

SYNTHESIS OF 4-PYRIDINE-BASED CHALCONE AND N-PHENYLPYRAZOLINE DERIVATIVES, ALONG WITH ITS ACTIVITY ASSAY AS ANTICANCER AGENTS

MUHAMMAD ARIF ARKAN

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ABSTRACT

The synthesis of pyridine-based chalcone and phenylpyrazoline derivatives and its activity also selectivity assay as anticancer agent against cervical, breast, and colorectal cancer, has been conducted. This research aimed to synthesize chalcone compounds from 4-acetylpyridine and benzaldehyde derivatives using claisen-schmidt condensation reaction which produced chalcone **A** ((E)-1-(pyridin-4-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one) and **B** ((E)-3-(benzo[d][1,3]dioxol-5-yl)-1-(pyridin-4-yl)prop-2-en-1-one). Subsequently, cyclocondensation reaction of these chalcones with phenylhydrazine under alkaline condition yielded pyrazoline **A** (4-(1-phenyl-5-(3,4,5-trimethoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl)pyridine) and **B** (4-(5-(benzo[d][1,3]dioxol-5-yl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl)pyridine). The synthesized product were then characterized by GC-MS, ATR-IR spectroscopy, ¹H-NMR for pyrazolines. The anticancer activity of Chalcone **A** and **B** also Pyrazoline **A** and **B** were assessed using MTT assay against HeLa, MCF-7, T47D, and WiDr cell lines, together with Vero cells used to evaluate the selectivity.

The synthesis of Chalcone **A** and Chalcone **B** yielded a white product with 82% and 89% efficiencies, respectively. In contrast, the synthesis of Pyrazoline **A** and Pyrazoline **B** resulted in white-green and yellow-red solids with 61% and 50% yields, respectively. Results from anticancer activity assays demonstrated that Chalcone **B** exhibited the lowest IC₅₀ values of 27 µg/mL against HeLa and T47D cell lines, and 45.72 µg/mL against the MCF-7 cell line, compared to Chalcone **A**. However, Chalcone **A** showed greater potency against the WiDr cell line, with an IC₅₀ of 0.15 µg/mL, compared to 0.64 µg/mL for Chalcone **B**, both exhibiting high selectivity. Pyrazolines **A** and **B** displayed significant cytotoxicity against HeLa and WiDr cell lines, with IC₅₀ values of approximately 13 µg/mL for HeLa. Notably, Pyrazoline **A** and Pyrazoline **B** demonstrated IC₅₀ values of 0.02 µg/mL and 0.45 µg/mL, respectively, against WiDr, both with high selectivity indices. The low IC₅₀ values and high selectivity indices suggest that Chalcone **A** and Pyrazoline **A** possess promising potential as treatments for colorectal cancer.

Keyword: 4-acetylpyridine, anticancer, chalcone, pyrazoline.

SINTESIS KALKON DAN N-PIRAZOLINA BERBASIS 4-PIRIDIN, SERTA UJI AKTIVITAS SEBAGAI AGEN ANTIKANKER

MUHAMMAD ARIF ARKAN

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INTISARI

Sintesis senyawa turunan kalkon dan fenilpirazolina berbasis piridin, beserta uji aktivitas dan selektivitasnya sebagai agen antikanker terhadap kanker serviks, payudara, dan kolorektal telah dilakukan. Tujuan penelitian ini adalah untuk mensintesis senyawa kalkon dari 4-asetilpiridin dan turunan benzaldehida melalui reaksi kondensasi Claisen-Schmidt yang menghasilkan Kalkon **A** ((E)-1-(pyridin-4-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one) dan **B** ((E)-3-(benzo[d][1,3]dioxol-5-yl)-1-(pyridin-4-yl)prop-2-en-1-one). Selanjutnya, reaksi siklokondensasi dari kalkon tersebut dengan fenilhidrazin di bawah kondisi basa menghasilkan Pirazolina **A** (4-(1-phenyl-5-(3,4,5-trimethoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl)pyridine) dan **B** (4-(5-(benzo[d][1,3]dioxol-5-yl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl)pyridine). Produk yang disintesis kemudian dikarakterisasi menggunakan spektroskopi GC-MS dan ATR-IR, juga ¹H-NMR untuk pirazolina. Aktivitas antikanker dari Kalkon **A** dan **B** serta Pirazolin **A** dan **B** diuji menggunakan uji MTT terhadap lini sel HeLa, MCF-7, T47D, dan WiDr, dengan lini sel Vero digunakan untuk mengevaluasi selektivitasnya.

Sintesis Kalkon **A** dan Kalkon **B** menghasilkan produk berwarna putih dengan efisiensi masing-masing sebesar 82% dan 89%. Sebaliknya, sintesis Pirazolin **A** dan Pirazolin **B** menghasilkan padatan berwarna putih-hijau dan kuning-merah dengan hasil masing-masing sebesar 61% dan 50%. Hasil uji aktivitas antikanker menunjukkan bahwa Kalkon **B** memiliki nilai IC₅₀ terendah yaitu 27 µg/mL terhadap lini sel HeLa dan T47D, serta 45,72 µg/mL terhadap lini sel MCF-7, dibandingkan dengan Kalkon **A**. Namun, Kalkon **A** menunjukkan potensi yang lebih besar terhadap lini sel WiDr, dengan IC₅₀ sebesar 0,15 µg/mL, dibandingkan dengan 0,64 µg/mL untuk Kalkon **B**, keduanya menunjukkan selektivitas yang tinggi. Pirazolin **A** dan **B** menunjukkan sitotoksitas yang signifikan terhadap lini sel HeLa dan WiDr, dengan nilai IC₅₀ sekitar 13 µg/mL untuk HeLa. Secara khusus, Pirazolin **A** dan Pirazolin **B** menunjukkan nilai IC₅₀ sebesar 0,02 µg/mL dan 0,45 µg/mL, masing-masing, terhadap WiDr, dengan indeks selektivitas yang tinggi. Nilai IC₅₀ yang rendah dan indeks selektivitas yang tinggi menunjukkan bahwa Kalkon **A** dan Pirazolin **A** memiliki potensi yang menjanjikan sebagai pengobatan untuk kanker kolorektal.

Keywords: 4-asetilpiridin, antikanker, kalkon, pirazolin.