L-365,260, a Potent CCK-B/Gastrin Receptor Antagonist, Suppresses Gastric Acid Secretion Induced by Histamine and Bethanechol as Well as Pentagastrin in Rats

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ABSTRACT — We evaluated the effects of a potent cholecystokinin (CCK)-B/gastrin receptor antagonist, L-365,260 (3R(+)-N-(2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N’-(3-methylphenyl)urea); a selective CCK-A receptor antagonist, devazepide (L-364,718); and cimetidine on gastric acid secretion induced by pentagastrin, histamine and bethanechol in anesthetized rats. We also evaluated the effects of L-365,260 and cimetidine on acid secretion in pylorus-ligated rats. Intravenous administration of L-365,260, L-364,718 and cimetidine dose-dependently reduced acid secretion induced by pentagastrin (20 nmol/kg/hr), with ED50 values of 0.63, 19.1 and 2.5 μmol/kg, respectively. Of interest was the finding that L-365,260, like cimetidine, dose-dependently inhibited acid secretion induced by histamine (100 μmol/kg/hr) and bethanechol (5 μmol/kg/hr) with ED50 values of 5.9 and 4.3 μmol/kg, respectively. L-364,718, even at 30 μmol/kg, i.v., had only a slight effect on histamine- or bethanechol-induced acid secretion. Gastric acid secretion was suppressed by treatment with L-365,260 (3–100 μmol/kg, i.v.) and cimetidine (11.9–396.4 μmol/kg, i.v.) in pylorus-ligated rats, with ED50 values of 13.3 and 96.9 μmol/kg, respectively. These results indicate that L-365,260 suppresses acid secretion induced by histamine and bethanechol in rats and that the gastrin receptor plays an important role in acid secretion in pylorus-ligated rats.

Gastrin plays an important role in the gastric phase of acid secretion in animals (1) and humans (2). There is a good correlation between the serum gastrin concentration and the amount of gastric acid secretion during feeding (2, 3). However, few studies have examined the role of gastrin in basal and histamine- or cholinomimetic-induced gastric acid secretion, as no potent and selective gastrin receptor antagonists have been developed. Proglumide, which has been reported to be a gastrin receptor antagonist, inhibits basal (4) and acetylcholine-induced gastric acid secretion (5). However, it is unclear whether endogenous gastrin participates in gastric acid secretion induced by histamine or cholinomimetics or whether it plays an important role in basal acid secretion, since the gastrin receptor antagonistic activity of proglumide is very weak and shows low selectivity.
A highly potent cholecystokinin (CCK)-B/gastrin receptor antagonist, L-365,260 (3R-\((+)-N-(2,3\text{-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl})\)-N'-(3-methylphenyl)urea), and a selective CCK-A antagonist, devazepide (L-364,718), have been recently developed. L-365,260, given p.o. or i.d., does not affect basal acid secretion in mice, rats and guinea pigs; and it does not antagonize histamine or carbachol-stimulated acid secretion in mice (6). However, there have been no detailed dose-response studies on the effects of L-365,260 on basal and secretagogues-induced gastric acid secretion in rats. Therefore, in the present study, we performed dose-response studies on the effect of L-365,260 on acid secretion induced by pentagastrin, histamine and bethanechol in anesthetized rats and examined the role of the CCK-B/gastrin receptor in gastric acid secretion in pylorus-ligated rats.

MATERIALS AND METHODS

Male Wistar rats (Japan SLC, Inc.), weighing 200–250 g, were kept in individual cages with a mesh bottom. They were allowed free access to tap water but were deprived of food for 18 hr before the experiments. Each study was performed using 3 to 10 rats per group.

Determination of gastric acid secretion in anesthetized rats

We measured the gastric acid secretion in rats anesthetized with urethane at 1.25 g/kg, i.p. After tracheostomy, a polyethylene tube was inserted to ensure a patent airway. The abdomen of the anesthetized rat was incised, and the stomach and duodenum were exposed (7). An acute gastric fistula was placed in the forestomach using a polyethylene tube. Another polyethylene tube was inserted into the stomach through a slit in the duodenum and held in place by a ligature around the pylorus. The stomach was perfused at a flow rate of 1.5 ml/min with saline adjusted to pH 7.0, which was gassed with 100% oxygen, heated to 37°C, and kept in a reservoir. Acid secretion was measured at pH 7.0 using the pH-stat method (Toa Electronics AUT-201, Tokyo, Japan) and adding 0.025 N NaOH to the reservoir. In the first experiment, we performed a dose-response study of gastric acid secretion using pentagastrin, histamine dihydrochloride and bethanechol chloride. Approximately 30 min after the basal secretion had stabilized, pentagastrin (7, 20, 70 and 200 nmol/kg/hr), histamine (10, 30, 100 and 200 µmol/kg/hr) or bethanechol (0.5, 1.5, 5 and 15 µmol/kg/hr) was infused through the femoral vein.

