SYNTHESIS AND CYTOTOXICITY ASSAY OF CHALCONE AND PYRAZOLINE COMPOUNDS FROM 4-CHLOROACETOPHENONE AND 4-(DIMETHYLAMINO)BENZALDEHYDE

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ABSTRACT

Synthesis of chalcone derivatives has been carried out starting from 4-chloroacetophenone and 4-(dimethylamino)benzaldehyde (DMAB) as the starting material. Then, treatment of the chalcone derivatives followed with further derivatization allowed the formation of several pyrazoline derivative. Cytotoxicity assay of the synthesized compounds has been conducted against various cancer cells.

The synthesis was started by reacting 4-chloroacetophenone and DMAB in the presence of NaOH to give chalcone derivative (1-(4-chlorophenyl)-3-(4-(dimethylamino)phenyl)prop-2-en-1-one (**chalcone**)) via Claisen-Schmidt condentation. To synthesize pyrazoline derivative, hydrazine monomonohydrate was added dropwise into solution of chalcone in ethanol. Further addition of glacial acetic acid or benzoyl chloride into reaction mixture would produce 1-(3-(4-chlorophenyl)-5-(4-(dimethylamino)phenyl)-4,5-dihydro-1H-pyrazol-1-yl) ethan-one (**Pyrazoline 1**) or 3-(4-chlorophenyl)-5-(4-(dimethylamino)phenyl)-4,5-dihydro-1H-pyrazol-1-yl)(phenyl)methanone **(Pyrazoline 2),** respectively. In addition, **Pyrazoline 3** (4-(3-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-5-yl)-N,N-dimethylaniline) was obtained by adding hydrazine monomonohydrate to chalcone in ethanol. The mixture was irradiated in ultrasonic bath for 2 hours.All the products were then analyzed by FTIR, GC-MS, ^{1}H- and ^{13}C-NMR spectrometer. Anticancer assay on MCF-7, T47D and Vero cell done by MTT methods.

The **chalcone** was obtained as bright yellow solid and in 64.32% yield. **Pyrazoline 1** and **Pyrazoline 3** were produced as bright yellow solid in 25.0 and 86.66% yield, repectively, while **Pyrazoline 2** was yielded as broken white solid in 45.9%. The compounds with high purity, **chalcone** and **Pyrazoline 3**, were tested for their biological activity as anticancer. The IC_{50} values of **chalcone** towards MCF-7, T47D and normal Vero cell were 2086.3, 0.59 and 627.87 μg/mL, respectively. The IC_{50} values of **Pyrazoline 3** was tested against MCF-7 and T47D were 23.69 and 81.45 μg/mL.

Keywords: chalcone, pyrazoline, anticancer, cytotoxicity, MTT method.

SINTESIS DAN UJI SITOTOKSISITAS SENYAWA KALKON DAN PIRAZOLINA DARI KLOROASETOFENON DAN 4-(DIMETILAMINO)BENZALDEHIDA

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INTISARI

Sintesis turunan kalkon dilakukan dengan menggunakan 4-kloroasetofenon dan 4-(dimetilamino)benzaldehida (DMAB) sebagai bahan dasar. Reaksi siklisasi terhadap turunan kalkon diikuti dengan derivatisasi menghasilkan beberapa senyawa turunan pirazolina. Uji sitotoksisitas senyawa kalkon dan pirazolina dilakukan terhadap beberapa sel kanker.

Sintesis diawali dengan mereaksikan 4-kloroasetofenon dan DMAB dalam suasana basa NaOH menghasilkan senyawa turunan kalkon 3-(4-dimetil-amino)fenil)-1-(4-klorofenil)prop-2-enone(**kalkon**) melalui reaksi kondensasi Claisen-Schmidt. Pada sintesis turunan pirazolina, hidrazin monohidrat diteteskan perlahan ke dalam larutan **kalkon** dalam etanol. Penambahan selanjutnya dengan asam asetat glasial atau benzoil klorida menghasilkan berturut-turut (5-(4-(dimetilamino)fenil)-1-(3-(4-klorofenil)-4,5-dihidro-1H-pirazolina)etanon (**pirazolina 1**) atau (5-(4-(dimetilamino)fenil)-(3-(4-klorofenil) -4,5-dihidro-1H-pirazolina)(fenil)metanon (**pirazolina 2**). **Pirazolina 3**, (3-(4-klorofenil)-4,5-dihidro-1H-pirazolina)-N,N-dimetilanilin dihasilkan melalui penambahan hidrazin monohidrat ke dalam larutan kalkon dalam etanol. Campuran diiradiasi menggunakan penangas ultrasonik selama 2 jam. Semua produk dianalisis dengan FTIR, GC-MS, ^{1}H- and ^{13}C-NMR spektrometer. Uji sitotoksisitas dilakukan terhadap sel kanker MCF-7, T47D dan sel normal Vero cell dengan metode MTT.

Senyawa kalkon yang diperoleh berupa padatan kuning **muda/terang** dengan rendemen 64,3%. **Pirazolina 1** dan **Pirazolina 3** didapatkan dengan warna yang serupa berupa kuning **terang/muda** dengan rendemen berturut-turut 25.0 dan 86.7%, sedangkan **Pirazolina 2** dihasilkan sebagai padatan putih tulang dengan rendemen 45.9%. Senyawa dengan kemurnian tinggi yaitu **kalkon** dan **pirazolina 3** diuji aktivitas biologinya sebagai senyawa antikanker. Nilai IC_{50} untuk **kalkon** terhadap sel kanker MCF-7, T47D dan normal sel Vero adalah 2086,3; 0,59 dan 627,87 μg/mL. Nilai IC_{50} **Pirazolina 3** terhadap sel MCF-7 dan T47D masing-masing sebesar 23.69 dan 81.45 μg/mL.

Kata Kunci : kalkon, pirazolina, antikanker, sitotoksisitas, Metode MTT