

[*Chem. Pharm. Bull.*, **47**, 177-181 (1999)]

[Lab. of Pharmacology]

**Synthesis of Trimethylhydroquinone Derivatives as Anti-allergic Agents with Anti-oxidative Actions.**

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A novel series of trimethylhydroquinone derivatives was synthesized and evaluated for their anti-lipid peroxidation activity in rat liver microsomes, inhibition of rat basophilic leukemia-1 (RBL-1) cell 5-lipoxygenase and 48h homologous passive cutaneous anaphylaxis (PCA) activity in rats. 4-[4-[4-(Diphenylmethyl)-piperazinyl]-butoxy]-2,3,6-trimethylphenol exhibited the ability to inhibit  $\text{Fe}^{3+}$ -ADP induced NADPH dependent lipid peroxidation ( $\text{IC}_{50}=5.3 \times 10^{-7}\text{M}$ ), 5-lipoxygenase ( $\text{IC}_{50}=3.5 \times 10^{-7}\text{M}$ ) and PCA reaction (57% inhibition at 100 mg/kg p.o.).

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[Lab. of Pharmacology]

**Participation of Histamine  $\text{H}_1$  and  $\text{H}_2$  Receptors in Passive Cutaneous Anaphylaxis-induced Scratching Behavior in ICR Mice.**

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Scratching behavior associated with passive cutaneous anaphylaxis (PCA) was examined and compared to that induced compound 48/80 or histamine in ICR mice. Elicitation of PCA, and intradermal injection of compound 48/80, histamine or serotonin induced both scratching behavior and vascular permeability increase in ICR mice. The histamine  $\text{H}_1$  receptor antagonists inhibited the histamine- or PCA-induced vascular permeability increase almost completely, whereas they failed to abolish the scratching behavior. In contrast,  $\text{H}_2$  receptor antagonists did not affect the vascular permeability increase caused by histamine, but inhibited scratching behavior. The combination of  $\text{H}_1$  and  $\text{H}_2$  antagonists abolished the histamine-induced scratching behavior.

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[Lab. of Pharmacology]

**Terreic acid, a Quinone Epoxide Inhibitor of Bruton's Tyrosine Kinase.**

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Bruton's tyrosine kinase (Btk) plays pivotal roles in mast cell activation as well as in B cell development. By using an in vitro assay to measure the activity that blocks the interaction between protein kinase C and the pleckstrin homology domain of Btk, terreic acid was identified and characterized in this study. This quinone epoxide specifically inhibited the enzymatic activity of Btk in mast cells and cell-free assays. Therefore, this study confirmed the important roles of Btk in mast cells and other immune system cells.

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[Lab. of Pharmacology]

**IPD-1151T (Suplatast Tosilate) Inhibits Interleukin (IL)-13 Release but not IL-4 Release from Basophils.**

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The effect of suplatast tosilate (IPD-1151T), which is known to suppress interleukin (IL)-4 release from T cells, on the release of IL-4 and IL-13 from human peripheral basophils was investigated. Basophils were obtained from 16 mite-sensitive atopic asthmatic patients. IPD-1151T clearly inhibited the antigen-induced release of IL-13 but not IL-4. Present results suggest that IPD-1151T possess different activity for the regulation of cytokine release in basophils and T cells.