were produced by restraining rats in wire mesh for 6 h at 16 ± 1.5°C (Brodie & Hanson, 1960; Senay & Levine, 1967). After the restraint or starvation period, or 6 h after drug administration, the rats were killed and their stomachs examined for mucosal damage. The rate of incorporation of *N*-acetyl-0[1-^{3}H] glucosamine was measured in a circular portion of fundus, 14 mm diameter, by modifications of the method of Lukie & Forstner (1972).

From the results shown in Table 1 it may be seen that significant decreases in the rate of [^{3}H]-*N*-acetylglucosamine incorporation occur after 24 h starvation, restraint, or administration of phenylbutazone, but only the latter two treatments result also in the formation of gastric erosions. However, a relationship between erosion formation and the rate of [^{3}H]-*N*-acetyl-glucosamine incorporation does exist since in the restrained group of rats those with erosions showed a much greater reduction in the rate of incorporation (59%, $n = 6$, $P < 0.01$) than those showing no mucosal damage (31%, $n = 5$, $0.2 > P > 0.1$).

References

BRODIE, D.A. & HANSON, H.M. (1960). A study of the factors involved in the production of gastric ulcers by the restraint technique. *Gastroenterology*, **38**, 352-360.

LUKIE, B.E. & FORSTNER, G. (1972). Synthesis of intestinal glycoproteins: Incorporation of (1-^{14}C)-glucosamine *in vitro*. *Biochim. Biophys. Acta*, **273**, 353-364.

SENAY, E.C. & LEVINE, R.J. (1967). Synergism between cold and restraint for rapid production of stress ulcers in rats. *Proc. Soc. exp. Biol. Med.*, **124**, 1221-1223.

WALDRON-EDWARD, D. (1970). Gastric mucin and mucinous secretions. *Can. J. Surg.*, **13**, 341-349.

Effects of bombesin and bombesin-like peptides on gastrointestinal myo-electric activity

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Bombesin produces an inhibitory effect *in vivo* on human upper intestinal motility and a stimulating effect *in vitro* on intestinal muscle strips both in human and in various animal species. Studies on smooth muscle electric activity however are lacking. The present investigation was carried out on the effect of bombesin on the electric activity of gastrointestinal tract *in vivo*. Three synthetic peptides, C-terminal fragments of the bombesin molecule, were also investigated in order to identify the shortest active amino acid sequence in the bombesin molecule.

Thirty-seven experiments were performed in three healthy, conscious dogs with bipolar silver electrodes chronically implanted at different levels between the stomach and the rectum. After a 20 min control period each compound was infused i.v. for 20 minutes. A 20 min recovery period followed. Bombesin was infused at 5, 10, 15, 30 ng kg^{-1} min^{-1}; C-terminal heptapeptide at 20, 80 ng kg^{-1} min^{-1}; C-terminal nonapeptide at 10, 15, 30 ng kg^{-1} min^{-1}. The effects of the drugs on frequency, amplitude, rhythm and propagation velocity of pacesetter potentials (PP) and on incidence of spikes were evaluated.

Bombesin significantly increased the frequency of PP in the antrum ($P = 0.01$), duodenum ($P = 0.01$), jejunum ($P = 0.01$) and ileum ($P = 0.05$). In the duodenum and jejunum the increase of PP frequency showed linear correlation with the reduction of PP amplitude. The propagation velocity was reduced from 8.0 ± s.e. mean 0.41 to 4.1 ± 0.60 cm/second. Spikes were not affected in the antrum and ileum, whereas they were abolished in the duodenum and jejunum. In the duodenum and jejunum the increase of PP frequency and the slowing down of propagation velocity was followed by the loss of PP phase lock and appearance of a characteristic electric pattern, consisting of an irregular sequence of slow and small potentials ('electric disorganization'). The mechanical counterpart, controlled by means of an intraluminal microballoon, was the disappearance of motility. In the colon the effect of bombesin on electric activity was not consistent.

Neither the C-terminal heptapeptide nor the octapeptide showed a significant effect on myo-electric activity, whereas the effect of nonapeptide was similar to that of bombesin showing, however, an activity which was 75% of that of bombesin.

