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Galanin Inhibits Rat Pancreatic Amylase Release via Cholinergic Suppression

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FLOWE, K. M., K. M. LALLY AND M. W. MULHOLLAND. *Galanin inhibits rat pancreatic amylase release via cholinergic suppression.* PEPTIDES **13**(3) 487–492, 1992.—The effects of galanin on pancreatic exocrine function were examined using rat pancreatic tissues. In anesthetized rats, galanin (40 μg/kg/h) decreased amylase secretion stimulated by 2-deoxy glucose (5.8 ± 0.1 vs. 3.1 ± 0.1 times basal) and cholecystokinin octapeptide (21.5 ± 0.6 vs. 16.8 ± 0.5), while not inhibiting bethanechol-stimulated secretion. In dispersed acini, there was no effect of galanin alone (10^{-8} to 10^{-13} M) on amylase release, nor did galanin (10^{-6} or 10^{-8} M) coincubation affect amylase release stimulated by bethanechol (10^{-3} to 10^{-7} M) or CCK-8 (10^{-8} to 10^{-13} M). Using pancreatic lobules, coincubation with galanin (10^{-6} M) suppressed 75 mM KCl-stimulated amylase secretion and ACh release (10.1 ± 0.6% vs. 7.3 ± 0.4%). Veratridine-stimulated (10^{-4} M) amylase secretion and ACh release (12.4 ± 1.7% vs. 8.5 ± 0.7%) were similarly diminished.

Amylase Acetylcholine Urethane anesthesia Acini Lobules Rats Inbred strains

GALANIN is a 29 amino acid peptide that was initially isolated from the porcine intestine (7). Galanin shares only minor sequence homology with other known peptides and is expressed in both central and peripheral nervous systems (7,15,27). Galanin-immunoreactive nerve fibers are distributed widely throughout the digestive tract of a number of mammalian species (16). The peptide has been localized immunocytochemically to nerve fibers within both the endocrine and the exocrine portions of the pancreas (9).

To date, investigation of the pancreatic effects of galanin have focused mainly on the endocrine portion of the gland, although prior studies have suggested that galanin may inhibit exocrine function in rats and dogs (1,13,31). In rats and dogs, galanin inhibits the release of insulin and somatostatin and stimulates release of glucagon (10,17). Galanin is released from intrapancreatic nerves by mixed pancreatic nerve stimulation in concentrations that are sufficient to inhibit insulin secretion (11). Because of these effects, and because the peptide is localized to nerves innervating acinar tissues, we investigated the effects of galanin on exocrine pancreatic function.

The current study sought to employ in vivo and in vitro techniques to investigate potential inhibitory effects of galanin in the rat pancreas. The general goals of the investigation were to: 1) determine if galanin is an inhibitor in vivo of stimulated pancreatic exocrine function in rats 2) determine if inhibitory actions are exerted directly on the acinar cell; and 3) examine the ability of galanin to affect exocrine function by modulation of intrapancreatic neurotransmission. In order to achieve these goals, experiments were performed to: 1) determine if galanin inhibits stimulated amylase secretion in anesthetized rats; 2) determine if galanin affects amylase release from purified acini; and 3) determine if galanin decreases amylase secretion and acetylcholine release from pancreatic lobules, containing islet tissues and intrapancreatic neurons, in addition to acini.

METHOD

Supplies

Rat galanin and cholecystokinin octapeptide (CCK-8) were obtained from Peninsula Laboratories, Belmont, CA. Peptides were reconstituted in 1% (w/v) bovine serum albumin to a concentration of 10^{-4} M. Aliquoted peptides were stored at −40°C until use. Collagenase, 2-deoxy glucose (2-DG), bethanechol, atropine, veratridine, tetrodotoxin, bovine serum albumin (BSA), soybean trypsin inhibitor, and aprotinin were purchased from Sigma Chemical Company, St. Louis, MO. [^{3}H]Methyl choline chloride was purchased from New England Nuclear, Boston, MA. [^{14}C]Acetylcholine was purchased from Amersham, Arlington Heights, IL.

In Vivo Studies

Male Sprague–Dawley rats from Charles River (Wilmington, MA), weighing 200–300 g, were used for all experiments. Animals were cared for under specific pathogen-free guidelines prior to use, and housed at constant temperature with alternating light-dark cycles of 12 h. Rats received water ad lib and were fed Purina Rodent Laboratory Chow. After an overnight fast, during

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which they were allowed water ad lib, rats were weighed and given an intraperitoneal injection of urethane, 1.25 mg/g body weight. Through a short midline laparotomy incision, the entrance of the bile pancreatic duct into the duodenum was cannulated with polyethylene tubing (PE-50, Becton–Dickinson, Parsippany, NJ) for total diversion of endogenous bile pancreatic secretion. A duodenostomy tube was placed to allow reinfusion of previously harvested bile pancreatic juice. This juice was collected from other male Sprague–Dawley rats and stored at −20°C until reinfused. Intravenous access was secured via the femoral veins and normal saline was infused at a rate of 1.6 cc/h throughout the experiment. A tracheostomy was placed to insure a patent airway.

