MASTER'S THESIS

Immunomodulatory effects of tryptanthrin on human bronchial epithelial cells

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Immunomodulatory Effects of Tryptanthrin on Human Bronchial Epithelial Cells

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Abstract

Cytokine is a group of low molecular weight glycoproteins produced by both immune and non-immune cells. One of the major functions of cytokines is to regulate the immune reactions. Influenza is caused by RNA viruses of the *orthomyxovirus* group. During influenza virus infection, bronchial epithelial cell is not only the primary target of infection, but also the source of pro-inflammatory cytokines and chemokines. Bronchial epithelial cell-derived cytokines have been shown to play an important in regulating airway inflammation. Control of influenza infection can be carried out by vaccination or by the use of antiviral or immuno-modulatory drugs.

Banlangen, a common name refers to *Polygonum tinctorium*, *Isatis indigoticum* and *Strobilanthes cusia*. These herbal plants are used for the treatment of various diseases in China, Korea and Japan. Tryptanthrin is one of the ingredients identified in these medicinal plants, tryptanthrin has previously been reported to mediate various biological activities, such as anti-microbial, anti-tumor, and the anti-inflammatory activities. However, the effects of tryptanthrin on the production of pro-inflammatory cytokines by influenza virus infected cells have not been investigated. In this study, we adopted the human bronchial epithelial cell line as a model to examine the effects of tryptanthrin on the production and secretion of cytokines by influenza virus infected bronchial epithelial cells. The expression and production of cytokines was determined using RT-PCR and ELISA method, respectively.

To evaluate the immunomodulatory activities of tryptanthrin, we have initially optimized the conditions on the influenza virus infected cell cultures. These included the evaluation of the toxicity of tryptanthrin, virus titer (A/NWS/33 and B/Lee) determination, and the cytopathic damage of virus infected bronchial epithelial H292 cells. Our results showed that tryptanthrin is not cytotoxic to H292 cell at the concentration up to 20 μM. And tryptanthrin was found to exert a cytostatic effect on the H292 by inhibiting the DNA synthesis. At a non-cytotoxic concentration, tryptanthrin slightly reduced the replication (4-fold reduction) of influenza A virus in H292 cells.

After the optimization of the culture conditions, the effects of tryptanthrin on cytokines expression by influenza virus infected bronchial epithelial H292 cells were examined. Both cytokines involved in the regulation of immunity (e.g. IL-6, IL-12) and inflammation (e.g. IL-1β, IL-8, MIP-1β, and RANTES) were studied. Tryptanthrin was found to differentially modulate the expression of IL-1β, IL-6, IL-8, IL-12 p35, MIP-1β, and RANTES in influenza A and influenza B virus infected H292. Tryptanthrin was found to increase the expression of IL-6 in influenza A or influenza B virus infected H292 cells. The expression of IL-12 p35, MIP-1β, and IL-8 was also significantly increased in influenza A virus infected cell. The results suggest that tryptanthrin may modulate the immune response by enhancing the expression of IL- 6 (a cytokine involved in the protection against influenza virus infection), IL-8 (a chemotactic cytokine for neutrophil), and MIP-1β (a cytokine involved in T cell stimulation) in influenza virus infected epithelial cells.

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