ANALOG KURKUMIN DARI 3-METOKSIBENZALDEHIDA SEBAGAI SENYAWA ANTIMALARIA: KAJIAN PENAMBATAN MOLEKUL, SINTESIS DAN UJI AKTIVITASNYA

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INTISARI

Telah dilakukan penelitian penambatan molekul senyawa analog kurkumin dari 3-metoksibenzaldehida dengan variasi keton dan kurkumin terhadap protein PfLDH dan PfENR, sintesis dan aktivitasnya sebagai senyawa antimalaria. Penambatan molekul menggunakan software AutoDock4 dilakukan untuk mengetahui nilai energi afinitas ikatan dan interaksi yang terbentuk antara senyawa analog kurkumin 2,5-bis(3-metoksibenzilidin)siklopentanon (**A**), 2,6-bis(3-metoksibenzilidin)sikloheksanon (**B**), 1,5-bis(3-metoksifenil)-penta-1,4-diena-3-on (**C**) dengan sisi aktif enzim PfLDH (PDB ID: 1U4O) dan PfENR (PDB ID: 1NNU). Analog kurkumin dengan nilai energi afinitas dan interaksi terbaik disintesis dengan mereaksikan 3-metoksibenzaldehida dan keton menggunakan katalis NaOH. Produk hasil sintesis diidentifikasi dengan KLT, spektrofotometer FT-IR, spektrometer DI-MS, spektrometer ^{1}H-NMR dan ^{13}C-NMR. Senyawa analog kurkumin hasil sintesis dan kurkumin diuji aktivitasnya sebagai senyawa antimalaria secara *in vitro* terhadap *P. falciparum strain* FCR-3.

Hasil penelitian diperoleh nilai energi afinitas ikatan senyawa analog kurkumin **A**; **B**; **C**; dan kurkumin terhadap sisi aktif enzim PfLDH secara berurutan sebesar -7,57; -7,51; -6,63; dan -5,96 kkal mol^{-1}. Penambatan molekul senyawa analog kurkumin **A**; **B**; **C**; dan kurkumin terhadap sisi akif enzim PfENR menghasilkan nilai energi afinitas ikatan secara berurutan sebesar -8,59; -8,27; -7,15; dan -6,69 kkal mol^{-1}. Senyawa analog kurkumin **A** menunjukkan afinitas ikatan paling negatif dan berinteraksi spesifik berupa ikatan hidrogen dengan sisi aktif PfLDH dan PfENR. Sintesis senyawa analog kurkumin **A** diperoleh *yield* 45,0%. Senyawa analog kurkumin **A** terbukti sangat aktif dalam uji antimalaria secara *in vitro* terhadap *P. falciparum strain* FCR-3 dengan IC_{50} sebesar 1,70 µg/mL dan kurkumin terbukti aktif dengan IC_{50} 6,49 µg/mL.

Kata kunci: Analog kurkumin, antimalaria, penambatan molekul, PfENR, PfLDH.

CURCUMIN ANALOGUE FROM 3-METHOXYBENZALDEHYDE AS AN ANTIMALARIAL COMPOUND: STUDY OF MOLECULAR DOCKING, SYNTHESIS AND ITS ACTIVITY TEST

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ABSTRACT

Molecular docking of curcumin analogues from 3-methoxybenzaldehyde using ketone variations on PfLDH and PfENR proteins, synthesis and its activity as antimalarial compounds have been carried out. Molecular docking using AutoDock4 software was carried out to determine the bond affinity energy values and the interactions formed between curcumin analogues 2,5-bis(3-methoxybenzylidine)cyclopentanone (**A**), 2,6-bis(3-methoxybenzylidine)-cyclohexanone (**B**), 1,5-bis(3-methoxyphenyl)-penta-1,4-diene-3-one (**C**) with active sites of PfLDH (PDB ID: 1U4O) and PfENR (PDB ID: 1NNU) enzymes. The curcumin analogue with the best affinity energy values and interactions was synthesized by reacting 3-methoxybenzaldehyde and ketone using NaOH catalyst. The synthesized product was identified by TLC, FT-IR spectrophotometer, DI-MS spectrometer, ^{1}H-NMR and ^{13}C-NMR spectrometer. The synthesized curcumin analogue was tested for its activity as an antimalarial compound in vitro against *P. falciparum* strain FCR-3.

The results showed that the bonding affinity energy value for curcumin analogues **A**; **B**; **C**; and curcumin to the active site of PfLDH enzyme respectively of -7.57; -7.51; -6.63; and -5,96 kcal mol^{-1}. Molecular docking of curcumin analogues **A**; **B**; **C**; and curcumin to the active site of PfENR enzyme resulted in a bond affinity energy value of -8.59; -8.27; -7.15; -6,69 kcal mol^{-1}. The curcumin analogue **A** showed the most negative bonding affinity and interacted specifically in the form hydrogen bonds with the active sites of PfLDH and PfENR. Synthesis of curcumin analogue **A** obtained yield 45,0%. The curcumin analogue **A** proved to be very active in antimalarial assays in vitro against *P. falciparum* strain FCR-3 with an IC_{50} of 1.70 µg/mL and curcumin proved to be active with an IC_{50} of 6.49 µg/mL.

Keywords: Antimalarial, curcumin analogue, molecular docking, PfENR, PfLDH.