PENAMBATAN MOLEKULER TERHADAP ENZIM P*f*ENR, SINTESIS SENYAWA ANALOG KURKUMIN BERBAHAN DASAR 3,4-DIMETOKSIBENZALDEHIDA DENGAN VARIASI KETON DAN UJI *IN VITRO* SEBAGAI ANTIPLASMODIUM

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INTISARI

Penambatan molekuler terhadap enzim P*f*ENR, sintesis senyawa analog kurkumin berbahan dasar 3,4-dimetoksibenzaldehida dengan variasi keton dan uji *in vitro* sebagai antiplasmodium telah berhasil dilakukan. Penambatan molekuler dilakukan antara enzim P*f*ENR (PDB ID: 1NNU) dengan senyawa analog kurkumin A-F, ligan alami, kurkumin, dan klorokuin untuk mengetahui bentuk interaksi dan nilai afinitas yang terjadi. Senyawa analog kurkumin yang memiliki nilai afinitas paling rendah dan membentuk interaksi spesifik kemudian disintesis. Sintesis dilakukan dengan metode kondensasi Claisen–Schmidt antara 3,4-dimetoksibenzaldehida dengan 1-benzilpiperidin-4-on menggunakan katalis KOH 10%. Reaksi dilakukan dengan variasi pengadukan, refluks, dan sonikasi. Hasil sintesis diidentifikasi dengan *TLC Scanner* dan hasil yang paling baik dikarakterisasi dengan spektrofotometer FT-IR, spektrometer ^{1}H-NMR dan ^{13}C-NMR. Uji aktivitas antiplasmodium senyawa analog kurkumin hasil sintesis dilakukan secara *in vitro* terhadap *Plasmodium falciparum* galur 3D7.

Hasil penelitian diperoleh nilai afinitas ikatan senyawa analog kurkumin A-F, ligan alami, kurkumin, dan klorokuin terhadap enzim *Pf*ENR secara berurutan sebesar -6,79; -7,79; -7,91; -6,95; -7,13; -8,39; -7,26; -7,11; dan -6,12 kkal/mol. Hasil penambatan molekuler menunjukan senyawa analog kurkumin F merupakan kandidat terbaik untuk disintesis. Hasil sintesis senyawa analog kurkumin F terbaik diperoleh melalui metode sonikasi berupa serbuk kuning dengan rendemen sebesar 77%, kemurnian 100%, dan titik lebur berkisar antara 148,6-150,1 ºC. Aktivitas antiplasmodium senyawa analog kurkumin F terhadap *P. falciparum* galur 3D7 termasuk kategori aktif dengan nilai IC_{50} sebesar 1,020 μg/mL.

Kata kunci: 3,4-dimetoksibenzaldehida, analog kurkumin, antiplasmodium, penambatan molekuler, P*f*ENR

MOLECULAR DOCKING OF PfENR ENZYME, SYNTHESIS OF CURCUMIN ANALOGUE FROM 3,4-DIMETHOXYBENZALDEHYDE WITH VARIATION OF KETONES AND IN VITRO ASSAY AS ANTIPLASMODIUM

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ABSTRACT

Molecular docking of P*f*ENR enzyme, synthesis of curcumin analogue from 3,4-dimethoxybenzaldehyde with variation of ketones and *in vitro* assay as antiplasmodium has been successfully carried out. Molecular docking was carried out between the P*f*ENR enzyme (PDB ID: 1NNU) and the curcumin analogue compounds A-F, native ligand, curcumin, and chloroquine in order to determine the interactions and affinity values that occur. Compound with the lowest affinity value and forming specific interactions is then synthesized. Synthesis was carried out using the Claisen–Schmidt condensation method between 3,4-dimethoxybenzaldehyde and 1-benzylpiperidine-4-one using KOH catalyst. The reaction methods were carried out with variation of stirring, reflux, and sonication. The results of the synthesis were identified by TLC Scanner and the best results were followed by characterization with the FT-IR spectrophotometer, ^{1}H-NMR, and ^{13}C-NMR spectrometers. Antiplasmodium assay activity of the choosen curcumin analogue was carried out *in vitro* against *Plasmodium falciparum* strain 3D7.

The results showed that the affinity values of curcumin analogues A-F, native ligand, curcumin, and chloroquine for the *PfENR* enzyme were -6.79; -7.79; -7.91; -6.95; -7.13; -8.39; -7.26; -7.11; and -6.12 kcal/mol. The results of molecular docking showed that curcumin analougue F was the best candidate for synthesis. The best synthesis results were obtained by the sonication method as solid yellow powder with 77% yield, 100% purity, and a melting point of 148.6-150.1 ºC. Antiplasmodium assay activity of the curcumin F analogue compound against *P. falciparum* strain 3D7 was classified as active with an IC_{50} value of 1.020 µg/mL.

Keywords: 3,4-dimethoxybenzaldehyde, antiplasmodium, curcumin analogue, molecular docking, P*f*ENR