After bile pancreatic flow was demonstrated, serial collection at 10-min intervals was maintained for 120 min. The volume of secretion for each interval was measured gravimetrically. Amylase activity was measured by the method of Bernfeld (6). All assays were performed in duplicate.

Inhibitory effects were examined by infusing galanin (40 μg/kg/h) continuously starting before 2-DG (100 mg/kg subcutaneously), bethanechol (3 mg/kg/h intravenously), or CCK-8 (0.25 μg/kg/h intravenously).

In Vitro Studies

Dispersed acini. After an overnight fast, rats were weighed and sacrificed. The pancreas was harvested; adherent fat and lymphatic tissue was removed. The gland was cut into 12 to 15 pieces and placed in chilled Krebs ringer HEPES buffer, pH 7.4. The buffer contained (each in mM) NaCl 103, KCl 4.8, KH_2PO_4 1.2, glutamine 2, glucose 5, HEPES 25, $CaCl_2$ 1.3, and $MgSO_4$, 0.6. Also included were minimal essential media amino acids, 1% (v/v) (GIBCO BRL, Gaithersburg, MD), nonessential amino acids, 0.5% (v/v) (GIBCO), and BSA, 0.2% (w/v). The pancreatic tissues were dispersed with collagenase as previously described (4,19,29). Briefly, under 100% oxygen, three 15-min collagenase (0.1 mg/ml buffer) digestions were performed at 37°C (with fresh buffer instilled between each digestion), and acini were then dispersed by trituration with pipettes of decreasing tip diameter. Acini were diluted with buffer and aliquoted into tubes containing galanin alone, or into tubes containing stimulant plus either galanin or equal volume of 1% (w/v) BSA (control). The concentration range used for galanin alone was 10^{-8} to 10^{-13} M. Stimulant concentration ranges used were 10^{-7} to 10^{-3} M for bethanechol, and 10^{-13} to 10^{-8} M for cholecystokinin. Galanin concentration in the presence of stimulant was either 10^{-8} M or 10^{-6} M. After incubation at 37°C for 30 min, the tubes were chilled and centrifuged. Amylase activity was determined in duplicate for the media and for the acini. Acini were lysed with a 0.1% Triton X-100 buffer, pH 8.0, containing 0.01 M NaH_2PO_4 and 0.1% BSA (w/v). Amylase release was expressed as percentage of total cellular content. Mean percent of total amylase release from duplicate incubations for each rat was used for statistical analysis.

Isolated lobules. Amylase release. A technique modified from Scheele and Palade (24) was used for isolated lobule studies. After an overnight fast, rats were weighed and sacrificed. The pancreas was harvested and pinned to a wax plate. Using 2.0 power optical magnification, individual lobules from throughout the pancreas were identified and excised, taking special care not to damage the pancreatic tissue with instruments. Lobules were kept in an oxygenated HEPES-bicarbonate buffer, pH 7.4, during harvest. Buffer contained (each in mM) NaCl 103, KCl 4.7, $CaCl_2$ 2.6, $MgCl_2$ 1.1, NaH_2PO_4 1.2, glucose 11, HEPES 25, $NaHCO_3$ 25, and L-glutamine 2, as well as minimal essential

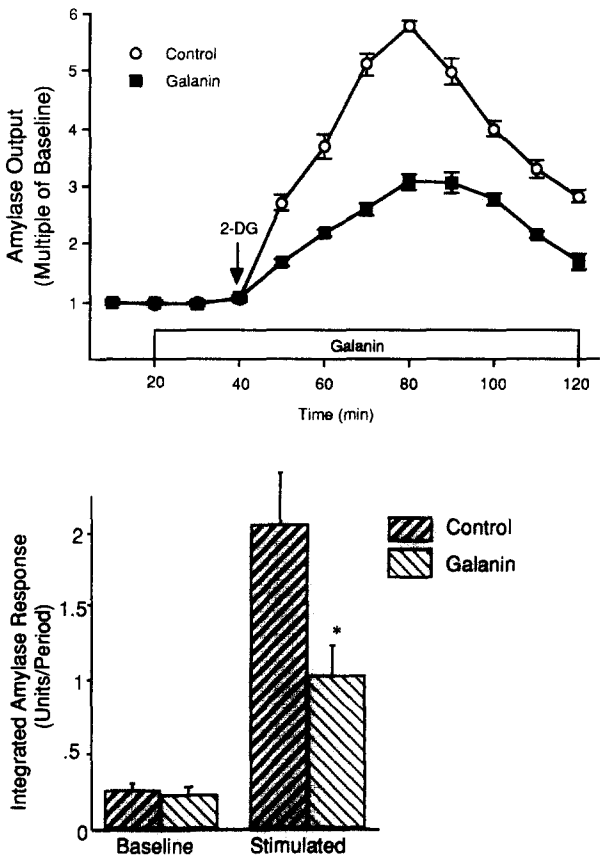

FIG. 1. Effects of galanin on 2-deoxy glucose (2-DG)-stimulated exocrine pancreatic function. Galanin (40 μg/kg/h) was infused from 20–120 min, and 2-DG (100 mg/kg) was injected subcutaneously at 40 min. All values for galanin-treated animals were significantly different from controls from 50–120 min for amylase release. Integrated amylase secretion was significantly decreased for rats receiving galanin infusion and 2-DG injection. For both groups, $n = 6$.

