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Effect of Big and Little Gastrins on Pancreatic and Gastric Secretion (40322)

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Gastrin exists in several molecular forms, two of which, big gastrin (G34) and little gastrin (G17), account for most of the gastrin in the circulation (1). The molar concentration of G34 in blood plasma is about twice that of G17. Infusion of equimolar doses of exogenous G34 and G17 produces approximately equal gastric acid secretory responses but leads to molar blood concentrations of G34 about five to seven times greater than G17, reflecting the slower removal of G34 from the circulation.

It is not known whether the different molecular forms of gastrin have different relative potencies for various target organs. To examine this question we studied simultaneously the gastric acid and pancreatic protein secretory responses to G34 and G17 in dogs with gastric and pancreatic fistulas. The dog is favorable for such studies since in this species the doses of gastrin needed to stimulate pancreatic protein secretion and gastric acid secretion are in the same range (2).

Materials and Methods. Natural human unsulfated little gastrin (G17-I) and natural porcine sulfated big gastrin (G34-II) were kind gifts of Professor R. A. Gregory and Doctor H. J. Tracy, University of Liverpool, England. Cholecystokinin (CCK), 20% pure, was purchased from the G.I.H. Research Unit, Karolinska Institutet, Stockholm, Sweden.

Animals. Four dogs weighing 20 to 24 kg were prepared with a Thomas gastric fistula (GF) and a pancreatic fistula (PF) by a modified Herrera technique (3). Studies were started no sooner than 4 weeks after surgery. Food but not water was withheld for 18 hr before each test. The interval between tests was at least 48 hr.

Experiments. NaCl (0.15 *M*) was infused intravenously into a leg vein at 30 ml hr^{-1}. The peptides were added to the saline infusion to give the required doses (25, 50, 100, 200, 400, 800, and 1600 pmol kg^{-1} hr^{-1} of gastrins and 53, 106, 213, 425, and 851 pmol kg^{-1} hr^{-1} of CCK). Each dose was given during 45 min starting with the lowest dose and doubling it until the highest dose was given. Gastric and pancreatic juices were collected continuously and separated into 15-min samples. Volumes were measured to the nearest 0.1 ml. Acid concentration was determined by titrating 0.2-ml samples with 0.2 *M* NaOH to pH 7 on an automatic titrator (Radiometer, Copenhagen). Total protein concentration was measured spectrophotometrically at 280 nm, using bovine serum albumin as standard. The responses were expressed as the mean of the last two 15-min collections from each dose. Two tests were done with each stimulant in each of three dogs and a fourth dog had one test with each stimulant. Basals were subtracted from each 15-min sample, and results of the two tests in each dog were averaged. Before averaging, the square root of acid output was computed and used in all analyses to make variances more uniform and straighten out the response curves.

Results. G34-II and G17-I were found to be approximately equipotent in stimulating gastric acid secretion (Fig. 1), confirming earlier studies (6). The relative potency of G17 with respect to G34 was 0.7 with 95% limits of 0.4 to 1.5 using doses 100, 200, and 400 for G17 and 50, 100, and 200 for G34. G34-II and G17-I appeared to differ from each other in potency in stimulating pancreatic protein secretion (Fig. 2). Relative potency of G17 with respect to G34 was about 0.3 to 0.4, depending on the doses used, with limits of about 0.1 to 0.6. The response to CCK is shown for comparison. CCK did not stimulate acid secretion. Relative potency of CCK to G17 was 1.5 (0.99 to 2.4) and to G34 was 0.5 (0.3 to 0.7).

The data do not, however, show a significant difference in selectivity for gastric acid and pancreatic protein secretion between G17 and G34. Comparison of the relative potency of G17 to G34 for acid secretion to that for protein secretion was made by computing

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potency of G17 to G34 for each dog separately for acid and for protein. The mean differences ± SE for relative potency for acid secretion minus relative potency for protein secretion were 0.49 ± 0.29 and 0.58 ± 0.30 depending on the G34 doses used for estimating protein potency. These differences were not significant by paired t test. As a further comparison, we computed the equation: protein = $a + b$ (acid)$^{\frac{1}{2}}$ for each dog for each test. The slopes were similar for G17 and G34. Figure 3 shows means for pancreatic protein response plotted against gastric acid response.

Discussion. These studies show that the potency of G34 relative to G17 is not significantly different for gastric acid and pancreatic protein secretion, indicating that one of these gastrins is not more selective than the other for these targets. Although the present results do not show a large difference in selectivity, further studies with other gastrins or other targets or in other species might reveal such differences.

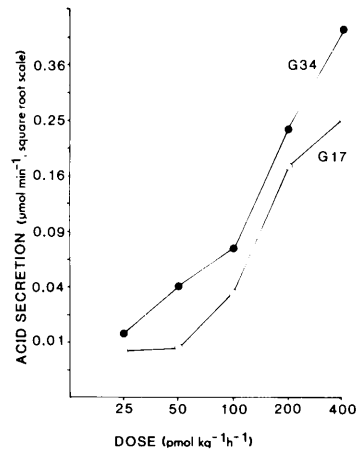

FIG. 1. Acid secretion in response to graded doses of G34 and G17.

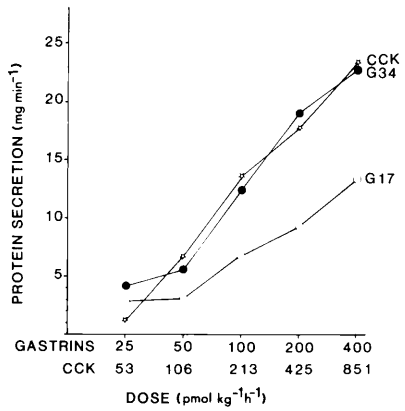

FIG. 2. Pancreatic protein secretion in response to graded doses of G34, G17, and CCK.

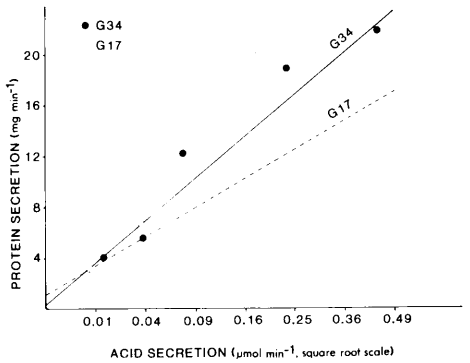

FIG. 3. Linear regression of protein secretion on acid secretion.

Summary. In dogs with gastric and pancreatic fistulas the potency of porcine big gastrin (G34-II) relative to human little gastrin (G17-I) was not significantly different for stimulation of gastric acid and pancreatic protein secretion.

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