SYNTHESIS AND ACTIVITY ASSAY OF CHALCONE AND PYRAZOLINE DERIVATIVES BASED ON 2-THIOPHENE CARBOXALDEHYDE AS ANTIMALARIAL AGENTS

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ABSTRACT

Chalcone and pyrazoline derivatives were synthesized from 2-thiophene carboxaldehyde as antimalarial agents and underwent activity assay. Synthesis of chalcone derivatives was carried out using 2-thiophene carboxaldehyde and acetophenone derivatives, which were 2,3-dimethoxy acetophenone, 3,4-dimethoxy acetophenone and 4-methoxy acetophenone as starting materials. Each acetophenone derivative and 2-thiophene carboxaldehyde were reacted in ethanol and 20% NaOH catalyst by stirring to give **chalcone A, B,** and **C** via Claisen-Schmidt condensation reaction. Then, each products were refluxed with phenylhydrazine in ethanol solvent and 20% NaOH catalyst to synthesize ***N*-phenylpyrazoline A** and **B**. Finally, structure elucidation of the synthesized product was done using FTIR, GC-MS, ^{1}H- and ^{13}C-NMR. All the products' activity as antimalarial agents was also tested by *in vitro* assay method against *Plasmodium falciparum* FCR-3.

Based on the research, **chalcone A, B** and **C** were obtained as yellow solids with yields of 72.73%, 76.36%, 75.72%, and melting points of 84-86, 109-110, and 105-106 °C, respectively. Cyclo-condensation reaction produced ***N*-phenylpyrazoline A** as a broken white solid with a 58.33% yield and a melting point of 128-130 °C. While ***N*-phenylpyrazoline B** was yielded as a yellow solid in 54.09% and melting points of 173-175°C. Antimalarial activity assay of **chalcone A, B**, **C**, ***N*-phenylpyrazoline A,** and **B** obtained the IC_{50} values of 14.45; 9.69; 5.80; 6.05; and 254.11 μM. It was concluded that **chalcone A, B**, **C**, and ***N*-phenylpyrazoline A** were categorized as good antimalarial agents, and ***N*-phenylpyrazoline B** was considered inactive.

Keywords: 2-thiophene carboxaldehyde, antimalaria, chalcone, *Plasmodium falciparum* FCR-3, pyrazoline.

SINTESIS DAN UJI AKTIVITAS SENYAWA TURUNAN KALKON DAN PIRAZOLINA BERBAHAN DASAR 2-TIOFEN KARBOKSALDEHIDA SEBAGAI AGEN ANTIMALARIA

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INTISARI

Senyawa turunan kalkon dan pirazolina disintesis dari 2-tiofen karboksaldehida sebagai agen antimalaria dan aktivitasnya diuji. Sintesis turunan kalkon dilakukan dengan menggunakan bahan dasar senyawa 2-tiofen karboksaldehida dan turunan asetofenon, yaitu 2,3-dimetoksi asetofenon, 3,4-dimetoksi asetofenon dan 4-metoksi asetofenon. Setiap turunan asetofenon direaksikan dengan 2-tiofena karboksaldehida dalam pelarut ethanol dan katalis NaOH 20% untuk menghasilkan **kalkon A**, **B** dan **C** melalui reaksi kondensasi *Claisen-Schmidt*. Produk yang dihasilkan selanjutnya direaksikan dengan fenilhidrazin dalam pelarut ethanol dan katalis NaOH 20% menggunakan metode refluks untuk mensintesis ***N*-fenilpirazolina A** dan **B**. Akhirnya, elusidasi struktur dilakukan terhadap produk hasil sintesis menggunakan instrumen FTIR, GC-MS, ^{1}H- dan ^{13}C-NMR.. Produk hasil sintesis diuji aktivitasnya sebagai senyawa antimalaria secara *in vitro* terhadap *Plasmodium falciparum* FCR-3.

Reaksi kondensasi *Claisen-Schmidt* menghasilkan yang **kalkon A**, **B** dan **C** berbentuk padatan berwarna kuning yang masing-masing memiliki titik leleh 84-86, 109-110 dan 105-106 °C dengan rendemen 72,73, 76,36, dan 75,72%. Senyawa ***N*-fenilpirazolina A** dan **B** berbentuk padatan berwarna putih gading dan kuning berhasil disintesis melalui reaksi siklokondensasi dengan rendemen 58,33 dan 54,09% dengan titik leleh of 128-130 dan 173-175°C, secara berurutan. Hasil uji antimalaria **kalkon A**, **kalkon B**, **kalkon C**, ***N*-fenilpirazolina A** dan ***N*-fenilpirazolina B** menghasilkan nilai IC_{50} berturut-turut 4,45; 9,69; 5,80; 6,05; dan 254,11 μM. Dapat disimpulkan bahwa **kalkon A**, **kalkon B**, **kalkon C** dan ***N*-fenilpirazolina A** memiliki aktivitas antimalaria yang baik dan ***N*-fenilpirazolina B** tergolong tidak aktif.

Kata kunci: 2-tiofena karboksaldehida, antimalaria, kalkon, pirazolina, *Plasmodium falciparum* FCR-3.