amino acids, 2% (v/v), BSA, 1% (w/v), soybean trypsin inhibitor, 0.1% (w/v), and aprotinin 680 KIU/ml. Four lobules were added to each incubation flask. The flasks contained buffer plus atropine 10^{-5} M, tetrodotoxin 10^{-5} M, galanin 10^{-8} or 10^{-6} M, or above medium alone. After a 30-min incubation at 37°C under a 95% O_2/5% CO_2 atmosphere, the lobules were washed. A second incubation was then performed including agonists (75 mM KCl or veratridine 10^{-4} M) in the presence or absence of the above antagonists or galanin. Two control flasks were prepared with no antagonist or agonist for each experiment. Lobules and media were separated, and lobules were mechanically homogenized in a 1% Triton X-100 buffer, pH 8.0, containing $CaCl_2$ 2.5 mM, HEPES 25 mM, and KCl 0.1 M. The media and diluted homogenate were analyzed for amylase content. Mean percentage of total cellular amylase released during incubations for each rat was used for statistical analysis.

Tritiated acetylcholine release. Acetylcholine (ACh) release from isolated lobules was determined using [^{3}H]ACh as a marker. The same incubation buffer was used as in other lobule studies, with the addition of physostigmine (50 μM). Two lobules in 1 ml buffer per flask were incubated with 0.2 μM [^{3}H]methyl choline chloride (specific activity, 88 Ci/mmol) for 1 hour at 37°C under 95%O_2/5%CO_2. After initial radiolabeling, lobules were washed twice with fresh buffer containing hemicholinium (10

μM). A 30-min period for equilibration was followed by incubation in buffer (30 min, 37°C) with veratridine (10^{-4} M) or KCl (75 mM). After removal of media, lobules were solubilized with 1 ml Solvable (Du Pont) for 2 h at 55°C. Glacial acetic acid (100 μl) was then added to the solubilized tissue, and finally 10 ml Ecolite was added for scintillation counting. Measured counts per minute was used for analysis. Released tritium was confirmed to be acetylcholine by separation on a 0.5 × 50 cm ion exchange column (Bio-Rex 70, 200–400 mesh, Bio-Rad) eluted with Na_2HPO_4 0.1 M at pH 7.0 (14).

Statistical Methods

Two-way analysis of variance was performed on all in vivo and acinar preparation results, and when significant differences ($p < 0.05$) were noted, individual Bonferroni t-tests were performed on analogous pairs to ascertain differences. Lobule preparation results were analyzed with paired Student's *t*-tests. All results are reported as mean ± SEM.

RESULTS

In Vivo Effect of Galanin on Pancreatic Exocrine Function

Intravenous infusion of galanin (40 μg/kg/h) did not affect basal amylase output from anesthetized rats (Fig. 1). Administration of 2-deoxy glucose (100 mg/kg subcutaneously) significantly stimulated amylase release. Increases were noted within 10 min of injection, were maximum by 40 min, and remained elevated relative to baseline throughout the entire study period. 2-Deoxy glucose-stimulated amylase secretion was significantly reduced by intravenous infusion of galanin, with inhibitory effects noted throughout the 80-min experimental period, $F(1, 11) = 36.6$, $p < 0.001$ (Fig. 1). Maximal amylase secretion was 5.8 ± 0.1 times baseline for control rats, and 3.1 ± 0.1 times baseline for galanin-treated rats, a 47% reduction relative to control. Total integrated amylase secretion was calculated for the 80-min experimental period for both galanin infusion and control groups. Integrated amylase secretion was significantly decreased in the group of rats exposed to galanin, $F(1, 1) = 7.14$, $p < 0.02$ (Fig. 1).

Pancreatic secretory response to intravenous CCK-8 (0.25 μg/kg/h) was significantly increased throughout the experimental period (Fig. 2). Continuous intravenous infusion of galanin (40 μg/kg/min) produced significant suppression of CCK-8-stimulated exocrine secretion during the 80-min experimental period, $F(1, 11) = 12.2$, $p < 0.001$ (Fig. 2). Integrated amylase secretion following CCK stimulation was decreased by 41% in animals receiving galanin coinfusion, $F(1, 1) = 3.45$, $p = 0.07$.

Bethanechol infusion (3 mg/kg/h) also stimulated pancreatic amylase secretion, with significant increases noted by 10 min and plateau values by 30 min. Continuous intravenous infusion of galanin (40 μg/kg/h) during bethanechol infusion resulted in no significant suppression of integrated amylase output, $F(1, 1) = 0.51$, $p = 0.48$ (Fig. 3).

In Vitro Effects of Galanin on Pancreatic Exocrine Function

Dispersed acini. Galanin had no effect on basal amylase release from dispersed acini. Basal amylase release was 4.5 ± 0.6% of total cellular content and incubation of acini in the presence of varying concentrations of galanin (10^{-13} to 10^{-8} M) produced no significant change (Table 1).

