# CATECHOLAMINE CONTENT IN THE GASTRIC JUICE

# OF DOGS SECRETED IN RESPONSE TO FOOD AND TO HISTAMINE

#### L. L. Grechishkin

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The catecholamine concentration in the gastric juice of dogs was determined by the fluorometric method of Von Euler and Floding and its proteolytic activity and acidity also were investigated. After feeding with meat the gastric juice has a high concentration of catecholamines  $(0.092 \pm 0.019~\mu g/ml)$  and possesses high proteolytic activity. In the gastric juice secreted in response to histamine (0.05~mg/kg) the concentration of these amines was several times lower  $(0.037 \pm 0.008~\mu g/ml)$  and the proteolytic activity was almost down to zero. The author suggests that the intensity of function of the chief (peptic) cells is connected with liberation of endogenous catecholamines of the gastric mucous membrane.

High concentrations of catecholamines are found in the gastric mucous membrane of animals and man [3,19]. Their level in this tissue is maintained not only by retention of amines from the circulatory system but also by synthesis with the aid of specific enzymes. This is shown by the high DOPA-decarboxylase activity found in the mucous membrane [29]. Catecholamines are also found in the gastric juice, as Mirzoyan and co-workers first showed [14,17,18]. The participation of these amines in the secretory process is confirmed by results obtained by various authors [13,15,16,20,21,23,24,26], and also by the writer's earlier investigations which demonstrated their connection with the function of the chief cells [2,4].

The object of the present investigation was to study the relationship between the proteolytic activity of gastric juice and its catecholamine content.

# EXPERIMENTAL METHOD

Experiments (16) were carried out on 2 noninbred male dogs weighing 21 and 24 kg. An isolated Pavloy pouch was formed in one dog by Danilov's method [12], and a Basow gastric fistula was formed in the second dog. The animals were kept on a mixed diet and were fed once a day. Before each experiment the dogs were kept without food for 18 h. To obtain gastric juice the dog with an isolated gastric pouch was given 300 g minced meat in broth. The animal with a gastric fistula was given a single subcutaneous injection of histamine dichloride (0.05 mg/kg). The gastric juice was investigated in samples obtained 1 h after the beginning of secretion. The pH of the juice was determined electrometrically, after which the proteolytic activity was measured by the method of Gates [31] as modified in the writer's laboratory [1], and by comparison with a standard it was expressed as pepsin concentration in mg/ml. To determine the catecholamines (adrenalin and noradrenalin) in the gastric juice the fluorometric method of Von Euler and Floding [28] in Govyrin's [11] modification was used. For this purpose, freshly obtained gastric juice was filtered through paper and protein was precipitated by the addition of 0.4 N perchloric acid solution. After centrifugation 20 ml of the supernatant was transferred into another tube with a ground-glass stopper and the pH adjusted to 8.2 by the addition of alkaline solutions. A weighed sample of alumina (200 mg) was then added to the sample, the tube was shaken for 5 min, and the contents centrifuged. The amines were extracted with 0.25 N acetic acid. Fluorescence was measured with a high-sensitivity Soviet BIAN fluorometer with filters of 365 and 510 nm at the entrance and exit, respectively.

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## EXPERIMENTAL RESULTS AND DISCUSSION

A high concentration of catecholamines  $(0.092 \pm 0.019 \,\mu\text{g/ml})$  was found in the gastric juice obtained from the isolated gastric pouch after a meal of meat. Most of these amines consisted of noradrenalin  $(0.084 \pm 0.020 \,\mu\text{g/ml})$ , and adrenalin accounted for only  $0.008 \pm 0.002 \,\mu\text{g/ml}$ .

The concentration of catecholamines in the juice obtained from the dog with a fistula in response to subcutaneous injection of histamine was 3 times lower  $(0.037 \pm 0.008 \ \mu g/ml)$ , of which noradrenalin accounted for  $0.036 \pm 0.008 \ \mu g/ml$  while adrenalin was virtually absent. The proteolytic activity in the samples of juice obtained in response to histamine was negligible  $(0.13 \pm 0.05 \ mg/ml)$  while the acid values were high  $(1.57 \pm 0.5)$ . By contrast, the proteolytic activity in the gastric juice secreted in response to meat was  $1.40 \pm 0.42 \ mg/ml$  pepsin at pH  $1.8 \pm 0.4$ .

Many investigators of gastric secretion regard the juice obtained after injection of histamine as secretion entirely of the parietal cells. This conclusion is based on numerous experimental facts [5, 7-9, 22, 25, 30, 32-34] and it derives from the idea that histamine stimulates only the parietal cells of the mucous membrane and does not affect the chief cells. This accounts for the low concentration of pepsin in such gastric juice.

Gastric secretion in response to meat as a food stimulus is the result of the combined function of both parietal and chief pepsin-forming cells, and the proteolytic activity of this juice is accordingly high.

