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[Lab. of Pharmacology]

**Ca<sup>2+</sup> and Protein Kinase C Signaling for Histamine and Sulfidoleukotrienes  
Released from Human Cultured Mast Cells.**

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We analyzed the Ca<sup>2+</sup> and protein kinase C (PKC) signaling in human cultured mast cells (HCMC) and compared it to that in rodent mast cells. In HCMC, after IgE-mediated stimulation, an elevation of [Ca<sup>2+</sup>]<sub>i</sub> and PKC translocation to the membrane fraction was observed. As concerns Ca<sup>2+</sup> signaling, IgE-mediated histamine and leukotrienes (LTs) release was abolished after Ca<sup>2+</sup> depletion. As regards PKC signaling, staurosporine inhibited IgE-mediated mediator release. These results demonstrated that HCMC might be useful for analysis of the signal transduction pathway for mediator release, such as histamine and LTs.

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[Lab. of Pharmacology]

**The Effect of Mesoporphyrin on the Production of Cytokines by Inflammatory  
Cells in vitro.**

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This study was conducted to investigate a mechanism of the anti-inflammatory action of mesoporphyrin (MP), especially the effect on the production of cytokines by some cultured inflammatory cells. MP had no effect on lipopolysaccharide-induced TNF- $\alpha$  production by RAW 264.7 cells. MP inhibited IFN- $\gamma$  production by 1E10.H2 cells (murine T helper-1 cells), but not IL-4 production by D10G4.1 cells (murine T helper-2 cells). MP inhibited IL-6 production by human osteoblast-like MG-63 cells. This inhibition of IL-6 production is closely related to the suppression of PGE<sub>2</sub> generation by interfering cyclooxygenase 1 and 2 enzymatic activities. These data suggest that the inhibition of cytokine production is one of the anti-inflammatory mechanisms of MP.

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[Lab. of Pharmacology]

**The Effects of Methanolic Extract from Corydalis Tuber on Cytokine  
Production and Allergic Reactions in Experimental Animals.**

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The effects of methanolic extract of Corydalis Tuber (MECT) on the production of cytokine and some allergic reactions in experimental animals were investigated. MECT inhibited bacterial lipopolysaccharide (LPS)-induced TNF- $\alpha$  production in mice that had been pretreated with *Propionibacterium acnes*. MECT inhibited TNF- $\alpha$  production by J774.1 cells, whereas it failed to affect the TNF- $\alpha$ -induced cytotoxicity to L929 cells. MECT inhibited IgE-mediated biphasic cutaneous reaction in mice. MECT also inhibited dinitrofluorobenzene-induced contact dermatitis in mice. The inhibitory action of TNF- $\alpha$  production is one of the possible mechanisms of anti-allergic action of MECT.

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[Lab. of Pharmacology]

**Role of Cyclic 3',5'-Adenosine Monophosphate in the Regulation of Chemical  
Mediator Release and Cytokine Production from Cultured Human Mast Cells.**

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The role of cyclic 3',5'-adenosine monophosphate (cAMP) in chemical mediator release and cytokine production by human mast cells was determined.  $\beta$ -Agonists significantly suppressed IgE-mediated release of histamine, leukotriene and prostaglandin D<sub>2</sub> and the production of cytokine, GM-CSF and IL-5. Phosphodiesterase inhibitors had no effect on chemical mediator release but suppressed cytokine production. Dibutyryl cAMP significantly suppressed both chemical mediator release and cytokine production. Elevation of cAMP may be responsible for the inhibitory effect of  $\beta$ -agonist and phosphodiesterase inhibitors on chemical mediator release and cytokine production in human mast cells.