AMINES AND THE RAT EXOCRINE PANCREAS: (3)  
EFFECTS OF AMINES ON PANCREATIC SECRETION

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Abstract—Effects of L-dopa, L-5HTP, a few amines, and related compounds on the pancreatic rate of flow, protein secretion, and bicarbonate secretion were studied in conscious rats. Single injections of L-dopa, DA and apomorphine did not modify the rate of flow, while an increase was seen with infusion of DA. L-dopa stimulated the protein secretion. L-5HTP and 5-HT decreased the rate of flow and protein secretion. Effects of L-dopa and L-5HTP on the protein secretion were prevented by DA- and 5-HT blockers, respectively. Neither L-dopa nor L-5HTP had any effect on the bicarbonate secretion. Secretin and cholinergic agents (acetylcholine and carbamylcholine) strongly stimulated the rate of flow of pancreatic juice. α-Agonists (phenylephrine and clonidine) decreased the rate of flow, and the effects were inhibited by an α-blocker. The α-agonists had no effect on protein secretion. Although, α-blockers (phenoxybenzamine and phentolamine) had no effects on the rate of flow, they did decrease the protein secretion. Isoproterenol was a potent secretagogue, and the effect was suppressed by a β-blocker. Histamine had no effect on the rate of flow. The results were discussed in relation to our previous histochemical and chemical findings, and the species difference between rats and dogs in response to the amines.

Acinar cells of the exocrine pancreas of rats efficiently take up and metabolize L-dopa (1, 2) and L-5HTP (3, 4). In previous histochemical and chemical studies, some differences and similarities between the L-dopa and L-5HTP metabolism were observed. The main findings were: 1) L-dopa was more rapidly metabolized than L-5HTP, 2) the pretreatment with DA-blockers increased markedly the accumulation of pancreatic DA after injection of L-dopa, whereas pretreatment with 5-HT blocker decreased the accumulation of 5-HT after injection of L-5HTP, 3) the pretreatment with α-blocker resulted in the increase of both DA and 5-HT content after injection of L-dopa and L-5HTP, respectively, and 4) iproniazide, a MAO inhibitor, was more effective in increasing the accumulation of 5-HT. The excretion of DA and 5-HT appeared to be associated with the secretion of zymogen granules, thus the amines can serve as indicator of pancreatic secretory activity, particularly enzyme secretion. Because DA- and 5-HT blockers produced an increase and decrease in accumulation of pancreatic DA and 5-HT contents, respectively, it was suggested that DA and 5-HT, formed from their corresponding precursors, could modify the pancreatic secretion of rats, particularly enzyme secretion.

The present experiments were an attempt to correlate the histochemical and chemical findings with possible pharmacological effects of L-dopa, L-5HTP, their corresponding amines, and the blockers on the pancreatic secretion of rats. Effects of other amines were also studied.
MATERIALS AND METHODS

Animals used: Male Sprague-Dawley rats weighing 330-430 g were used. The animals had free access to food and water before operation.

Operation procedure: An external pancreatic fistula was made. Under pentobarbital anesthesia (30 mg/kg i.p.) the abdomen was opened by a midline incision. After the duodenal loop and pancreas had been brought forward through the incision the common hepatic duct was ligated with silk close to the duodenum. The duct was cannulated immediately proximal to the ligature with a 30 cm long polyethylene tube (PE 10, Clay Adams). The tube was passed about 5 mm towards the liver and was secured by a silk ligature tied around the duct. The bile was then diverted from the proximal part of the common hepatic duct to the duodenum by another polyethylene tube. The fistula tube was brought out from the abdomen through a small incision to the right of the wound and fixed to the abdominal muscle and skin by silk sutures. The abdominal incision was closed. For the injection of drugs, a polyethylene tube filled with heparin solution (PE 50, Clay Adams) was inserted into the femoral vein and tied in place. The other end of the tube was stoppered by Kocher’s forceps. After operation, the animals were placed in restraining cages of Bollman type with access to food and water, and were used for experiments the next day. To compensate for the loss of electrolytes with the pancreatic juice, Ringer solution was given s.c. after the operation (10 ml) and physiological saline was provided as drinking water.

