The effect of methoxy-derivatives of catecholamines on histamine release from sensitized human leucocytes and its inhibition by the parent compounds

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It has been shown that catecholamines inhibit the anaphylactic histamine release from sensitized human leucocytes, an action which is apparently mediated through stimulation of β-adrenoceptors (Lichtenstein & Margolis, 1968; Assem & Schild, 1969). In general, the rank order of the potency of various β-receptor stimulants in this respect seemed to bear a positive correlation with their rank order as relaxants of bronchial muscle. Catecholamines are partly metabolized by catechol-O-methyltransferase, and the methoxy derivatives thus formed may antagonize the effect of the parent compounds on bronchial and gastrointestinal smooth muscle (Paterson, Conolly, Davies & Dollery, 1968; Hornsey, Gailer, Turner & Griffin, 1971).

A study has been carried out in order to investigate the relative potency of three catecholamines, isoprenaline, isoetharine (an α-ethyl derivative of isoprenaline), and rimiterol which has a piperidyl methanol side chain, as inhibitors of the anaphylactic release of histamine from isolated human leucocytes. This was found to be of the order of 1,000, 20 and 3, respectively. Their reported mean relative potency in guinea-pig tracheal chain preparations is of the order of 1,000, 200 and 400, respectively, whilst in the rabbit atrial strip preparation it is 1,000, 3 and 3. Thus, the relative potencies for isoetharine and rimiterol as cardiac stimulants seemed to be closer to their relative potencies as inhibitors of histamine release.

The anti-anaphylactic effect (inhibition of antigen-induced histamine release) of the methoxy derivatives of these three catecholamines has also been investigated. Both 3-methoxy isoprenaline, and to a much smaller extent 3-methoxyisoetharine, produced partial inhibition of histamine release, particularly with concentrations exceeding 10^{-5} M. Each of these two compounds possessed less than 10% of the activity of the parent compound, which varied in different experiments within the range of 0.5 to 10%. 3-methoxy rimiterol did not produce any inhibition in the concentrations used (up to 10^{-3} M).

The interaction between the three catecholamines used and their 3-methoxy derivatives was studied. Both 3-methoxy isoetharine and 3-methoxy rimiterol antagonized the inhibitory activity of their parent compounds, while 3-methoxy isoprenaline often potentiated the effect of isoprenaline (Table 1).

Table 1

Treatment	*% histamine release from isolated leucocytes of a pollen-allergic patient*
Control (Tyrode solution)	3
Mixed grass pollen (20 Noon Units/ml)	39
Mixed grass pollen + isoprenaline (2×10^{-6} M)	25
Mixed grass pollen + 3-methoxy isoprenaline (10^{-5} M)	28
Mixed grass pollen + isoprenaline (2×10^{-6} M) + 3-methoxy isoprenaline (10^{-5} M)	17

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