References

BLACK, J.W. & WELCH, L.A. (1977). Are gastrin receptors located on patietal cells? *Br. J. Pharmac.*, **59**, 476P.

BRADHAM, L.S., HOLT, D.A. & SIMS, M. (1970). The effect of Ca^{2+} on the adenylate cyclase of calf brain. *Biochim. biophys. Acta*, **201**, 250–260.

BUNCE, K.T. & PARSONS, M.E. (1976). A quantitative study of metiamide, a histamine H_2-antagonist, on the isolated whole rat stomach. *J. Physiol., Lond.*, **258**, 453–465.

JACOBSON, A., SCHWARTZ, M. & REHM, W.S. (1965). Effects of removal of calcium from bathing media on frog stomach. *Am. J. Physiol.*, **209**, 134–140.

KASBEKAR,D.K. (1974). Calcium—secretagogue interaction in the stimulation of gastric acid secretion. *Proc. Soc. exp. Biol. Med.*, **145**, 234–239.

MAIN, I.H.M. & PEARCE, J.B. (1977). Effect of calcium on acid secretion by the isolated rat gastric mucosa. *Br. J. Pharmac.*, **61**, 124P.

β-Adrenoceptor agonist stimulation of acid secretion in rat isolated stomach

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β-Adrenoceptor agonists inhibit pentagastrin-induced acid secretion from gastric pouches in conscious dog (Curwain, Holton and Spencer, 1972; Daly & Stables, 1977) and rat (Lundell and Svensson, 1974). Salmefamol, a β_2-adrenoceptor agonist inhibits bethanechol-induced acid secretion (Canfield, Curwain, King & Price, 1978) whilst in high doses the related drug, salbutamol will inhibit histamine-stimulated secretion in the dog (Daly, Long & Stables, 1978). We have recently shown that salmefamol does not inhibit acid secretion stimulated by pentagastrin, histamine or bethanechol in the rat isolated stomach (Canfield *et al.*, 1978), but appears to act as a stimulant of secretion. The present results extend this finding to include salbutamol and isoprenaline and the action of various antagonists on this stimulation by β-adrenoceptor agonists of acid secretion in the isolated stomach.

The rat stomach preparations were set up as described for the guinea pig by Holton & Spencer, 1976. All drugs were applied to the serosal bathing fluid. When required the tissues were pre-incubated with an inhibitor for one hour before addition of the β-adrenoceptor agonist for a further 60–90 minutes. Each tissue was exposed to only one concentration of salmefamol, salbutamol or isoprenaline, and the acid output was measured over fifteen-min periods. The change in rate of secretion is expressed as the ratio of the rate at the plateau of response to the average rate in the two control periods in the same tissue immediately before exposure to the agonist. The average control secretion in one series was 3.39 ± 0.190 μmol H^+ $cm^{-2}h^{-1}$ (s.e. mean, $n = 36$).

Both salmefamol (0.2–20 μM) and isoprenaline (0.06–6 μM) caused a concentration-dependent increase in the rate of acid secretion. The mean maximum observed value for the secretory ratio with salmefamol was 1.90 ± 0.09 ($n = 21$) and with isoprenaline 2.33 ± 0.28 ($n = 12$). Although the full concentration response curve remains to be investigated, salbutamol (0.1–20 μM) also caused an increase in acid secretion.

The responses to isoprenaline (1.25 μM) or salmefamol (5 μM) were not reduced by atropine (10 μM), metiamide (100 μM) or practolol (20 μM). However, propranolol (20 μM) did cause a significant decrease in the secretory ratio for both salmefamol and isoprenaline (t-test $P < 0.01$ in each case; $n = 12$ and 10 respectively) and caused a shift in the salmefamol concentration—response curve to the right with no change in slope of the linear region.

These results confirm that β-adrenoceptor agonists stimulate acid secretion by the rat isolated stomach. This action appears not to involve either histamine or cholinergic receptors and may be mediated by β_2 receptors. The reasons for the difference in response between the isolated preparation and the intact animal remain to be investigated.

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References

CANFIELD, S.P., CURWAIN, B.P., KING, J.A. & PRICE, CAROLYN (1978) Salmefamol: Inhibitor or stimulant of gastric acid secretion? *Br. J. Pharmac.* **62**, 445P.

