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Experimental Studies on the Effect of Histidine upon the Secretory Function of the Gastric Gland Cells.

II. On the Actional Differences between Injected Histidine and Injected Histamine.

ヒスチジンが胃腺細胞分泌機能に及ぼす影響に関する実験的研究.

II. ヒスチジンとヒスタミンの作用的相違に就て.

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FUJIE has claimed that the gastric hormone *productin* which was discovered and so named by him, must be histamine or at least a histamine-like substance, and recently demonstrated, histochemically, that *productin* contains an imidazol group. On the other hand, the author demonstrated in a previous study that the lack of protein in the diet causes the functional inhibition of the discharge of *productin* into the blood from the gastric surface cells and that histidine in the diet, which is very amino-acid containing an imidazol group, can prevent this inhibition even if protein is completely lacking. The results suggest that the discharge of *productin* may be promoted by an amino-acid containing the imidazol group.

The author, here, proved on the one hand that histidine when injected shows the same effects as when contained in the diet, on the other hand the activities of histidine on the secretory function of the gastric gland cells. The author compared the latter results with those of histamine, so that the true nature of *productin* might be determined, viz. whether it is histamine-like or histidine-like.

I. Materials and Methods.

Adult and male rats, weighting between 100—120 g, which were accustomed to constant and regular feeding with Mc COLLUM's artificial diet, were used in the following experiments.

1. Histidine monohydrochloride 0.3% 1 cc (described below as Histidine) and histamine dihydrochloride 0.3% 1 cc (described below as Histamine) were injected respectively into the normal rats while they were still unfed.

2. The same injections were given to rats fed with the non-protein diet (concerning which see Arch. hist. jap. Vol. 14, No. 1, p. 42 1958) for 10 and 20 days.

3. Histidine and Histamine were injected respectively into the normal fasting rats, then 20 min. later, Mc COLLUM's artificial diet was given.

4. Histidine and Histamine were injected respectively into the normal fasting rats, then at once sesame oil was injected into the stomach using a sonde.

5. Atropin sulfate 0.05% 1 cc (described below as Atropin) was injected into

the normal fasting rats, then 10 min. later, Histidine and Histamine was injected respectively.

The materials have been taken, in the experiments 1, 2, 5, at the periods of 1/3, 2/3, 1, 2 and 3 hrs. after the injection, and in the experiments 3, 4 where the diet or sesame oil was administered, at the periods of $\frac{1}{2}$, 1, $1\frac{1}{2}$, 2 and 3 hrs. after these administrations. Concerning the methods used to take materials and to make the microscopic specimens, see the previous report in Arch. hist. jap. 14.

II. Observations.

In the present study, the gastric peptic cells in which the action of *productin* and of Histamine are positively recognizable were observed as were also the gastric surface cells from which *productin* vacuoles are discharged. To summarize the observations on these cells, the author used the same methods which have been described in former study.

a) *The gastric peptic cells.*

1. Histidine and Histamine was injected respectively into normal rats fasting for 24 hrs. (Table 1 and Table 2).

2. Histidine and Histamine was injected respectively into fasting rats which were fed with non-protein diet for 10 and 20 days (Tables 3, 4, 5, 6).

Table 1. Histidine was injected into the normal rats.

Hrs. after the injection	Total result			Representative result		Gland lumen
	Quantity of the intracel- lular secretory substance		Form of pls.			
	Granules	Vacuoles		Granules	Vacuoles	
Before	— ~ ±	— ~ ±	long rod, filament	— ~ ±	— ~ ±	narrow
$\frac{1}{3}$	± ~ + + +	± ~ +	short rod, granule, long rod	+	+	wide, a little wide
$\frac{2}{3}$	+ ~ + + + +	± ~ + + + +	long rod, short rod, granule	+ + ~ + + + + + + +	± + + + + + +	wide
1	± ~ + + +	— ~ +	long rod, short rod, supra-short rod	+ ~ + + +	+	a little wide, narrow
2	± ~ + + +	± ~ + + +	long rod, short rod, granule	± ~ + + +	+	wide, a little wide
3	— ~ + + + +	— ~ + + + +	long rod, granule, short rod	+ + + + + + — ~ +	— + + + + + +	wide, a little wide, narrow

Table 2. Histamine was injected into the normal rats.