Measurements of the rate of flow: The number of drops was counted for estimation of the pancreatic rate of flow. The number of drops during the continuous two 15-min periods after injection of a solvent was counted and the average was used as a control value. Within 5-15 min after the control experiment, a test substance was given and the number of drops during 15-min periods was counted.

Measurement of the protein concentration: The pancreatic juice was collected in a test tube for 60 min after injection of a solvent, and then for 60 min after injection of a test substance. Samples were stored frozen until assay. The enzyme content was followed indirectly in terms of protein. Protein concentration (mg/ml) was determined according to the method of Lowry et al. (5). Bovine serum albumin (Sigma) was used for the standard solution.

Measurement of the bicarbonate concentration: The juice was collected under 0.1 ml of paraffin oil in a test tube for 30 min after injection of a solvent, and then for 30 min after injection of a test substance. Samples were stored frozen pending analysis. A sample of 0.1 ml was transferred to a 20 ml messflask, and a known excess of N/100 hydrochloric acid and distilled water was added to make up 20 ml. The mixture was heated for 5 min in a boiling water bath. The bicarbonate was back-titrated with N/40 sodium hydroxide to the pH of the distilled water used. A digital meter of model HM-20B (TOA Electronics Ltd. Tokyo) was used. The concentration was expressed in terms of mEq/L.

Substances used: Dopamine hydrochloride (DA) (Sigma), apomorphine hydrochloride (August Brandes), 5-hydroxytryptamine creatinine sulfate (5-HT) (Sigma), secretin (Boots), acetylcholine chloride (Ovisot®, Dai-ichi), carbamylcholine chloride (Nakarai Chemicals),
L-phenylephrine hydrochloride (Sigma), clonidine hydrochloride (synthesized in our research laboratories), histamine dihydrochloride (Nakarai Chemicals), DL-isoproterenol hydrochloride (Sigma), cyproheptadine hydrochloride (Nihon Merck Banyu), phenoxybenzamine hydrochloride (Tokyo Kasei), atropine sulfate (Nakarai Chemicals), and iproniazide phosphate (Aldrich) were dissolved in 0.9% saline. Phentolamine mesylate (Regitin®, CIBA-Geigy) and DL-propranolol hydrochloride (Inderal®, Sumitomo) were diluted with 0.9% saline. 3,4-Dihydroxy-L-phenylalanine (L-dopa) (Sigma) and 5-hydroxy-L-tryptophan (L-5HTP) (Sigma) were dissolved in 0.9% saline with the aid of a minimum amount of 0.1 N HCl. Sulpiride (Delagrange) and haloperidol (Janssen) were dissolved in 0.9% saline with the aid of a minimum amount of 1N H2SO4 and 50% (v/v) acetic acid, respectively. All drugs were given i.v. L-dopa, L-5HTP, cyproheptadine, and iproniazide were given in a volume of 0.3 ml/100 g body weight. All the remaining drugs were given in a constant volume of 0.2 ml/100 g body weight. Doses were expressed in terms of salts.

Treatments with drugs: DA was infused at the rate of 6, 15, and 30 mg/2 ml/30 min/animal. The rate of infusion was controlled by hand. In the control experiments, saline was given in a volume of 0.2 ml/100 g. When studying the antagonism of blockers on effects of agonists on the rate of flow and protein concentration, blockers were given 10 min before injection of the agonists. In the control experiments, vehicles of blocker and agonists were given.

Statistical analysis: Student’s t-test (paired) was used to analyse the significance of differences between control and treated groups.