CURWAIN, B.P., HOLTON, P. & SPENCER, J. (1972) The effect of β_2 adrenoceptor stimulants, salbutamol and terbutaline on gastric acid secretion and mucosal blood flow in conscious dogs with Heidenhain pouches. *Br. J. Pharmac.*, **46**, 566–567P.

DALY, M.J., LONG, JANET M. & STABLES, R. (1978) The effects of (−)-isoprenaline, salbutamol and nylidrin on gastric acid secretion in conscious dogs with Heidenhain pouches. *Br. J. Pharmac.* **63**, 376P.

DALY, M.J. & STABLES, R. (1977) The effect of (−)-isoprenaline and (±)-salbutamol on pepsinogen and acid secretion in the dog. *Br. J. Pharmac.* **59**, 323–325.

HOLTON, PAMELA & SPENCER, JAN (1976). Acid secretion by guinea pig isolated stomach. *J. Physiol., (Lond.)*, **255**, 465–479.

LUNDELL, L. & SVENSSON, S.E. (1974). Implication of gastric mucosal histamine in inhibition by isoprenaline of pentagastrin induced gastric secretion. *Br. J. Pharmac.*, **52**, 69–75.

Mucosal cell turnover in the upper gut of the mouse and its modification by carbenoxolone

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In 1970 Lipkin claimed that carbenoxolone reduced the rate of mucosal cell proliferation in the acid secreting part of the mouse stomach (fundus) and increased the time these cells took to migrate to the point of exfoliation. Neither effect was apparent in duodenum or colon. This work has now been repeated and extended.

Mice received radioactive [^{3}H]-thymidine i.v. and the radioactivity remaining in the fundic, antral and duodenal mucosae was measured during the six days following this injection. A minimum of 22 mice were used to derive each value.

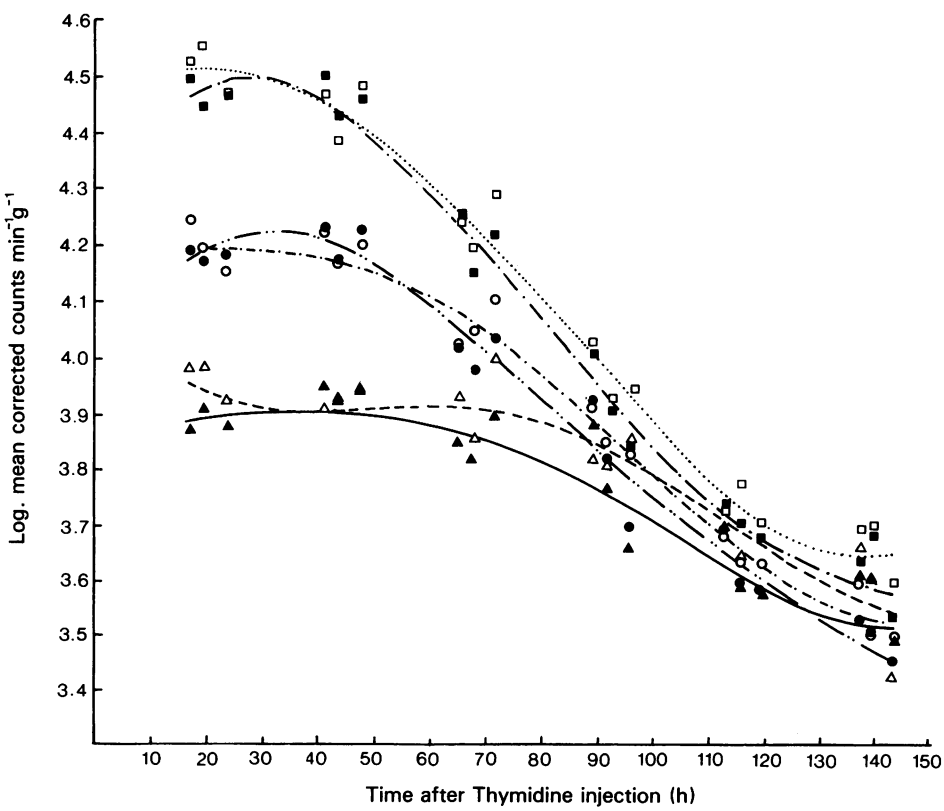

Figure 1 Mouse mucosal cell lifespan. Cells were taken from the (■) duodenal, (●) antral and (▲) fundic mucosae before (filled symbols) and after (open symbols) carbenoxolone.