SINTESIS KLORO-PIRAZOLINA TERSUBSTITUSI PADA NITROGEN DAN UJI AKTIVITASNYA SEBAGAI ANTIMALARIA

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INTISARI

Telah dilakukan sintesis turunan pirazolina serta uji aktivitasnya sebagai antimalaria. Penelitian ini bertujuan untuk menemukan turunan senyawa kloropirazolina yang potensial sebagai senyawa aktif antimalaria. Penelitian dilakukan melalui dua tahapan, yaitu: sintesis senyawa turunan N-substituen pirazolina dan uji aktivitasnya sebagai senyawa antimalaria.

Sintesis pirazolina **A**-**D** dilakukan dengan mereaksikan 4-kloro-(3',4'-dimetoksi)-kalkon dan turunan hidrazina, yaitu formil hidrazina, benzoil hidrazina, fenil hidrazina dan klorofenil hidrazina. Reaksi dilakukan dengan metode konvensional dan sonikasi dalam etanol sebagai pelarut dan dengan adanya asam asetat glasial sebagai katalis untuk menghasilkan 1-formil-(3-(4-klorofenil)-5-(3,4-dimetoksi)-4,5-dihidro-2-pirazolina (pirazolina **A**), 1-benzoil-(3-(4-klorofenil)-5-(3,4-dimetoksi)-4,5-dihidro-2-pirazolina (pirazolina **B**), 1-fenil-(3-(4-klorofenil)-5-(3,4-dimetoksi)-4,5-dihidro-2-pirazolina (pirazolina **C**) dan 1-klorofenil-(3-(4-klorofenil)-5-(3,4-dimetoksi)-4,5-dihidro-2-pirazolina (pirazolina **D**). Elusidasi struktur seluruh senyawa hasil sintesis dilakukan menggunakan FT-IR, GC-MS, ^{1}H- dan ^{13}C-NMR. Produk hasil sintesis diuji aktivitasnya sebagai senyawa antimalaria secara *in vitro* terhadap *Plasmodium falciparum* 3D7.

Berdasarkan hasil penelitian diperoleh pirazolina **A** dan **B** berupa padatan putih dengan *yield* berturut-turut 91,27 dan 90,47% dan titik leleh 109-110 dan 101-103 °C, pirazolina **C** berupa padatan putih kekuningan dengan *yield* 75,53% dan titik leleh 143-144 °C, sedangkan pirazolina **D** berupa padatan kuning dengan *yield* 86,68% dan titik leleh 191-193 °C. Uji aktivitas antimalaria terhadap senyawa pirazolina **A**-**D** menghasilkan nilai IC_{50} berturut-turut 8,25; 2,79; 551,25 dan 272,91 µM. Dapat disimpulkan bahwa perbedaan substituen pada Nitrogen pirazolina memberikan aktivitas sebagai antimalaria yang berbeda dimana pirazolina **A** dan **B** dikategorikan senyawa yang aktif sebagai antimalaria. Sebaliknya, pirazolina **C** dan **D** dikategorikan senyawa tidak aktif sebagai antimalaria.

Kata kunci: N-substituen pirazolina, sonokimia, antimalaria, *Plasmodium falciparum* 3D7

SYNTHESIS OF N-SUBSTITUTED CHLORO-PYRAZOLINE AND ITS ACTIVITY ASSAY AS ANTIMALARIAL AGENTS

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ABSTRACT

Synthesis of pyrazoline derivatives and their activity assay as antimalarial have been carried out. The aim of this study is to discover potent chloropyrazoline derivatives as candidates for active antimalarial compounds. This research was carried out through two main steps, i.e., synthesis of N-substituted pyrazoline derivatives, and its activity assay as antimalarial agents.

Synthesis of pyrazoline **A**-**D** was carried out by reacting 4-chloro-(3',4'-dimethoxy)-chalcone with hydrazine derivatives, i.e.formyl hydrazine, benzoyl hydrazine, phenyl hydrazine and chlorophenyl hydrazine. The reactions were performed using conventional and sonication methods in ethanol as a solvent and in the presence of glacial acetic acid as a catalyst to produce 1-formyl-(3-(4-chlorophenyl)-5-(3,4-dimethoxy)-4,5-dihydro-2-pyrazoline (pyrazoline **A**), 1-benzoyl -(3-(4-chlorophenyl)-5-(3,4-dimethoxy)-4,5-dihydro-2-pyrazoline (pyrazoline **B**), 1-phenyl-(3-(4-chlorophenyl)-5-(3,4-dimethoxy)-4,5-dihydro-2-pyrazoline (pyrazoline **C**), and 1-chlorophenyl-(3-(4-chlorophenyl)-5-(3,4-dimethoxy)-4,5-dihydro-2-pyrazoline (pyrazoline **D**). The structure elucidation of all synthesized compounds was confirmed by FT-IR, GC-MS, ^{1}H-and ^{13}-CNMR spectrometers. The synthesized products were tested for its activity as antimalarial compounds *in vitro* assay against *Plasmodium falciparum* 3D7.

The results showed that pyrazoline **A** and **B** were yielded as white solids in 91.27 and 90.47% with m.p 109-110 and 101-103 °C, respectively. Pyrazoline **C** was obtained as a yellowish-white solid in 75.53% yield with m.p 143-144 °C, while pyrazoline **D** was yielded as yellow solid in 86.68% and m.p 191-193 °C. Antimalarial activity test of pyrazoline **A**-**D** gave IC_{50} values of 8.25; 2.79; 551.25 and 272.91 µM, respectively. It can be concluded that the differences in substituents of Nitrogen pyrazoline resulted in different antimalarial activities. Pyrazoline **A** and **B** were categorized as good antimalarial agents. In contrast, pyrazoline **C** and **D** were classified as inactive as antimalarial agents.

Keyword: N-substituted pyrazoline, sonochemical, antimalarial, *Plasmodium falciparum* 3D7