

Do β adrenergic agents directly stimulate gastrin secretion?

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Summary. Isoproterenol if given during methacholine stimulation in dogs neither depresses gastric secretion nor elevates serum gastrin. Therefore, we conclude that β adrenergics (isoproterenol) are unlikely to be direct liberators of gastrin, but raise serum gastrin indirectly only if they inhibit gastric secretion.

It has been suggested that β adrenergic agents stimulate the release of gastrin from the pyloric G cells because administration of epinephrine raised serum gastrin in anesthetized dogs². Phenoxybenzamine was found to depress the elevated serum gastrin seen in patients with pheochromocytoma².

Another explanation for this suggested itself to us based on the fact that many agents and procedures which depress gastrin stimulated gastric secretion also elevate serum gastrin. The extreme example of this is the elevated serum gastrin in achlorhydria³. Our hypothesis is that the depressed parietal cell itself signals the G cell to produce more gastrin. Isoproterenol does depress gastrin stimulated secretion, and propranolol inhibits the decrease, however, isoproterenol does not depress cholinergically stimulated gastric secretion⁴. If isoproterenol causes liberation of gastrin, serum levels should rise whether isoproterenol is administered, alone, with gastrin or with methacholine. If

gastrin levels do not rise when isoproterenol is given with methacholine this then is an argument in favour of the notion that the increase in serum gastrin is a consequence of inhibition of fundic secretion.

Methods. In 4 fasted, conscious dogs, with Heidenhain pouches, innervated pyloric pouches and gastric fistulae, methacholine was administered i.v. at 4 μ g/min for 1 h. Then isoproterenol was added at 0.25 μ g/min for a further h. Collections were at 10 min intervals. The last 3 collections of each period were used for calculating group means and paired t. Pouch secretion was collected by the washout method, pepsin was determined by Anson⁵ technique and gastrin by Cataland et al.⁶ method.

Results. It will be noted from the table that gastrin levels in control experiments with methacholine are not significantly different from those with added isoproterenol. The dose of isoproterenol used invariably produced a marked depression in pentagastrin stimulated secretion, but not (see table) in cholinergically promoted secretion.

	Pouch H ⁺ mEq	Pepsin units	Fistula H ⁺ mEq	Pepsin units	Gastrin μ g/ml
Control	0.2871	115.59	1.1861	415.6	22.25
methacholine	$\pm 0.0662 \pm 11.65$		$\pm 0.4366 \pm 169.5$		± 1.493
Methacholine	0.2766	90.56	1.6421	341.5	28.50
plus isoproterenol	$\pm 0.0533 \pm 25.17$		$\pm 0.6946 \pm 142.2$		± 3.775

Each figure group mean of 4 experiments in 4 dogs \pm SE.

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- 2 J. R. Hayes, J. Ardill, T.L. Kennedy, R.G. Shanks and K.D. Buchanan, *Lancet* *1*, 819 (1972).
- 3 J. Hansky, *Med. Clins N. Am.* *58*, 1217 (1974).
- 4 D.F. Magee, *Proc. Soc. exp. Biol. Med.* *151*, 659 (1976).
- 5 M. L. Anson, *J. gen. Physiol.* *22*, 79 (1938).
- 6 S. Cataland, T.M. O'Dorisio, R. Brooks and G.S. Mekhjian, *Gastroenterology* *73*, 19 (1977).

Profound hypothermia in golden hamsters (*Mesocricetus auratus*) induced by serotonergic potentiating and noradrenergic inhibiting drugs

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Summary. Profound hypothermia (6°C) was induced in cold exposed golden hamsters (*Mesocricetus auratus*) by a combination of drugs that potentiate brain serotonergic activity (fluoxetine and pargyline) and inhibit noradrenergic activity (alpha-methyl-p-tyrosine). Individual drugs and combinations of 2 were ineffective.

Serotonin and norepinephrine are neurotransmitters involved in temperature regulation²⁻⁵. Drugs that influence serotonin and norepinephrine synthesis or activity modify body temperature by as much as 6°C. These drugs include p-chlorophenylalanine (PCPA), an inhibitor of serotonin synthesis; fluoxetine, a potentiator of serotonergic activity; alpha-methyl-p-tyrosine (α -MPT), an inhibitor of norepinephrine synthesis; pargyline, a potentiator of both serotonin and norepinephrine. Inhibition of serotonin synthesis with PCPA elevated the body temperature of rats^{6,7}, whereas enhancement of serotonergic activity by fluoxetine⁸ or pargyline⁹ lowered the temperature. Inhibition of norepinephrine synthesis with α -MPT also slightly lowered body temperature of rats¹⁰. Because serotonergic and nora-

drenergic mechanisms may have antagonistic effects, drug-induced alteration in one might be compensated by the other, thereby limiting the hypothermia. Therefore, drugs that simultaneously stimulate serotonergic and inhibit noradrenergic mechanisms should produce a deep hypothermia (figure).

Adult golden hamsters, *Mesocricetus auratus* (100-150 g b. wt) of mixed sexes, were maintained on a 10-h daily photoperiod (07.00-17.00 h). From March 15 to May 16, 1977, on various dates, a total of 73 hamsters were injected i.p. at 13.00 h with one or more of the following drugs: 10 mg α -MPT (Sigma Chemical Company, St. Louis) in 0.2 ml, 8 mg pargyline (Sigma) in 0.2 ml, 5 mg fluoxetine (Lilly Research Laboratories, Indianapolis) in 0.5 ml, and