analogues **a** and **b** against *P.falciparum* strain 3D7 resulted in IC50 values of 10.03; 3.72; and 2.68 μM. Based on these results, analogues of curcumin **a** and **b** as good antimalarials and have better inhibition against the parasite *P.falciparum* strain 3D7 than curcumin.

Keywords : curcumin, analogue curcumin, antimalarial, *P. faciparum*