

The research was carried out on white rats from our own breed at the Department of Histology and Embryology in Lublin. The animals were on the standard diet. They were divided into one control group and three experimental groups. Every day the experimental rats were administered on empty stomach mefenamic acid produced by the Fabianice Pharmaceutical Plants "Polfa", Mefacit, by means of a gastric tube. The experimental group I was given an amount of 30 mg/kg of body weight for two weeks, the group II — 430 mg/kg of body weight for two weeks, and the group III — 860 mg/kg of body weight for four days. The sections

to be examined were taken from duodenum 24 hrs after the last administration of the drug. The succinic dehydrogenase was discovered on non-fixed material according to Nachlas method. On the sections fixed in Baker fluid, histochemical reactions to the acid and alkaline phosphatase activity were carried out according to Gomori method, and to the activity of adenosinetriphosphatase — according to Wachstein and Meisel. On paraffin sections stained in Carnoy fluid the PAS reaction was carried out with a control digestion with diastase and Brachet reaction with a control digestion with ribonuclease.

EXPERIMENTAL

Control group

In the cytoplasm of absorbing cells of the intestinal epithelium and in the cytoplasm of glandular cells a strong pyronine-absorbing reaction was observed, proving the presence of RNA (Fig. 1). There was found a positive reaction to acid phosphatase and a strong reaction to alkaline phosphatase and adenosinetriphosphatase. They were most strongly marked in the striated limbus of enterocytes. The activity of succinic dehydrogenase was high in absorbing cells covering villi, and lower — in intestinal glands. The mucocytes and the striated limbus of enterocytes showed a PAS-positive reaction. The cells of connective tissue stroma showed a positive reaction to all hydrolytic enzymes and to Brachet reaction.

Experimental group I

The intensity of PAS and Brachet reaction (Fig. 2) in epithelium and connective tissue stroma of the duodenum was similar to that in the duodenum of the control animals. No changes were observed in the distribution and intensity of reaction to the acid phosphatase and succinic dehydrogenase. The activity of alkaline phosphatase and of adenosinetriphosphatase, however, slightly decreased.

Experimental group II

The intensity and distribution of PAS and Brachet was similar to that in the control group and in the experimental group I. The activity of acid phosphatase in enterocytes considerably increased. It had a form of thick, intensively saturated granules in the whole cytoplasm of absorbing cells. In this group, in comparison with the experimental group I, further decrease in alkaline phosphatase activity was observed (Fig. 3) uniform in all the absorbing cells of epithelium, as well as decrease in

activity of adenosinetriphosphatase concerning enterocytes covering the apical part of intestinal villi (Fig. 4). The activity of succinic dehydrogenase in epithelium also decreased in comparison with the control group and the experimental group I (Fig. 5).

Experimental group III

The pyronine-absorbing reaction in the intestinal epithelium and in connective tissue stroma did not change. Among enterocytes the reaction to acid phosphatase was strong, as in the experimental group II (Fig. 6). The activity of reaction to alkaline phosphatase, however, considerably decreased. The reaction to adenosinetriphosphatase and to succinic dehydrogenase in these cells also decreased considerably, especially in the intestinal glands. Among the mucous cells of intestinal glands an increase of intensity of PAS reaction was observed. The cells were bulgy and profusely dilatated with secretion.

RESULTS OF INVESTIGATIONS AND DISCUSSION

Mefenamic acid, a derivative of antranil acid (the chemical term: N-(2,3-xylilo)-antranil acid) is an analgesic, anti-inflammatory and antipyretic drug, similar to salicylates, phenylbutazone and flufenamic acid (1, 9). The degree of absorbing drugs depends, among others, on the metabolic activity of thin epithelium mucous membrane whose active surface is considerable. The changeability of histochemical reactions in the mucosa of the alimentary duct was described in various stages of its development and after some of the drugs were administered (2, 3, 6, 7, 8).

In our investigations, after administering mefenamic acid in various doses, no changes in Brachet reaction were observed in the duodenal mucous membrane in comparison with histochemical reaction in the intestine of the control animals. The intensity of PAS reaction in the mucous cells of epithelium changed only in the control group of animals receiving the drug in 860 mg/kg dose of body weight can be said for stimulating the cells towards an increased production and myxiosis. The activity of the investigated enzymes in enterocytes was different in the particular groups of experimental animals. After applying 30 mg/kg of body weight for two weeks only a small decrease was observed in the activity of reaction to alkaline phosphatase and adenosinetriphosphatase in enterocytes. After the administration of the drug in the dose of 430 mg/kg of body weight for two weeks the activity of reaction to acid phosphatase increased, whereas the intensity of reaction to alkaline

phosphatase, adenosinetriphosphatase and succinic dehydrogenase decreased in those cells. After administering the drug in the amount of 860 mg/kg of body weight for four days there was observed a more intensive, than in the former groups, decrease of activity of alkaline phosphatase, adenosinetriphosphatase and succinic dehydrogenase.

