TURUNAN PIRAZOLINA TERKONJUGASI DAN DIBENZALSIKLOHEKSANON SEBAGAI ANTIMALARIA: *MOLECULAR DOCKING,* SINTESIS, DAN UJI AKTIVITAS SECARA *IN VITRO*

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INTISARI

Molecular docking, sintesis dan uji bioaktivitas antimalaria senyawa dibenzalsikloheksanon (2,6-bis(*E*)-benzilidin)sikloheksanon (**DS 1**); 2,6-bis(E)-4-metoksibenzilidin)sikloheksanon (**DS 2**); 2,6-bis(*E*)-3,4-metoksibenzilidin)sikloheksanon (**DS 3**); serta (*E*)-7-benzilidin-2,3-difenil-3,3a,4,5,6,7-heksahidro-2*H*-indazol (**PT 1**); (*E*)-7-(4-metoksibenzilidin)-3-(4-metoksifenil)-3,3a,4,5,6,7-heksahidro-2*H*-indazol (**PT 2**); dan (*E*)-7-(4-metoksibenzilidin)-3-(3,4-dimetoksifenil)-3,3a,4,5,6,7-heksahidro-2*H*-indazol (**PT 3**) telah dilakukan. *Molecular docking* dilakukan terhadap protein *Pf*LDH. Sintesis senyawa dibenzalsikloheksanon **DS 1-3** dilakukan melalui reaksi kondensasi *Claisen Schmidt* antara sikloheksanon dan turunan aldehida aromatik benzaldehida, *p*-anisaldehida, dan veratraldehida terkatalisis basa NaOH. Sintesis senyawa pirazolina terkonjugasi **PT 1-3** dilakukan dengan mereaksikan senyawa dibenzalsikloheksanon hasil sintesis dengan fenilhidrazin dengan NaOH sebagai katalis menggunakan metode refluks. Elusidasi struktur senyawa sintesis dilakukan menggunakan spektrometer FTIR, GC-MS, MS-MS, ^{1}H-NMR dan ^{13}C-NMR. Senyawa hasil sintesis diuji bioaktivitasnya sebagai antimalaria secara *in vitro* terhadap *Plasmodium falciparum strain* 3D7.

Hasil penelitian *molecular docking* senyawa **DS 1, DS 2**, dan **DS 3**, serta **PT 1, PT 2,** dan **PT 3** menghasilkan afinitas ikatan yang lebih rendah dan terbentuk interaksi secara spesifik dengan sisi aktif *Pf*LDH. Nilai afinitas ikatan yang dihasilkan setiap senyawa secara berturut-turut adalah -7,82; -6,96; -7,44; -8,68; -8,07; dan -8,59 kkal/mol. Senyawa kontrol positif pada percobaan ini dilakukan terhadap senyawa kurkumin yang memberikan nilai energi interaksi sebesar -6,46 kkal/mol. Elusidasi senyawa **DS 1, DS 2, DS 3, PT 1, PT 2** dan **PT 3** yang disintesis menunjukkan kesesuaian pada data spektroskopi IR, GC-MS/ MS-MS, ^{1}H-NMR, dan ^{13}C-NMR. Hasil uji aktivitas malaria secara *in vitro* terhadap *P. falciparum strain* 3D7 menunjukkan bahwa senyawa **DS 1** dan **DS 3** dikategorikan aktif dan berpotensi sebagai antimalaria dengan IC_{50} 12,99 dan 8,07 μM, sedangkan senyawa **DS 2, PT 1, PT 2,** dan **PT 3** dikategorikan cukup aktif dengan IC_{50} 86,39; 39,59; 41,31; dan 32,48 μM.

Kata kunci: Dibensikloheksanon, pirazolina terkonjugasi, uji antimalaria secara *in vitro*, *molecular docking*

THE CONJUGATED PIRAZOLINE AND DIBENZALCYCLOHEXANONE DERIVATIVES AS ANTIMALARIAL: MOLECULAR DOCKING SYNTHESIS, AND IN VITRO BIOACTIVITY TEST

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ABSTRACT

Molecular docking, synthesis, and antimalarial bioactivity test of dibenzalcyclohexanone (2,6-bis(*E*)-benzylidine)cyclohexanone (**DS 1**); 2,6-bis(*E*)-4-methoxybenzylidine)cyclohexanone (**DS 2**); 2,6-bis(*E*)-3,4-methoxybenzylidine)cyclohexanone (**DS 3**); (*E*)-7-benzylidin-2,3-diphenyl-3,3a,4,5,6,7-hexahydro-2*H*-indozole (**PT 1**); (*E*)-7-(4-methoxybenzylidine)-3-(4-methoxyphenyl)-3,3a,4,5,6,7-hexahydro-2*H*-indozole (**PT 2**); and (*E*)-7-(4-methoxybenzylidine)-3-(3,4-dimethoxyphenyl)-3,3a,4,5,6,7-hexahydro-2*H*-indozole (**PT 3**) have been carried out. Molecular docking has been done using *Pf*LDH protein. Synthesis of dibenzalcyclohexanone DS 1-3 was conducted through *Claisen Schmidt* condensation reaction between cyclohexanone and aromatic aldehyde derivatives for benzaldehyde, *p*-anisaldehyde, and veratraldehyde catalyzed by NaOH. Synthesis of conjugated pyrazoline compounds **PT 1-3** was carried out by reacting the synthesized dibenzalcyclohexanone and phenylhydrazine with NaOH as catalyst using reflux. Structural elucidation of the synthesized compounds was carried out using FTIR, GC-MS, MS-MS, ^{1}H-NMR and ^{13}C-NMR spectrometers. The synthesized compounds have been tested *in vitro* for their bioactivity as antimalarial against *Plasmodium falciparum strain* 3D7.

Molecular docking studies of compounds **DS 1, DS 2, and DS 3** as well as **PT 1, PT 2,** and **PT 3** resulted in lower binding affinity and interacted specifically with the active site of *Pf*LDH. The binding affinities of each compound were -7.82; -6.96; -7.44; -8.68; -8.07; and -8.59 kcal/mol respectively. The positive control compound in this experiment was carried out on curcumin resulted ini binding affinity value of -6.46 kcal/mol. The elucidation of the synthesized compounds **DS 1, DS 2, DS 3, PT 1, PT 2** and **PT 3** showed suitability with IR, ^{1}H-NMR, ^{13}C-NMR and MS-MS spectroscopy data. *In vitro* antimalarial activity test against *P. falciparum strain* 3D7 showed that compounds **DS 1** and **DS 3** were categorized as active and potential antimalarial with IC_{50} 12.99 and 8.07 μM, while compounds **DS 2, PT 1, PT 2**, and **PT 3** were quite active with IC_{50} of 86.39; 39.59; 41.31; and 32.48 μM respectively.

Keywords: dibenzalcyclohexanone, conjugated pyrazoline, *in vitro* antimalarial test, molecular docking