Extracts from Lotus Leaf (*Nelumbo nucifera*) induced human pancreatic cancer cell apoptosis

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Pancreatic cancer is one of the most malignant tumors with poor prognosis and lack of response to conventional therapy. Here, we attempted to investigate the anti-cancer effect of methanolic extract from lotus leaf (*Nelumbo nucifera*), an aquatic perennial plant and cultivated in eastern Asia and India and widely used in the traditional Chinese herb medicine in human pancreatic cancer cells. Lotus leaf (*Nelumbo nucifera*) methanolic extract (NNE) induced cell death and apoptosis (increase in sub-G1 DNA fragmentation) in human pancreas epithelioid carcinoma cell lines (PANC-1 cells) after exposure for 24 h with a dose-dependent manner. NNE also displayed several features of mitochondrial-dependent apoptotic signals, including: mitogen-activated protein kinases (MAPKs) activation, loss of mitochondrial membrane potential, increase in cytosolic cytochrome *c* release, and activation of PARP and caspase cascades in NNE-exposed PNAC-1 cells. Moreover, we also found that treatment of PANC-1 cells with NNE resulted in triggering endoplasmic reticulum (ER) stress as indicated by the enhancement in ER stress-related molecules induction (including: glucose-regulated protein (GRP)78, GRP94, and CHOP), caspase 12 and calpain activation. This study demonstrates that lotus leaf (*Nelumbo nucifera*) may be a useful anti-cancer efficacy targeting pancreatic cells.

Keyword: Lotus leaf (*Nelumbo nucifera*) methanolic extract; Human pancreatic cancer; Apoptosis; MAPKs; Mitochondria dysfunction; ER stress