The obtained results show that mefenamic acid, though rapidly absorbed from the alimentary duct and rapidly excreted from the organism (4, 5, 10), may affect the active part of intestinal mucous membrane, especially the intestinal epithelium, stuffing the villi and intestinal glands. The most sensitive to action of the drug proved to be the absorbing cells of epithelium in which the most important changes were observed in enterocytes taking part in the active transport through membranes. The decrease in the activity of reaction to alkaline phosphatase and adenosinetriphosphatase concerned all the experimental groups and was proportional to the dose of the administered drug. This proves that the influence of mefenamic acid on the permeability of cellular membranes, and thereby on metabolism of duodenal epithelium cells is possible.

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Fig. 1

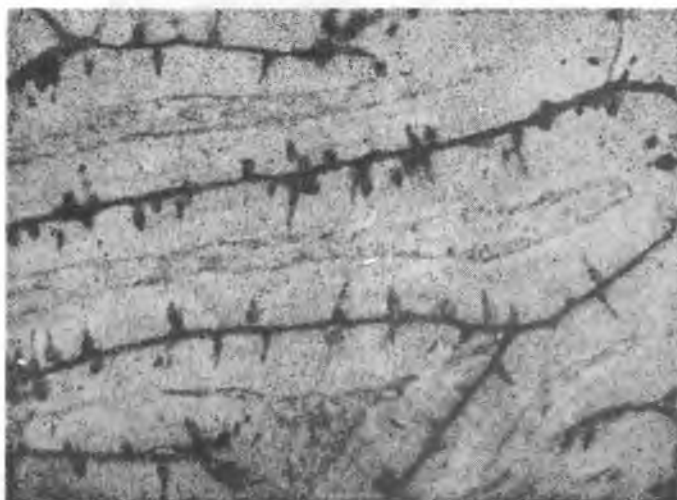


Fig. 2



Fig. 3

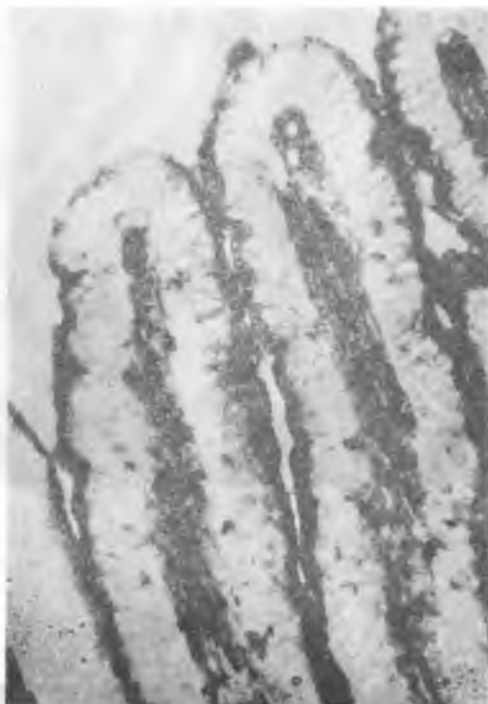


Fig. 4

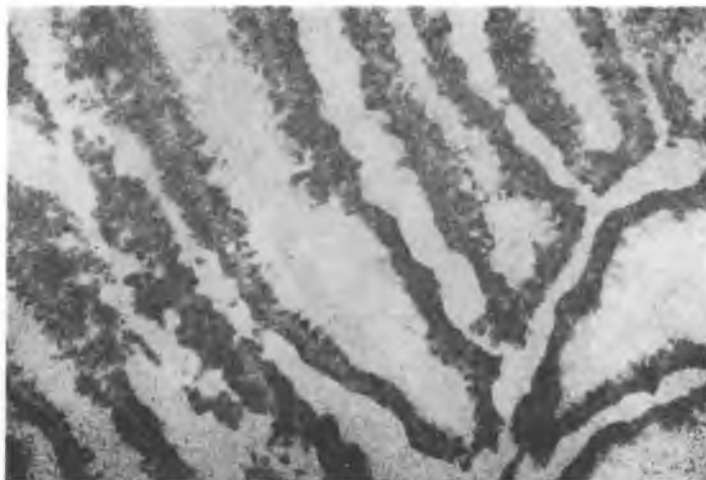


Fig. 5

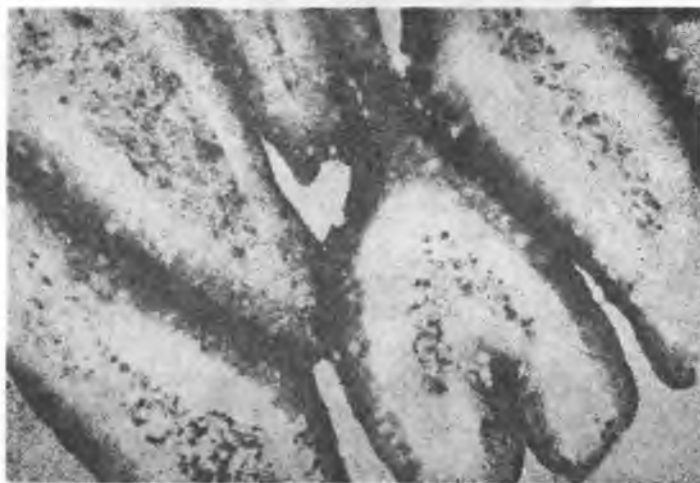


Fig. 6

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EXPLANATION TO FIGURES

Fig. 1. Brachet reaction in duodenal mucous membrane of the control rat. Magn. ca 200×.

Fig. 2. PAS reaction in duodenal mucous membrane of the rat from the experimental group I. Magn. ca 200×.

Fig. 3. Reaction to the activity of alkaline phosphatase in duodenal mucous membrane of the rat from the experimental group II. Magn. ca 200×.

Fig. 4. Reaction to the activity of adenosinetriphosphatase in duodenal mucous membrane of the rat from the experimental group II. Magn. ca 200×.

Fig. 5. Reaction to the activity of succinic dehydrogenase in the duodenal mucous membrane of the rat from the experimental group II. Magn. ca 200×.

Fig. 6. Reaction to the activity of acid phosphatase in the duodenal mucous membrane of the rat from the experimental group III. Magn. ca 200×.

STRESZCZENIE

Badano błonę śluzową dwunastnicy szczurów białych, którym uprzednio podawano dożołądkowo kwas mefenaminowy w postaci preparatu Mefacit produkcji „Polfa”. Zwierzęta podzielono na 4 grupy: kontrolną oraz 3 grupy doświadczalne. Grupa I doświadczalna otrzymywała lek w dawce 30 mg/kg m.c. przez 2 tygodnie, grupa II doświadczalna — w dawce 430 mg/kg m.c. przez 2 tygodnie, grupa III doświadczalna — w dawce 860 mg/kg m.c. przez 4 dni. W pobranych po 24 godz. od ostatniego podania leku wycinkach dwunastnicy wykrywano aktywność fosfatazy kwaśnej i zasadowej, adenozynotrójfosfatazy i dehydrogenazy bursztynianowej oraz wykonano reakcje PAS i Bracheta.

