SINTESIS DAN UJI AKTIVITAS ANTIKANKER SENYAWA KALKON DAN PIRAZOLINA BERBAHAN DASAR 2-ASETILTIOFENA DAN TURUNAN METOKSI BENZALDEHIDA

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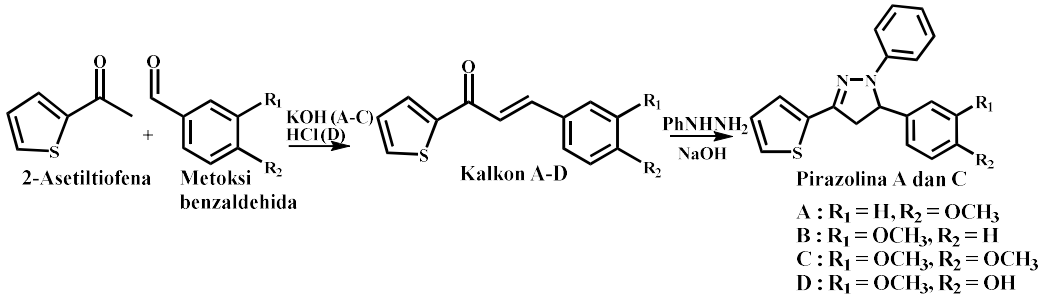
INTISARI

Sintesis dan uji sitotoksisitas senyawa turunan kalkon dan pirazolina yang mengandung cincin tiofena telah berhasil dilakukan. Senyawa kalkon disintesis melalui reaksi kondensasi *Claisen-Schmidt* dari 2-asetiltiofena dan metoksi benzaldehida menghasilkan kalkon **A, B**, **C**, dan **D**. Pirazolina disintesis melalui reaksi siklokondensasi antara senyawa kalkon (**A** dan **C**) dengan fenilhidrazin. Skema sintesis kalkon dan pirazolina disajikan pada Gambar 1.

Kalkon **A**, **B**, dan **C** disintesis dari 2-asetiltiofena dan metoksi benzaldehida menggunakan katalis basa KOH 40% (b/v) melalui pengadukan selama 24 jam pada suhu ruang. Kalkon **D** disintesis menggunakan katalis asam HCl 10% (v/v dalam asam asetat glasial) yang diaduk selama 24 jam pada suhu ruang. Kalkon **A** dan **C** hasil sintesis dilarutkan dengan etanol, ditambahkan katalis basa NaOH dan fenilhidrazin, kemudian dilanjutkan refluks selama 24 jam hingga terbentuk produk akhir senyawa pirazolina. Elusidasi struktur kalkon dan pirazolina dilakukan dengan spektrometer FTIR, GC-MS, ^{1}H- dan ^{13}C-NMR. Uji antikanker kalkon dan pirazolina terhadap beberapa sel kanker dan sel normal dilakukan dengan menggunakan MTT *assay* untuk mengetahui IC_{50}nya.

Hasil penelitian menunjukkan bahwa senyawa kalkon **A**, **B**, **C** dan **D** telah berhasil disintesis dengan *yield* berturut-turut sebesar: 98,63; 83,63; 97,56; dan 50%. Senyawa pirazolina **A** dan **C** juga berhasil disintesis dengan *yield* sebesar 60,37 dan 74,85%. Uji antikanker senyawa kalkon (**A-D**) dan pirazolina (**A** dan **C**) dilakukan secara *in vitro* terhadap sel kanker payudara (T47D dan 4T1), sel kanker leher rahim (HeLa), sel kanker kolon (WiDr) dan sel normal (Vero). Hasil menunjukkan bahwa kalkon **C** memiliki aktivitas antikanker terbaik dengan IC_{50} 0,18 µg/mL terhadap sel WiDr dan selektivitasnya tinggi terhadap sel normal.



Gambar 1. Skema sintesis senyawa kalkon dan pirazolina

Kata kunci: Antikanker, kalkon, tiofena, pirazolina, MTT *assay*.

SYNTHESIS AND ANTICANCER ACTIVITY TESTS OF CHALCONE AND PYRAZOLINE COMPOUNDS FROM 2-ACETYLTHIOPHENE AND METHOXY BENZALDEHYDE DERIVATIVES

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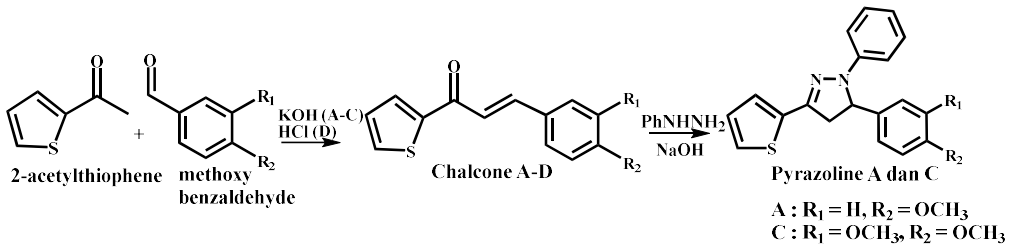
ABSTRACT

Synthesis and cytotoxicity assays of chalcone and pyrazoline compounds containing a thiophene ring have been carried out. Chalcones were synthesized via *Claisen-Schmidt* condensation reaction of 2-acetylthiophene and methoxy benzaldehyde to produce chalcones **A**, **B**, **C**, and **D**. Pyrazolines were synthesized by cyclocondensation reaction of chalcones (**A** and **C**) with phenylhydrazine. Synthethic pathway for chalcone and pyrazoline is presented in Figure 1.

Chalcone **A**, **B**, and **C** were obtained from the reaction of 2-acetylthiophene and methoxy benzaldehyde using a 40% (w/v) KOH base catalyst under stirring for 24 h at room temperature. Chalcone **D** was produced using 10% HCl as an acid catalyst under stirring for 24 h at room temperature. The synthesized chalcones **A** and **C** were dissolved in ethanol and then reacted with phenylhydrazine in the presence of NaOH as a base catalyst under reflux for 24 h to give pyrazolines. Structures of chalcones and pyrazolines were confirmed by FTIR, GC-MS, ^{1}H, and ^{13}-CNMR spectrometers. Cytotoxicity test of chalcones and pyrazolines on several cancer cells and normal cells was done using the MTT assay to determine the IC_{50}.

The results showed that chalcones **A, B, C**, and **D** had been successfully synthesized with 98.63, 83.63, 97.56, and 50% yield, respectively. Pyrazolines **A** and **C** were also successfully synthesized in 60.37 and 74.85% yields, respectively. *In vitro* anticancer tests of chalcones (**A-D)** and pyrazolines (**A** and **C**) were evaluated against breast cancer cell lines (T47D and 4T1), cervical cancer cell line (HeLa), colorectal cancer cell line (WiDr), and normal cell line (Vero) via MTT assay. It showed that chalcone **C** had the best anticancer activity with an IC_{50} of 0.18 µg/mL against WiDr cells and high selectivity against normal cells.



Scheme 1. Synthetic pathway for chalcone and pyrazoline

Keywords: Anticancer, chalcone, pyrazoline, thiophene, MTT assay.