Are gastrin receptors located on parietal cells?

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Gastric acid secretion stimulated by either food or pentagastrin is as sensitive to inhibition by histamine H_2-receptor antagonists as is histamine-stimulated secretion. This could be explained if parietal cells have separate receptors for histamine and gastrin such that blockade of one alters the other (Grossman & Konturek, 1974). Alternatively, histamine may act directly on parietal cells and gastrin indirectly by releasing histamine from local histamine-secreting cells (Kahlson & Rosengren, 1972). Secretion of histamine from rat mast cells is critically dependent on calcium (Foreman & Mongar, 1972), while stimulation of cat salivary secretion, particularly of electrolytes, is not (Martinez & Petersen, 1972). If gastrin releases histamine, then there is a possibility that the two exogenous agonists exhibit different degrees of calcium dependence.

This possibility was tested on isolated, lumen perfused, mouse stomach preparations, suspended in organ baths at 37°C (Wan, 1975). The calcium concentration of the unbuffered lumen perfusate was 1.3 mM and that of the phosphate buffered bathing solution was 0.65 mM. Agonists were added to the bath, but to avoid desensitisation, each stomach was only equilibrated with one agonist concentration. The pH of the lumen-perfusate was sensed by a flow electrode system. The peak secretory responses were calculated by the change in hydrogen ion concentration and expressed as ΔH^+ nmoles/ml. Submaximal doses of histamine 10^{-5}M and pentagastrin 10^{-7}M were given in a randomized block design with six preparations run concurrently.

The mean and standard error of the response to histamine ($n=6$) was 202 ± 34 and that to pentagastrin 101 ± 31. In the absence of calcium, the responses were 141 ± 32 ($P > 0.1$) and 15 ± 5 ($P < 0.05$) respectively.

Since magnesium can reduce the release of histamine through competitive inhibition of Ca^{++} uptake (Foreman & Mongar, 1972), mouse stomachs were exposed to the bathing solution and perfusate containing 5 or 20 mM Mg^{++} replacing sodium. Histamine responses in control and 5 mM Mg^{++} solutions were 135 ± 11 and 114 ± 22 ($n=6$, $P > 0.2$) respectively; corresponding pentagastrin responses were 158 ± 19 and 46 ± 16 showing significant inhibition ($n=6$, $P < 0.001$). No further inhibition of pentagastrin responses occurred at 20 mM Mg^{++}, but histamine responses were significantly increased to 303 ± 31 ($n=6$, $P < 0.05$).

The results could be interpreted so that histamine and pentagastrin still act on the same cell if histamine mobilised intracellular Ca^{++} and pentagastrin increased the membrane permeability to Ca^{++}. However, our finding that acid secretion evoked by the calcium ionophore, A23187 (Foreman, Gomperts & Mongar, 1973), can be inhibited by metiamide, is incompatible with this hypothesis unless metiamide is also a calcium antagonist. Since there is no evidence for this, our results therefore reinforce the hypothesis that gastrin stimulates acid secretion indirectly, via histamine secreting cells.

References

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