SINTESIS DAN UJI SITOTOKSISITAS TURUNAN PIRAZOLINA BERBAHAN DASAR VANILIN DAN 4-KLOROASETOFENON

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INTISARI

Sintesis turunan pirazolina berbahan dasar vanilin dan 4-kloroasetofenon telah dilakukan. Senyawa hasil sintesis diuji sitotoksisitasnya sebagai agen antikanker secara *in vitro* melalui penentuan nilai IC_{50} terhadap beberapa sel kanker.

Sintesis dilakukan dengan mereaksikan vanilin dalam metanol dan 4-kloroasetofenon dengan adanya katalis NaOH 60% dan digunakan metode pengadukan selama 20 jam sehingga dihasilkan 1-(4-klorofenil)-3-(4-hidroksi-3-metoksifenil)-2-propen-1-on (**kalkon**). Kalkon direaksikan dengan hidrazin monohidrat dan asam asetat glasial kemudian direfluks selama 12 jam sehingga dihasilkan 1-asetil-3-(4-klorofenil)-5-(4-hidroksi-3-metoksifenil)-2-pirazolina (pirazolina **1**). Senyawa 1-fenil-3-(4-klorofenil)-5-(4-hidroksi-3-metoksifenil)-2-pirazolina (pirazolina **2**) diperoleh dengan mereaksikan kalkon dan fenilhidrazin dalam asam asetat glasial kemudian direfluks selama 4 jam. Produk yang terbentuk diukur titik leburnya dan diidentifikasi strukturnya dengan menggunakan spektrometer FT-IR, GC-MS, ^{1}H- serta ^{13}C-NMR. Uji sitotoksisitas dilakukan terhadap sel T47D, HeLa dan WiDr dengan metode MTT.

Kalkon yang dihasilkan berupa padatan berwarna kuning terang dengan titik lebur 84,0-85,6 °C dan rendemen 80,55%. Pirazolina **1** yang diperoleh berupa padatan berwarna coklat dengan titik lebur 104,3-107,8 °C dan rendemen 20,33% sedangkan pirazolina **2** berupa padatan berwarna putih tulang dengan titik lebur 157,9-159,8 °C dan rendemen 73,68%. Pirazolina **2** dengan kemurnian tinggi diuji sitotoksisitasnya. Nilai IC_{50} terhadap sel T47D, HeLa dan WiDr berturut-turut adalah 10,21, 14,45 dan 7,89 μg mL^{-1}. Berdasarkan nilai tersebut dapat disimpulkan bahwa pirazolina **2** toksik terhadap sel kanker dan berpotensi sebagai agen antikanker baru.

Kata kunci: vanilin, kalkon, pirazolina, uji sitotoksisitas, sel kanker.

SYNTHESIS AND CYTOTOCICITY ASSAY OF PYRAZOLINE DERIVATIVES FROM VANILLIN AND 4-CHLOROACETOPHENONE

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ABSTRACT

Synthesis of pyrazolines from vanillin and 4-chloroacetophenone had been conducted. The synthesized compounds were tested by in vitro cytotoxicity assay as anticancer agent by determining its IC_{50} values against several cancer cell lines.

Synthesis was performed by reacting vanillin in methanol and 4-chloroacetophenone with the presence of NaOH 60% as catalyst and stirred for 20 h to produce 1-(4-chlorophenyl)-3-(4-hydroxy-3-methoxyphenyl)-2-propen-1-one (**chalcone**). Chalcone was reacted with hydrazine monohydrate and glacial acetic acid then refluxed for 12 h to produce 1-acetyl-3-(4-chlorophenyl)-5-(4-hydroxy-3-methoxyphenyl)-2-pyrazoline (pyrazoline **1**). Compound of 1-phenyl-3-(4-chlorophenyl)-5-(4-hydroxy-3-methoxyphenyl)-2-pyrazoline (pyrazoline **2**) was obtained by reacting chalcone with phenylhydrazine in glacial acetic acid then refluxed for 4 h. All syntheses were controlled by TLC. The melting points of the obtained products were measured and its structures were identified with spectrometer FT-IR, GC-MS, ^{1}H- and ^{13}C-NMR. The cytotoxicity assay against T47D, HeLa and WiDr cancer cells was performed by MTT method.

The chalcone was obtained as bright yellow solid with melting point 84.0-85.6 °C in 80.55% yield. Pyrazoline **1** was produced as brown solid with melting point 104.3-107.8 °C in 20.33% yield. Pyrazoline **2** was obtained as broken white solid with melting point 157.9-159.8 °C in 73.68% yield. Pyrazoline **2** with the highest purity was tested for its cytotoxicity. The IC_{50} values against T47D, HeLa and WiDr cells were 10.21, 14.45 and 7.89 μg mL^{-1} respectively. It was concluded that pyrazoline **2** showed toxicity against cancer cell lines and potential to be a new anticancer agent.

Keywords: vanillin, chalcone, pyrazoline, cytotoxicity assay, cancer cell.