Effect of gastrin I and caerulein on gastric acid secretion in rats

Anastasi, Erspamer & Endean (1967) isolated a polypeptide from the skin of an Australian amphibian *Hyla caerulea*, which they called "caerulein". Caerulein [Pyr.Gln.Asp.Tyr(SO_3H).Thr.Gly.Trp.Met.Asp.Phe–NH_2] is a dekapeptide amide (*M* 1352), whose C-terminal tetrapeptide amide is the same as that of gastrin.

Caerulein has a powerful stimulating effect on several exocrine organs of the gastrointestinal tract and has been reported to be more active on gastric acid secretion in rats and dogs than gastrin (Erspamer, Bertaccini & others, 1967). According to Mantegazza, Naimzada & Riva (1968), with caerulein "a clear dose-response relationship was not obtained due to the individual variation in sensitivity to the peptide".

In the perfused rat stomach preparation (Lai, 1964) we established a dose-response relation for synthetic human gastrin I and caerulein. The infusion time was 15 min for each dose (Fig. 1). The threshold doses were $<2 \times 10^{-12}$ mole/kg min^{-1} for caerulein and $<1 \times 10^{-10}$ mole/kg min^{-1} for gastrin I. From the dose-response curves it can be calculated that caerulein is on a molar basis about 45 times, and on a weight basis about 70 times, more active than gastrin I.

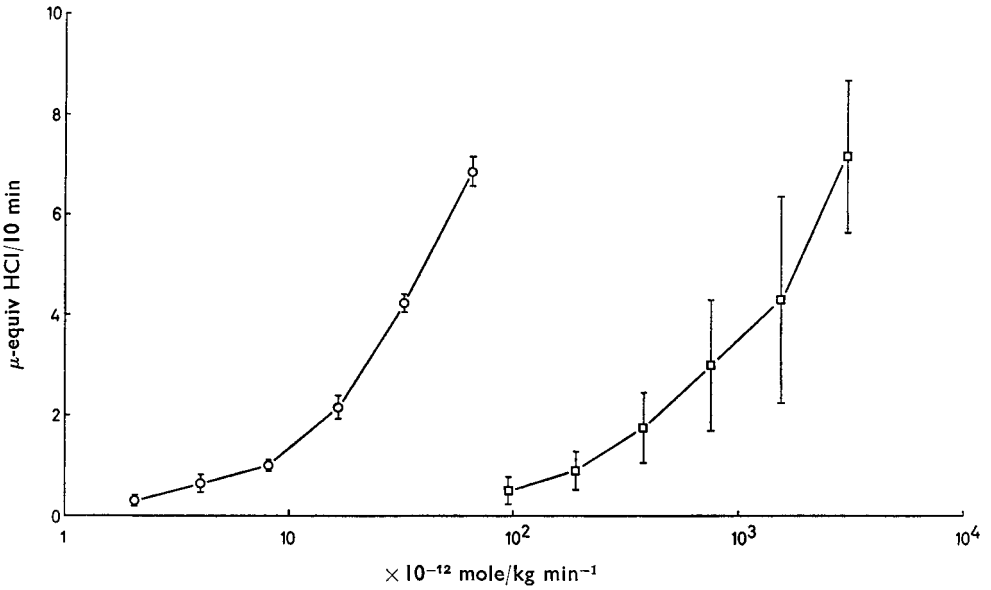

FIG. 1. Dose-response curves for synthetic human gastrin I □——□ and caerulein ○——○ in rats. Each point on the curves represents the mean value of 6 experiments in different animals. Vertical bars: s.e.

Morley, Tracy & Gregory (1965) assayed many synthetic peptides resembling gastrin I. They were unable to detect one which was more active than gastrin I. Stening & Grossman (1968) could not estimate relative potencies for gastrin I and caerulein in gastric fistula dogs since the dose-response curves were not parallel over a dose range of 1–4 μg/kg for gastrin and of 0·03–0·75 μg/kg for caerulein. 0·75 μg/kg caerulein was less active than 1 μg/kg gastrin I.

Our results demonstrate a clear dose-response relation for both gastrin I and caerulein for gastric acid secretion in rats. From the data given by Stening &

Grossman (1968) it can be calculated that in dogs caerulein is less active than gastrin I or II on a molar basis.

Gastrin I was purchased from the American Gastroenterological Association, caerulein was kindly donated by Professor Bertaccini (Parma, Italy) and supplied as a methanolic extract from the skin of *Hyla caerulea* containing 55 μg/ml caerulein.

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Department of Pharmacology,
University of Tübingen,
7400 *Tübingen,*
Wilhelmstrasse 56,
Germany.

K.-FR. SEWING
MARGITTA ALBINUS

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On the mechanism of lipomobilizing effect of chlordiazepoxide

Previously, Arrigoni Martelli & Tóth (1968) have shown that chlordiazepoxide provokes hyperglycaemia possibly through an activation of adrenergic mechanisms. The potentiation of hyperglycaemia observed in rats treated with chlordiazepoxide and theophylline or with chlordiazepoxide and cyclic 3′,5′-AMP led us to suppose that chlordiazepoxide, like theophylline (Butcher & Sutherland, 1962), interferes in some of the biochemical steps connecting the release of noradrenaline with phosphorylase activation. Since theophylline, through a blockade of phosphodiesterase, enhances lipolysis (Hynie, Krishna & Brodie, 1966), we decided to examine the effects of chlordiazepoxide on free fatty acid mobilization.

Female albino rats, Wistar strain, weighing about 250 g were used. Plasma free fatty acids (FFA) were determined according to Dole (1966). The experimental design and the results obtained are reported in Table 1. Chlordiazepoxide (40 mg/kg, i.p.) produced a sustained elevation of the plasma FFA levels; a similar effect was elicited by theophylline (20 mg/kg, i.p.).

The lipomobilizing effect of noradrenaline was potentiated by pretreatment of rats with chlordiazepoxide or with theophylline. Cyclic 3′,5′-AMP (10 mg/kg, i.p.) had no effect on plasma FFA levels. When the same dose was given to rats pretreated with chlordiazepoxide the FFA levels rose about 3-fold. Likewise, in rats pretreated with theophylline, cyclic 3′, 5′-AMP produced a significant elevation of plasma FFA. The