L-365,260, L-364,718 and cimetidine were injected intravenously 1 hr after the start of pentagastrin or bethanechol infusion and 1.5 hr after the start of histamine infusion.

Determination of basal acid secretion in pylorus-ligated rats

Under ether anesthesia, the abdomen was incised and the pylorus ligated. Four hours later, the animals were sacrificed with ether, and the gastric contents were collected and analyzed for volume and acidity. Acidity was determined by automatic titration of the gastric juice against 0.05 N NaOH to pH 7.0 (Hiranuma Comite-7, Tokyo, Japan). Titratable acid output was expressed as µEq/4 hr. L-365,260, cimetidine or their corresponding vehicle (polyethylene glycol 300 or physiological saline) was given intravenously immediately after ligation.

Drugs

L-365,260, L-364,718 and cimetidine were prepared by Yamanouchi Pharmaceutical Co. Urethane was purchased from Tokyo Kasei Co. (Tokyo, Japan). L-365,260 and L-364,718 were dissolved and diluted in polyethylene glycol 300. These drugs were given in a volume of 0.5 ml/kg body weight. Cimetidine was dissolved in a small volume of 0.1 N HCl. The pH of this solution was adjusted to 6 with 0.1 N NaOH after dilution with physiological saline for intravenous injection (1 ml/kg). Pentagastrin (ICI Pharma Co., Osaka, Japan),
histamine dihydrochloride (Sigma Chemical Co., St. Louis, MO) and bethanechol hydrochloride were prepared, at appropriate concentrations to be given at 1ml/kg/hr, with physiological saline.

Statistics
Data are presented as means ± S.E. and 95% confidence limits from 3 to 10 rats per group. ED50 values were determined using a probit method.

RESULTS

Dose-response studies of secretagogues
Basal gastric acid secretion in anesthetized rats was 1–3 μEq/10 min (n = 4). This value is consistent with the findings of Takeuchi et al. (7). Intravenous infusion of pentagastrin (7–200 nmol/kg/hr), histamine (10–200 μmol/kg/hr) or bethanechol (0.5–15 μmol/kg/hr) dose-dependently stimulated gastric acid secretion (Fig. 1). Maximal acid secretion was 13.9 ± 2.8 μEq/10 min (n = 6) at 200 nmol/kg/hr of pentagastrin, 27.6 ± 3.6 μEq/10 min (n = 6) at 200 μmol/kg/hr of histamine, and 25.3 ± 1.9 μEq/10 min (n = 6) at 15 μmol/kg/hr of bethanechol. In the following studies, we used 20 nmol/kg/hr of pentagastrin, 100 μmol/kg/hr of histamine and 5 μmol/kg/hr of bethanechol, because these doses were not supramaximum and produced stable acid secretion for at least 1 hr. A stable acid secretory rate was observed 1 hr after the start of pentagastrin or bethanechol infusion and 1.5 hr after the start of histamine infusion in these doses (Fig. 1). Therefore, the antagonists were injected to the rat with a different time schedule in each experiment.

