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Immunostimulating activity effect of water extract of *Acanthopanax divaricatus* vat. *albeofructus* leaf in human peripheral blood mononuclear cells

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Acanthopanax divaricatus vat. *albeofructus* is a typical Oriental herb. It has been used as anti-rheumatic and hypertension, anti-stress. It has also an immunostimulating activity effect. Various cytokines are related to immune reaction. The production of IL-2, IFN- γ , TNF- α and IL-12 lead to a Th1-type cellular response, while production of IL-6 lead to Th2-type humoral immunity. IL-2, together with other factors and in conjunction with antigens, mitogens, or anti-immunoglobulin antibodies, controls B cell proliferation and differentiation into antibody-producing plasma cells. IFN- γ is also an important cytokine in the host defense against infection by viral and microbial pathogens. IL-12 is primarily produced by activated macrophages and stimulates T cells and NK cells. TNF- α also modulates immune response by triggering the production of number of other regulatory cytokines. In this study, we investigated that the cytokine (IL-2, IL-12, IL-6, IFN- γ , TNF- α) released from peripheral blood mononuclear cells (PBMC) by treatment of extract of *Acanthopanax divaricatus* vat. *albeofructus* leaves. Cytokine production were evaluated by enzyme-linked immunosorbent assay (ELISA) and, respectively.

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Immunosuppressive activity of poly(RGD) in mice

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The domain of fibronectin in cellular recognition is carried by an Arg-Gly-Asp-Ser (RGDS) sequence. The RGD sequence exists commonly in many adhesion molecules. Poly(RGD) was prepared by the subsequent polymerization procedure with diphenylphosphoryl azide (DPPA). Here, we investigated the effect of poly(RGD) peptide on induction of cytolytic T lymphocyte (CTL) against allogenic tumor cells in mice. CTL activity was measured using spleen cells harvested from C57BL/6 mice (H-2b) that had immunized with an allogenic P815 cells (H-2d) 10 days before assay. Immunization of poly(RGD) admixed with P815 cells showed a significant decrease in CTL activity against P815 cells compare with that immunized with P815 cells without poly(RGD). The suppressive effect of poly(RGD) on CTL induction was dose-dependent, and the best result was obtained by treatment with poly(RGD) on day 0, 1, 2 and 3 after P815 immunization. In addition treatment with poly(RGD) resulted in a significant decrease in P815-specific T cell proliferation and IL-2 production. These results indicate that poly(RGD) acts as an immuno-suppressor to inhibit cellular immune responses.

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Inhibition of IL-2 production mediated through the down-regulation of ERK1/2 signaling pathway by naturally occurring small molecules in murine T lymphocytes

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In the present study, we investigate the effect of the small molecules on IL-2 expression in murine T lymphocytes. Of the small molecules tested, three structurally related compounds, IMB-104, IMB-105, and IMB-112, markedly inhibited IL-2 production in B6C3F1 mouse splenocytes and thymocytes. The decrease in IL-2 production was found to correlate well with a decrease in T-cell proliferation as well as mRNA expression. To further characterize the inhibitory mechanisms of the small molecules at the transcriptional level, we examined the upstream signaling for IL-2 gene expression. We found that those small molecules inhibited DNA binding activity of NF-AT and they also inhibited the phosphorylation of ERK1/2. These results suggest that naturally occurring small molecules, IMB-104, IMB-105 and IMB-112, inhibits IL-2 production mediated through the down-regulation of ERK1/2 as well as NF-AT signaling pathway, which may explain their potentials for immune modulation. Supported by a grant from MOCIE and ITEP through the BPRC of Inje University.

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Inhibition of nitric oxide production mediated through the down-regulation of NF-kB signaling pathway by naturally occurring small molecules in LPS-stimulated RAW264.7 cells

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Here we investigate the effect of the small molecules on NO production and iNOS expression in RAW264.7 murine macrophages stimulated with lipopolysaccharide (LPS). Of the small molecules tested, interestingly, two structurally related compounds, IMB-104 and IMB-105, markedly inhibited NO production in dose- and time-dependent manners. The decrease in NO production was found to correlate well with a decrease in iNOS protein and mRNA expression as determined by Western blot and real-time RT-PCR, respectively. To further characterize the inhibitory mechanisms of the small molecules at the transcriptional level, we examined the DNA binding and transcriptional activity of NF-kB. We found that IMB-104 and IMB-105 inhibited NF-kB-dependent transcriptional activity and DNA binding activity. IMB-104 and IMB-105 inhibited the degradation of I-kBa, which leads to decrease of the nuclear translocation of p65, a component of NF-kB. These results suggest that naturally occurring small molecules, IMB-104 and IMB-105, inhibits NO production mediated through the down-regulation of NF-kB signaling pathway, which may explain their potentials for immune modulation. Supported by a grant from MOCIE and ITEP through the BPRC of Inje University.