

**Title :** Evaluation of Cytotoxicity of Synthetic Heterocyclic Compounds Against Lung Cancer Cell Line

**Author(s) :** 1. Woranittha Laiad

**Student ID :** 650510100

**Major :** Biochemistry and Biochemical Innovation

**Advisor(s) :** 1. Associate Professor Dr. Panchika Prangkio

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## ABSTRACT

Lung cancer is the most diagnosed cancer and the leading cause of death worldwide. Despite advances, current therapies are limited by resistance, toxicity, and poor selectivity. Therefore, the development of synthetic compounds with high efficacy and cancer cell specificity is essential. Benzopyrano[4,3-c]pyrazolines and their derivatives have been reported to exhibit anti-lung-cancer activity. This study investigated the anticancer activity of four synthetic heterocyclic compounds (TLWP01, TLWP07, TLWP08, and TLWP09) against lung cancer cells using the MTT assay. These compounds differ in methoxy substitution positions on the benzopyran ring. TLWP01 is the parent compound lacking substituents, whereas TLWP07, TLWP08, and TLWP09 are methoxy-substituted derivatives containing a methoxy (-OCH<sub>3</sub>) group that may affect interactions with biological targets. Half-maximal inhibitory concentration (IC<sub>50</sub>) values were determined. Gefitinib was used as a reference drug and showed a mean IC<sub>50</sub> value of 6.661 ± 1.477 μM. In A549 lung cancer cells, TLWP08 exhibited the highest cytotoxic activity (IC<sub>50</sub> = 8.273 ± 0.784 μM), followed by TLWP01 (8.784 ± 2.558 μM) and TLWP07 (11.792 ± 2.458 μM), while TLWP09 showed no inhibitory effect within the tested concentration range. Selectivity was assessed in normal HEK293T cells, where IC<sub>50</sub> values were not determined. Overall, %cell viability decreased with increasing compound concentration but remained higher than the control due to cell detachment. Notably, TLWP08 showed higher cytotoxicity in A549 cells than in HEK293T cells, indicating favorable selectivity. Benzopyrano[4,3-c]pyrazolines derivatives, particularly TLWP08, therefore demonstrate potential as lead compounds for anti-lung-cancer drug development. Further studies are required to confirm their mechanisms and safety.

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