## Effect of Trasylol® on Paneth Cells of the Mouse

The characteristic feature of Paneth cells is the apical cytoplasmic secretory granules. It is assumed that these cells secrete digestive enzymes, especially peptidases, into the intestinal lumen[1-3]. It has been shown also that Paneth cells are able to phagocytose bacteria[4,5] and secrete amino acids[6]. The secretory granules of the Paneth cells contain also lysozyme[7] and enzyme activities characteristic of lysosomal organelles[8]. The cells are able to take up L-dopa and dopamine from the circulation[9,10]. It has been shown that a rapid turnover is characteristic of secretory granules of Paneth cells and that the standard food does not have any apparent effect on them[11]. Recent morphological observations on Paneth cells have indicated that the sympathetic and parasympathetic nervous systems control the secretory mechanisms of these cells[12]. Paneth cells are morphologically also quite identical to the acinar cells of the pancreas[13]. It is well known that an inhibitor of trypsin present in dietary soybean can induce hypertrophic growth of pancreatic acinar cells of the rat[14]. Therefore it was studied whether Trasylol®, a trypsin and proteinase inhibitor, could exert any morphological effects on intestinal Paneth cells.

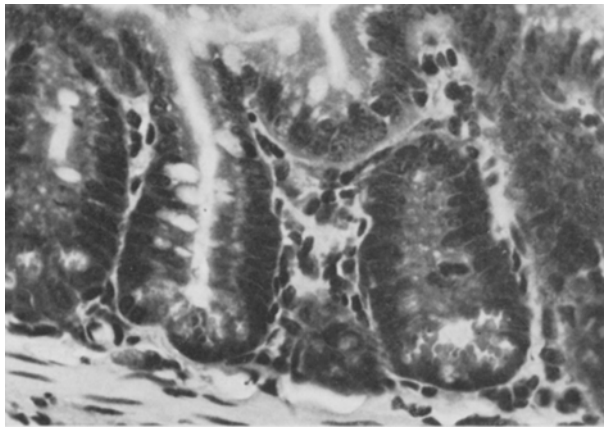

Fig. 1. A light microscope photograph of a formaline-fixed and Best's carmine stained 7 µm thick section of the jejunum of the control mouse. Some granular Paneth cells at the bottom of the crypts of Lieberkühn are seen. ×900.

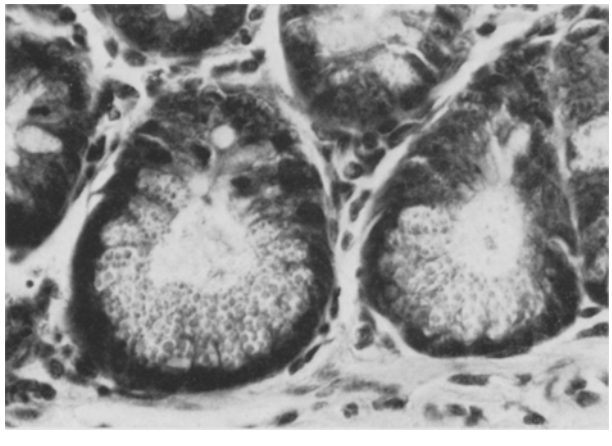

Fig. 2. A light microscope photograph of the jejunum of the mouse which received an i.p. dose of 40,000 UI/kg of Trasylol® 1 h before killing. The fixation and staining methods were identical to those in Figure 1. The number of recognizable Paneth cells per crypt was markedly increased after Trasylol® treatment. There was also a significant increase of the count and size of cytoplasmic granules. ×900.

*Material and methods.* The material consisted of 17 adult albino mice of both sexes. The animals were descendants of a strain used at the Department of Anatomy. The mice were fasted for 1 day before the experiments but were allowed to drink tap water ad libitum. The experimental group of mice received an i.p. dose of 40,000 IU/kg of Trasylol®. 1 h later the mice were killed by decapitation and tissue samples were taken from the mid-duodenum and the mid-jejunum. The pieces were fixed in a buffered 4% formaldehyde solution, pH 7.2, embedded in paraffin wax, sectioned at 7 µm and stained with Best's carmine method[15]. The control mice received only an equal dose of 0.9% saline solution. The experimental group contained 10 mice, and 7 mice served as controls. The number of cytoplasmic coarse granules of Paneth cells was counted under a light microscope. The objective and ocular lenses with magnifications of ×90 and ×10, respectively, were used. A total of 400 cells were studied in the experimental and 600 cells in the control group. No thickness correction of sections was made because only the relative number of granules per cell between the experimental and control groups was determined.

*Results.* The number of the indentifiable Paneth cells in an intestinal crypt was higher in the mice treated with Trasylol® than in the control group 1 h after administration of the drug (Figures 1 and 2). The mean diameter of Paneth cell secretory granules was also somewhat larger after Trasylol® treatment than in controls (Figure 2). The mean number of secretory granules per cell increased from 12.1 ± 0.1 to 17.1 ± 0.2 in the duodenum and from 8.3 ± 0.1 to 19.7 ± 0.2 in the jejunum afte trreatment of the mice with Trasylol® (Figures 3 and 4). Both differentials were highly significant ($p < 0.001$).

