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[Lab. of Pharmacology]

**Recovery of purification-associated reduction in antigen-induced histamine release from rat peritoneal mast cells.**

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Immunoglobulin E (IgE)-dependent histamine release from purified rat peritoneal mast cells (PMC) is very low in comparison to that from a non-purified preparation (PEC). The reduced histamine release from PMC is recovered or potentiated by reconstitution with separated non-mast cells (NMC). In the present study, further characterization was undertaken to elucidate the mechanisms involved. IgE-dependent histamine release was significantly potentiated by NMC reconstitution to PMC. The potentiation was dependent on the concentration of NMC reconstituted and reached a plateau after 30 min incubation. Membrane fraction prepared from NMC also potentiated PMC histamine release in a dose-dependent manner. Fibronectin, laminin and collagen failed to potentiate PMC histamine release.

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[Lab. of Pharmacology]

**VUF-K-8788, a periphery-selective histamine H1 antagonist with anti-pruritic activities.**

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The pharmacological properties of VUF-K-8788 were investigated in vitro and in vivo. VUF-K-8788 inhibited [<sup>3</sup>H]-mepyramine from binding to the cell membrane of lung parenchyma and the histamine-induced contraction of isolated guinea pig ileum without affecting ileal contractions induced by acetylcholine, serotonin, KCL and BaCl<sub>2</sub>. The increase of vascular permeabilities induced by histamine and passive cutaneous anaphylaxis (PCA) in guinea pigs were inhibited by VUF-K-8788 in a dose-dependent fashion. Moreover, the anti-histaminic effect of VUF-K-8788 was also observed in rats. These results suggested that VUF-K-8788 would be useful in the treatment of allergic disorders such as atopic dermatitis and eczema.

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[Lab. of Pharmacology]

**Psychosocial stress enhances IgE-mediated triphasic cutaneous reaction in mice: Antagonism by yokukan-san (a Kampo medicine) and diazepam.**

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In the present study, we investigated the effect of social isolation stress on IgE-mediated triphasic cutaneous reactions after 2,4-dinitrofluorobenzene (DNFB) challenge in male BALB/c mice passively sensitized with anti-dinitrophenol (DNP) IgE antibody, and examined the effects of Yokukan-san and a reference drug (diazepam) on the stress-enhanced cutaneous reaction. Oral administration of Yokukan-san attenuated the isolation stress-exacerbated triphasic skin reactions in a dose-dependent manner, whereas it had no significant effect on cutaneous reactions in the unstressed group-housed mice.

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[Lab. of Pharmacology]

**Disruption of antigen-induced airway inflammation and airway hyper-responsiveness in low affinity neurotrophin receptor p75 gene deficient mice.**

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The present study was conducted to clarify the role of neurotrophin low affinity receptor (p75N) in allergic airway inflammation and hyperresponsiveness (AHR) in mice by employing p75N gene deficient mice. Mice were immunized twice by intraperitoneal injections of ovalbumin (OA) at intervals of 12 days. OA was inhaled 10 days after the secondary immunization and repeated 3 times at 4 days interval. In wild-type mice, repeated antigen provocation resulted in airway eosinophilia, AHR and elevations in serum IgE and interleukin (IL) -4 and -5 in BALF. In p75N gene deficient mice, none of the above parameters was observed after antigen provocation. The present findings suggest that p75 gene deficiency disrupt an allergic airway inflammation and AHR in mice.