

[J. Pharmacobio-Dyn., 14, 309-314 (1991)]

[Lab. of Pharmacology]

Effect of Tranilast on Endothelin-Induced Bronchoconstriction in Guinea Pigs.

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Effect of tranilast on endothelin (ET)-induced bronchoconstriction was investigated in guinea pigs. Intravenous injection of ET caused an asthma like respiratory obstruction and an increase in inflation pressure. Oral administration of tranilast at a dose of 200 mg/kg inhibited both responses. Tranilast at concentration between 10^{-5} and 10^{-4} g/ml inhibited ET-induced contraction of isolated guinea pig tracheal muscle. However, the agent did not affect ET-induced tracheal muscle contraction in Ca^{2+} -free Tyrode's solution and ET-induced neither histamine nor $PGF_{2\alpha}$ release. These results suggest that tranilast inhibits ET-induced bronchoconstriction by inhibiting calcium influx into tracheal muscle.

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[Lab. of Pharmacology]

In vitro Development and Functions of Human Mast Cells.

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A long-term co-culture of mononuclear cells of human cord blood with mouse 3T3 fibroblasts resulted in the development of human mast cells. These cells were morphologically and functionally mature cells, containing 1.4-2.8 μ g histamine per million cells and bore approximately 10^5 $E_{c\epsilon}RI$ per cell. The mast cells sensitized with human IgE released histamine upon challenge with anti-IgE. Further experiments revealed that soluble factors released from 3T3 fibroblasts are essential and sufficient for the differentiation of human mast cell progenitors in vitro. Cultured mast cells also responded to calcium ionophore A23187 and substance P for histamine release, but failed to respond to compound 48/80 and FMLP.

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[Lab. of Pharmacology]

Bleomycin-Induced Pulmonary Fibrosis in Genetically Mast Cell-Deficient WBB6F₁-W/W^v Mice and Mechanism of the Suppressive Effect of Tranilast, an Antiallergic Drug Inhibiting Mediator Release from Mast Cells, on Fibrosis.

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Pulmonary fibrosis could be induced in genetically mast cell-deficient WBB6F₁-W/W^v mice by treating with bleomycin (BLM). Tranilast suppressed BLM-induced fibrosis in WBB6F₁-W/W^v mice, suggesting little role of mast cells in the development of fibrosis. Tranilast may act through suppressing BLM-induced activation of lymphoid cells including macrophage and neutrophil.