Classification of the β-adrenoceptors that mediate inhibition of pentagastrin-induced gastric acid secretion in the dog

M.J. DALY, JANET M. LONG & R. STABLES

Department of Pharmacology, Allen & Hanburys Research Ltd., Ware, Hertfordshire SG12 0DJ, UK

β-Adrenoceptor agonists inhibit pentagastrin-induced gastric acid secretion in the dog (Curwain & Holton, 1972; Daly & Stables, 1977), but the type of receptor involved is not clear. Curwain, Holton & Spencer (1972) have reported that propranolol blocks the anti-secretory effect of salbutamol but not that of isoprenaline, whereas Magee (1976) found that propranolol does block the antisecretory action of isoprenaline. The experiments reported here were carried out to resolve this discrepancy and to characterize the adrenoceptors that mediate inhibition of gastric secretion.

We have studied the interactions between the agonists (−)-isoprenaline and salbutamol, and the antagonists (±)-propranolol, practolol and (+)-propranolol. Four male beagles (13–18 kg) with well-established Heidenhain pouches were used. Pentagastrin was infused at doses (1–4 $\mu g\ kg^{-1}\ h^{-1}$ i.v.) which produced 50% of maximal secretion in each dog (Daly & Stables, 1977). The doses of (−)-isoprenaline (3–10 $ng\ kg^{-1}\ min^{-1}$ for 60 min) and salbutamol (100–300 $ng\ kg^{-1}\ min^{-1}$ for 60 min) required to produce approximately 70% inhibition of gastric acid secretion were determined in each dog. These doses were tested at least 3 times in each dog 15 min after saline, (±)-propranolol (0.1 mg/kg i.v.), practolol (1.0 mg/kg i.v.) or (±)-propranolol (0.1 mg/kg i.v.). At the dose levels used (±)-propranolol blocks bronchial and vascular β_2-adrenoceptors as well as cardiac β_1-adrenoceptors, but practolol only blocks the cardiac β_1-adrenoceptors (Daly, Flook & Levy, 1975). (+)-Propranolol is devoid of β-adrenoceptor blocking activity (Barrett & Cullum, 1968).

Preliminary experiments showed that the selected doses of (±)-propranolol, practolol and (+)-propranolol had no direct effect on gastric acid secretion. Results for the interaction studies are summarized in Table 1. (±)-Propranolol, but not (+)-propranolol, blocked the antisecretory actions of (−)-isoprenaline and salbutamol. Practolol blocked the antisecretory action of the non-selective β-adrenoceptor agonist (−)-isoprenaline but not that of the selective β_2-adrenoceptor agonist salbutamol.

It is concluded that the antisecretory actions of (−)-isoprenaline and salbutamol are mediated through β-adrenoceptors and that both β_1- and β_2-sub-types are involved. The antisecretory action of (−)-isoprenaline certainly involves activation of β_1-adrenoceptors since it was reduced by both propranolol and practolol and may also involve β_2-adrenoceptors. The antisecretory action of salbutamol clearly results from the selective activation of β_2-adrenoceptors.

Table 1 The effects of (−)-isoprenaline and salbutamol on pentagastrin induced acid secretion after saline, (±)-propranolol, (+)-propranolol or practolol in conscious dogs with Heidenhain pouches

Agonist	*% reduction in acid secretion (mean ± s.e. mean) after:*			
	Saline	*(±)-Propranolol*	*(+)-Propranolol*	*Practolol*
(−)-Isoprenaline	72.2 ± 2.4	47.7 ± 6.5*	67.2 ± 3.1	33.4 ± 3.7*
(*n*)	(14)	(12)	(13)	(12)
Salbutamol	69.1 ± 4.1	12.6 ± 4.4*	63.5 ± 4.8	61.8 ± 3.9
(*n*)	(14)	(12)	(12)	(13)

(*n*) = number of observations.
* = significantly different from control, by *t* test $P < 0.001$.

References

BARRETT, A.M. & CULLUM, V.A. (1968). The biological properties of the optical isomers of propranolol and their effects on cardiac arrhythmias. *Br. J. Pharmac.*, **34**, 43–55.

CURWAIN, B.P. & HOLTON, P. (1972). The effects of isoprenaline and noradrenaline on pentagastrin stimulated gastric acid secretion and mucosal blood flow in the dog. *Br. J. Pharmac.*, **46**, 225–233.

CURWAIN, B.P., HOLTON, P. & SPENCER, J. (1972). The effects 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., FLOOK, J.J. & LEVY, G.P. (1975). The selectivity of β-adrenoceptor antagonists on cardiovascular and bronchodilator responses to isoprenaline in the anaesthetized dog. *Br. J. Pharmac.*, **53**, 173–181.

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.

MAGEE, D.F. (1976). Adrenergic activity and gastric secretion. *Proc. Soc. exp. Biol. Med.*, **151**, 659–662.