

**SINTESIS TURUNAN N-FENIL PIRAZOLINA DARI
VERATRALDEHIDA DAN UJI SITOTOKSISITASNYA
TERHADAP BEBERAPA SEL KANKER**

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INTISARI

Sintesis turunan N-fenil pirazolina dari veratraldehida dan variasi asetofenon serta uji sitotoksitasnya terhadap beberapa sel kanker telah dilakukan. Sintesis N-fenil pirazolina dilakukan melalui dua tahap yaitu kondensasi aldol dan siklokondensasi sedangkan uji sitotoksitas senyawa pirazolina terhadap beberapa sel kanker dilakukan menggunakan metode 3-(4,5-dimetiltiazol-2-il)-2,5-difenil tetrazolium bromida (MTT).

Kondensasi *Claisen-Schmidt* dilakukan dengan cara mereaksikan campuran antara veratraldehida dengan asetofenon, 2-hidroksiasetofenon, 4-hidroksiasetofenon dalam etanol dan adanya katalis NaOH 40% menggunakan metode sonokimia untuk menghasilkan 1-fenil-3-(3',4'-dimetoksifenil)-2-propen-1-on (kalkon **A**), 1-(2'-hidroksifenil)-3-(3',4'-dimetoksifenil)-2-propen-1-on (kalkon **B**) dan 1-(4'-hidroksifenil)-3-(3',4'-dimetoksifenil)-2-propen-1-on (kalkon **C**). Siklisasi kalkon dengan fenilhidrazin dilakukan dengan metode konvensional dan sonokimia untuk menghasilkan 1-fenil-3-(fenil)-5-(3',4'-dimetoksifenil)-2-pirazolina (pirazolina **A**), 1-fenil-3-(2'-hidroksifenil)-5-(3',4'-dimetoksifenil)-2-pirazolina (pirazolina **B**), 1-fenil-3-(4'-hidroksifenil)-5-(3',4'-dimetoksifenil)-2-pirazolina (pirazolina **C**). Semua produk dielusidasi menggunakan FT-IR, GC-MS, ¹H- dan ¹³C-NMR. Uji sitotoksitas senyawa pirazolina terhadap sel kanker (HeLa, MCF-7, T47D, WiDr) and sel normal (Vero) dilakukan menggunakan metode MTT.

Hasil menunjukkan bahwa kalkon **A**, **B**, dan **C** telah berhasil disintesis dengan metode sonokimia dengan rendemen sebesar 81, 67, dan 79%. Siklisasi kalkon dengan metode konvensional menghasilkan pirazolina **A**, **B**, dan **C** dengan rendemen sebesar 75, 63, dan 74%. Metode sonokimia gagal menghasilkan pirazolina **A** tetapi berhasil menghasilkan pirazolina **B** and **C** dengan rendemen sebesar 20 dan 58%. Uji sitotoksitas pirazolina menunjukkan bahwa pirazolina **C** memiliki sitotoksitas tinggi terhadap sel kanker HeLa, MCF-7, T47D dan WiDr namun toksik terhadap sel Vero.

Kata kunci : N-fenil pirazolina, antikanker, MTT, kalkon.

SYNTHESIS OF N-PHENYL PYRAZOLINE DERIVATIVES FROM VERATRALDEHYDE AND ITS CYTOTOXICITY TOWARDS CANCER CELLS

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ABSTRACT

Synthesis of N-phenyl pyrazoline derivatives from veratraldehyde and various acetophenone and its cytotoxicity test towards cancer cells have been done. The synthesis of N-phenyl pyrazoline was carried out in two-step reactions, i.e., aldol condensation, and cyclocondensation while the cytotoxicity test of pyrazoline against several cancer cell lines was conducted by 3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay.

The Claisen-Schmidt condensation was performed by reacting the mixture of veratraldehyde with acetophenone, 2-hydroxyacetophenone, 4-hydroxyacetophenone in ethanol in the presence of NaOH 40% as a catalyst using sonochemistry method to give 1-phenyl-3-(3',4'-dimethoxyphenyl)-2-propen-1-one (chalcone **A**), 1-(2'-hydroxyphenyl)-3-(3',4'-dimethoxyphenyl)-2-propen-1-one (chalcone **B**) dan 1-(4'-hydroxyphenyl)-3-(3',4'-dimethoxyphenyl)-2-propen-1-one (chalcone **C**). The cyclization of chalcone with phenylhydrazine was carried out with conventional and sonochemistry methods to yield 1-phenyl-3-(phenyl)-5-(3',4'-dimethoxyphenyl)-2-pyrazoline (pyrazoline **A**), 1-phenyl-3-(2'-hydroxyphenyl)-5-(3',4'-dimethoxyphenyl)-2-pyrazoline (pyrazoline **B**), 1-phenyl-3-(4'-hydroxyphenyl)-5-(3',4'-dimethoxyphenyl)-2-pyrazoline (pyrazoline **C**). All of the products were elucidated using FT-IR, GC-MS, ¹H- dan ¹³C-NMR spectrometers. Finally, the cytotoxicity test towards cancer cells (HeLa, MCF-7, T47D, WiDr) and normal cell (Vero) were performed using MTT assay.

The result showed that chalcone **A**, **B**, and **C** had been successfully synthesized by sonochemistry method in 81, 67, and 79% yields. Cyclization of chalcone by conventional methods yielded pyrazoline **A**, **B**, and **C** in 75, 63, and 74%, respectively. Unfortunately, the sonochemistry method failed to give pyrazoline **A**, but pyrazoline **B** and **C** produced in 20 and 58% yield. Cytotoxicity test of pyrazoline showed that pyrazoline **C** has high cytotoxicity towards cancer cells HeLa, MCF-7, T47D, and WiDr but toxic towards Vero cell.

Keywords: N-phenylpyrazoline, anticancer, MTT assay, chalcone.