Hrs. after the injection	Total result			Representative result		Gland lumen
	Quantity of the intracel- lular secretory substance		Form of pls.			
	Granules	Vacuoles		Granules	Vaucoles	
$\frac{1}{3}$	$\pm \sim + + +$	$- \sim +$	short rod, short rosary form, supra- short rod, long rod	$+ \sim + +$	$\pm$	a little wide
$\frac{2}{3}$	$+ \sim + + + +$	$\pm \sim +$	short rod, supra-short rod, long rod	$+ +$	$\pm \sim +$	a little wide, narrow
1	$\pm \sim + + + +$	$\pm \sim + + +$	supra-short rod, short rod, granule	$+ + \sim + + + +$	$+$	wide, a little wide
2	$+ \sim + + + +$	$+ \sim + + +$	short rod, long rod (a few)	$+ +$	$+ \sim + + +$	narrow
3	$\pm \sim + + + +$	$+ \sim + + + +$	short rod, supra-short rod, long rod	$\pm \sim + + + +$	$+$	narrow

Table 3. Histidine was injected into the rats fed with the non-protein diet for 10 days.

Hrs. after the injection	Total result			Representative result		Gland lumen
	Quantity of the intracel- lular secretory substance		Form of pls.			
	Granules	Vacuoles		Granules	Vacuoles	
Before	$\pm \sim +$	$- \sim \pm$	short rod, long rod	$\pm \sim +$	$- \sim \pm$	narrow
$\frac{1}{3}$	$- \sim + + +$	$\pm \sim +$	short rod, guitar form, long rod	$- \sim + + +$	$\pm \sim +$	a little wide, narrow, wide
$\frac{2}{3}$	$- \sim + + +$	$\pm \sim +$	short rod, long rod, supra-short rod, guitar form	$- \sim + +$	$\pm$	narrow, a little wide
1	$- \sim +$	$\pm \sim + + +$	short rod, long rod, guitar form	$- \sim +$	$+ \sim + +$	wide, a little wide
2	$- \sim + +$	$+ \sim + + +$	long rod, short rod, guitar form	$- \sim + +$	$+ + \sim + + +$	a little wide, narrow, wide
3	$- \sim \pm$	$- \sim +$	long rod, short rod, filament	$-$	$\pm$	a little wide, narrow

Table 4. Histamine was injected into the rats fed with the non-protein diet for 10 days.

Hrs. after the injection	Total result			Representative result		Gland lumen
	Quantity of the intracel- lular secretory substance		Form of pls.			
	Granules	Vacuoles		Granules	Vacuoles	
$\frac{1}{3}$	$\pm \sim ++$	$-\sim \pm$	short rod, long rod, supra-short rod	$+\sim ++$	$-$	narrow, a little wide
$\frac{2}{3}$	$+\sim ++$	$-\sim +$	short rod, long rod, granule	$++$	$\pm$	wide, a little wide
1	$+\sim +++$	$+\sim ++$	short rod, guitar form, long rod	$++$	$+(+)$	wide, a little wide
2	$++\sim +++$	$-\sim +$	short rod, supra-short rod, long rod	$++\sim +++$	$\pm$	narrow, a little wide
3	$++\sim +++$	$-\sim +$	short rod, long rod, granule	$+++$	$\pm$	narrow

Table 5. Histidine was injected into the rats fed with the non-protein diet for 20 days.

Hrs. after the injection	Total result			Representative result		Gland lumen
	Quantity of the intracel- lular secretory substance		Form of pls.			
	Granules	Vacuoles		Granules	Vacuoles	
Before	— ~ ±	— ~ ±	long rod	— ~ ±	— ~ ±	narrow
$\frac{1}{3}$	— ~ ++	— ~ ±	supra-short rod, short rod, long rod	± ~ +	—	narrow, a little wide
$\frac{2}{3}$	± ~ ++	± ~ ++	short rod, guitar form, long rod, supra-short rod	+ + + ±	± + ++	a little wide, narrow
1	± ~ ++	± ~ ++	long or short rod, supra- short rod	± ~ +	+	a little wide, narrow
2	— ~ +	— ~ ±	long or short rod, guitar form	±	— ~ ±	a little wide, narrow
3	— ~ ±	— ~ ±	long or short rod, guitar form	— ~ ±	— ~ ±	narrow, a little wide

Table 6. Histamine was injected into the rats fed with the non-protein diet for 20 days.

