

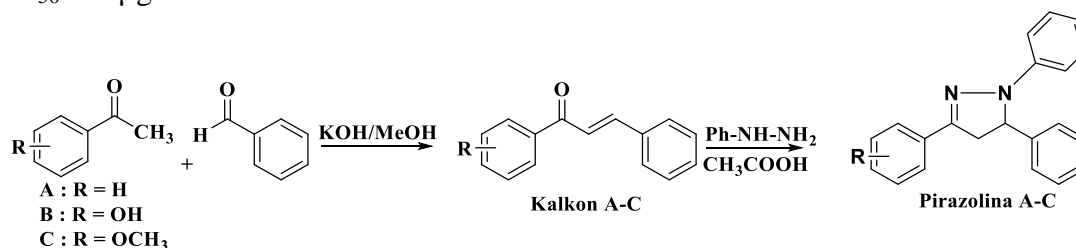
SINTESIS DAN UJI AKTIVITAS ANTIMALARIA SENYAWA TURUNAN KALKON DAN N-FENILPIRAZOLINA DARI BENZALDEHIDA DAN TURUNAN ASETOFENON

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INTISARI

Sintesis turunan *N*-fenilpirazolina berbahan dasar benzaldehida dan turunan asetofenon berupa *n*-asetofenon, 4-hidroksiasetofenon, 4-metoksiasetofenon serta uji aktivitasnya sebagai antimalaria dengan metode polimerisasi heme dan *P. falciparum* telah dilakukan. Penelitian diawali dengan sintesis kalkon dengan mereaksikan turunan asetofenon, benzaldehida, dan KOH dengan metode pengadukan dan sonokimia untuk menghasilkan 1,3-difenil-2-propen-1-on (kalkon **A**), 1-(4-hidroksifenil)-3-fenil-2-propen-1-on (kalkon **B**), dan 1-(4-metoksifenil)-3-fenil-2-propen-1-on (kalkon **C**). Sintesis senyawa turunan *N*-fenilpirazolina dilakukan dengan cara siklokondensasi senyawa kalkon hasil sintesis dengan fenilhidrazin dan penambahan asam asetat glasial menggunakan metode refluks selama 6 jam untuk menghasilkan 1,3-5-trifenil-2-pirazolina (pirazolina **A**), 1-fenil-3-(4-hidroksifenil)-5-fenil-2-pirazolina (pirazolina **B**), dan 1-fenil-3-(4-metoksifenil)-5-fenil-2-pirazolina (pirazolina **C**). Kebenaran struktur senyawa hasil sintesis dielusidasi struktur dengan spektrometer FTIR, GC-MS, ¹H- dan ¹³C-NMR.

Berdasarkan hasil penelitian diperoleh senyawa turunan kalkon berupa padatan kuning (kalkon **A** dan **B**) dan putih (kalkon **C**) dengan persen hasil berturut-turut sebesar 89,40; 80,35; dan 77,30%. Senyawa *N*-fenilpirazolina yang diperoleh berupa padatan kuning kecoklatan (pirazolina **A** dan **B**) dan putih kecoklatan (pirazolina **C**) dengan persen hasil masing-masing sebesar 79,31; 83,87; dan 78,12%. Uji penghambatan polimerisasi heme menghasilkan nilai IC₅₀ kalkon **A-C** lebih rendah dibandingkan klorokuin difosfat sebagai kontrol positif. Senyawa pirazolina **A** dan **B** terbukti aktif pada penghambatan polimerisasi heme dengan nilai IC₅₀ kurang dari 37,5 mM. Senyawa pirazolina **A-C** juga diuji aktivitasnya terhadap *P. falciparum* dan hanya diperoleh nilai IC₅₀ senyawa pirazolina **B** yang tergolong sangat aktif sebagai antimalaria dalam menghambat pertumbuhan *P. falciparum* strain FCR3 dengan nilai IC₅₀ < 5 µg/mL.



Skema 1. Jalur sintesis turunan kalkon dan *N*-fenilpirazolina

Kata kunci: antimalaria, *N*-fenilpirazolina, kalkon.

***SYNTHESIS AND ANTIMALARIA ACTIVITY ASSAY OF CHALCONE AND
N-PHENYLPYRAZOLINE DERIVATIVES FROM BENZALDEHYDE AND
ACETOPHENONE DERIVATIVES***

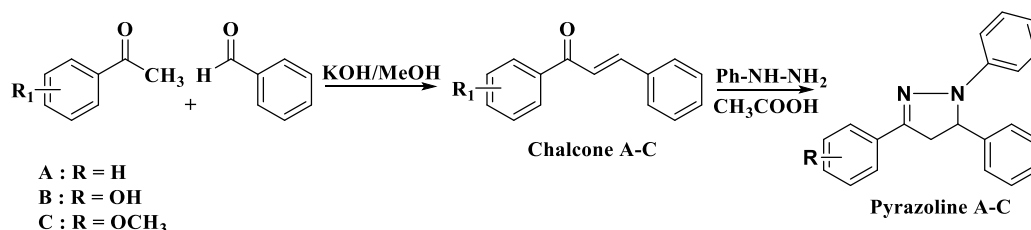
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ABSTRACT

Synthesis *N*-phenylpyrazoline derivatives from benzaldehyde and acetophenone derivatives such as *n*-acetophenone, 4-hydroxyacetophenone, 4-methoxyacetophenone and the activity assay as an antimalarial using heme polymerization method and *P. falciparum* have been carried out. Chalcones was synthesized from benzaldehyde, acetophenone derivatives, and KOH by stirred method and sonochemical method to give 1,3-diphenyl-2-propen-1-one (chalcone **A**), 1-(4-hydroxyphenyl)-3-phenyl-2-propen-1-one (chalcone **B**), and 1-(4-methoxyphenyl)-3-phenyl-2-propen-1-one (chalcone **C**). Synthesis of *N*-phenylpyrazoline derivatives was carried out by cyclocondensation of chalcone with phenylhydrazine and the addition of glacial acetic acid by reflux method for 6 hours to yield 1,3-5-triphenyl-2-pyrazoline (pyrazoline **A**), 1-phenyl-3-(4-hydroxyphenyl)-5-phenyl-2-pyrazoline (pyrazoline **B**), and 1-phenyl-3-(4-methoxyphenyl)-5-phenyl-2-pyrazoline (pyrazoline **C**). The structure elucidations of product were confirmed by FTIR spectrophotometer, GC-MS, ¹H- and ¹³C-NMR spectrometers.

Based on the results, chalcones were obtained as yellow solids (chalcone **A** and **B**) and white (chalcone **C**) in 89.40; 80.35; and 77.30%, respectively. *N*-phenylalpyrazoline derivatives were obtained brownish yellow solids (pyrazoline **A** and **B**) and brownish white (pyrazoline **C**) in 79.31; 83.87; and 78.12%. The heme polymerization assay produced IC₅₀ value of chalcone **A-C** showed lower activity than chloroquine diphosphate as positive control. It was proven that the pirazolina **A** and **B** compounds were active in inhibition of heme polymerization with IC₅₀ value less than 37,5 mM. Pirazolina A-C was also tested for its activity against *P. falciparum* and only obtained IC₅₀ value of pyrazolina **B** is the most active as antimalarial in inhibiting the growth of *P. falciparum* strain FCR3 IC₅₀ < 5 µg/mL.



Scheme 1. Synthetic pathway for chalcone and *N*-phenylpyrazoline derivatives

Keywords: antimalarial, *N*-phenylpyrazoline, chalcone.