SINTESIS DAN UJI AKTIVITAS ANTIMALARIA ANALOG KURKUMIN DARI 2-METOKSIBENZALDEHIDA DENGAN VARIASI KETON SERTA PENAMBATAN MOLEKUL TERHADAP PROTEIN PFLDH

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INTISARI

Telah dilakukan penelitian sintesis dan uji aktivitas antimalaria analog kurkumin hasil sintesis 2-metoksibenzaldehida dengan variasi keton serta penambatan molekul terhadap protein PfLDH. Penelitian ini bertujuan untuk melakukan sintesis senyawa analog kurkumin dari 2-metoksibenzaldehida dengan aseton, siklopentanon, sikloheksanon menggunakan katalis basa, mengetahui aktivitas senyawa analog kurkumin hasil sintesis dan kurkumin sebagai antimalaria secara *in vitro* dengan uji antiplasmodium terhadap *P. falciparum strain* FCR3, dan mengetahui nilai energi afinitas ikatan yang terbentuk antara senyawa analog kurkumin dan kurkumin dengan sisi aktif enzim PfLDH menggunakan uji *in silico* metode penambatan molekul.

Sintesis dilakukan dengan bahan awal 2-metoksibenzaldehida dalam etanol dengan aseton (analog kurkumin **A**), siklopentanon (analog kurkumin **B**), sikloheksanon (analog kurkumin **C**). Reaksi ini menggunakan katalis NaOH. Campuran tersebut diaduk selama 24 jam pada suhu ruang. Larutan dinetralisasi dengan HCl 37% hingga pH 6-7 dan terbentuk padatan. Padatan difiltrasi dan direkristalisasi menggunakan etanol. Produk hasil sintesis diidentifikasi dengan KLT, spektrofotometer FT-IR, spektrometer ^{1}H-NMR, ^{13}C-NMR, spektrometer DI-MS, dan LC-MS. Uji aktivitas antimalaria dilakukan dengan metode *in vitro* menggunakan parasit *Plasmodium falciparum strain* FCR3 dan studi interaksi dilakukan dengan metode penambatan molekul terhadap protein PfLDH.

Hasil penelitian diperoleh senyawa analog kurkumin (1E,4E)-1,5-bis(2-metoksifenil)-1,4-pentadiena-3-on (analog kurkumin **A**), analog kurkumin (2E,5E)-2,5-bis(2-metoksibenzilidin)siklopentanon (analog kurkumin **B**), dan analog kurkumin (2E,6E)-2,6-bis(2- metoksibenzilidin)sikloheksanon (analog kurkumin **C**) dengan *yield* yang diperoleh dari hasil sintesis berurutan adalah 56,6%; 51,7%;dan 47,5%. Senyawa analog kurkumin **A**, **B**, dan **C** terbukti sangat aktif dalam uji *in vitro* terhadap *P. falciparum strain* FCR3 dengan nilai IC_{50} berurutan 1,09; 0,69;dan 2,01 µM. Senyawa analog kurkumin **A**, **B**, dan **C** berinteraksi stabil dengan protein reseptor PfLDH memberikan energi afinitas ikatan berurutan -5,47; -5,69;dan -4,60 kkal mol^{-1}. Ketiga analog kurkumin berinteraksi spesifik dengan asam amino Arg171 melalui ikatan hidrogen.

Kata kunci : antimalaria, penambatan molekul, senyawa analog kurkumin.

SYNTHESIS AND ANTIMALARIAL ACTIVITY TEST OF CURCUMIN ANALOGUES FROM 2-METOXYBENZALDEHYDE USING KETONES VARIATIONS WITH MOLECULAR DOCKING ON PFLDH PROTEIN

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ABSTRACT

Synthesis and antimalarial activity test of synthesized curcumin analogues from starting material 2-metoxybenzaldehyde using ketones variations with molecular docking on PfLDH protein has been carried out. The aims of this study were to synthesize curcumin analogue compounds from 2-methoxybenzaldehyde with acetone, cyclopentanone, cyclohexanone used base catalysts, to determine the activity of curcumin analog compounds produced and curcumin as antimalarials *in vitro* with antiplasmodium test against *P. falciparum strain* FCR3, and to determine the energy value of the bond affinity formed between curcumin and curcumin analog compounds with the active site of the PfLDH enzyme using *in silico* with method molecular docking.

The synthesis analogue curcumines were carried out with the starting material 2-methoxybenzaldehyde in ethanol with acetone (analogue curcumin **A**), cyclopentanone (analogue curcumin **B**), cyclohexanone (analogue curcumin **C**). The reaction used NaOH as catalyst. The mixture is stirred for 24 hours at room temperature. The solution was neutralized with 37% HCl to pH 6-7 and a solid is formed. The solid was filtered and recrystallized using ethanol. The synthesized products were identified by TLC, FT-IR spectrophotometer, ^{1}H-NMR spectrometer, ^{13}C-NMR, DI-MS spectrometer, and LC-MS. The antimalarial activity test was carried out by *in vitro* method using the parasite *P. falciparum strain* FCR3 and interaction studies were carried out using the molecular docking method of PfLDH protein.

The results showed curcumin analog compounds (1E, 4E)-1,5-bis(2-methoxyphenyl) -1,4-pentadiene-3-on (analogue curcumin **A**), curcumin analogue (2E, 5E)-2,5-bis(2-methoxybenzilidine) cyclopentanone (analogue curcumin **B**), and curcumin analogue (2E, 6E)-2,6-bis(2- methoxybenzilidine) cyclohexanone (analogue curcumin **C**) with the *yield* obtained from the synthesis results, respectively 56.6%, 51.7%, 47.5%. Curcumin analogue compounds **A**, **B**, and **C** proved to be very active in *in vitro* tests against *P. falciparum strain* FCR3 with a value of IC_{50}, sequentially 1.09; 0.69; and 2.01 µM. Curcumin analogue compounds **A**, **B**, and **C** gived negative values for bond affinity energy when interacting with PfLDH protein, respectively -5.47; -5.69; and -4.60 kcal mol^{-1}. The three curcumin analogues bonded specifically with the amino acid Arg171 through hydrogen bond.

Keywords : antimalarial, molecular docking, curcumin analogue compounds.