J. Physiol. (1982), **325**, *pp.* 419–421
Printed in Great Britain

COMPARISON OF GASTRIN BIOACTIVITY AND IMMUNOREACTIVITY OF ANTRAL EXTRACTS FROM MAN, PIG AND CAT

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(*Received 29 September 1981*)

SUMMARY

1. The gastrin bioactivity and immunoreactivities of human, porcine and feline antral extracts were compared.
2. Human and porcine had similar activities but cat had much less.
3. The ratio of gastrin bioactivity to immunoreactivity was much greater with feline antral extracts than with human and porcine extracts.

INTRODUCTION

Radioimmunoassay has helped in the understanding of hormonal control of the stomach but there is always the problem that results expressed as immunoreactivity may be completely different from bioactivity. Radioimmunoassay is nearly always the only method of hormone assay for blood samples. Tissue extracts can be bioassayed easily but they must be diluted several times to be measured by radioimmunoassay.

Here we compare the bioactivities and immunoreactivities of partially purified extracts of three human, nine pig and twenty-six cat antra.

METHODS

The extracts consisted of boiling water extracts of homogenized antral mucosa which were filtered and extracted with acetone and then ether as described by Blair, Harper, Lake, Reed & Scratcherd (1961) to produce a histamine-free gastrin-containing extract. The bioactivity was measured in anaesthetized cats (Blair & Wood, 1968; Blair, Keenlyside, Newell, Reed & Richardson, 1968) and this bioassay could detect 1 ng ml^{-1} synthetic human gastrin 17NS. Gastrin activity of antral extracts was also measured by radioimmunoassay. The ^{125}I-labelled gastrin was prepared and used as described by Blair, Grund, Reed, Sanders, Sanger & Shaw (1975). The detection limit of the assay varied from 21 to 41 pg ml serum because of differences in the slopes of the standard curves. The antral extracts were run on Sephadex G50 superfine columns (Blair, Grund, Lund, Piercy, Reed, Sanders, Shale, Shaw & Wilkinson, 1977). The fractions were estimated by an assay which used ^{125}I-labelled SHG17NS purified by AE cellulose chromatography (Rehfeld & Stadil, 1972; Blair *et al.* 1977). The detection limit of this assay was 3·6 pg ml^{-1}.

The antibody R6/4.2.72 recognizes SCatG17NS, SHG17NS, NHG17NS, NPG17NS, NPG17S, SHG13NS, SHG15NS, SHG16NS and NHG34NS equally but is 417 times less sensitive to G4.

RESULTS

The bioactivity and immunoreactivity of partially purified antral extracts of human and porcine tissue were similar, with slightly greater bioactivity than immunoreactivity (Table 1). The cat antral extracts had much less gastrin activity both by bioassay and immunoassay compared with the porcine and human extracts The ratio of bioactivity to immunoreactivity was much greater with the cat extracts. Nearly all the gastrin immunoreactivity eluted from chromatography columns in the same position as gastrin 17.

TABLE 1. Comparison of gastrin bioactivity and immunoreactivity of partially purified antral extracts

Source		No of antra	Bioactivity (μg SHG17NS g^{-1} mucosa)	Immunoreactivity (μg SHG17NS g^{-1} mucosa)	Ratio of bioactivity to immunoreactivity
Human	1	1	15·1	6·5	2·32
	2	1	3·1	1·85	1·67
	3	1	9·2	5·85	1·57
Porcine	1	9	3·83	1·37	2·9
Cat	1	14	0·36	0·023	15·7
	2	12	0·94	0·132	7·2

DISCUSSION

These results are different from those of Nilsson, Yalow & Berson (1973) who reported the concentrations of immunoreactive gastrin found in aqueous extracts of human, pig and cat antra. In their results, porcine antra had the highest gastrin contents by immunoassay; cat and human antra had equal concentrations but less than porcine. However they used porcine gastrin as their standard whereas we used synthetic human gastrin 17NS as standard both in the bioassay and radioimmunossay.

That the cat antral extracts contained less biologically active gastrin than porcine or human extracts is at first sight surprising because the samples were bioassayed in cats. These results are confirmed by the immunossay data which also show that the cat antral extracts have less immunoreactive gastrin (Table 1), despite the use of an antibody which cross-reacts equally with human and feline gastrin 17NS (Blair *et al.* 1977). Nevertheless,the ratio of bioactivity to immunoreactivity was much greater with the cat antral extracts than with the porcine and human extracts (Table 1). The antral extracts may contain differing amounts of the C-terminal tetrapeptide of gastrin G4. This is not easily detected by the gastrin antibody used here nor is it as biologically active as gastrin 17. The ratio of bioactivity to immunoreactivity of G4 is about 35 (Blair, Hirst, Lund, Reed, Sanders & Shaw, 1980). If the cat antral extracts contain larger proportions of G4 than the human or porcine extracts then this might account for the higher rate of bioactivity to immunoreactivity (Table 1). The G4 would not be detected in column chromatography because the antibody cross-reacts about 420 times less with G4.

The gastrin in the cat antral extracts could have a different structure compared

with the human and porcine materials though we have not sequenced the gastrins. Kenner & Sheppard (1973) reported that cat gastrin 17NS has alanine at position 10 whereas human and porcine gastrin 17 have glutamic acid, porcine gastrin has methionine at position 5 and human and feline gastrins have leucine. The presence of alanine at position 10 in cat gastrin may conceivably account for its apparently greater bioactivity in the cat. However, Blair *et al.* (1980) have shown that, in the cat, synthetic cat gastrin 17NS in low doses has similar activity to synthetic human gastrin 17NS.

It would appear from these data that natural cat gastrin is more biologically active in the cat than human or porcine gastrins.

We gratefully acknowledge the technical assistance of Mrs E. Nicholson and the financial support of the North of England Cancer Research Campaign and The Royal Society to develop the assays.

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