Exposure of acini to incremental concentrations of bethanechol (10^{-7} to 10^{-3} M) resulted in a dose-dependent increase in amylase release (Fig. 4). Maximal release was noted at 3 × 10^{-5} M bethanechol. Coincubation of bethanechol with galanin

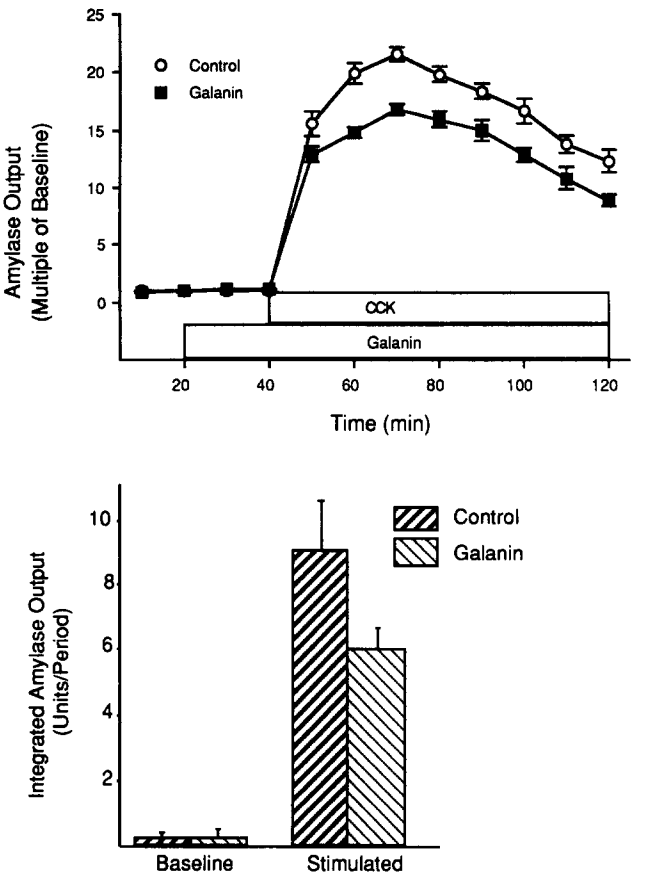

FIG. 2. Effects of galanin on cholecystokinin octapeptide (CCK-8)-stimulated exocrine pancreatic function. Galanin (40 μg/kg/h) was infused from 20–120 min, and CCK-8 (0.25 μg/kg/h) was infused from 40–120 min. All values beyond 40 min are significantly different from control. Decreases in integrated amylase secretion did not achieve statistical significance ($p = 0.07$); $n = 6$ for both groups.

(10^{-8} or 10^{-6} M) produced no change in amylase release relative to bethanechol alone, $F(2,9) = 0.24$, $p = 0.99$. Amylase release from acini incubated with cholecystokinin (10^{-13} to 10^{-8} M) increased in a dose-dependent fashion, with maximal release at 10^{-10} M. Coincubation with galanin (10^{-8} or 10^{-6} M) had no significant effect on CCK-8 stimulated amylase release, $F(2, 11) = 1.4$, $p = 0.12$.

Isolated lobules. Amylase release. Basal amylase release from isolated lobules averaged 2.8 ± 0.5% of tissue content. Lobules incubated with KCl (75 mM) released 4.6 ± 0.4% of total amylase content (Fig. 5). Release in response to potassium was significantly inhibited by preincubation of lobules with galanin (10^{-6} M). Atropine (10^{-5} M) completely abolished potassium-stimulated amylase release.

Lobules incubated with veratridine (10^{-4} M) released 5.9 ± 0.6% of total cellular amylase. Veratridine-stimulated amylase release was significantly inhibited by preincubation with galanin (10^{-6} M). Preincubation with atropine (10^{-5} M) significantly suppressed amylase release, while tetrodotoxin (10^{-5} M) resulted in complete inhibition of veratridine-stimulated amylase release.

Tritiated acetylcholine release. Basal [^{3}H]ACh release from pancreatic lobules was 5.5 ± 0.5% of total tissue content. When stimulated by KCl (75 mM), [^{3}H]ACh release was increased to 10.1 ± 0.6% (Fig. 6). Galanin 10^{-6} M significantly inhibited potassium-stimulated [^{3}H]ACh release. Incubation of labeled

