TURUNAN KALKON BERBAHAN DASAR 3-ASETILINDOLA: PENAMBATAN MOLEKUL, SINTESIS, DAN UJI *IN VITRO* SEBAGAI SENYAWA AKTIF ANTIPLASMODIUM

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INTISARI

Penelitian untuk menemukan senyawa aktif antiplasmodium yang didasarkan pada senyawa kalkon berkerangka indola telah dilakukan. Dua belas kalkon yang dapat disintesis dengan bahan dasar 3-asetilindola dirancang dan ditambatkan terhadap enzim *Pf*-DHFR sensitif dan mutan menggunakan AutoDock Vina dan dievaluasi interaksinya menggunakan Discovery Studio. Evaluasi didasarkan pada interaksi yang terbentuk di sisi aktif enzim dan afinitas ikatan. Lima senyawa rekomendasi penambatan molekul disintesis menggunakan reaksi kondensasi *Claisen-Schdmidt* berkatalis basa. Struktur kalkon dikarakterisasi dengan menggunakan spektroskopi FTIR, GC-MS, MS/MS, *TLC Scanner*, ^{1}H, dan ^{13}C-NMR. Aktivitas antiplasmodium kalkon ditentukan dengan uji *in vitro* terhadap *Plasmodium falciparum strain* FCR-3.

Evaluasi penambatan molekul dari 12 senyawa kalkon (kalkon **A** – **L**) dihasilkan 5 senyawa kalkon terbaik yaitu Kalkon **B**, **G**, **H**, **I**, dan **J**. Lima senyawa kalkon hasil rekomendasi penambatan molekul berhasil disintesis melalui reaksi kondensasi *Claisen-Schdmidt* dengan katalis basa NaOH 10% atau KOH 10% dari bahan dasar 3-asetilindola dengan berbagai turunan aldehida aromatik yaitu 1-metil-2-imidazolkarbaldehid (kalkon **B**), benzaldehida (kalkon **G**), 4-metoksibenzaldehida (kalkon **H**), 3,4-dimetoksibenzaldehida (kalkon **I**), dan 3-bromo-4-metoksibenzaldehida (kalkon **J**). Rendemen yang diperoleh untuk kalkon **B**, **G, H, I,** dan **J** sebesar 50,60; 68,82; 57,76; 42,34; dan 42,13%. Uji aktivitas antiplasmodium secara *in vitro* terhadap *P. falciparum strain* FCR-3 diperoleh nilai IC_{50} 12,82 μM (kalkon **B**), 14,46 μM (kalkon **G**), 11,01 μM (Kalkon **H**), 14,36 μM (Kalkon **I**), dan 7,58 μM (Kalkon **J**). Senyawa kalkon berkerangka indola menunjukkan aktivitas yang lebih baik daripada kalkon pembanding yang membuktikan bahwa kerangka indola berperan dalam aktivitas antiplasmodium.

Kata kunci: Penambatan molekul, antiplasmodium, kalkon, 3-asetilindola, indola

CHALCONE DERIVATIVES FROM 3-ACETYLINDOLE: MOLECULAR DOCKING, SYNTHESIS, AND IN VITRO TEST AS ACTIVE ANTIPLASMODIUM COMPOUNDS

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ABSTRACT

The research to find antiplasmodial based on indole scaffold chalcone has been carried out. Twelve chalcones that can be synthesized from 3-acetylindole were designed and docked to the sensitive and resistant *Pf*-DHFR enzyme using AutoDock Vina and their interactions evaluated using Discovery Studio. The evaluation is based on the interaction formed at the active site of the enzyme and binding affinity. Five recommended molecules from molecular docking were synthesized using base catalysed *Claisen-Schdmidt* condensation reaction. Chalcone structures were characterized using FTIR, GC-MS, MS/MS, *TLC Scanner*, ^{1}H, and ^{13}C-NMR spectroscopy. The antiplasmodial activity of chalcone was determined in vitro against *Plasmodium falciparum* strain FCR-3.

The molecular docking evaluation of 12 chalcone compounds (Chalcone **A-L**) gave 5 best chalcone compounds, namely Chalcone **B**, **G**, **H**, **I**, and **J**. The 5 chalcone compounds were successfully synthesized through *Claisen-Schdmidt* condensation reaction in presence of base catalyst NaOH 10% or KOH 10% from 3-acetylindole with various aromatic aldehyde derivatives, namely 1-methyl-2-imidazolcarbaldehyde (chalcone **B**), benzaldehyde (chalcone **G**), 4-methoxybenzaldehyde (chalcone **H**), 3,4-dimethoxybenzaldehyde (chalcone **I**), and 3-bromo-4-methoxybenzaldehyde (chalcone **J**). The yield obtained for chalcones **B**, **G, H, I,** and **J** were 50,60; 68,82; 57,76; 42,34; and 42,13%. In vitro antiplasmodial activity test against *P. falciparum* FCR-3 strain gave IC_{50} values of 12.82 μM (chalcone **B**), 14.46 μM (chalcone **G**), 11.01 μM (chalcone **H**), 14.36 μM (chalcone **I**), and 7.58 μM (chalcone **J**). The indole scaffold chalcone compounds showed better activity than chalcone as standard proves that the indole scaffold plays a role in antiplasmodial activity.

Keywords: Molecular docking, antiplasmodial, chalcone, 3-acetylindole, indole.