Effects of L-365,260, L-364,718, and cimetidine on pentagastrin-induced gastric acid secretion in anesthetized rats
Intravenous injection of L-365,260 (0.3–3 μmol/kg) dose-dependently inhibited gastric acid secretion induced by pentagastrin (Fig. 2A) with an ED50 value of 0.63 μmol/kg (Table 1). Maximal inhibition appeared 30 or

Fig. 1. Dose-response studies of pentagastrin, histamine and bethanechol on gastric acid secretion in anesthetized rats. Pentagastrin (□, control; △, 7 nmol/kg/hr; ■, 20 nmol/kg/hr; ▲, 70 nmol/kg/hr; ●, 200 nmol/kg/hr), histamine (□, control; △, 10 μmol/kg/hr; ■, 30 μmol/kg/hr; ▲, 100 μmol/kg/hr; ●, 200 μmol/kg/hr) and bethanechol (□, control; △, 0.5 μmol/kg/hr; ■, 1.5 μmol/kg/hr; ●, 5 μmol/kg/hr) were injected after basal gastric acid secretion had been well-stabilized. Data represent the means ± S.E. of values measured every 10 min from 4 to 6 rats.
40 min after the drug injection and persisted for at least 30 min. L-364,718 (3–30 μmol/kg, i.v.) and cimetidine (1–10 μmol/kg, i.v.) also inhibited gastric acid secretion caused by pentagastrin in a dose-dependent manner (Fig. 2, B and C). When ED50 values were estimated from the maximal inhibition of each dose, L-365,260 was found to be 30 and 4 times more potent than L-364,718 and cimetidine, respectively (Table 1).

Effects of L-365,260, L-364,718 and cimetidine on histamine-induced gastric acid secretion in anesthetized rats

Intravenously administered L-365,260 (1–30 μmol/kg) and cimetidine (3–30 μmol/kg) dose-dependently inhibited gastric acid secretion induced by histamine (Fig. 3, A and C), with ED50 values of 5.9 and 13.1 μmol/kg, respectively (Table 1). Maximal inhibition appeared 20 min after injection of L-365,260, after which gastric acid secretion rapidly recovered to the predosing values (Fig. 3A). On the other hand, L-364,718 given i.v. did not inhibit gastric acid secretion even at the high dose of 30 μmol/kg (Fig. 3B).

Effects of L-365,260, L-364,718 and cimetidine on bethanechol-induced gastric acid secretion in anesthetized rats

L-365,260 (1–10 μmol/kg) injected intravenously inhibited gastric acid secretion caused by bethanechol in a dose-dependent manner (Fig. 4A), with an ED50 value of 4.3 μmol/kg (Table 1). This inhibitory effect was transient, and gastric acid secretion rapidly recovered to the pre-drug value as in the case of histamine-induced gastric acid secretion (Fig. 4A). Cimetidine (3–30 μmol/kg, i.v.) also reduced gastric acid secretion (Fig. 4C), with an ED50 value of 15.0 μmol/kg (Table 1). L-364,718 did not inhibit bethanechol-induced gastric acid secretion, even at 30 μmol/kg, i.v. (Fig. 4B).

Effects of L-365,260 and cimetidine on gastric acid secretion in pylorus-ligated rats

The amount of acid in rats treated with phy-
Fig. 3. Effects of L-365,260, L-364,718 and cimetidine on gastric acid secretion induced by histamine (100 μmol/kg/hr) in anesthetized rats. L-365,260 (○, 1 μmol/kg; ▲, 3 μmol/kg; ■, 10 μmol/kg; ○, 30 μmol/kg), L-364,718 (●, 3 μmol/kg; ▲, 10 μmol/kg; ■, 30 μmol/kg) and cimetidine (●, 3 μmol/kg; ▲, 10 μmol/kg; ■, 30 μmol/kg) were given intravenously 60 min after starting histamine infusion. Data are expressed as percentages of the values observed immediately before administration of these antagonists and are means ± S.E. from 3 to 6 rats.

Fig. 4. Effects of L-365,260, L-364,718 and cimetidine on gastric acid secretion induced by bethanechol (5 μmol/kg/hr) in anesthetized rats. L-365,260 (○, 1 μmol/kg; ▲, 3 μmol/kg; ■, 10 μmol/kg), L-364,718 (●, 3 μmol/kg; ▲, 10 μmol/kg; ■, 30 μmol/kg) and cimetidine (●, 3 μmol/kg; ▲, 10 μmol/kg; ■, 30 μmol/kg) were given intravenously 60 min after starting bethanechol infusion. Data are expressed as percentages of the values observed immediately before administration of these antagonists and are means ± S.E. from 3 to 6 rats.
siological saline was 317.9 ± 48.0 μEq/4 hr (n = 10). Intravenously administered polyethylene glycol 300, the vehicle for L-365,260, decreased acid secretion to 82.8% as compared to acid secretion in saline-treated rats. L-365,260 (3–100 μmol/kg, i.v.) dose-dependently inhibited gastric acid secretion in pylorus-ligated rats (Fig. 5), with an ED50 value of 13.3 μmol/kg (Table 1). Cimetidine (11.9–396.4 μmol/kg, i.v.) also inhibited gastric acid secretion, with an ED50 value of 96.9 μmol/kg.