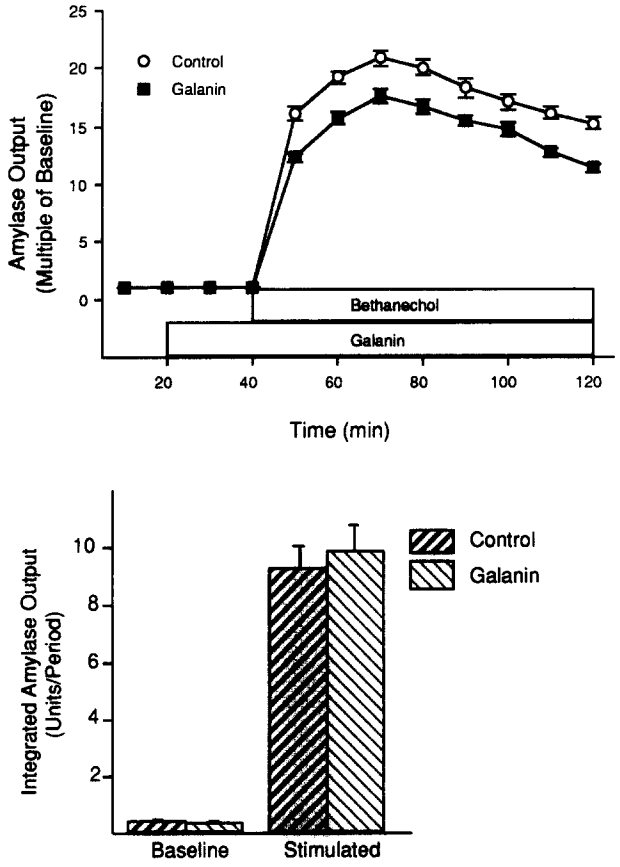

FIG. 3. Effects of galanin on bethanechol-stimulated exocrine pancreatic function. Galanin (40 μg/kg/h) was infused from 20–120 min, and bethanechol (3 mg/kg/h) was infused from 40–120 min. The lower panel illustrates integrated amylase secretion in the presence or absence of galanin. $n = 6$ for both groups.

lobules with veratridine (10^{-4} M) increased [^{3}H]ACh release to 12.4 ± 1.7%. Stimulated release of ACh was significantly inhibited by galanin 10^{-6} M. Tetrodotoxin further inhibited veratridine-stimulated [^{3}H]ACh release.

DISCUSSION

The results of the current study suggest that galanin is an inhibitor of rat pancreatic exocrine secretion in vivo. When administered by continuous infusion, galanin caused sustained inhibition of pancreatic exocrine secretion stimulated by 2-DG or CCK-8. Yagci and coworkers have also recently reported that galanin inhibits CCK-8-stimulated pancreatic secretin in the anesthetized rat (31). In the present investigation, bethanechol-stimulated amylase secretion was not affected by galanin. Inhibitory actions do not appear to be exerted directly upon the acinar cell, as galanin had no inhibitory activity in vitro upon dispersed acini. Galanin did not affect basal amylase release from dispersed acini, and amylase release in dispersed acini stimulated by bethanechol or CCK-8 incubation was not altered by coincubation with galanin. For dispersed acini, the current results differ significantly from those of Ahren and coworkers (1). These investigators have previously reported that galanin inhibits amylase release when isolated rat acini were exposed to CCK-8 in concentrations similar to those used in the current study.

The current studies utilizing pancreatic lobules suggest that inhibition of pancreatic exocrine function by galanin may be

TABLE 1

DISPERSED ACINI INCUBATED WITH GALANIN OVER A RANGE OF CONCENTRATIONS

Galanin Concentration	Amylase Released*	SEM
Zero (control)	4.5	0.6
1×10^{-13} M	4.9	0.4
3×10^{-13} M	5.4	0.6
1×10^{-12} M	4.9	0.5
3×10^{-12} M	5.2	0.2
1×10^{-11} M	5.4	0.5
3×10^{-11} M	5.6	0.5
1×10^{-10} M	5.7	0.5
3×10^{-10} M	5.5	0.5
1×10^{-9} M	5.5	0.6
3×10^{-9} M	5.5	0.6
1×10^{-8} M	5.4	0.7

* Expressed as mean percentage of total cellular amylase released into the media.

mediated, at least in part, by modulation of intrapancreatic cholinergic neurotransmission. Galanin significantly decreased the release of amylase when pancreatic lobules, which contain intrapancreatic nerve terminals as well as islets, were exposed to the depolarizing agents veratridine or KCl. In separate experi-