W wyniku przeprowadzonych obserwacji wykazano zmiany histochemiczne w porównaniu z preparatami kontrolnymi, dotyczące zwłaszcza nabłonka jelitowego. W grupie I doświadczalnej zaobserwowano niewielki spadek aktywności fosfatazy zasadowej i adenozynotrójfosfatazy. W grupie II doświadczalnej wyraźnie zmniejszyła się intensywność reakcji na dehydrogenazę bursztynianową, fosfatazę zasadową i adenozynotrójfosfatazę, natomiast zwiększyło się nasilenie reakcji na fosfatazę kwaśną. W grupie III doświadczalnej nastąpił dalszy spadek aktywności fosfatazy zasadowej, adenozynotrójfosfatazy i dehydrogenazy bursztynianowej w enterocytach oraz wzrost intensywności reakcji PAS w komórkach śluzowych gruczołów jelitowych.

РЕЗЮМЕ

Исследовано слизистую оболочку двенадцатиперстной кишки белых крыс, которые получали в желудок мефанаминовую кислоту в виде препарата Мефацил производства Польфа. Животные были разделены на четыре группы, т.е. на одну контрольную и три опытные. Первая опытная группа получала препарат в дозе 30 мг/кг в.т. в течение двух недель; вторая опытная группа — в дозе 430 мг/кг в.т. в течение двух недель; третья опытная группа — в дозе 860 мг/кг в.т. в течение четырех дней. Спустя 24 часа от последней принятой животными дозы препарата были взяты срезы двенадцатиперстной кишки и исследовано активность кислой и щелочной фосфатазы, аденозинотрифосфатазы и сукцинатной дегидрогеназы, а также проведено реакцию PAS и Брашета.

В результате проведенных наблюдений показано гистохимические изменения выступившие в кишечном эпителии и сопоставлено с контрольными препаратами. В I опытной группе замечено небольшое понижение активности щелочной фосфатазы и аденозинотрифосфатазы. Во II опытной группе значительно понизилась интенсивность реакции на сукцинатную дегидрогеназу, щелочную фосфатазу и аденозинотрифосфатазу, зато повысилась интенсивность реакции на кислую фосфатазу. В III опытной группе выступало дальнейшее понижение активности щелочной фосфатазы, аденозинотрифосфатазы и сукцинатной дегидрогеназы в энтероцитах и повышение интенсивности реакции PAS в слизистых оболочках кишечных желез.

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