

# STRUCTURE CHANGES OF THE ENTEROCHROMAFFIN CELLS OF THE SMALL INTESTINE OF GUINEA PIGS UNDER THE INFLUENCE OF ROTUNDIN

(UDC 611.341-018 : 615.717 + 615.717-092 : 611.341-018)

I. V. Skorodumova and V. V. Berezhinskaya

All-Union Scientific Research Institute of Therapeutic and Aromatic Plants

(Director, P. T. Kondratenko), USSR Ministry of Health, Moscow

(Presented by Academician V. N. Chernigovskii)

Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 58, No. 7,  
pp. 113-115, July, 1964

Original article submitted March 29, 1963

It is now firmly established that many drugs act on the body through mediators. In particular the action of the recently widely used reserpine is related to the metabolism of 5-hydroxytryptamine (serotonin) and of the catecholamines (adrenaline and noradrenaline) [4, 5].

In our Institute from the plant *Stephania glabra*, we separated the alkaloid rotundin, which belongs to the group of benzoquinolysins, and is closely related chemically to tetrabenazine. This latter is an active tranquillizing substance, which, like reserpine, exerts a strong influence on the metabolism of serotonin [6, 7].

The object of the present work has been to study the histochemical changes in enterochromaffin cells of the small intestine under the influence of rotundin. According to published reports [1, 3] enterochromaffin cells (cells of Kol'chitskii) contain up to 1% of serotonin.

## EXPERIMENTAL METHOD

The investigations were made on guinea pigs of both sexes weighing 330-520 g. The animals of the first (control) group received no drugs. Those of the second group received 50, 100, and 200 mg/kg of rotundin. Animals of the third group were studied to determine the effect of rotundin given together with iproniazid, which is an inhibitor of monoaminoxidase, which destroys serotonin. Animals of the fourth group received reserpine, so that its action could be compared with that of rotundin.

After 24 h the animals were decapitated, and the duodenum was removed for histological examination. The material was fixed in 12% neutral formalin, and embedded in paraffin. Sections 5 $\mu$  thick were cut. To reveal the argentaffin grains we used the method of Masson-Fontana. The sections were also stained by various other histological methods.

## EXPERIMENTAL RESULTS

It has been shown that rotundin produces an appreciable and statistically significant reduction in the number of enterochromaffin cells in the duodenal mucosa of the guinea pigs (see table).

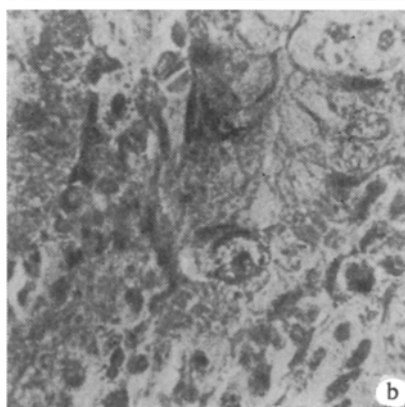
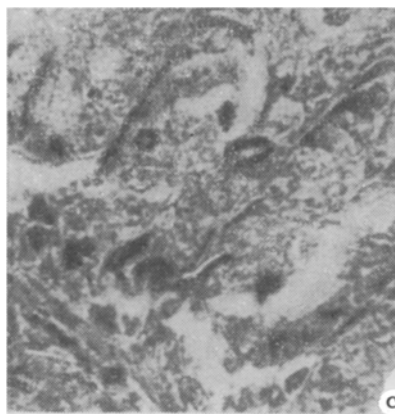
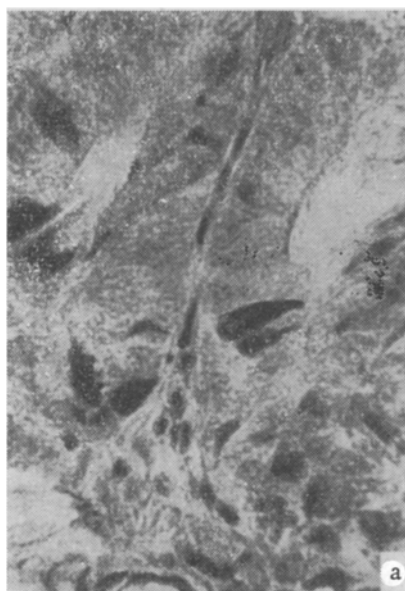
In control animals the greatest number of enterochromaffin cells was found at the base of the villi (see figure a). The cells were triangular in shape with a structure which was difficult to make out because the cytoplasm was strongly argentophil.

