PENAMBATAN MOLEKULER, SINTESIS, DAN UJI AKTIVITAS SENYAWA ANALOG KURKUMIN MONOKARBONIL BERBAHAN DASAR 3-HIDROKSIBENZALDEHIDA DENGAN VARIASI KETON TERHADAP ENZIM *Pf*LDH SEBAGAI ANTIMALARIA

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INTISARI

Penelitian penambatan molekuler, sintesis dan uji aktivitas senyawa analog kurkumin monokarbonil berbahan dasar 3-hidroksibenzaldehida dengan variasi keton terhadap enzim *Pf*LDH sebagai antimalaria telah berhasil dilakukan. Penambatan molekuler senyawa analog kurkumin A-F terhadap enzim *Pf*LDH (PDB ID: 1CET) dilakukan dengan tujuan untuk mengetahui nilai afinitas ikatan dan interaksi yang terjadi. Senyawa analog kurkumin dengan nilai afinitas ikatan paling besar dan membentuk interaksi spesifik dari hasil penambatan molekuler, dilakukan sintesis menggunakan metode kondensasi Claisen-Schmidt dengan mereaksikan 3-hidroksibenzaldehida dan satu varian keton menggunakan katalis NaOH. Produk sintesis selanjutnya dikarakterisasi dengan spektrofotometer FT-IR, spektrometer MS/MS, spektrometer ^{1}H-NMR dan ^{13}C-NMR. Uji aktivitas antimalaria senyawa analog kurkumin hasil sintesis dan kurkumin dilakukan secara *in vitro* terhadap *Plasmodium falciparum strain* FCR-3.

Hasil penelitian diperoleh nilai afinitas ikatan senyawa analog kurkumin A-F dan kurkumin terhadap enzim *Pf*LDH secara berurutan sebesar -6,40; -7,48; -7,82; -7,74; -7,96; -8,86; dan -6,53 kkal/mol. Berdasarkan hasil penambatan molekuler diketahui senyawa analog kurkumin F merupakan senyawa kandidat terbaik karena memiliki nilai afinitas ikatan paling besar dan interaksi spesifik dengan sisi aktif enzim *Pf*LDH. Senyawa analog kurkumin F disintesis dengan kondensasi Clasien-Schmidt menghasilkan rendemen sebesar 71,9% dan kemurnian 100%. Pengujian aktivitas antimalaria senyawa analog kurkumin F terhadap *P. falciparum strain* FCR-3 sangat aktif dengan nilai IC_{50} sebesar 0,851 µM.

Kata kunci: 3-hidroksibenzaldehida, analog kurkumin, antimalaria, penambatan molekuler, *Pf*LDH

MOLECULAR DOCKING, SYNTHESIS, AND ACTIVITIES TEST OF 3-HYDROXYBENZALDEHYDE MONOCARBONYL ANALOGUES OF CURCUMIN COMPOUND USING KETONES VARIATION ON PfLDH ENZYME AS ANTIMALARIA

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ABSTRACT

The experiment of molecular docking, synthesis, and activity test of 3-hydroxybenzaldehyde based monocarbonyl curcumin analog compound with ketone variations on *Pf*LDH enzyme as an antimalarial had been carried out. Molecular docking of A-F curcumin analog compounds with *Pf*LDH enzyme (PDB ID: 1CET) was carried out to determine the value of the binding affinity and the interactions. The curcumin analog compound with the best binding affinity and interaction from the molecular docking was synthesized using the Claisen-Schmidt condensation method by reacting 3-hydroxybenzaldehyde and one of the ketone variants using a NaOH catalyst. The synthesized product was further characterized by FT-IR spectrophotometer, MS/MS spectrometer, ^{1}H-NMR spectrometer, and ^{13}C-NMR. Antimalarial activity tests of synthetic curcumin analog compounds and curcumin were conducted in vitro against *Plasmodium falciparum strain* FCR-3.

The results showed that the binding affinity of curcumin analogue compounds A-F and curcumin to *Pf*LDH enzyme respectively was -6.40; -7.48; -7.82; -7.74; -7.96; -8.86; and -6.53 kcal/mol. Based on the results of molecular docking, it was found that F curcumin analogue were the best candidate compound which were indicated by the highest binding affinity values and had specific interactions with the active site of *Pf*LDH enzyme. The analogue compound of curcumin F was synthesized by Clasien-Schmidt condensation obtained 71.9% yield and 100% purity. Testing the antimalarial activity of curcumin F analogue compounds against *P. falciparum strain* FCR-3 was very active with an IC_{50} of 0.851 µM.

Keywords: 3-hydroxybenzaldehyde, antimalarial, curcumin analogue, molecular docking, *Pf*LDH