Hrs. after the injection	Total result			Representative result		Gland lumen
	Quantity of the intracel- lular secretory substance		Form of pls.			
	Granules	Vacuoles		Granules	Vacuoles	
$\frac{1}{3}$	$\pm \sim + + +$	$- \sim \pm$	short rod, long rod, supra-short rod	$+ \sim + +$	$- \sim \pm$	narrow, a little wide
$\frac{2}{3}$	$\pm \sim + + +$	$- \sim +$	short rod, long rod, granule	$+ +$	$\pm$	narrow, a little wide, wide
1	$+ \sim + + +$	$\pm \sim +$	long rod, short rod, granule	$+ +$	$+$	wide, a little wide
2	$+ \sim + + +$	$- \sim +$	long rod, short rod, guitar form, granule	$+ +$	$- \sim +$	a little wide, narrow
3	$+ \sim + + +$	$- \sim +$	long or short rod, guitar form	$+ +$	$- \sim +$	narrow, a little wide

Table 7. Histidine was injected, and 20 min. later an artificial diet was administered.

Hrs. after ad- minist- ration of the diet.	Total result			Representative result		Gland lumen
	Quantity of the intracel- lular secretory substance		Form of pls.			
	Granules	Vacuoles		Granules	Vacuoles	
Before	± ~ + + +	± ~ +	short rod, guitar form, long rod	+ ~ + +	± ~ +	a little wide, narrow
$\frac{1}{2}$	± ~ + + +	± ~ +	short rod, guitar form, supra-short rod	+ + ~ + + +	±	a little wide, narrow
1	± ~ + + +	+ ~ + + +	short rod, supra-short rod, long rod	± + + + + +	+ + + + + +	a little wide, narrow
$1\frac{1}{2}$	± ~ + + +	+ ~ + + +	short rod, supra-short rod, long rod	+ + + + + ± ~ +	+ + + + + +	a little wide, narrow
2	± ~ + + +	+ ~ + +	short rod, long rod, supra-short rod	+ +	+	a little wide, narrow
3	± ~ + + +	± ~ + + +	short rod, long rod, supra-short rod	± ~ + + +	± ~ + + +	narrow, a little wide

Table 8. Histamin ewas injected, and 20 min. later an artificial diet was admi nistered

Hrs. after ad- ministration of the diet.	Total result			Representative result		Gland lumen
	Quantity of the intracel- lular secretory substance		Form of pls.			
	Granules	Vacuoles		Granules	Vacuoles	
Before	± ~ + +	± ~ +	short rod, guitar form, long rod, granule	+ ~ + +	±	a little wide, narrow
½	+ ~ + + +	± ~ +	short rod, guitar form, granule	+ + ~ + + +	+	a little wide
1	+ ~ + + +	± ~ +	shrot rod, guitar form, long rod	+ +	+	narrow, a little wide
1 ½	+ + ~ + + +	± ~ +	short rod, long rod	+ + ~ + + +	+	a little wide
2	± ~ + + +	± ~ + + +	long rod, short rod, supra-short rod	+ + + ±	± + + +	a little wide
3	± ~ + + +	± ~ + + +	short rod, supra-short rod, long rod	+ + + + + ±	± + + + + +	a little wide, wide

3. Histidine and Histamine was injected respectively into normal fasting rats, then 20 min. later Mc COLLUM's artificial diet was administered (Tables 7 and 8).

Table 9. Histidine was injected into normal fasting rats, then at once sesame oil 1cc was injected into the stomach.

Hrs. after the injection into the stomach	Total result			Representative result		Gland lumen
	Quantity of the intracel- lular secretory substance		Form of pls.			
	Granules	Vacuoles		Granules	Vacuoles	
$\frac{1}{2}$	++~+++	±~+	short rod, granule, long rod	++~+++	±~+	a little wide, narrow
1	+~+++	±~++	short rod, guitar form, granule	++~+++	+	a little wide, wide
$1\frac{1}{2}$	±~+++	±~+++	short rod, guitar form, long rod	++~+++ ±	+ +++	a little wide, wide
2	±~+++	±~+++	short rod, long rod, guitar form	++~+++	++	narrow, a little wide
3	±~++	+~+++	short rod, long rod	++ +	+ ++	narrow, a little wide

4. Histidine and Histamine was injected respectively into normal fasting rats, then at once sesame oil was injected into the stomach using a sonde (Tables 9 and 10).

Table 10. Histamine was injected into normal fasting rats, then at once sesame oil 1 cc was injected into the stomach.

