MASTER'S THESIS

Anti-cancer effect of ginsenosides on nasopharyngeal carcinoma

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Anti-cancer Effect of Ginsenosides on Nasopharyngeal Carcinoma

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Abstract

Nasopharyngeal carcinoma (NPC) is a head and neck cancer which has a high incidence rate in Southern China. Radiotherapy, chemotherapy and radiochemotherapy are the current therapies commonly used on NPC patients. However, these therapies have the problems of side effects, chemoresistance and toxicity. In view of this, alternative therapy is needed.

In the first part of my study, the anti-cancer effect of ginsenosides on NPC cells was investigated. Ginsenosides are the active compound in ginseng. NPC cell lines: HK-1 and C666-1 cells were used at the beginning of this study. Later on, only HK-1 cells were studied because of its sensitivity towards ginsenosides. It was shown that five ginsenosides: protopanaxadiol (PPD), panaxadiol (PD), compound K (CK), 20(S)-Rh_2 and Rp1 exhibited higher cytotoxicity and induced apoptosis on NPC cells. The mitogen-activated protein kinase (MAPK) signaling pathways were revealed to be independent of the ginsenoside-induced cell death. Besides, it was found that ginsenosides modulated the ROS level in NPC cells, but relationship was not conclusive. Furthermore, ginsenoside-induced caspase-3, -8 and -9 activations were shown to be independent of the cell death. Apart from that, ginsenoside CK was found to induce depolarization of mitochondrial membrane potential as well as translocation of apoptosis-inducing factor (AIF) from cytoplasm to nucleus. This study suggested that the ginsenoside-induced cell death was mediated through the mitochondrial apoptotic pathway.

The second part was about the effect of NPC cell conditioned medium on human umbilical vein endothelial cells (HUVECs). In tumor microenvironment, tumor cells secrete various angiogenic and migratory factors affecting the behavior of HUVECs. In this study, it was found that both NPC cell conditioned media induced angiogenesis and migration of HUVECs. Furthermore, the vascular endothelial growth factor (VEGF) and matrix metalloproteinases (MMPs) expressions in both NPC cell conditioned media were higher than uncultured medium. This indicated that the NPC cells may affect the HUVECs behavior through secretion of VEGF and MMPs.

The third part was to study the anti-cancer effect of Cetuximab with conventional anti-cancer drugs, cisplatin or docetaxel, on both NPC cells. The use of anti-epidermal growth factor receptor (EGFR) antagonist with current chemotherapy on NPC patients has been reported in clinical studies. However, *in vitro* study about this issue is lacking. In the present study, the cotreatment with Cetuximab did not show significant synergistic effect on the anti-cancer effect of cisplatin or docetaxel in both NPC cell lines by MTT assay. This study shed light

on the clinical trial that this combination of drugs and treatment schedule may not have beneficial effect on NPC therapy.

Taken together, the anti-cancer effect and underlying mechanism of ginsenosides on NPC cells has been demonstrated in this study. The angiogenic effect of NPC cells on HUVECs was also studied, in which further investigation with anti-angiogenic therapy on NPC cells was suggested. In addition, the anti-cancer effect of Cetuximab with cisplatin or docetaxel was revealed. Alternative combination of drugs and treatment schedule were recommended.

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