These experiments show that bombesin induces characteristic gastrointestinal myo-electric changes

and that these are dependent on the sequence of the nine C-terminal amino acids of the bombesin molecule.

References

BERTACCINI, G., IMPICCIATORE, M., MOLINA, M. *ET AL.* (1973). Action of some natural and synthetic peptides on the motility of human gastrointestinal tract *in vitro*. *Rendic. Gastroenterol.*, 5, 136.

CORAZZIARI, E., DELLE FAVE, G.F., MELCHIORRI, P. *ET AL.* (1973). Effects of a new polypeptide, Bombesin, on gallbladder and duodeno-jejunal mechanical activity in man. *Rendic. Gastroenterol.*, 5, 140.

ERSPAMER, V., FALCONIERI ERSPAMER, G., INSELVINI, M. *ET AL.* (1972). Occurrence of Bombesin and Alytesin in extracts of the skin of three European discoglossid frogs and pharmacological action of Beombesin on extravascular smooth muscle. *Br. J. Pharm.*, 45, 333-348.

Supersensitivity to the inhibitory effect of catecholamines on intestinal peristaltic reflex after sympathetic denervation

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Morphological and functional evidence indicates that in the intestinal musculature postganglionic sympathetic fibres make contact with both the smooth muscle cells and the intrinsic cholinergic neurons (Beani, Bianchi & Crema, 1969; Silva, Ross & Osborne, 1971). Sympathetic adrenergic transmission seems to involve, at postsynaptic sites, both α- and β-receptors on smooth muscle cells and only α-receptors at the level of cholinergic structures (Lee, 1970; Kosterlitz & Lees, 1972). Physiological sympathetic modulation of peristaltic reflex seems more likely to be accomplished indirectly through an action on the nervous pathway subserving peristaltic reflex than through a direct inhibition on the effector cells (Crema, Frigo & Lecchini, 1970).

The ability of reserpine and uptake inhibitors to alter adrenoreceptor sensitivity in longitudinal muscle is controversial (Fleming & Schmidt, 1962; Govier, Sugrue & Shore, 1969) and no attempt has been made to study the potency changes of catecholamines in inhibiting intestinal intrinsic reflex after sympathetic denervation.

Adrenergic-induced inhibition of peristaltic reflex has been investigated in the guinea-pig isolated distal colon. Quantal dose-response curves were constructed for noradrenaline (NA), isoprenaline (IPNA) and methoxamine, the observed response being the prevention of propulsion elicited by localized intraluminal distention. Papaverine was employed as a non-specific inhibitor. The rank order of activity (Table 1) in preventing peristalstic reflex was: NA > methoxamine = IPNA > papaverine. However, when the inhibitory activity was assayed in circular muscle strips, against the carbachol-induced contraction, the rank order was: IPNA > NA > papaverine > methoxamine.

Sympathetic denervation was carried out surgically by freezing the periarterial plexus of the inferior mesenteric artery and by removing the colon 10 days after. In denervated preparations the efficacy of the adrenergic agents in blocking peristalsis was significantly increased as compared with control preparations, while the activity of papaverine was not modified. The activity changes

Table 1 ED_{50} (g/ml) against peristalsis (95% fiducial limits in brackets)

Drugs	*Control*	*After denervation*	*Activity ratio (95% F.L. in brackets)*
Noradrenaline	$1.38\ (1.74\text{-}1.11) \times 10^{-7}$	$6.22\ (7.72\text{-}5.02) \times 10^{-9}$	17.82 (25.21-12.72)
Isoprenaline	$1.95\ (2.64\text{-}1.43) \times 10^{-6}$	$2.09\ (2.82\text{-}1.56) \times 10^{-7}$	9.16 (13.58-6.09)
Methoxamine	$1.56\ (2.09\text{-}1.16) \times 10^{-6}$	$1.69\ (2.16\text{-}1.33) \times 10^{-7}$	9.26 (13.5-6.36)
Papaverine	$3.70\ (6.31\text{-}2.66) \times 10^{-6}$	$3.23\ (4.47\text{-}2.22) \times 10^{-6}$	1.02 (2.14-0.32)

P values for NA *vs* IPNA and for NA *vs* methoxamine < 0.05.