

STUDI PENAMBATAN MOLEKUL, SINTESIS, DAN UJI AKTIVITAS ANTIPLASMODIUM SENYAWA ANALOG KURKUMIN MONOKETON BERBAHAN DASAR 4-METOKSIBENZALDEHIDA

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INTISARI

Telah dilakukan penelitian studi penambatan molekul, sintesis, dan uji aktivitas antiplasmodium senyawa analog kurkumin monoketon berbahan dasar 4-metoksibenzaldehida. Penelitian ini bertujuan untuk mengetahui hasil studi penambatan molekul senyawa analog kurkumin dari 4-metoksibenzaldehida dan 6 senyawa keton (aseton, siklopentanon, sikloheksanon, 4-piperidon, 1-benzil-4-piperidon, dan N-metil-4-piperidon) dengan protein reseptor *Acyl Carrier Protein Reductase (PfENR)* (PDB ID:1NNU); Sintesis senyawa analog kurkumin terbaik hasil penambatan molekul; dan Menguji aktivitas antiplasmodium serta skrining profil ADMET dari senyawa analog kurkumin. Senyawa analog kurkumin dengan hasil terbaik berdasarkan studi penambatan molekul disintesis melalui reaksi kondensasi aldol silang. Sintesis dilakukan dengan mereaksikan 4-metoksibenzaldehida dan senyawa keton dalam pelarut etanol dengan menggunakan katalis NaOH 40%. Sintesis dilakukan dengan pengadukan selama 3 jam pada temperatur 37 °C. Hasil sintesis diidentifikasi dengan uji KLT serta di karakterisasi menggunakan TLC *scanner*, FT-IR, ¹H-NMR, dan ¹³C-NMR. Produk sintesis juga diuji aktivitas antiplasmodium secara *in vitro* menggunakan parasit *P. falciparum strain 3D7* serta dievaluasi terhadap profil ADMET.

Hasil penelitian terbaik dari penambatan molekul yaitu senyawa analog kurkumin F, yaitu N-benzil-3,5-bis[(4-metoksifenil)metiliden]-4-piperidon dengan nilai afinitas ikatan sebesar -8,55 kkal/mol serta membentuk ikatan hidrogen dengan residu asam amino Ala219, Asn218, Gly313, Ala217, dan Ser215. Sintesis analog kurkumin didapatkan padatan berwarna kuning dengan persen hasil sebesar 68,39% dan titik leleh 161-163 °C. Senyawa tersebut memiliki IC₅₀ sebesar 4,48 µg/mL dan berdasarkan profil ADMET senyawa analog kurkumin F dapat dijadikan senyawa kandidat obat malaria dengan aktivitas lebih baik daripada senyawa kurkumin.

Kata Kunci: 4-metoksibenzaldehida, analog kurkumin monoketon, antiplasmodium, *PfENR*

MOLECULAR DOCKING STUDY, SYNTHESIS, AND ANTIPLASMODIAL ACTIVITY ASSAY OF MONOKETONE CURCUMINE ANALOGUE FROM 4-METHOXYBENZALDEHYDE

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ABSTRACT

A molecular docking study, synthesis, and antiplasmodial activity assay of monoketone curcumin analogue from 4-methoxybenzaldehyde have been carried out. The aims of this study were to find the best molecular docking study of monoketone curcumin analogue from 4-methoxybenzaldehyde and 6 ketone compounds variation (acetone, cyclopentanone, cyclohexanone, 4-piperidone, 1-benzyl-4-piperidone, and N-methyl-4-piperidone) against Acyl Carrier Protein Reductase (*Pf*ENR) enzyme (PDB ID:1NNU); to synthesize monoketone curcumin analogue based on the best of molecular docking study results; and to perform curcumin analogue antiplasmodial activity assay on *P. falciparum*. The study was initiated with a molecular docking study of a curcumin analogue with the *Pf*ENR enzyme. Based on molecular docking study results, the curcumin analogue would be synthesis by reacting 4-methoxybenzaldehyde with a ketone compound (1-benzyl-4-piperidone) in ethanol. The reaction used a 40% NaOH catalyst. The mixture is stirred for 3 hours at room temperature. The synthesized product will be characterized by TLC scanner, FT-IR, ¹H-NMR, and ¹³C-NMR. The antiplasmodial activity of the curcumin analogue will be carried out by an in vitro method using the parasite *P. falciparum* strain 3D7.

The results showed the binding affinity of curcumin analogue compounds A-F and curcumin to *Pf*ENR enzyme respectively. -6.66, -7.00, -7.34, -7.85, -7.39, -8.55, and -6.72 kcal/mol. Based on the results of molecular docking, it was found that the F curcumin analogue was the best candidate compound which was indicated by the highest binding affinity values and had specific interactions with specific amino acid residues Ala219, Asn218, Gly313, Ala217, and Ser215 of *Pf*ENR enzyme. The analogue compound of curcumin F was synthesized by Claisen-Schmidt condensation reaction and obtained a 68.39% yield and 100% purity. Testing the antimalarial activity of curcumin F analogue compounds against *P. falciparum* strain 3D7 was antiplasmodial active with an IC₅₀ of 4.48 µg/mL. Curcumin F analogue compound has a good ADMET profile than curcumin compound so it has the potential to be developed as an antimalarial drug candidate.

Keywords: 4-methoxybenzaldehyde, antiplasmodial, monoketone curcumin analogue, *Pf*ENR