AKTIVITAS ANTIMALARIA ANALOG KURKUMIN HASIL SINTESIS SINAMALDEHIDA DENGAN VARIASI KETON DAN STUDI *IN SILICO* TERHADAP ENZIM *Plasmodium falciparum LACTATE DEHYDROGENASE* (PfLDH)

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INTISARI

Telah dilakukan sintesis dan uji aktivitas antimalaria senyawa analog kurkumin berbahan dasar sinamaldehida dengan variasi keton berupa sikloheksanon (analog kurkumin **A**), siklopentanon (analog kurkumin **B**), dan aseton (analog kurkumin **C**) dan studi *in silico* terhadap enzim *Plasmodium falciparum Lactate Dehydrogenase* (PfLDH). Penelitian ini bertujuan untuk melakukan sintesis senyawa analog kurkumin melalui reaksi kondensasi aldol Claisen-Schmidt, melakukan uji antiplasmodium terhadap *P. falciparum strain* FCR-3, dan menentukan jenis interaksi antara senyawa analog kurkumin dengan reseptor enzim dengan studi *in silico* menggunakan teknik penambatan molekul.

Sintesis dilakukan dengan mereaksikan sinamaldehida dengan variasi keton menggunakan katalis HCl 37% pada pengadukan di suhu ruang selama 24 jam. Reaksi dipantau dengan uji KLT setiap 30 menit dengan campuran eluen n-heksana:etil asetat (7:3). Reaksi kemudian dinetralkan dengan NaOH 40% (w/w) dan direkritalisasi dengan etanol. Karakterisasi senyawa hasil sintesis dilakukan dengan analisis elemental, FTIR, DI-MS, ^{1}H-NMR dan ^{13}C-NMR. Aktivitas antimalaria diuji secara *in vitro* terhadap *P. falciparum strain* FCR-3 dengan inkubasi 72 jam. Studi *in silico* dilakukan terhadap protein dari enzim PfLDH (PDB ID: 1U4O) dengan metode penambatan molekul menggunakan *software* AutoDock4.

Senyawa analog kurkumin 2,5-bis(3-fenilalilidin)sikloheksanon (**A**); 2,5-bis(3-fenilalilidin)siklopentanon (**B**); dan 1,9-difenilnona-1,3,6,8-tetraen-5-on (**C**) berhasil disintesis dengan menghasilkan rendemen secara berurutan sebesar 69,9%; 75,6%; dan 54,5%. Uji *in vitro* terhadap *P. falciparum strain* FCR-3 senyawa analog kurkumin **A**, **B**, **C** memiliki aktivitas yang sangat aktif dengan nilai IC_{50} secara berurutan sebesar 2,27; 3,42; 3,85 µg/mL, sedangkan kurkumin memiliki aktivitas yang aktif dengan nilai IC_{50} 5,11 µg/mL. Studi *in silico* analog kurkumin **A**, **B**, **C,** dan kurkumin dengan penambatan molekul menghasilkan nilai energi ikatan secara berurutan sebesar -6,12; -5,79; -5,16; dan -5,02 kkal mol^{-1} yang menunjukkan adanya afinitas ikatan yang tinggi dalam berikatan dengan sisi aktif enzim PfLDH sebagai antimalaria.

Kata kunci: antimalaria, kurkumin, penambatan molekul, PfLDH, *Plasmodium falciparum*.

ANTIMALARIAL ACTIVITIES OF ANALOGUES CURCUMIN SYNTHESIZED FROM CINNAMALDEHYDE WITH VARIATIONS OF KETONE AND ITS *IN SILICO* STUDY TO *Plasmodium falciparum LACTATE DEHYDROGENASE* (PfLDH) ENZYME

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ABSTRACT

Curcumin analogue compounds based on cinnamaldehyde with variations of ketones in the form of cyclohexanone (analogue curcumin **A**), cyclopentanone (analogue curcumin **B**), and acetone (analogue curcumin **C**) were synthesized and tested for antimalarial activity, as well as *in silico* study of the *Plasmodium falciparum Lactate Dehydrogenase* (PfLDH) enzyme. The goal of this research were to synthesize curcumin analogue compounds using the Claisen-Schmidt aldol condensation method, to perform antiplasmodium tests on *P. falciparum* strain FCR-3, and to evaluate the bond energy of interaction between curcumin analogue compounds and enzyme receptors using *in silico* study by the molecular docking technique.

The synthesis was carried out by reacting cinnamaldehyde with a variety of ketones with HCl 37% as a catalyst at room temperature for 24 hours while stirring. TLC tests with a mixture of eluent N-hexane:ethyl acetate (7:3) were performed every 30 minutes to monitor the reaction. The reaction was then recrystalized with ethanol after being neutralized with NaOH 40% (w/w). The characterization of the synthesized compounds was carried out by elemental analysis, FTIR, DI-MS, ^{1}H-NMR and ^{13}C-NMR. The antimalarial activity was assessed in vitro against the *P. falciparum* strain FCR-3 with a 72-hour incubation period. The protein of the PfLDH enzyme (PDB ID: 1U4O) was studied by *in silico* using tilizing the molecular docking method with AutoDock4 software.

Analogue curcumin compounds 2,5-bis (3-phenylalilidine) cyclohexanone (**A**); 2,5-bis (3-phenylalilidine) cyclopentanone (**B**); 1,9-diphenylnona-1,3,6,8-tetraen-5-on (**C**) were successfully synthesized by producing 69.9%; 75.6%; and 54.5% yield. *In vitro* test against *P. falciparum* strain FCR-3 of analogue curcumin compounds **A**, **B**, **C** remarked good activity as antimalarial with its IC_{50} values were 2.27; 3.42; 3.85 µg/mL respectively than curcumin that was remarked moderately active and its IC_{50} was 5.11 µg/mL. *In silico* studies of analogue curcumin **A**, **B**, **C,** and curcumin control with molecular docking yielded bond energy values of -6.12; -5.79; -5.16; and -5.02 kcal mol^{-1} that showed its high bond affinity for bonding with the active site of the PfLDH enzyme as antimalarial.

Keywords: antimalarial, curcumin, molecular docking, PfLDH, *Plasmodium falciparum*.