*Discussion.* It was previously shown that Trasylol® has various biological effects on different cell types. Very high doses of the drug can destroy the mast cells of the rat mesenterium, whereas this phenomenon does not occur in the guinea-pig[16]. Trasylol® can, on the other hand, protect the mucosa of the small intestine from hemorrhages during prolonged shock[17]. The underlying mechanisms


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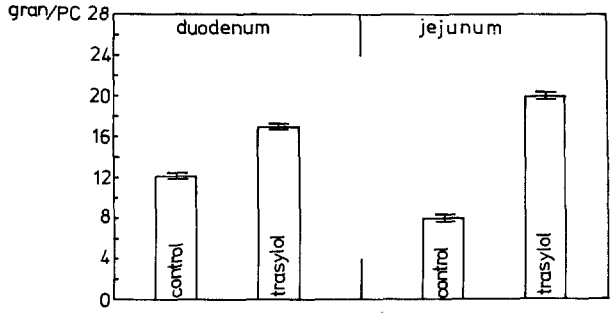


Fig. 3. The mean number (± S.E.) of secretory granules of Paneth cells after Trasylol® administration. The granule count per cell is marked on the ordinate. There is statistically a highly significant increase of the granule count per cell both in the duodenum and jejunum. Abbrevations: gran, granule; PC, Paneth cell.

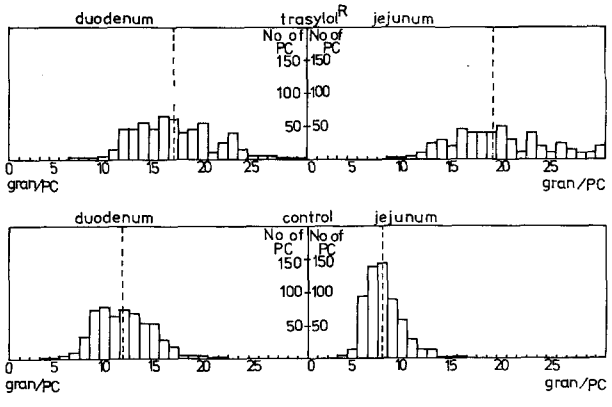


Fig. 4. The distribution of the Paneth cells as a function of the number of coarse cytoplasmic granules after Trasylol® administration. The number of granules per cell is marked on the axis and the number of Paneth cells on the ordinate. The average number of granules per cell is marked with dotted lines. The same material was used for Figures 3 and 4.

for these diverse phenomena have mainly remained obscure. It is shown that Trasylol® is able to inhibit the activity of zymogenic proteases of the acinar cells of the rat pancreas[18]. The present results indicated that Trasylol®, which is an inhibitor of various proteinases and trypsin, has obviously an identical effect on Paneth cells of the intestine. This appeared as an increased number of secretory granules of the cells as well as an increased granule size. Similar phenomenoma have been described to occur in acinar cells of the rat pancreas after soybean ingestion which contains trypsin inhibitors[14]. The origin and the relation of the Paneth cells to other cell types in the gastrointestinal tract is not wholly understood. The present observations further support the view that Paneth cells are morphologically and functionally and even embryologically related to the pancreatic acinar cells, as suggested previously on the basis of numerous morphological studies[13]. The underlying mechanism for the increase of the counts of secretory granules may either result from increased production of material necessary for granule formation or delayed extrusion of the granules from the cytoplasm of the cells into the intestinal lumen. The marked increase of the granule size in the present Trasylol® experiments favours the latter mechanism.

*Zusammenfassung.* Nachweis, dass Trasylol®, ein Hemmstoff für proteolytische Enzyme, im Duodenum und Jejunum der Maus eine Zunahme der Panethschen Zellen bewirkt und ausserdem eine Vermehrung der Sekretgranula pro Zelle verursacht.

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## Stereological Measurements of Atrial Ultrastructures in the Guinea-Pig

Examination of the excitation-contraction coupling process in atrial muscle has suggested that the frequency-dependent mechanical response of the tissue[1,2] is associated with calcium derived from multiple calcium stores[3-5]. These stores have been suggested to be the sarcolemmal membrane, subsarcolemmal cisterns (SSC), sarcoplasmic reticulum (SR) and mitochondria (Mt). Electron microscopic examination of these and other intracellular structures have been performed in several atrial preparations[6,7]. However, in order to develop a better understanding of the contractile behavior of the tissue, a quantitative examination of cell structure is desirable. Previous determinations of this kind have been made on ventricular myocardium[8-11] and skeletal muscle[12,13]. In this paper, we report the results of stereological measurements made on the contraction-related structures of a typical mammalian atrial preparation: the guinea-pig left atrium.

*Materials and methods.* Left atria from guinea-pigs of either sex, weighing between 400 and 800 g, were isolated in oxygenated Krebs-Henseleit solution at 24 °C. Prior to fixation, mechanical characteristics of the tissue were examined with a standard isometric recording apparatus. Only atria exhibiting normal behavior were prepared for stereological examination.

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