The results of previous investigations [4, 6, 10] showed that catecholamines in the gastric mucous membrane participate in the function of the chief cells where they play the role of activators of both synthesis and liberation of the proteolytic enzymes which they contain.

The results of this investigation show that after activation of the secretion of the chief cells, the concentration of both pepsin and catecholamines in the gastric juice is increased. Conversely, if secretion takes place entirely without the participation of these cells, both the proteolytic activity and the catecholamine concentration of the juice are very low. This is further confirmation of the view that the liberation of these amines from the depots in the mucous membrane is dependent on the work of the peptic cells.

## LITERATURE CITED

- 1. S. V. Anichkov and L. L. Grechishkin, Farmakol. i Toksikol., No. 5, 587 (1965).
- 2. S. V. Anichkov and L. L. Grechishkin, Byull. Éksperim. Biol. i Med., 64, 37 (1967).
- 3. S. V. Anichkov, I. S. Zavodskaya, and E. V. Moreva, Byull. Éksperim. Biol. i Med., No. 11, 89 (1967).
- 4. S. V. Anichkov (Anitchkov) and L. L. Grechishkin, Arch. Internat. Pharmacodyn., 180, 281 (1969).
- 5. L. L. Grechishkin, Farmakol. i Toksikol., 29, 655 (1966).
- 6. L. L. Grechishkin, Farmakol. i Toksikol., 30, 612 (1967).
- 7. L. L. Grechishkin, Farmakol. i Toksikol., 31, 193 (1968).
- 8. L. L. Grechishkin, Farmakol. i Toksikol., 31, 450 (1968).
- 9. L. L. Grechishkin, Farmakol. i Toksikol., 32, 485 (1969).
- 10. L. L. Grechishkin, Farmakol. i Toksikol., 32, 556 (1969).
- 11. V. A. Govyrin, in: Adrenalin and Noradrenalin [in Russian], Moscow (1964), p. 282.
- 12. N. V. Danilov, Fiziol. Zh. SSSR, 48, 1512 (1962).
- 13. M. G. Dateshidze, Role of the Sympathetic Nervous System in the Secretory Activity of the Stomach. Author's Abstract of Candidate's Dissertation, Tbilisi (1955).
- 14. E. K. Kazarova and N. A. Esayan, Biol. Zh. Armenii, 19, 58 (1966).
- 15. L. N. Karpenko, Neurohumoral Mechanics of Regulation of the Secretory Activity of the Gastric Glands. Author's Abstract of Doctoral Dissertation, L'vov (1966).
- 16. A. S. Karlova, Role of Cholinergic and Adrenergic Structures of the Brain in the Secretory Activity of the Gastric Glands. Author's Abstract of Candidate's Dissertation, Yaroslavl' (1968).
- 17. S. A. Mirzoyan and I. L. Virabyan, Dokl. Akad. Nauk Arm. SSR, 45, 134 (1967).
- 18. S. A. Mirzoyan, N. A. Esayan, I. L. Virabyan, et al., Byull. Éksperim. Biol. i Med., 65, 20 (1968).
- 19. E. V. Moreva, Dystrophic States Evoked by Hypothalamic Stimulation and the Effect of Neurotropic Drugs on Them. Author's Abstract of Doctoral Dissertation, Leningrad (1969).
- 20. Ya. P. Sklyarov, in: Mechanism of Action of Hormones [in Russian], Kiev (1959), p. 237.
- 21. I. I. Triger, in: Proceedings of the Fourth Volga Conference of Physiologists, Pharmacologists, and Biochemists with the Participation of Morphologists and Clinicians [in Russian], Saratov (1966), p. 403.

- 22. B. P. Babkin, Secretory Mechanism of the Digestive Glands, New York (1950), p. 125.
- 23. P. Bass and M. Patterson, J. Pharmacol. Exp. Ther., <u>156</u>, 142 (1967).
- 24. C. F. Code, Pharmacol. Rev., 3, 59 (1951).
- 25. C. F. Code, Fed. Proc., 24, 1311 (1965).
- 26. I. Corral-Salenta, Rev. Esp. Fisiol., 4, 289 (1960).
- 27. H. A. Demand, K. Weichmann, and G. Berg, Gastroenterology, 55, 272 (1968).
- 28. U.S. Von Euler and I. Floding, Acta Physiol. Scand., 33, 45 (1955).
- 29. R. Hakanson and C. Owman, Biochem. Pharmacol., <u>15</u>, 489 (1966).
- 30. E. H. Harries, J. Physiol. (London), <u>133</u>, 498 (1956).
- 31. F. L. Gates, Proc. Soc. Exp. Biol. (New York), 4, 936 (1926-1927).
- 32. A. P. Forest and C. F. Code, J. Pharmacol. Exp. Ther., 110, 447 (1954).
- 33. G. Kahlson and E. Rosengren, Ann. Rev. Pharmacol., 5, 305 (1955).
- 34. W. Lorenz and K. Pfleger, Klin. Wschr., <u>46</u>, 57 (1968).