(4) Blockage of aspartic and glutamic carboxylate (and C-terminal) groups by conversion to an ester or an amide increases the activity of SPF by factors ranging from 4 to 24-fold.

Our interpretation of these results is that unique features of tertiary structure are not responsible for SPF activity. Intact primary amino groups are largely responsible for activity. The enhanced activity seen after the conversion of carboxylate groups to electroneutral derivatives may be caused by the destruction of charge interactions and/or hydrogen bonding between carboxylate and primary amino groups, allowing the latter to exist in a free state at the surface of the protein molecules.

The effects of β_2-adrenoceptor stimulants, salbutamol and terbutaline on gastric acid secretion and mucosal blood flow in conscious dogs with Heidenhain pouches

B. P. CURWAIN*, PAMELA HOLTON and JAN SPENCER

Department of Physiology, St. Mary's Hospital Medical School, University of London, London W2

Isoprenaline is a potent inhibitor of pentagastrin-induced gastric acid secretion in dogs; this inhibition is not secondary to decreased mucosal blood flow, nor antagonized by propranolol (Curwain & Holton, 1972). In order to investigate whether these properties are shared by other drugs which stimulate β_2 receptors, we have examined the effect of salbutamol and terbutaline.

Gastric acid secretion was stimulated by pentagastrin [1·0–4·0 (μg/kg)/h] and gastric mucosal blood flow measured by radioactive aniline clearance (Curwain & Holton, 1971; Curwain, 1972). Both salbutamol sulphate [0·1–0·5 (μg/kg)/min] and terbutaline sulphate [0·1–0·5 (μg/kg)/min], infused intravenously for 30 min, decreased gastric acid secretion, and the effect was dose related. In 5 experiments in 3 dogs salbutamol [0·1 (μg/kg)/min] reduced acid secretion to a mean of 54% ±S.E. of mean 12% and the effect was antagonized by propranolol (1 mg/kg, I.V.) given 25 min earlier (3 experiments in 3 dogs).

In 6 experiments in 3 dogs terbutaline [0·2 (μg/kg)/min] reduced acid secretion to 48% ±4% and in each case the effect was abolished by propranolol. Heart rate, measured by palpation, rose to 163% of pre-dose level during salbutamol infusion and 127% during terbutaline. Propranolol abolished the tachycardia.

The effects of salbutamol and terbutaline on mucosal blood flow were studied in 3 dogs. Salbutamol 0·1 (μg/kg)/min for 30 min in each of 2 experiments in 2 dogs decreased acid secretion and mucosal blood flow, but the ratio of blood flow to secretion (G/P) increased markedly. Terbutaline 0·2 (μg/kg)/min for 30 min gave similar results (2 experiments in 2 dogs).

In a dose of 1 (μg/kg)/min both salbutamol and terbutaline increased gastric mucosal blood flow without affecting secretion when given on a plateau of histamine-induced secretion.

These results are similar to those previously reported for isoprenaline (Curwain, Endersby & Holton, 1971; Curwain & Holton, 1972) except that isoprenaline inhibition of gastric secretion is not sensitive to blockade by propranolol. The inhibi-

tion of pentagastrin-induced gastric acid secretion by terbutaline and salbutamol, like the inhibition by isoprenaline, is not secondary to a fall in mucosal blood flow.

The development of β-adrenoceptor stimulants which, in man, have no direct effect on the heart, raises the possibility of using these drugs for their anti-secretory action. A substance which inhibits acid secretion but causes a relative increase in mucosal blood flow might be expected to hasten the healing of some types of gastric lesions.

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Development of acetylcholine, choline acetyltransferase and acetylcholinesterase in rabbit corneal epithelium

R. O. HOWARD and W. S. WILSON* (introduced by D. POLLOCK)

Department of Ophthalmology, Yale University School of Medicine, New Haven, Connecticut, U.S.A. and Department of Pharmacology, Glasgow University, Glasgow G12 8QQ

The mammalian corneal epithelium contains a very high concentration of acetylcholine (ACh) and high activities of choline acetyltransferase (ChAc) and acetylcholinesterase (AChE), but the function of the cholinergic system in this tissue is unknown. Hemicholinium-induced depletion of epithelial ACh is accompanied by loss of the corneal reflex, suggesting involvement of ACh in sensory mediation (Fitzgerald & Cooper, 1971). However, significant amounts of ACh remain in the cornea after denervation (Brücke, Hellauer & Umrath, 1949).

Corneal epithelia from female rabbits and their offspring were scraped off under pentobarbitone anaesthesia. Material from one eye of each animal was bioassayed for ACh while ChAc activity was estimated in the extract from the contralateral eye using the method of Schrier & Shuster (1967). AChE was assayed by the technique of Ellman, Courtney, Andres & Featherstone (1961) on any remaining material, as well as on that from several other litters of rabbits. In the case of very young animals, it was necessary to pool tissue from several littermates.

Great variation in ACh content was found, although this was less noticeable within each family. Thus, after expressing ACh levels in terms of %ACh content of the mother's corneal epithelium, a logarithmic increase with age could be observed. At 12 days after birth the corneal ACh was about 3% of that of the mother, reaching 100% at about 50 days. ChAc activities were also subject to considerable variation, but showed a linear increase with age. The enzyme was