**DISCUSSION**

Lotti and Chang (6) reported that L-365,260 given orally inhibited gastric acid secretion induced by pentagastrin in rats. Although our results could not be exactly compared with their results because of the different route of administration, it is considered that the inhibitory effect of L-365,260 is due to antagonization of gastrin receptors as described in their report.

In the present study, we evaluated the role of endogenous gastrin in histamine- and bethanechol-induced gastric acid secretion as well as basal acid secretion in rats. Therefore, 100 μmol/kg/hr of histamine and 5 μmol/kg/hr of bethanechol were chosen as the submaximal dosages. Under these conditions, L-365,260, a potent CCK-B/gastrin receptor antagonist, inhibited not only pentagastrin-stimulated gastric acid secretion but also histamine- and bethanechol-stimulated gastric acid secretion in anesthetized rats. Hirst et al. (8) reported that intravenously administered L-365,260 in a dose of 10 μmol/kg significant-
ly inhibited histamine-induced gastric acid secretion in anesthetized rats. These observations disagree with another report (6) in which L-365,260 did not antagonize histamine- or carbachol-stimulated acid secretion in mice. We observed that L-365,260 intravenously dosed at 3 μmol/kg (1.2 mg/kg) or more markedly inhibited histamine- and bethanechol-induced acid secretion. In their report (6), however, the authors only determined the inhibitory effects of this drug at 1 mg/kg, p.o. on acid secretion induced by histamine and carbachol, despite results in which the drug not significantly but slightly inhibited these secretions. Therefore, it is likely that the dosage used in the previous report was insufficient to inhibit acid secretion induced by histamine and carbachol. Another possible reason for this discrepancy is that different species were used.

The mechanism of the inhibitory effects of L-365,260 against histamine- and bethanechol-stimulated acid secretion is unknown. A benzodiazepine derivative of L-365,260 has no effect on muscarine M₁ and M₂ receptors, but does show a low potency for benzodiazepine receptors in binding assays (6). In preliminary experiments, diazepam, a typical benzodiazepine receptor agonist, even at 30 μmol/kg did not reduce histamine- and bethanechol-induced gastric acid secretion in anesthetized rats (data not shown). In the isolated right atrium of guinea pigs, a high concentration of L-365,260 (10⁻⁵ M) had no effect on the chronotropic response to histamine (data not shown). These results indicate that the inhibitory effects of L-365,260 do not result from antagonism of muscarinic and histamine H₂ receptors and agonism of benzodiazepine receptors. L-365,260 also interacts with CCK-A receptors at higher concentrations than CCK-B receptors in vitro (6). However, L-364,718, a potent CCK-A receptor antagonist, did not affect histamine- and bethanechol-induced acid secretion, suggesting that CCK-A receptor antagonism did not contribute to inhibition of histamine- and bethanechol-induced acid secretion in rats.

A possible mechanism for the inhibitory effect of L-365,260 is antagonism of CCK-B receptors in the central nervous system. CCK-8 administered intracerebroventricularly (i.c.v.) stimulates gastric acid secretion in anesthetized rats (9). On the other hand, pentagastrin administered i.c.v. does not stimulate or inhibit gastric acid secretion. These results indicate that CCK-B receptors do not participate in the regulation of gastric acid secretion in the central nervous system.