RESULTS

(A) Effects on the rate of flow

The animals tolerated the surgical procedure well and their physical condition the next morning was good. Although the rats did not appear to have taken much food, the rate of secretion (0.53 ± 0.02 ml/hr, n = 10) was almost comparable to the value (0.6 ml/hr) reported by Grossman (6) for the non-anesthetized, non-starved rats.

(1) Effects of DA, 5-HT, and related compounds: Results are shown in Table 1.

Single injections of DA (1 and 2 mg/kg), apomorphine (1 mg/kg), a DA agonist, and L-dopa (16 and 32 mg/kg) had no effects on the secretion from the exocrine pancreas, whereas infusion of DA (15 or 30 mg/animal/30 min) increased the secretion slightly, but significantly. The increased rate of flow rapidly returned to normal levels after the cessation of infusion of DA, and in the 3rd 15-min period the increase was not significant. Although 5-HT and L-5HTP were without effect at lower doses (0.25 and 16 mg/kg, respectively), the two compounds produced significant inhibitory effects on the secretion at higher doses (0.5 and 32 mg/kg, respectively). However, the inhibitory effects showed great individual variations. For example, L-5HTP (32 mg/kg) produced little effect in 6 of 12 rats, and slight to moderate effects in the remaining 6 rats. In the latter rats, the effects persisted for two hours. Death sometimes occurred with rapid injections of larger doses of 5-HT possibly due to cardiovascular and respiratory effects of the amine. After larger doses of DA, the animals were
left in a poor condition. Therefore, their precursors, L-dopa and L-5HTP were used in the further studies. In the dog exocrine pancreas, L-dopa is known to stimulate the secretion after being converted to DA (7).

(2) Effects of some other amines: Results are shown in Table 2.

Secretin (2-32 U/kg), used as a reference substance, increased the secretion in a dose-dependent manner. The effects of secretin (16 and 32 U/kg) lasted for 30-60 min. However, as has been reported (6, 8), a lower sensitivity to secretin was noted. Acetylcholine (0.125 mg/kg) produced a transient increase of the secretion. Another cholinergic agent carbamylcholine (0.125 mg/kg), which is resistant to the enzymatic degradation by acetylcholine esterase, elicited increase of the secretion which lasted for 90 min. Phenylephrine (1 mg/kg) slightly decreased the secretion for a short period. Another α-agonist clonidine (0.5 mg/kg) also produced a slight, but significant decrease in secretion, the action lasting over two hours. Histamine (1 and 2 mg/kg) had no effect, whereas isoproterenol (0.064-1.0 mg/kg) increased the secretion in a dose-dependent manner. The effect of isoproterenol (1 mg/kg) lasted about one hour.

(3) Effects of blockers and MAO inhibitor: Results are shown in Table 3.

Two DA-blockers, haloperidol (2 mg/kg) and sulphiride (32 mg/kg), did not modify the pancreatic secretion. Cyproheptadine, a 5-HT blocker, produced a slight inhibitory effect on the secretion at a dose of 4 mg/kg and this effect lasted for over one hour. Two α-blockers, phentolamine (8 mg/kg) and phenoxybenzamine (8 mg/kg), were without effects. Propranolol, β-blocker, had no effect when given in a dose of 1 mg/kg. There was a slight
significant inhibitory effect at a dose of 2 mg/kg and this effect lasted for about one hour.
An anticholinergic agent, atropine (1-8 mg/kg), inhibited the secretion in a dose-dependent