Hrs. after the injection into the stomach	Total result		Form of pls.	Representative result		Gland lumen
	Quantity of the intracel- lular secretory substance			Granules	Vacuoles	
	Granules	Vacuoles				
$\frac{1}{2}$	$\pm \sim + + +$	$- \sim \pm$	short rod, long rod, granule	$++$	$-$	a little wide
1	$++ \sim + + +$	$\pm \sim +$	supra-short rod, granule, short rod, guitar form	$++ \sim + + +$	$\pm$	a little wide
$1\frac{1}{2}$	$\pm \sim + + +$	$\pm \sim + +$	short rod, granule, long rod	$++ \sim + + +$	$\pm \sim +$	a little wide
2	$+ \sim + + +$	$\pm \sim +$	short rod, long rod	$++ \sim + + +$	$\pm$	a little wide, narrow
3	$+ \sim + + +$	$\pm \sim +$	short rod, long rod	$++ \sim + + +$	$\pm$	a little wide, narrow

5. Atropin was injected into normal fasting rats, then 10 min. later, Histidine and Histamine was injected respectively (Tables 11 and 12).

Table 11. Atropin was injected into normal fasting rats, then 10 min. later, Histidine was injected.

Hrs. after the Histidine injection	Total result			Representative result		Gland lumen
	Quantity of the intracel- lular secretory substance		Form of pls.			
	Granules	Vacuoles		Granules	Vacuoles	
Before	— ~ +	± ~ + (+)	long or short rod, guitar form	± ~ +	± ~ +	narrow
$\frac{1}{3}$	± ~ + +	+ ~ + + +	long rod, short rod	± ~ + + ~ + +	+ + ~ + + + +	a little wide, narrow, wide
$\frac{2}{3}$	— ~ + + +	± ~ + + +	short rod, guitar form, supra-short rod, long rod	+ + ~ + + + —	± + + +	a little wide
1	+ ~ + + +	± ~ +	long or short rod	+ ~ + + +	±	narrow
2	— ~ + + +	± ~ + + +	long or short rod	+ + ~ + + + — ~ ±	± + + ~ + + +	a little wide
3	— ~ + + +	± ~ + + +	long or short rod	+ + ~ + + + — ~ ±	± + + ~ + + +	a little wide, narrow

Table 12. Atropin was injected into normal fasting rats, then 10 min. later, Histamine was injected.

Hrs. after the Hista- mine injection	Total result			Representative result		Gland lumen
	Quantity of the intracel- lular secretory substance		Form of pls.			
	Granules	Vacuoles		Granules	Vacuoles	
$\frac{1}{3}$	$\pm \sim + + +$	$\pm \sim +$	short rod, guitar form	$\pm \sim + + +$	$\pm \sim +$	narrow, a little wide
$\frac{2}{3}$	$+ \sim + + +$	$\pm \sim +$	short rod, guitar form, rosary form	$+ + \sim + + +$	$\pm \sim +$	a little wide, narrow
1	$- \sim + + +$	$\pm \sim +$	short rod, supra-short rod, guitar form	$+ \sim + +$	$+$	a little wide, narrow
2	$\pm \sim + + +$	$\pm \sim + +$	short rod, rosary form, long rod	$++$ $+$ $\pm$	$\pm$ $+$ $++$	a little wide, narrow
3	$- \sim + + +$	$\pm \sim + +$	short rod, long rod, guitar form, rosary form	$+ + \sim + + +$ $+$ $- \sim \pm$	$\pm$ $++$ $\pm \sim +$	a little wide

b) The 'productin' vacuoles in the gastric surface cells (Table 13).

Table 13. Observations on the quantity of *productin* vacuoles in the surface cells (B: Before the injection, or before administration of the diet).