Under the influence of reserpine the enterochromaffin cells became indistinguishable from other epithelial cells of the mucosa. Only in two animals were enterochromaffin cells found having solitary argentophil granules in the form of a fine dust (see figure b).

When 50 mg/kg of rotundin was injected there was a reduction in the number of argentophil cells to half the value found in the controls. The remaining cells were greatly enlarged and had an immense broadly oval or poly-

# Influence of Rotundin on the Number of Enterochromaffin Cells in the Guinea Pig Duodenal Mucosa

Preparation and method of administration	No. of animals	Dose (in mg/kg)	Mean number of argentophil cells in a cross section of the duodenum	P
Control	4		587 $\pm$ 42.5	
Rotundin (subcutaneous)	5	50	275 $\pm$ 43.5	< 0.01
	5	100	231 $\pm$ 26.0	< 0.001
	5	200	229 $\pm$ 36.8	< 0.002
Iproniazid (intraperitoneally 18 h before rotundin) + rotundin	5	100	320 $\pm$ 25.9	< 0.01
		100		
Reserpine (by mouth)	4	20	6 $\pm$ 2	< 0.001



Enterochromaffin cells (cells of Kol'chitskii) in the mucosa of the guinea pig duodenum. a) General view of cells at the base of a villus of a normal guinea pig; b) loss of granules by the enterochromaffin cells in a guinea pig killed 24 h after introduction of 20 mg/kg reserpine into the gut; c) enterochromaffin cell changed by vacuolization 24 h after subcutaneous injection of 50 mg/kg rotundin. Micrograph. Magnification 400 x.

gonal shape. As the cytoplasm became saturated with granules, three types of cells could be distinguished. The first group included cells which were densely packed with granules, so that the nucleus could not be made out. In this set of experiments the number of such cells was very small—only 56. Cells containing a moderate number of granules formed the second group. The third group consisted of cells with solitary granules scattered in the cytoplasm. In the last two groups these cells were distributed (about 116 and 94). The irregular form of the cells was largely due to the uneven distribution of the argentophil granules in the cytoplasm. In some parts of the cell body they were grouped together, while in other places there were gaps (figure c).

With rotundin doses of 100 and 200 mg/kg the number of cells tightly packed with granules became still smaller (37). The remaining groups had approximately the same number of cells.

It should be noted that independently of the dose of rotundin in the enterochromaffin cells we found changes of a particular type showing a characteristic cytomorphosis with the development of forms distinguishable from the cells found in the control animals. These changes are apparently related to the condition of functional stimulation which in certain regions showed up as a renewal of the intestinal mucosa.

A comparison of the structural changes of the enterochromaffin cells induced by the injection of rotundin with the morphological manifestations of reserpine shows that they are of the same nature, though quantitatively the latter has a much stronger action.

The results we have reported indicate that rotundin exerts a definite action on the system of enterochromaffin cells, and that serotonin is possibly involved in the mechanism.

#### SUMMARY

A study was made on guinea pigs of both sexes of the histochemical changes in the enterochromaffin cells of the small intestine under the influence of the alkaloid rotundin. The Masson-Fontana method was used to investigate the state of the enterochromaffin cells. Argentophil granules of these cells have recently been identified with serotonin (5-hydroxytryptamine). Analysis of the data obtained showed that rotundin had a definite effect on the enterochromaffin cell system halving the number of these cells, and causing stimulation of the remainder to produce the morphological appearance of regenerating tissue. This evidence points to a possible role played by serotonin in the action of rotundin.

#### LITERATURE CITED

1. E. Benditt and R. Wong, J. Path., Vol. 32, p. 638 (1956).
2. Idem, Proc. Inst. Med., Chic., Vol. 21, p. 279 (1957).
3. Idem, J. exp. Med., Vol. 105, p. 509 (1957).
4. A. Pletscher, P. Shore, and B. Brodie, Science, Vol. 122, p. 374 (1955).
5. Idem, J. Pharmacol. exp. Ther., Vol. 116, p. 84 (1956).
6. A. Pletscher, H. Besendorf, and H. Bächtold, Arch. exp. Path. Pharmac., Bd. 232, S. 499 (1958).
7. M. Vialli and F. Ghiringhelli, Rend. Inst. Lomb. Sc. e Lett., Vol. 92, p. 511 (1958).

---

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

---