### TABLE 2. Effects of various amines on the rate of flow of pancreatic juice in rats

| Drugs          | Dose mg/kg | N | Number of drops/15 min |
|----------------|------------|---|------------------------|
|                |            |   | Control | 1st 15-min | 2nd 15-min |
| Secretin       | 2          | 5 | 6.2±0.6 | 7.0±0.9 | 6.0±0.8 |
|                | 4          | 6 | 7.2±0.8 | 9.3±1.1** | 7.7±1.1 |
|                | 8          | 6 | 6.4±0.9 | 9.2±1.3*** | 6.7±0.8 |
|                | 16         | 6 | 5.7±0.6 | 8.8±1.2** | 7.3±0.8** |
|                | 32         | 5 | 6.7±0.8 | 12.8±0.9*** | 8.8±0.9*** |
| Acetylcholine  | 0.125      | 5 | 9.7±0.9 | 11.2±1.1* | 9.8±1.0 |
| Carbamylcholine| 0.125      | 5 | 10.3±1.0| 12.6±2.3** | 16.2±2.7** |
| Phenylephrine  | 1          | 6 | 9.2±1.3 | 6.3±0.6* | 8.8±1.0 |
| Clonidine      | 0.5        | 5 | 11.8±0.6| 8.2±1.0** | 8.4±0.7** |
| Histamine      | 1          | 5 | 9.7±1.3 | 9.4±1.5 | 9.8±1.7 |
|                | 2          | 5 | 10.1±1.5| 11.0±1.4| 10.4±1.2 |
| Isoproterenol  | 0.064      | 5 | 8.0±0.9 | 9.0±1.0 | 8.0±0.9 |
|                | 0.250      | 5 | 6.9±0.7 | 9.8±0.9** | 7.0±0.9 |
|                | 1.0        | 5 | 6.3±0.7 | 9.8±1.1***| 7.2±0.7***|

The dose of secretin is in terms of U/kg. N: number of animals. Values are mean±S.E. *; p<0.1, **; p<0.05, and ***; p<0.01, as compared to control. For the duration of action of drugs, see text.

### TABLE 3. Effects of various blockers and MAO inhibitor on the rate of flow of pancreatic juice in rats

| Drugs            | Dose mg/kg | N | Number of drops/15 min |
|------------------|------------|---|------------------------|
|                  |            |   | Control | 1st 15-min | 2nd 15-min |
| Haloperidol      | 2          | 5 | 7.5±1.1 | 7.6±0.9 | 7.4±0.8 |
| Sulpiride        | 32         | 7 | 13.8±3.1| 13.3±2.9| 14.0±3.4 |
| Cyproheptadine   | 2          | 4 | 11.1±1.0| 10.3±0.3| 10.8±0.6 |
|                  | 4          | 4 | 8.4±0.6 | 7.5±0.6* | 7.3±0.8** |
| Phenolamine      | 8          | 5 | 8.1±1.7 | 8.0±1.5 | 7.0±1.3 |
| Phenoxybenzamine | 8          | 5 | 10.4±1.4| 11.0±1.9| 10.2±1.8 |
| Propranolol      | 1          | 5 | 7.2±0.5 | 6.8±0.6 | 7.2±0.4 |
|                  | 2          | 5 | 7.8±0.9 | 6.2±0.7** | 6.6±1.0*** |
| Atropine         | 1          | 4 | 9.1±1.3 | 8.0±2.1 | 7.8±1.7 |
|                  | 2          | 7 | 6.8±0.9 | 4.6±0.6** | 3.3±0.4*** |
|                  | 8          | 5 | 6.5±0.5 | 3.0±0.6***| 3.6±0.5** |
| Iproniazide      | 100        | 5 | 7.4±0.6 | 12.2±1.7** | 13.0±2.0** |

N: number of animals. Values are mean±S.E. *; p<0.1, **; p<0.05, and ***; p<0.01, as compared to control.
manner. The effect of atropine (2 and 8 mg/kg) lasted for over two hours. A MAO inhibitor, iproniazide (100 mg/kg), exerted a profound stimulatory effect (over 5 hr) on the secretion.

(4) Antagonism of blockers to phenylephrine-, isoproterenol-, and carbamylcholine-induced secretion: Results are shown in Table 4.

Phenoxybenzamine (8 mg/kg), propranolol (1 mg/kg), and atropine (1 mg/kg) blocked the secretory effects of phenylephrine (1 mg/kg), isoproterenol (0.25 mg/kg), and carbamylcholine (0.125 mg/kg), respectively.