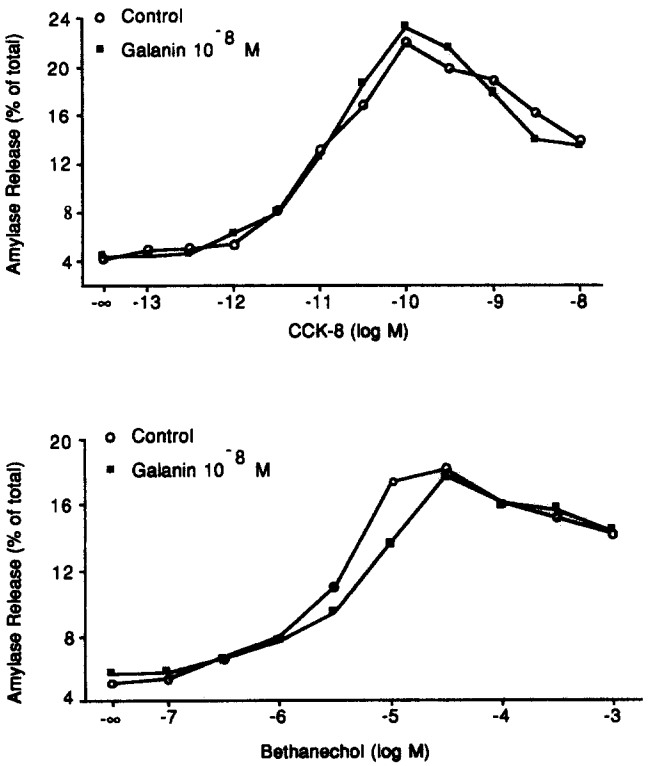

FIG. 4. Amylase release from dispersed acini incubated with bethanechol or cholecystokinin octapeptide (CCK-8) in the absence or presence of galanin 10^{-8} M. Bethanechol concentrations ranged from 10^{-7} to 10^{-3} M and CCK-8 concentrations ranged from 10^{-13} to to 10^{-8} M. Galanin at 10^{-6} M produced similar results. All assays were performed in duplicate. $n = 6$ for each group. Error bars are omitted for clarity; all SEMs < 10%.

ments, decreased release of [^{3}H]ACh from pancreatic lobules in response to stimulation by these agonists was also noted with galanin coincubation.

The ability of galanin to affect pancreatic function indirectly via actions on intrapancreatic neurons has also been suggested for other, structurally unrelated, pancreatic neuropeptides. Pancreatic polypeptide has been reported to inhibit bethanechol-, CCK-8-, and 2-DG-stimulated exocrine pancreatic function in vivo. (5,23). Inhibition is believed to involve presynaptic modulation of acetylcholine release (14). Neuropeptide Y, which shares sequence homology with pancreatic polypeptide, has also been shown to have indirect inhibitory effects on exocrine pancreatic function consistent with effects on cholinergic transmission (18). Somatostatin has also been shown to act indirectly to modulate exocrine secretion (25). From experiments using isolated perfused rat pancreas, Mulvihill et al. concluded that somatostatin inhibition was mediated via effects on intrapancreatic peptidergic neurons (20).

In enteric neurons, galanin does not affect basal acetylcholine release, but the peptide does inhibit acetylcholine release stimulated by electrical current, vasoactive intestinal peptide, or substance P (32). Galanin causes neuronal membrane hyperpolarization by opening potassium channels, thereby decreasing input resistance and suppressing excitability. Galanin has also been noted to block voltage-gated calcium channels (26). Effects are blocked by pertussis toxin (8). Galanin has been noted to inhibit acetylcholine release from hippocampal slices (22).

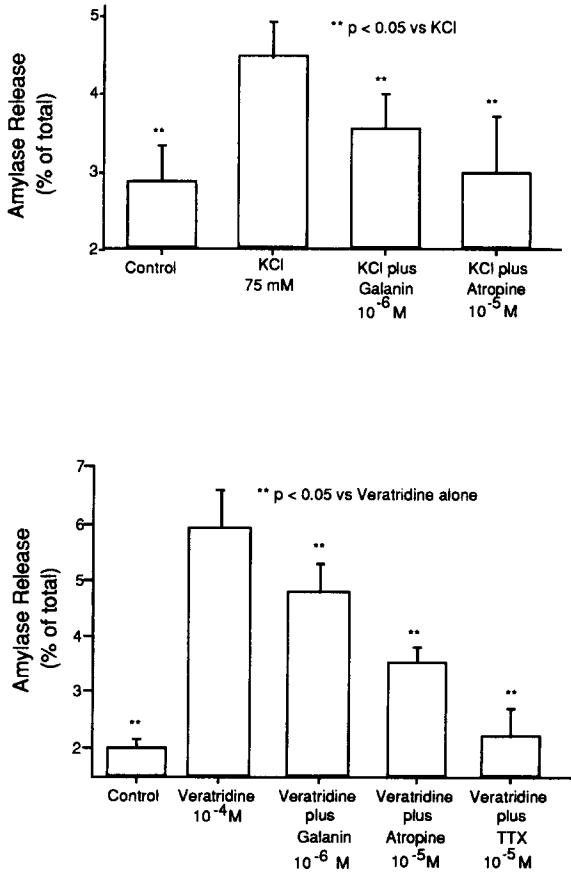

FIG. 5. Amylase release from isolated lobules incubated with KCl (75 mM) or veratridine (10^{-4} M) with or without galanin (10^{-6} M), atropine (10^{-5} M), or tetrodotoxin (TTX, 10^{-5} M). $n = 6$.

