Inhibitory Effects of Nedocromil Sodium on Cytokine Production from Mast and Epithelial Cells

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The effects of nedocromil sodium on cytokine release from various inflammatory cells and on cytokine induced responses in different cell types have been studied.

Upon stimulation, mast cells are known to release cytokines, e.g. tumour necrosis factor (TNF α) [1], which possess a range of biological activities including the up-regulation of adhesion receptor expression on endothelial cells [2]. The activity of mast cells is known to be influenced by various cytokines such as interleukin (IL)-2 [3], which potentiates histamine release induced by immunologic stimulation. The inhibitory effects of nedocromil sodium (10^{-5} – 10^{-3} M) on TNF- α release from rat peritoneal mast cells (RPMCs) and intestinal mucosal mast cells (IMMCs) [4] may explain in part the anti-asthmatic effects of this compound. Nedocromil sodium has been shown to exhibit tachyphylaxis against histamine release from RPMCs and no inhibitory effects on histamine release from rat IMMCs, thus contrasting markedly with the data on TNF- α release. In studies which have preincubated RPMCs cocultured on 3T3 fibroblasts with rat IL-2, an enhanced release of histamine was measured with both immunologic and non-immunologic (compound 48/80 challenge and this response was inhibited with nedocromil sodium (10^{-5} M) without showing any signs of tachyphylaxis [5].

Airway epithelial cells are also known to release a variety of cytokines and their expression is up-regulated in asthma. In experiments which exposed cultured human bronchial epithelial cells to ambient concentrations (up to 50 ppb) of the atmospheric pollutant ozone for 6 h, marked increases in the levels of TNF- α , granulocyte/macrophage-colony-stimulating factor and soluble ICAM-1 receptor were measured with a significant effect at 10–50 ppb ozone, and these were reduced by treatment of the cells with nedocromil sodium (10^{-5} M) [6].

These findings indicate the ability of nedocromil sodium to inhibit cytokine release from different cell types, and further studies are in progress to elucidate the stage at which cytokine release is modulated.

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