(B) Effects on the protein secretion

(1) Effects of agonists: Results are shown in Table 5.

Secretin (32 U/kg) did not change the protein concentration, whereas carbamylcholine (0.125 mg/kg) increased it significantly. L-dopa (32 mg/kg) produced a slight, but significant increase in the protein concentration, whereas L-5HTP (32 mg/kg) decreased it significantly. Two α-agonists, phenylephrine (1 mg/kg) and clonidine (0.5 mg/kg), were without effects.

### Table 4. Antagonism of blockers to phenylephrine-, isoproterenol-, and carbamylcholine-induced pancreatic secretion

| Drugs        | Dose mg/kg | N  | Control 1st 15-min | 2nd 15-min |
|--------------|------------|----|--------------------|------------|
| Phenoxybenzamine | 8.0        | 8  | 7.3±0.7            | 7.4±0.5    | 7.3±0.6 |
| + Phenylephrine | 1.0        |    |                    |            |
| Propranolol   | 1.0        | 5  | 7.3±0.6            | 7.6±0.8    | 7.4±0.7 |
| + Isoproterenol | 0.25      |    |                    |            |
| Atropine      | 1.0        | 4  | 7.9±1.1            | 8.5±0.3    | 8.3±0.3 |
| + Carbamylcholine | 0.125    |    |                    |            |

N: number of animals. Values are mean±S.E. The blocker was given 10 min before injection of agonist. No significant differences were observed.

### Table 5. Effects of amines on the pancreatic protein concentration in rats

| Drugs           | Dose mg/kg | N  | Concentration (mg/ml) Before adm. | After adm. |
|-----------------|------------|----|-----------------------------------|------------|
| Secretin        | 32         | 7  | 31.0±4.3                          | 29.1±3.8   |
| Carbamylcholine | 0.064      | 5  | 24.5±2.0                          | 31.7±2.9*  |
| L-dopa          | 32         | 8  | 20.2±4.0                          | 23.6±4.4*  |
| L-5HTP          | 32         | 7  | 21.8±3.5                          | 15.1±4.1***|
| Phenylephrine   | 1          | 5  | 21.6±6.4                          | 24.8±3.9   |
| Clonidine       | 0.5        | 4  | 31.2±3.5                          | 31.1±5.0   |

The dose of secretin is in terms of U/kg. N: number of animals. Values are mean±S.E. *: p<0.1, **: p<0.05, and ***: p<0.01, as compared to control.
(2) Effects of blockers: Results are shown in Table 6.

DA-blockers (haloperidol 2 mg/kg, and sulpiride 32 mg/kg) and 5-HT blocker (cyproheptadine 4 mg/kg) were without effects. α-Blockers (phentolamine and phenoxybenzamine, each 8 mg/kg) decreased the protein concentration, but a significant decrease was obtained only with phentolamine. Atropine (4 mg/kg) also decreased the protein concentration significantly.

(3) Antagonism of sulpiride and cyproheptadine to the changes in protein concentration induced by L-dopa and L-5HTP: Results are shown in Table 7.

Sulpiride (32 mg/kg) blocked the L-dopa (32 mg/kg)-induced increase in the protein concentration. The L-5HTP (32 mg/kg)-induced decrease in the protein concentration was blocked by cyproheptadine (4 mg/kg), but not by sulpiride (32 mg/kg).

(C) Effects on the bicarbonate concentration: Results are shown in Table 8.

Secretin (32 U/kg) markedly increased the bicarbonate concentration. DA (2 mg/kg given twice at 15 min intervals), or L-dopa (32 mg/kg), and L-5HTP (32 mg/kg) did not modify the bicarbonate concentration.

