

## Regulation of Apoptosis in Human Lung Cancer NCI-H226 Cells through Caspase - Dependent Mechanism by Benjakul Extract

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**Abstract :** Background: Benjakul, a Thai traditional herbal formulation, comprises of five plants: Piper chaba, Piper sarmentosum, Piper interruptum, Plumbago indica, and Zingiber officinale. It has been widely used to treat cancer patients in the context of folk medicine in Thailand. This study aimed to investigate the cytotoxic effect of the ethanol extract of Benjakul against three non-small cell lung cancer (NSCLC) cell lines (NCI-H226, A549, COR-L23), small cell lung cancer (SCLC) cell line NCI-H1688 and normal lung fibroblast cell line MRC-5. The study further examined the molecular mechanisms underlying its cytotoxicity via induction of apoptosis in NCI-H226 cells. Methods: The cytotoxic effect of Benjakul was determined by SRB assay. The effect of Benjakul on cell cycle distribution was assessed by flow cytometric analysis. The apoptotic effects of Benjakul were determined by sub-G1 quantitation and Annexin V-FITC/PI flow cytometric analyses as well as by changes in caspase-3 activity. Results: Benjakul exerted potent cytotoxicity on NCI-H226 and A549 cells but lower cytotoxicity on COR-L23 and NCI-H1688 cells without any cytotoxic effect on normal cells. Molecular studies showed that Benjakul extract induced G2/M phase arrest in human NCI-H226 cells in a dose-dependent manner. The highest concentration of Benjakul (150 µg/ml) led to the highest increase in the G2/M population at 12 h, followed by the highest increase in the sub-G1 population (apoptotic cells) at 60 h. Benjakul extract also induced early apoptosis (AnnexinV +/PI-) in NCI-H226 cells in a dose- and time- dependent manner. Moreover, treatment with 150 µg/ml Benjakul extract for 36 h markedly increased caspase-3 activity by 3.5-fold, and pretreatment with the general caspase inhibitor z-VAD-fmk completely abolished such activity. Conclusions: This study reveals for the first time the regulation of apoptosis in human lung cancer NCI-H226 cells through caspase-dependent mechanism by Benjakul extract.

**Keywords :** apoptosis, Benjakul, caspase activation, cytotoxicity

**Conference Title :** ICBPS 2015 : International Conference on Biomedical and Pharmaceutical Sciences

**Conference Location :** Tokyo, Japan

**Conference Dates :** May 28-29, 2015