DESAIN DAN SINTESIS SENYAWA TURUNAN PIRAZOLINA TERKONJUGASI DARI ANALOG KURKUMIN SIKLOPENTANON SEBAGAI ANTIMALARIA

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INTISARI

Desain dan sintesis senyawa turunan pirazolina terkonjugasi dari analog kurkumin siklopentanon sebagai antimalaria telah dilakukan. Desain senyawa antimalaria dilakukan melalui penambatan molekul senyawa analog kurkumin siklopentanon dan turunan pirazolina terkonjugasinya terhadap protein *Plasmodium falciparum* laktat dehidrogenase (1LDG.pdb). Hasil penambatan molekul selanjutnya dilakukan sintesis melalui reaksi kondensasi *Claisen-Schmidt* antara turunan benzaldehida dengan siklopentanon menggunakan katalis NaOH. Hasil reaksi dilanjutkan siklokondensasi dengan hidrazin untuk menghasilkan turunan pirazolina terkonjugasi.

Hasil penambatan molekul terhadap protein *Plasmodium falciparum* laktat dehidrogenase (*Pf*LDH) menunjukkan bahwa senyawa analog kurkumin siklopentanon maupun turunan pirazolina terkonjugasi memiliki interaksi yang menyerupai ligan aslinya. Sintesis 2,5-bis(4-metoksibenzalidin) siklopentanon (**AK 1**), 2,5-bis-(3,4-dimetoksibenzalidin) siklopentanon (**AK 2**) dan 2,5-dibenzalidin-siklopentanon (**AK 3**) diperoleh dengan rendemen reaksi 97,32; 71,31 dan 54,04%. Senyawa 6-(4-metoksibenzil)-3-(4-metoksifenil)-hexahidrosiklopentapirazolina (**PT 1**) dan 6-(3,4-dimetoksibenzil)-3-(3,4-dimetoksifenil)-hexahidrosiklopentapirazolina (**PT 2**) dihasilkan dengan rendemen reaksi 23,28 dan 19,82%. Uji aktivitas antimalaria menggunakan strain *Plasmodium falciparum* 3D7 menghasilkan nilai IC_{50} senyawa **AK 1-7** serta **PT 1-10** berturut sebesar 35,43; 18,63; 73,24; 4,55 dan 4,10 μM. Hasil uji aktivitas menunjukkan bahwa perubahan struktur analog kurkumin menjadi pirazolina terkonjugasi mampu meningkatkan aktivitas antimalarianya.

Kata kunci: siklopentanon, turunan pirazolina terkonjugasi, aktivitas antimalaria, penambatan molekul, PfLDH

DESIGN AND SYNTHESIS OF CONJUGATED PIRAZOLINE DERIVATIVES FROM CYCLOPENTANON CURCUMIN ANALOGUES AS AN ANTIMALARIA

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ABSTRACT

The design and synthesis of conjugated pyrazoline derivatives from cyclopentanone curcumin analogues as antimalarials have been carried out. The design of antimalarial compounds was carried out through the molecular docking of cyclopentanone curcumin analogues and conjugated pyrazoline derivatives to the protein *Plasmodium falciparum* lactate dehydrogenase (1LDG.pdb). The results of the molecular docking are then synthesised through the Claisen-Schmidt condensation reaction between benzaldehyde derivatives and cyclopentanone using NaOH catalysts. The reaction results were then continued to cyclocondensation with hydrazine to produce conjugated pyrazoline derivatives.

Molecular docking of the *Plasmodium falciparum* lactate dehydrogenase (*Pf*LDH) protein revealed that both cyclopentanone curcumin analogues and conjugated pyrazoline derivatives had binding pockets like the original ligands. Synthesis of 2,5-bis(4-methoxybenzylidene)-cyclopentanone (**AK 1**), 2,5-bis-(3,4-dimethoxy-benzylidene)-cyclopentanone (**AK 2**), and 2,5-benzylidene-cyclopentanone (**AK 3**) were obtained in 97.32, 71.31, and 54.04 % yields. Synthesis of 6-(4-methoxy-benzylidene)-3-(4-methoxyphenyl) hexahydrocyclopentapyrazoline (**PT 1**) and (6-(3,4-dimethoxybenzylidene)-3-(3,4dimethoxyphenyl) hexahydrocyclopentapyrazoline (PT 2) were obtained in 23.28 and 19.82 % yield respectively. An antimalarial activity assay using the *Plasmodium falciparum* 3D7 strain gave IC_{50} values for **AK 1-3** compound and **PT 1 - 2** of 35.43, 18.63, 73.24, 4.55 and 4.10 µM respectively. The results showed that the change of structure of curcumin analogues to conjugated pyrazoline enhanced their antimalarial activities.

Keywords: cyclopentanone, conjugated pyrazoline derivatives, antimalarial activity, molecular docking, PfLDH