Histamine H₂ receptor antagonists have been shown in vivo to inhibit not only histamine-stimulated acid secretion but also gastrin- or cholinomimetics-induced acid secretion through antagonism of histamine H₂ receptors (10). Our results confirmed the above findings, but the cimetidine dosage required in histamine- or bethanechol-induced acid secretion was 5 times greater than that required in pentagastrin-induced secretion (Table 1). It is likely that these differences of cimetidine’s potency are due to the differing stimulatory activities of each secretagogue. The ED₅₀ value of L-365,260 against pentagastrin-stimulated acid secretion was one-tenth that in histamine- or bethanechol-induced secretion. These differing ED₅₀ values apparently result from the same reasons mentioned in the case of cimetidine. We therefore suspect that L-365,260 inhibits gastric acid secretion induced by histamine and bethanechol through antagonism of gastrin receptors as cimetidine inhibits acid secretion induced by these secretagogues through antagonism of histamine H₂ receptors. L-365,260 produced transient inhibition of gastric acid secretion induced by histamine or bethanechol, despite the prolonged effect observed in pentagastrin-stimulated gastric acid secretion. These different modes of inhibition may suggest that the mechanism of the inhibitory effect of L-365,260 on histamine- or bethanechol-induced acid secretion differ from that on pentagastrin-induced acid secretion. Therefore, we could not exclude the possibility that unknown mechanisms underlie these effects.

An in vitro study showed that a low con-
centration of gastrin which had only a slight effect on acid secretion by itself potentiated acid secretion induced by histamine, which differed from gastrin in intracellular signal transduction (11). The present results on L-365,260 suggest that serum gastrin which basally exists in the blood flow may also potentiate histamine-induced gastric acid secretion in vivo. On the other hand, gastrin appeared to be released by cholinomimetic stimuli (12, 13) and has an additive effect on cholinomimetics-induced acid secretion (11) in vitro. The observation in which L-365,260 inhibited bethanechol-induced gastric acid secretion indicates that the released gastrin may participate in cholinomimetics-induced gastric acid secretion in the whole animal.

Vagotomy and atropine inhibit gastric acid secretion in pylorus-ligated rats, showing that this secretion in these rats is mediated mainly by cholinergic muscarinic pathways (14). Although a certain amount of gastrin basally exists in the blood flow, the precise role of gastrin in gastric acid secretion in pylorus-ligated rats is unknown. Proglumide, a weak gastrin receptor antagonist, inhibits gastric acid secretion in pylorus-ligated rats (4). We also observed that L-365,260 dose-dependently inhibited gastric acid secretion, and almost completely inhibited gastric acid secretion at the dose of 100 μmol/kg, indicating that gastrin plays an important role in gastric acid secretion in pylorus-ligated rats.

L-364,718 (3–30 μmol/kg) dose-dependently inhibited gastric acid secretion induced by pentagastrin. This result suggests that L-364,718 has antagonistic activity towards gastrin receptors. If gastrin receptors are implicated in histamine- and bethanechol-stimulated acid secretion, higher doses of L-364,718 should suppress these secretions. However, L-364,718 even at 30 μmol/kg did not inhibit histamine-induced gastric acid secretion and had only a slight inhibitory effect on bethanechol-induced gastric acid secretion. As mentioned above, the L-365,260 dosage required to inhibit histamine- or bethanechol-induced acid secretion was 10 times greater than that needed to inhibit pentagastrin-induced acid secretion. Larger doses of L-364,718 may be needed to produce obvious inhibition of histamine- and bethanechol-stimulated acid secretion; However, we could not examine this because of the poor solubility of the drug. Another possibility is that L-364,718 strongly suppresses the inhibitory mechanism of gastric acid secretion. Gastrin and CCK directly stimulate gastric acid secretion via gastrin receptors on parietal cells (15) and indirectly activate gastric acid secretion via histamine release from endocrine cells (enterochromaffin-like cells) through CCK-B/gastrin receptors (16–18). Simultaneously, these peptides inhibit gastric acid secretion via somatostatin release from D cells through the activation of CCK-A receptors (17, 18). It is likely that L-365,260, even in the maximum dose against CCK-B/gastrin receptors, does not thoroughly suppress the inhibitory system mediated by CCK-A receptors, whereas L-364,718 completely inhibits this pathway. Suppression of the inhibitory system may explain the lower potency of L-364,718 on stimulant-induced gastric acid secretion.

In summary, L-365,260, a potent CCK-B/gastrin receptor antagonist, inhibited not only pentagastrin-induced gastric acid secretion but also histamine- and bethanechol-induced gastric acid secretion in anesthetized rats and also suppressed basal acid secretion in pylorus-ligated rats. Therefore, it is suggested that gastrin plays an important role in basal and secretagogues-induced gastric acid secretion in rats.

