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Umbelliprenin is cytotoxic against QU-DB large cell lung cancer cell line but anti-proliferative against A549 adenocarcinoma cells

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Abstract

Background: Umbelliprenin is a natural compound, belonging to the class of sesquiterpene coumarins. Recently, umbelliprenin has attracted the researchers' attention for its antitumor activities against skin tumors. Its effect on lung cancer is largely unknown. The aim of our study was to investigate the effects of this natural compound, which is expected to have low adverse effects, on lung cancer.

Methods: The QU-DB large cell and A549 adenocarcinoma lung cancer cell lines were treated with umbelliprenin. IC_{50} values were estimated using methyl thiazolely diphenyl-tetrazolium bromide (MTT) assay, in which a decrease in MTT reduction can occur as a result of cell death or cell proliferation inhibition. To quantify the rate of cell death at IC_{50} values, flow cytometry using Annexin V-FITC (for apoptotic cells), and propidium iodide (for necrotic cells) dyes were employed.

Results: Data from three independent MTT experiments in triplicate revealed that IC_{50} values for QU-DB and A549 were 47 ± 5.3 μM and 52 ± 1.97 μM, respectively. Annexin V/PI staining demonstrated that umbelliprenin treatment at IC_{50} induced 50% cell death in QU-DB cells, but produced no significant death in A549 cells until increasing the umbelliprenin concentration to IC_{80}. The pattern of cell death was predominantly apoptosis in both cell lines. When peripheral blood mononuclear cells were treated with 50 μM and less concentrations of umbelliprenin, no suppressive effect was observed.

Conclusions: We found cytotoxic/anti-proliferative effects of umbelliprenin against two different types of lung cancer cell lines.

Keywords: Annexin, IC_{50}, Lung cancer, MTT assay, Propidium Iodide, Umbelliprenin

Background

Lung cancer is one of the most common causes of cancer related deaths in most countries [1]. In Iran, lung cancer is the third most frequent cancer in both men and women [2]. The current 5 year survival of lung cancer is about 10–15% mostly being attributed to late diagnosis and inefficient therapy [3,4]. The limited success and significant side effects of lung cancer treatment with classic chemotherapeutic agents has led researchers to find more efficient drugs with fewer side effects [5,6].

Umbelliprenin is synthesized by various *Ferula* plant species such as *Citrus Limon* [7]. It is a prenylated compound that belongs to the class of sesquiterpene coumarins, and possesses a similar structure to auraptene, a compound whose antitumor activities have largely been investigated [8]. Recently, umbelliprenin has attracted the researchers' attention for its antitumor activities. It has been shown that the cell susceptibility to umbelliprenin decreased in the order M4Beu (metastatic pigmented malignant melanoma) > A549 (non-small cell lung carcinoma) ≈ PC3 (androgen resistant prostate carcinoma) > PA1 (ovary teratocarcinoma) > human primary fibroblasts [9]. The anti-tumor effect of umbelliprenin has also been demonstrated in vivo in a mouse skin tumor model in which oral administration of

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