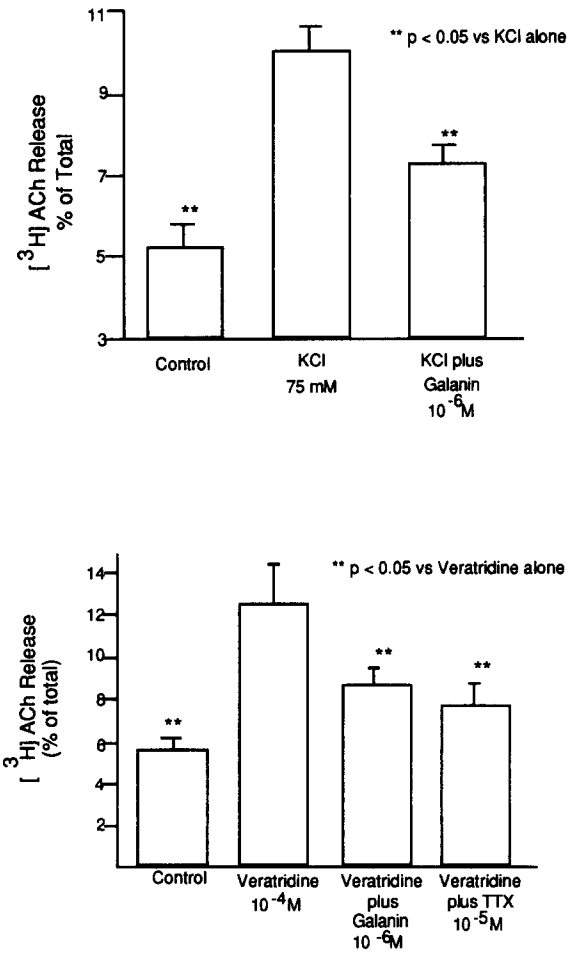

FIG. 6. Tritiated acetylcholine release from isolated lobules ($n = 6$ per group) incubated with KCl (75 mM) or veratridine (10^{-4} M) with or without galanin (10^{-6} M) or tetrodotoxin (TTX, 10^{-5} M).

Inhibitory effects of galanin have also been noted in pancreatic endocrine tissues. Galanin suppresses insulin release by inhibiting adenylate cyclase in the insulin-secreting cell line RINm5F (3). Galanin inhibition of insulin release appears to act via blockade of exocytosis secondary to effects on beta cell membrane G-proteins; inhibitory effects are blocked by pertussis toxin (21,28).

While the current data indicate that galanin affects exocrine function, at least in part, via inhibition of cholinergic neurons, other mechanisms of action for galanin are not excluded. The in vivo effects of galanin could be secondary to pancreatic vasoconstriction. Pancreatic galanin has been shown to be released by bilateral thoracic splanchnic nerve stimulation, and the peptide has been shown to coexist with epinephrine and norepinephrine in intrapancreatic and celiac neurons (2,18). Since galanin inhibits the release of somatostatin (10,17), and since somatostatin itself decreases with mixed pancreatic nerve stimulation, the involvement of this peptide seems unlikely (4).