REFERENCES

1. Kovacs, T.O.G., Walsh, J.H., Maxwell, V., Wong, H.C., Azuma, T. and Katt, E.: Gastrin is a major mediator of the gastric phase of acid secretion in dogs: Proof by monoclonal antibody neutralization. Gastroenterology 97, 1406–1413 (1989)
2. Feldman, M., Walsh, J.H. and Wong, H.C.: Role of gastrin heptadecapeptide in the acid secretory response to amino acids in man. J. Clin. Invest. 61, 308–313 (1978)
3. Eysselein, V.E., Maxwell, V., Reedy, T.,
Wunsch, E. and Walsh, J.H.: Similar acid stimulatory potencies of synthetic human big and little gastrins in man. J. Clin. Invest. 73, 1284–1290 (1984)

4 Tariq, M., Parmar, N.S. and Ageel, A.M.: Gastric and duodenal antiulcer and cytoprotective effects of proglumide in rats. J. Pharmacol. Exp. Ther. 241, 602–607 (1987)

5 Magous, R. and Bali, J.P.: Evidence that proglumide and benzotript antagonize secretagogue stimulation of isolated gastric parietal cells. Regul. Pept. 7, 233–241 (1983)

6 Lotti, V.J. and Chang, R.S.L.: A new potent and selective non-peptide gastrin antagonist and brain cholecystokinin receptor (CCK-B) ligand: L-365,260. Eur. J. Pharmacol. 162, 273–280 (1989)

7 Takeuchi, K., Furukawa, O., Tanaka, H. and Okabe, S.: A new model of duodenal ulcers induced in rats by indomethacin and histamine. Gastroenterology 90, 636–645 (1986)

8 Hirst, B.H., Elliott, K., Ryder, H. and Szelke, M.: Inhibition of gastrin- and histamine-stimulated gastric acid secretion by gastrin and cholecystokinin antagonists in the rat. Aliment. Pharmacol. Ther. 5, 31–39 (1991)

9 Ishikawa, T., Osumi, Y. and Nakagawa, T.: Cholecystokinin intracerebroventricularly applied stimulates gastric acid secretion. Brain Res. 333, 197–199 (1985)

10 Grossman, M.T. and Konturek, S.T.: Inhibition of acid secretion in dog by metiamide, a histamine antagonist action on H2 receptors. Gastroenterology 66, 517–521 (1974)

11 Soll, A.H.: The interaction of histamine with gastrin and carbachol on oxygen uptake by isolated mammalian parietal cells. J. Clin. Invest. 61, 381–389 (1978)

12 Duval, J.W., Saffouri, B., Weir, G.C., Walsh, J.H., Arimura, A. and Makhlouf, G.M.: Stimulation of gastrin and somatostatin secretion from the isolated rat stomach by bombesin. Am. J. Physiol. 241, G242–G247 (1981)

13 Schubert, M.L., Saffouri, B. and Makhlouf, G.M.: Identical patterns of somatostatin secretion from isolated antrum and fundus of rat stomach. Am. J. Physiol. 254, G20–G24 (1988)

14 Brodei, D.A.: Mechanism of gastric hyperacidity produced by pylorus ligation in the rat. Am. J. Dig. Dis. 11, 231–241 (1966)

15 Soll, A.H.: The actions of secretagogues on oxygen uptake by isolated mammalian parietal cells. J. Clin. Invest. 61, 370–380 (1978)

16 Kawabata, S., Kanayama, S., Shinomura, Y., Miyazaki, Y., Imamura, I., Moriwaki, K., Wada, H. and Tarui, S.: Effect of cholecystokinin receptor antagonists, MK-329 and L-365,260, on cholecystokinin-induced acid secretion and histidine decarboxylase activity in the rat. Regulatory Peptides 35, 1–10 (1991)

17 Roche, S., Gudsnar, T., Bali, J.P. and Magous, R.: “Gastrin” and “CCK” receptors on histamine-and somatostatin-containing cells from rabbit fundic mucosa—I; Characterization by means of agonists. Biochem. Pharmacol. 42, 765–770 (1991)

18 Roche, S., Gudsnar, T., Bali, J.P. and Magous, R.: “Gastrin” and “CCK” receptors on histamine-and somatostatin-containing cells from rabbit fundic mucosa—II; Characterization by means of selective antagonists (L-364,718 and L-365,260). Biochem. Pharmacol. 42, 771–776 (1991)