### Table 6. Effects of various blockers on the protein concentration of pancreatic juice in rats

| Drugs           | Dose (mg/kg) | N  | Concentration (mg/ml) |
|-----------------|--------------|----|-----------------------|
|                 |              |    | Before adm. | After adm. |
| Haloperidol     | 2            | 4  | 25.3±6.7   | 25.4±7.8   |
| Sulpiride       | 32           | 10 | 31.1±4.6   | 29.9±3.6   |
| Cyproheptadine  | 4            | 5  | 39.2±4.3   | 34.7±7.5   |
| Phentolamine    | 8            | 5  | 26.7±4.1   | 13.8±2.8**|
| Phenoxybenzamine| 8            | 6  | 25.9±6.4   | 18.5±3.9   |
| Oxprenolol      | 0.5          | 5  | 32.0±2.1   | 32.8±2.8   |
| Atropine        | 4            | 5  | 30.8±5.2   | 24.7±7.0**|

N: number of animals. Values are mean ± S.E. **: p < 0.05, as compared to control.

### Table 7. Antagonism of blockers to L-dopa- and L-5HTP-induced changes in protein concentration of pancreatic juice in rats

| Treatments       | Dose (mg/kg) | N  | Concentration (mg/ml) |
|------------------|--------------|----|-----------------------|
|                  |              |    | Before adm. | After adm. |
| Sulpiride        | 32           | 4  | 25.7±4.1   | 26.6±5.5   |
| L-dopa           | 32           |    |            |            |
| Cyproheptadine   | 4            | 5  | 26.6±4.3   | 27.8±3.5   |
| L-5HTP           | 32           |    |            |            |
| Sulpiride + L-5HTP| 32          | 5  | 24.5±5.6   | 16.3±3.6*  |

N: number of animals. Values are mean ± S.E. *: p < 0.1, as compared to control.
TABLE 8. Effects of secretin, DA, L-dopa, and L-5HTP on the bicarbonate concentration of pancreatic juice in rats

| Drugs  | Dose mg/kg | N | Concentration (mEq/L) |
|--------|------------|---|-----------------------|
| Secretin | 32         | 5 | 41.2 ± 2.6            |
| DA      | 4          | 6 | 49.8 ± 4.2            |
| L-dopa  | 32         | 5 | 42.5 ± 2.5            |
| L-5HTP  | 32         | 5 | 40.0 ± 1.4            |

The dose of secretin is in terms of U/kg. N: number of animals. Values are mean ± S.E. **: p<0.05, as compared to control.

DISCUSSION

In agreement with our previous histochemical and chemical findings, the present results showed that L-dopa and L-5HTP appear to have opposite effects on pancreatic secretion in rats, particularly on enzyme secretion. Moreover, the results with α-blockers and a MAO inhibitor, iproniazide, can explain the characteristic change found in our previous studies.

First, L-dopa increased, but L-5HTP decreased the protein concentration in the pancreatic juice. The effect of L-dopa and L-5HTP on the protein secretion were prevented by corresponding blockers at doses which had no effect either on the rate of flow or on the protein secretion, except for cyproheptadine which produced a slight, but a significant decrease in the rate of flow. The results suggest that the pancreas has a dopaminergic and serotonergic mechanism for protein secretion. According to a recent report by Furuta et al. (9), single injections of DA and L-dopa have stimulatory effects on the rate of flow of pancreatic juice in fasted, urethane-anesthetized rats, the potencies being approximately 100,000 times less than that of secretion. The stimulatory effect of DA was suppressed by propranolol, but not by haloperidol. Because the strong stimulatory effects of isoproterenol were also inhibited by propranolol, they suggested the presence of a β-adrenoceptor mechanism for the secretion from the exocrine pancreas of rats. In the present experiments, the effects of the blockers on the stimulatory and inhibitory effects of the amines and their precursors on the rate of flow were not studied, because the effects of amines and their precursors after single injections were not only weak but also variable. Accordingly, the receptor mechanism for the rate of flow could not be clarified. However, it is apparent that the stimulatory effects of DA on the exocrine pancreas in rats are weak as opposed to the strong secretin-like effects in dogs (7, 10–13).

