

Title : Anticancer Activity of Chalcones and Its Derivatives in NCI-H460 Lung Cancer Cells

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## ABSTRACT

Lung cancer is a leading cause of mortality worldwide with major risk factors including smoking, exposure to carcinogens, and air pollution. Current statistics indicate a continuous global rise in lung cancer incidence, particularly in Thailand. Phytochemicals are widely utilized as anticancer agents and anticancer development. In northern Thailand, *Syzygium nervosum* A. Cunn. ex DC. (locally known as Makiang) is a fruit plant contain bioactive properties including the ability to inhibit cancer cell proliferation in *in vitro* models. The primary chemical compound, 2',4'-dihydroxy-6'-methoxy-3',5'-dimethylchalcone (DMC), was isolated from the seeds of *S. nervosum* and exhibits various bioactive properties, including antioxidant, anti-inflammatory, and anticancer activities. Chemical structure modifications of parental compounds, such as semi-synthetic chalcone derivatives, have the potential to enhance their pharmacological activities, including anti-cancer properties. This study aims to investigate the anti-lung cancer properties of semi-synthetic chalcone derivatives from *S. nervosum*, specifically 7-*O*-acylated-4-hydroxycoumarin (C4-C12). These derivatives were investigated for antiproliferative activities in non-small cell lung cancer lines (NCI-H460) using the MTT assay. Compound **C4** and **C10** showed potential anti-lung cancer proliferative activities with  $IC_{50}$  of  $11.87 \pm 0.58$ , and  $9.983 \pm 0.57$   $\mu$ M in NCI-H460, respectively. The biological activities of 7-*O*-acylated-4-hydroxycoumarin were investigated by analyzing the live and dead cell populations, as well as apoptosis-induced cell death, using a confocal microscope with acridine orange (AO) and propidium iodide (PI) staining. Compound **C4** and **C10** increased dead cell populations in NCI-H460 when compared to untreated and 1% DMSO groups. Therefore, 7-*O*-acylated-4-hydroxycoumarin derivatives demonstrated potential anti-lung cancer activity in NCI-H460 cells. The findings revealed that 7-*O*-acylated-4-hydroxycoumarin exhibited significant anti-lung cancer activity, highlighting its potential as a promising candidate for anti-lung cancer drug development. Our data provides valuable insights and it will be further utilized to explore the cell-death mechanisms underlying its anti-lung cancer activities in both *in vitro* and *in vivo* models.

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