Experi- ment		Hrs.	Quantity of 'productin' vacuoles		Experi- ment	Hrs.	Quantity of 'productin' vacuoles		
			Total obser- vation	Representa- tive obser- vation			Total obser- vation	Representa- tive obser- vation	
Normal fasting rats	Histidine injection	B	+ ~ + + + +	+ + + +	Rats fed with the non protein diet for 10 days	Histidine injection	B	- ~ + + + +	+ ~ + + + +
		$\frac{1}{3}$	- ~ + + + +	- ~ + + + +			$\frac{1}{3}$	$\pm$ ~ + + + +	$\pm$ ~ +
		$\frac{2}{3}$	- ~ + + + +	- ~ + + + +			$\frac{2}{3}$	$\pm$ ~ + + + +	+ ~ + + + +
		1	- ~ + + + +	- ~ +			1	+ ~ + + + +	+ ~ + + + +
		2	$\pm$ ~ + + + +	+ ~ + + + +			2	- ~ + + + +	$\pm$ ~ + + + +
		3	$\pm$ ~ + + + +	+ ~ + + + +			3	+ ~ + + + +	+ ~ + + + +
	Histamine injection	$\frac{1}{3}$	$\pm$ ~ + + + +	+ ~ + + + +		Histamine injection	$\frac{1}{3}$	- ~ + + + +	+ ~ + + + +
		$\frac{2}{3}$	- ~ + + + +	+ ~ + + + +			$\frac{2}{3}$	$\pm$ ~ + + + +	+ ~ + + + +
		1	$\pm$ ~ + + + +	+ + ~ + + + +			1	$\pm$ ~ + + + +	+ ~ + + + +
		2	$\pm$ ~ + + + +	+ ~ + + + +			2	+ ~ + + + +	+ ~ + + + +
		3	+ ~ + + + +	+ + ~ + + + +			3	+ ~ + + + +	+ + ~ + + + +

An artificial diet was given 20 min. after the injection					Atropin was injected 10 min. before the injection					Sesame oil was injected into the stomach soon after the injection							
Histamine injection			Histidine injection		Histamine injection			Histidine injection		Histamine injection			Histidine injection				
B	$\frac{1}{2}$	$\frac{3}{4}$	1	2	3	B	$\frac{1}{2}$	$\frac{3}{4}$	1	2	3	B	$\frac{1}{2}$	$\frac{3}{4}$	1	2	3
+	~	+	+	+	+	-	~	+	+	+	+	+	~	+	+	+	+
+	~	+	+	+	+	-	~	+	+	+	+	+	~	+	+	+	+
+	~	+	+	+	+	-	~	+	+	+	+	+	~	+	+	+	+
+	~	+	+	+	+	+	~	+	+	+	+	+	~	+	+	+	+
+	~	+	+	+	+	+	~	+	+	+	+	+	~	+	+	+	+
+	~	+	+	+	+	+	~	+	+	+	+	+	~	+	+	+	+
+	~	+	+	+	+	+	~	+	+	+	+	+	~	+	+	+	+
+	~	+	+	+	+	+	~	+	+	+	+	+	~	+	+	+	+
+	~	+	+	+	+	+	~	+	+	+	+	+	~	+	+	+	+
+	~	+	+	+	+	+	~	+	+	+	+	+	~	+	+	+	+

III. Discussion.

In order to deduce the actions of Histidine and Histamine from the functional figures of the gastric peptic cells, the author described the average quantity of secretion granules, vacuoles in the peptic cells and of *productin* vacuoles in the surface cells, in the same figure (Figs. 1—6).

According to the experiments in which Histidine and Histamine alone was injected (Figs. 1, 2 and 3), it is noticed that, first, secretion granules increase in the cell after the injection of Histidine regardless of normally fed rats or protein deprived rats, but the production of secretion granules is less than in the case of Histamine injection, and secondly, secretion vacuoles increase in the cell to a greater extent than in the case of Histamine injections — this observation will be the important difference between Histidine and Histamine —, and thirdly, *productin* vacuoles in the gastric surface cells decrease positively after Histidine injection, but not so after Histamine injection.

Thus the actional characteristics of injected Histidine can be summarized as 1. not only secretion granules but secretion vacuoles increase in the peptic cells, 2. *productin* vacuoles are positively discharged from the surface cells. These characteristics of Histidine are also immediately recognizable in the results obtained by

Fig. 1. Histidine and Histamine was respectively injected into the normal rats fasted for 24 hrs. —●— Secretion granules in the peptic cells, —○— Secretion vacuoles in the peptic cells, ---x--- 'Productin' vacuoles in the surface cells.

Fig. 2. Histidine and Histamine was respectively injected into the rats fed with the non-protein diet for 10 days.

Fig. 3. Histidine and Histamine was respectively injected into the rats fed with the non-protein diet for 20 days.

the administration of the diet and sesame oil after the injection of Histidine (Tables 7—10, and Figs. 4 and 5). Usually there is only a slight production of secretion vacuoles after an administration of sesame oil and a copious production of them where artificial diet has been administered. But if Histidine is injected, secretion vacuoles are produced copiously in the peptic cells even after administration of sesame oil, and this is remarkably different from the case in which Histamine was injected before the administration of sesame oil (Fig. 5). On the other hand, it is also noticed that if Histamine is injected before administration of the artificial diet, secretion vacuoles are extremely less than those of the normal case in which the diet was administered without the injection of Histamine.

