SINTESIS ANALOG MONOKARBONIL KURKUMIN ASIMETRIS DAN PREDIKSI AKTIVITASNYA SEBAGAI ANTIMALARIA MELALUI PENAMBATAN MOLEKUL

Aisyah Mumtaziyah
17/412659/PA/17978

INTISARI

Penelitian sintesis analog monokarbonil kurkumin asimetris dan prediksi aktivitas antimalaria melalui penambatan molekul telah dilakukan. Penelitian ini bertujuan melakukan sintesis dua senyawa analog monokarbonil kurkumin asimetris dan mengetahui aktifitas antimalaria dari hasil penambatan molekuler terhadap *Plasmodium falciparum* DHFR-TS.

Senyawa analog monokarbonil kurkumin asimetris diperoleh dari kondensasi *Claisen-Schmidt* senyawa benzalaseton A dan B dengan benzaldehida dan veratraldehida dengan penambahan katalis NaOH 10% melalui metode pengadukan yang menghasilkan produk (1*E*,4*E*)-1-(4-hidroksi-3-metoksifenil)-5-fenilpenta-1,4-dien-3-on (**AMKA A**) dan (1*E*,4*E*)-1-(3,4-dimetoksifenil)-5-(2-hidroksi-3-metoksifenil) penta-1,4-dien-3-on (**AMKA B**). Benzalaseton A ((*E*)-4-(4-hidroksi-3-metoksifenil)-but-3-en-2-on) disintesis dari reaksi *kondensasi Claisen-Schmidt* vanillin dengan aseton menggunakan katalis NaOH 8% sedang benzalaseton B (*E*)-4-(2-hidroksi-3-metoksifenil)-but-3-en-2-on disintesis dari reaksi *kondensasi Claisen-Schmidt* o-vanillin dengan aseton menggunakan katalis NaOH 8%. Elusidasi struktur produk dilakukan menggunakan spektrometer FTIR, GC-MS, LC-MS/MS, ^{1}H NMR dan ^{13}C-NMR. Uji aktivitas antimalaria dilakukan dengan metode penambatan molekul untuk mengkaji afinitas ikatan dan interaksi senyawa terhadap protein PfDHFR-TS menggunakan *software* Autodock4.

Sintesis senyawa benzalaseton A, benzalaseton B, **AMKA A** dan **AMKA B** menghasilkan produk dengan rendemen 71,8, 61,5, 91,2, dan 47,1%. Hasil penambatan molekul benzalaseton A dan B memberikan afinitas ikatan antara protein-ligan sebesar -5,51 dan -5,87 kkal/mol yang kurang stabil dari ligan alami. Senyawa **AMKA A** dan **AMKA B** menunjukkan ikatan stabil dengan protein PfDHFR-TS resisten serta memberikan afinitas ikatan sebesar -7,30 dan -8,22 kkal/mol yang berinteraksi spesifik dengan asam amino Asp54, Leu164, Cys15, dan Ala16 melalui ikatan hidrogen. Senyawa **AMKA A** dan **AMKA B** menujukkan kenaikkan aktivitas antimalaria dibandingkan kurkumin.

Kata kunci: AMKA, antimalaria, penambatan molekul.

SYNTHESIS OF ASYMMETRIC MONOCARBONYL CURCUMIN ANALOGUES AND THEIR ANTIMALARIAL ACTIVITY PREDICTION WITH MOLECULAR DOCKING

Aisyah Mumtaziyah
17/412659/PA/17978

ABSTRACT

The experiment of asymmetric monocarbonyl curcumin analogues synthesis dan their antimalarial activity prediction through molecular docking had been carried out. The study aimed to synthesize two asymmetric monocarbonyl analogue compounds of curcumin and to determine the antimalarial activity of the molecular docking to *Plasmodium falciparum* DHFR-TS.

The asymmetric monocarbonyl analogue of curcumin was obtained from the Claisen-Schmidt condensation of benzalacetone compounds A and B with benzaldehyde and veratraldehyde with the addition of 10% NaOH catalyst through stirring method, which resulted in the product (1E,4E)-1-(4-hydroxy-3-methoxyphenyl)- 5-phenylpenta-1,4-diene-3-one (**AMKA A**) and (1E,4E)-1-(3,4-dimethoxyphenyl)-5-(2-hydroxy-3-methoxyphenyl) penta-1,4 -dien-3-on (**AMKA B**). Benzalacetone A ((E)-4-(4-hydroxy-3-methoxyphenyl)-but-3-en-2-one) was synthesized from the *Claisen-Schmidt* vanillin condensation reaction with acetone using 8% NaOH as a catalyst while benzalacetone B (E)-4-(2-hydroxy-3-methoxyphenyl)-but-3-en-2-one was synthesized from the condensation reaction of Claisen-Schmidt o-vanillin with acetone using 8% NaOH as a catalyst. The structure elucidation of the product was carried out using FTIR, GC-MS, LC-MS/MS, ^{1}H-NMR, and ^{13}C-NMR spectrometers. The antimalarial activity test was carried out using the molecular docking method to assess the binding affinity and interaction of the compound to the PfDHFR-TS protein using Autodock4 software.

The results showed that the yield of benzalacetone A, benzalacetone B, **AMKA A** and **AMKA B** were 71.8, 61.5, 91.2, and 47.1% respectively. Benzalacetone A and B compounds gave binding affinities between protein-ligands of -5.51 and -5.87 kcal/mol, which were less stable than natural ligands. **AMKA A** and **B** compounds bind stably to resistant PfDHFR-TS protein by providing binding affinities of -7.30 and -8.22 kcal/mol, which interact specifically with amino acids Asp54, Leu164, Cys15, and Ala16 through hydrogen bonds. The compounds **AMKA A** and **AMKA B** showed an enhancement in antimalarial activity compared to curcumin.

Keywords: AMKA, antimalarial, molecular docking