All these results taken together suggest that the pancreas has different receptor mechanisms for protein secretion and rate of flow of pancreatic juice, yet because these two functions are closely related, it is unlikely that they are controlled by different receptor mechanisms. We have no evidence as to whether the differences in experimental conditions—e.g. conscious vs. urethane-anesthetized rats, fed vs. fasted rats and sulpiride vs. haloperidol—would explain the difference. However, it must be emphasized that DA and L-dopa exerted their effects more consistently on the protein secretion than on the rate of flow. The situation holds true
also for 5-HT and L-5HTP. Therefore, DA, 5-HT and their precursors appear to act mainly on the enzyme secretion in the exocrine pancreas of rats. However, the effects of DA and L-dopa were not so potent as expected from our previous studies; the effects had a borderline significance. Therefore, there is the possibility that the excretion of DA is not so closely related to the discharge of zymogen granules to the extent suggested in the previous histochemical and chemical experiments.

Second, in our previous histochemical and chemical studies, DA- and \( \alpha \)-blockers produced an increased accumulation of DA in the exocrine pancreas after injection of L-dopa. However, the present results indicated that the two kinds of blockers had a different mechanism; DA-blockers, which themselves had no effect on the exocrine pancreatic secretion, caused an accumulation by inhibiting the stimulatory effect of DA, whereas \( \alpha \)-blockers produced the change by their own inhibitory effects on the secretion of zymogen granules (carriers of DA), not by inhibiting the \( \alpha \)-agonistic action of DA; the two \( \alpha \)-agonists did not affect the protein secretion. The characteristic effect of \( \alpha \)-blockers also explains why they produced an increased accumulation of 5-HT after injection of L-5HTP. The present results with phentolamine differ from those of Roze et al. (14) who reported that phentolamine increased the pancreatic flow and protein secretion, and atropine inhibited both these increases. We have no explanations for the discrepancy.

Third, we thought that iproniazide would increase greatly the contents of both DA and 5-HT after injection of L-dopa and L-5HTP, respectively. However, iproniazide had only a moderate effect on the DA content, although it did have a remarkable effect on the 5-HT content. In the present study, iproniazide exerted a profound stimulatory effect on the exocrine pancreas. The stimulatory effect of iproniazide is probably independent of its anti-MAO activity; a large amount of DA only slightly stimulated the secretion, and 5-HT and \( \alpha \)-agonists even depressed the secretion. When the stimulatory effects of iproniazide and DA were combined, the excretion of intracellular DA would necessarily be accelerated, and increase in accumulation of DA due to iproniazide would not be so great. On the other hand, when iproniazide and L-5HTP were given together, the stimulatory effect of iproniazide would probably be antagonized by the inhibitory effect of 5-HT, and the remaining anti-MAO activity may favour the increase of accumulation of 5-HT.

The control mechanism of pancreatic secretion in rats has been shown to differ in many respects from those in dogs and other animals (6, 8, 15–19). Hashimoto et al. (20) and Furuta et al. (9) have stressed a species difference in the sympathetic control of pancreatic secretion between dogs and rats. The present results confirmed the effects of amines on the exocrine pancreas of rats reported by Roze et al. (21), Furuta et al. (9), and Hashimoto et al. (20), and also showed that the dog and rat exocrine pancreas responded differently to 5-HT and histamine. On the basis of data reported thus far (7, 9, 20, 21, and present results), the main differences between dogs and rats in the response to various amines can be summarized as follows: 1) DA has a potent stimulatory effect in dogs while DA has only a weak stimulatory effect on the protein secretion and a very weak stimulatory effect on the rate of flow in rats, 2) 5-HT has inhibitory effects on the rate of flow and protein secretion in
rats, but no effect in dogs, 3) α-agonists decrease the rate of flow in rats, but have no effects in dogs, 4) β-agonist has a profound stimulatory effect on the rate of flow in rats, but has no effect in dogs, and 5) histamine is an effective stimulant in dogs, but not in rats.

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