SYNTHESIS OF CHALCONE AND *N*-PHENYL PYRAZOLINE DERIVATIVES BASED ON 4-CHLOROBENZALDEHYDE AND METHOXYACETOPHENONE AND ITS ACTIVITY ASSAY AS ANTIMALARIAL AGENTS

LAILY SALSABILA
18/425541/PA/18433

ABSTRACT

Synthesis of chalcone and pyrazoline derivatives based on 4-chlorobenzaldehyde and methoxyacetophenone has been carried out and their activity as an antimalarial compound has been checked. This study aimed to synthesize chalcone **A–D** and *N*-phenyl Pyrazoline **A** and **B**. The successfully synthesized chalcone and pyrazoline derivatives were tested for their activity as antimalarial compounds.

Chalcone **A–C** were synthesized by reacting 4-methoxyacetophenone, 2,4-dimethoxyacetophenone, or 3,4-dimethoxyacetophenone with 4-chloro-benzaldehyde in ethanol solvent and KOH 20% (w/v) catalyst with the stirring method at room temperature for 24 hours. Next, chalcone **D** was synthesized by reacting 3-methoxyacetophenone and 4-chloro-benzaldehyde at 15 °C. Finally, *N*-phenyl Pyrazoline **A** and **B** were synthesized by reacting chalcone **A** or **B** with phenylhydrazine in ethanol solvent with NaOH 20% (w/v) as a catalyst. The synthesized products were then characterized using GC-MS, FTIR, ^{1}H-, and ^{13}C-NMR spectrometers and tested for their activity as an antimalarial compound against *Plasmodium falciparum* FCR-3 strain.

Chalcone **A** as a yellow solid was obtained in 57.4% yield with a melting point of 138–140 °C. Chalcone **B** was produced as a pale-yellow solid with a yield of 53.3% and m.p. of 139–141 °C. Chalcones **C** and **D** as yellow solid were yielded in 85.43% and 26.1%, and m.p. of 132–134 and 108–110 °C, respectively. *N*-phenyl Pyrazoline **A** and **B** were obtained through cyclocondensation with yields and m.p. of 98.6% and 69.2% and 145–147 and 158–160 °C, respectively. The results of the antimalarial test against *Plasmodium falciparum* FCR-3 gave IC_{50} values for chalcones **A–D** 5.97; 1.95; 1.85; and 8.09 µM, respectively. Therefore, chalcone **B** and **C** were categorized as active, while chalcone **A** and **D** were weakly active compounds as antimalarial. *N*-phenyl Pyrazoline **A** and **B** have IC_{50} of 60.02 and 34.46 µM and are classified as inactive antimalarial agents.

Keywords: antimalarial, chalcone, methoxy-acetophenone, *N*-phenylpyrazoline, *Plasmodium falciparum* FCR-3.

SINTESIS TURUNAN SENYAWA KALKON DAN PIRAZOLINA BERBASIS 4-KLOROBENZALDEHIDA DAN METOKSIASETOFENON SERTA UJI AKTIVITASNYA SEBAGAI SENYAWA ANTIMALARIA

LAILY SALSABILA
18/425541/PA/18433

INTISARI

Telah dilakukan sintesis turunan kalkon dan pirazolina berbahan dasar 4-klorobenzaldehida dan metoksiasetofenon tersubstitusi serta uji aktivitasnya sebagai senyawa antimalaria. Tujuan dari penelitian ini adalah untuk melakukan sintesis senyawa kalkon **A–D** serta *N*-fenilpirazolina **A** dan **B**. Senyawa turunan kalkon dan pirazolina yang berhasil disintesis kemudian dilakukan uji aktivitasnya sebagai senyawa antimalaria.

Sintesis turunan kalkon **A–C** dilakukan dengan mereaksikan 4-metoksiasetofenon, 2,4-dimetoksiasetofenon, atau 3,4-dimetoksiasetofenon dengan 4-klorobenzaldehida dalam pelarut etanol dan katalis KOH 20% (b/v) dengan metode pengadukan pada suhu ruang selama 24 jam. Kalkon **D** disintesis dengan mereaksikan 3-metoksiasetofenon dan 4-klorobenzaldehida pada suhu 15 °C. Sintesis *N*-fenilpirazolina **A** dan **B** dilakukan dengan mereaksikan kalkon **A** atau **B** dengan fenilhidrazina dalam pelarut etanol dengan katalis NaOH 20% (b/v). Produk hasil sintesis kemudian dikarakterisasi dengan menggunakan spektrometer GC-MS, FTIR, ^{1}H- dan ^{13}C-NMR serta diuji aktivitasnya sebagai senyawa antimalaria terhadap *Plasmodium falciparum* FCR-3.

Dari hasil sintesis tersebut diperoleh padatan kuning kalkon **A** dengan rendemen 57.4% dan titik leleh 138–140 °C. Kalkon **B** menghasilkan padatan berwarna kuning pucat dengan rendemen 53,3% dan titik leleh 139–141 °C. Kalkon **C** dan **D** menghasilkan padatan berwarna kuning dengan rendemen berturut-turut 85,43% dan 26,1% serta titik leleh 132–134 °C dan 108–110 °C. Melalui reaksi siklokondensasi, diperoleh senyawa *N*-fenilpirazolina **A** dan **B** dengan rendemen dan titik leleh berturut-turut 98,6% dan 69,2% serta titik leleh 145–147 dan 158–160 °C. Hasil uji antimalaria terhadap *Plasmodium falciparum* galur FCR-3 memberikan nilai IC_{50} untuk kalkon **A–D** berturut-turut 5,97; 1,95; 1,85; dan 8,09 μM sehingga dikategorikan sebagai senyawa antimalaria yang aktif untuk senyawa kalkon **B** dan **C**, sementara untuk kalkon **A** dan **D** diketaegorikan sebagai senyawa antimalaria yang kurang aktif. *N*-fenilpirazolina **A** dan **B** menghasilkan IC_{50} 60,02 dan 35,36 μM dan dikategorikan sebagai senyawa antimalaria tidak aktif.

Kata kunci: antimalaria, kalkon, metoksi-asetofenon, *N*-fenilpirazolina, *Plasmodium falciparum* FCR-3.