Fig. 4. Histidine and Histamine was respectively injected, 20 min. later, an artificial diet was given.

Fig. 5. Histidine and Histamine was respectively injected, then at once sesame oil was injected into the stomach.

According to FUJIE's *productin* theory, the vacuolization of secretion granules in the peptic cells is promoted by a decomposed *productin* in the blood. If *productin* is for sure a histamine or a histamine-like substance, the present results obtained by Histidine injections will be explained by the anti-histamic action of histidine, which has been proved by EDLBACHER, JUCKER and BAUR (1937). (If so, it is not so wonderful as to be surprising.)

The most interesting point for the author is the production of secretion granules in the peptic cells, which can be observed after the injection of Histidine. Though a superior production of secretion granules in the peptic cells can be seen after the injection of Histamine, the discharge of *productin* vacuoles is, in this case, so little that the production of secretion granules may be connected with the Histamine injected. However, the discharge of *productin* is so active after the injection of Histidine, as mentioned above, that it must be determined whether the production of secretion granules is due to the Histidine injected or to the *productin* which was discharged into the blood after the injection of Histidine.

To answer these questions, the author injected Atropin so that the discharge of *productin* might be inhibited, then injected Histidine and Histamine respectively (Tables 11 and 12, Fig. 6). In case of Atropin + Histamine injection, the observations are almost similar to those of the case in which Histamine alone was injected (Fig. 1). In the case of Atropin + Histidine injection, secretion granules in the peptic cells are less numerous and secretion vacuoles are more numerous in the early period. And it is also noted that the discharge of *productin* is positively less than

Fig. 6. Atropin was injected, then 10 min. later, Histidine and Histamine was respectively injected.

in the case in which Histidine alone was injected (Fig. 1). Here is little proof of the fact that histidine is a substance which causes the production of secretion granules in the peptic cells.

According to all the observations mentioned above, it is believed that the production of secretion granules in the peptic cells is promoted by histamine, and not by histidine though the latter is similar to the former in so far as it contains an imidazol group, but that histidine, however, has another action viz. the discharge *productin* from the gastric surface cells, and that this difference will be due to the side chain combined with the imidazol group, i. e. the difference between $-\text{CH}_2-\text{NH}_2$

$\text{CH}-\text{COOH}$ (histidine) and $-\text{CH}_2-\text{CH}_2-\text{NH}_2$ (histamine). The observations will also suggest that the FUJIE's gastric hormone *productin* which promotes the production of secretion granules in the peptic cells, will probably be a histamine-like substance rather than a histidine-like substance.

IV. Summary.

As the effects of Histidine in the diet on the secretory function of gastric gland cells were investigated in author's former study, the author has studied here if the actional mechanisms of Histidine are similar to those of Histamine, and has obtained the following conclusions.

1. The production of secretion granules in the peptic cells is believed to be promoted by Histamine and not by Histidine.

2. Histamine does not promote the discharge of *productin* from the gastric surface cells but Histidine does actively promote it. Accordingly, Histidine seems as if it would promote the production of secretion granules in the peptic cells if man observed only the peptic cells.

3. Histidine seems to be related to the vacuolization of secretion granules (discharging stage of secretion granules) in the peptic cells.

4. The actional difference between Histidine and Histamine is deduced to be owing to the side chain combined with the imidazol group.

内 容 自 抄.

食餌中のヒスチジンが胃腺細胞分泌機能に及ぼす影響を追究した著者は、ヒスチジンのその作用機転がヒスタミンと同一か否かを此所に探究し、次の如き結果を得た。

1. 主細胞分泌顆粒はヒスタミンによって新生促進されるが、ヒスチジンによっては新生促進されないと信じられる。

2. ヒスタミンは胃粘膜表在細胞から *productin* を放出させないが、ヒスチジンはその放出を促進する。そのためヒスチジンも結果的には主細胞の分泌顆粒を新生するかの如くに見える。

3. ヒスチジンは主細胞分泌顆粒の非染色化（空胞化）、即ち放出に関与すると考えられる処がある。

4. 以上の如き作用的相違は imidazol 核以外の部分即ち側鎖にあると考えられる。

References.

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