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REFERENCES

1. Ahrén, B.; Andren-Sandberg, A.; Nilsson, A. Galanin inhibits amylase secretion from isolated rat acini. Pancreas 3:559–562; 1988.
2. Ahrén, B.; Bottcher, G.; Kowalyk, S.; Dunning, B. E.; Sundler, F.; Taborsky, G. J., Jr. Galanin is colocalized with noradrenaline and neuropeptide Y in dog pancreas and celiac ganglion. Cell Tissue Res. 261:49–58; 1990.
3. Amiranoff, B.; Lorinet, A. M.; Lagny-Pourmir, I.; Laburthe, M. Mechanism of galanin-inhibited insulin release. Occurrence of a pertussis-toxin-sensitive inhibition of adenylate cyclase. Eur. J. Biochem. 177:147–152; 1988.
4. Amsterdam, A.; Solomon, T. E.; Jamieson, J. D. Sequential dissociation of the pancreas into lobules, acini, and individual cells. New York; Academic Press; 1978:361–378. (Methods Cell Biol., vol. 20.)
5. Beglinger, C.; Taylor, I. L.; Grossman, M. I.; Solomon, T. E. Pancreatic polypeptide inhibits exocrine pancreatic responses to six stimulants. Am. J. Physiol. 246(3, pt. 1):G286–G291; 1984.
6. Bernfeld, P. Amylases α and β. Methods Enzymol. 1:149–158; 1955.
7. Bishop, A. E.; Polak, J. M.; Bauer, F. E.; Christofides, N. D.; Carlei, F.; Bloom, S. R. Occurrence and distribution of a newly discovered peptide, galanin, in the mammalian enteric nervous system. Gut 27:849–857; 1986.
8. Dunne, M. J.; Bullett, M. J.; Li, G. D.; Wollheim, C. B.; Petersen, O. H. Galanin activates nucleotide-dependent K+ channels in insulin-secreting cells via a pertussis toxin-sensitive G-protein. EMBO J. 8:413–420; 1989.
9. Dunning, B. E.; Ahrén, B.; Veith, R. C.; Böttcher, G.; Sundler, F.; Taborsky, G. J., Jr. Galanin: A novel pancreatic neuropeptide. Am. J. Physiol. 251:E127–E133; 1986.
10. Dunning, B. E.; Taborsky, G. J., Jr. Galanin—sympathetic neurotransmitter in endocrine pancreas? Diabetes 37:1157–1162; 1988.
11. Dunning, B. E.; Taborsky, G. J., Jr. Galanin release during pancreatic nerve stimulation is sufficient to influence islet function. Am. J. Physiol. 256:E191–E198; 1989.
12. Dunning, B. E.; Havel, P. J.; Veith, R. C.; Taborsky, G. J., Jr. Pancreatic and extrapancreatic galanin release during sympathetic neural activation. Am. J. Physiol. 258(3, pt. 1):E436–444; 1990.
13. Fisone, G.; Wu, C. F.; Consolo, S. Galanin inhibits acetylcholine release in the ventral hippocampus of the rat: Histochemical, autoradiographic, in vitro, and in vivo studies. Proc. Natl. Acad. Sci. USA 84:7339–7343; 1987.
14. Jung, G.; Louie, D. S.; Owyang, C. Pancreatic polypeptide inhibits pancreatic enzyme secretion via a cholinergic pathway. Am. J. Physiol. 253:G706–G710; 1987.
15. Koenig, J. I.; Hooi, S.; Gabriel, S. M.; Martin, J. B. Potential involvement of galanin in the regulation of fluid homeostasis in the rat. Regul. Pept. 24:81–86; 1989.
16. Melander, T.; Hökfelt, T.; Rökaeus, Å.; Fahrenkrug, J.; Tatemoto, K.; Mutt, V. Distribution of galanin-like immunoreactivity in the gastrointestinal tract of several mammalian species. Cell Tissue Res. 239:253–270; 1985.
17. Miralles, P.; Peiró, E.; Silvestre, R. A.; Vilanueva, M. L.; Marco, J. Effects of galanin on islet cell secretory responses to VIP, GIP, 8-CCK, and glucagon by the perfused rat pancreas. Metabolism 37: 766–770; 1988.
18. Mulholland, M. W.; Lally, K.; Taborsky, G. J., Jr. Inhibition of rat pancreatic exocrine function by neuropeptide Y: Studies in vivo and in vitro. Pancreas 6:433–440; 1991.
19. Mulholland, M. W.; Garcia, R.; Garcia, I.; Taborsky, G. J., Jr.; Helton, S. Inhibition of pancreatic exocrine secretion in the rat by calcitonin gene-related peptide: Involvement of circulating somatostatin. Endocrinology 124:1849–1856; 1989.
20. Mulvihill, S. J.; Bunnett, N. W.; Goto, Y.; Debas, H. T. Somatostatin inhibits pancreatic exocrine secretion via a neural mechanism. Metabolism 39(9, Suppl. 2):143–148; 1990.
21. Nilsson, T.; Arkhammar, P.; Rorsman, P.; Berggren, P. O. Suppression of insulin release by galanin and somatostatin is mediated by a G-protein. An effect involving repolarization and reduction in cytoplasmic free Ca2+ concentration. J. Biol. Chem. 264:973–80; 1989.
22. Powers, M. A.; Pappas, T. N. Galanin is a potent inhibitor of pancreatic exocrine secretion. Gastroenterology 96:A398; 1989.
23. Putnam, W. S.; Liddle, R. A.; Williams, J. A. Inhibitory regulation of rat exocrine pancreas by peptide YY and pancreatic polypeptide. Am. J. Physiol. 256(4, pt. 1):G698–G703; 1989.
24. Scheele, G. A.; Palade, G. E. Studies on the guinea pig pancreas. J. Biol. Chem. 250:2660–2670; 1975.
25. Shinozaki, H.; Funakoshi, A.; Miyasaka, K.; Miyazaki, K.; Kitani, K. Effect of somatostatin on pancreatic enzyme secretion. Gastroenterol. Jpn. 23:673–679; 1988.
26. Tamura, K.; Palmer, J. M.; Winkelmann, C. K.; Wood, J. D. Mechanism of action of galanin on myenteric neurons. J. Neurophysiol. 60:966–979; 1988.
27. Tatemoto, K.; Rökaeus, Å.; Jörnvall, H.; McDonald, T. J.; Mutt, V. Galanin—a novel biologically active peptide from porcine intestine. FEBS Lett. 164:124–128; 1983.
28. Ullrich, S.; Wollheim; C. B. Galanin inhibits insulin secretion by direct interference with exocytosis. FEBS Lett. 247:401–404; 1989.
29. Williams, J. A.; Korc, M.; Dormer, R. L. Action of secretagogues on a new preparation of functionally intact, isolated pancreatic acini. Am. J. Physiol. 235:E517–E524; 1978.
30. Wu, Z.; Kisslinger, S. D.; Gaginella, T. S. Functional evidence for the presence of cholinergic nerve endings in the colonic mucosa of the rat. J. Pharmcaol. Exp. Ther. 221:664–669; 1982.
31. Yagci, R. V.; Alptekin, N.; Zacharia, S.; Coy, D. H.; Ertan, A.; Rossowski, W. J. Galanin inhibits pancreatic amylase secretion in the phenobarbital-anesthetized rat. Regul. Pept. 34:275–282; 1991.
32. Yau, W. M.; Dorsett, J. A.; Youther, M. L. Evidence for galanin as an inhibitory neuropeptide on myenteric cholinergic neurons in the guinea pig small intestine. Neurosci. Lett. 72:305–308; 1986.