



## RESULTS

## Control group

Under the microscope the mucous membrane of the stomach of the particular individuals showed no major differences. It was covered with one layer of the characteristic cylindrical epithelium. The cytoplasm and cell nuclei of the epithelium were stained normally with H + E (Fig. 1). The gastric glands proper had a typical tubular structure. They consisted of normally distributed additional, chief and parietal cells. The lumen of the glands was narrow and the glands discharged into shallow gastric pits, whereas the bottoms of the tubules reached the muscular layer of the mucosa. In the region of the glands there were some lymphatic nodules. The structure of the gastric submucosal membrane was normal.

## Group I

In all animals of this experimental group the gastric mucosa was widened (Fig. 2). The covering epithelium showed foci of destruction. The lumen of the glands was markedly broadened and filled with acidophilic substance. Some changes of vacuolar degeneration of the cells forming the glands proper of the stomach were noted. They were accompanied by morphological changes of the cell nuclei. Some of them were pycnotic, others large with a broad ring "halo" round the nucleus (Fig. 3). Owing to the enlarged granules in the cytoplasm in the chief and their enhanced basophilicity, the physiological adelomorphism was substituted by delomorphism unnatural to them. In the interglandular connective tissue scarce macrophages were present. In the subglandular connective tissue the lumen of the capillary blood vessels was broadened and there were infiltrations.

## Group II

The mucous membrane was enormously widened (Fig. 4). Its epithelium had undergone extensive diffusive necrosis. The gland outlets were expanded widely and filled with granular coagulated secretion (Fig. 5). The additional cells of the glands exhibited a considerably flattened supranuclear cytoplasm. There were distinct morphological changes in the cell nuclei. The chief cells showed features of vacuolar degeneration and a wide perinuclear rings. Numerous parietal cells were nontypical in appearance. In most of them acidophilicity was depressed, and the pycnotic nuclei were pushed towards the cell periphery. The zone of parietal cells was widened. In some places of the glandular zone of the mucosa the parietal cells were found to build the body and bottom of the glands (Fig. 6).

### G r o u p III

The width of the gastric mucosa was close to the control picture. The morphological changes of gastric mucosa surface appeared as extensive desquamation and disintegration of the covering epithelial cells (Fig. 7). The glandular lumen was only slightly broadened. Flattening of the supranuclear part of the cytoplasm and poor staining of the additional cells were observed. Most of the cells constituting the glands exhibited vacuolar degeneration. The nuclear structures of the many cells were separated from the cytoplasm by a broad "halo". The nuclei of these cells were not typical in appearance, enlarged, even enormous or pycnotic and pushed to the periphery (Fig. 8). The chief cells of the body and bottom of the glands contained numerous intensively basophilic megagranules. There were lymphocytic infiltrations in the subglandular connective tissue.

### DISCUSSION

Morphological changes were found in all the experimental animals within the glandular part of the stomach. The changes appearing in all the groups appeared as destruction of the epithelium on the surface of the mucosa. Vacuolar degeneration appeared in all cells constituting the gastric glands proper. Cells were noted with a broad perinuclear "halo". The nuclei were deformed, modified in size and intensity of staining. The number of parietal cells increased, many of them exhibiting pycnosis or karyolysis. The intensity of morphological changes of the stomach varied in the particular experimental groups (I—III). They were most pronounced in the group II where Ukrain was given in a dose of 9.5 mg/kg b.wt. Microscopic inspection of the stomach wall in group III after the dose of 4.75 mg/kg b.wt. indicated the smallest changes. It may be concluded on the basis of the results obtained that the effects of the maximal Ukrain dose — 19 mg/kg b.wt. were not proportional to the amount of the drug applied. The destructive changes in the stomach of the group I can be described as intermediate between the maximal ones observed in group II and the minimal ones in group III.

It is difficult to decide within the range of this study whether the described changes were due to the preparation administered. The supposition that it was so is supported by the fact of occurrence of degenerative changes in the cells in their nuclear structure after Ukrain administration. Novicky et al. (4) observed *in vivo* destruction of neoplasm cells after application of Ukrain. According to these authors this drug inhibits the metabolism of cancer cells by affecting oxygen uptake, depression of nucleic acids and protein synthesis. It may, therefore, be indirectly inferred that the drug applied in the present study *in vivo* exerted a catabolic effect on the cells of the gastric wall. It is possible that the tested drug is a complex factor defactor depressing cytoprotection in the studied organ (1, 6, 9).

## REFERENCES

1. Allen A.: Structure and Function of Gastrointestinal Mucus. I [in:] Physiology of the Gastrointestinal Tract. Ed. Johnson L. R., Raven Press, N. Y. 1981.
2. Kleinrok Z. et al.: Basic Central Pharmacological Properties of Thiophosphoric Acid Alcaloid Derivatives from *Chelidonium majus* L. Polish Journal of Pharmacol. Pharm. 3, 227, 1992.
3. Novicky J. W.: Cancer Treatment Using Anticancer Preparation Alcaloid Derivative Ukrain. Chemioterapia Supp. 4, 1169, 1985.
4. Novicky J. W. et al.: Biological Activity of Ukrain *in vitro* and *in vivo*. Chemioterapia, Supp. 7, 683, 1987.
5. Novicky J. W. et al.: Macroscopic UV-Marking through Affinity. Journal of Tumor Marker Oncology 3 (4), 463, 1988.
6. Tarnowski A. et al.: Prostaglandin Protection of the Gastric Mucosa Against Alcohol Injury—Dynamic Time Related Process. Role of the Mucosal Proliferative Zone. Gastroenterology 88, 334, 1985.
7. Ukrain — Name of Company and Address of Pharmaceutical Company, Firma Novicky, Laimgrubengasse 19/5, A-1060 Vienna.
8. Zawistowski S.: Technika histologiczna. PZWL, Warszawa 1986.
9. Dzieniszewski J., Brandt Z.: Współczesne poglądy na etiopatogenezę choroby wrzodowej. Wiad. Lek. 13 (36), 1109, 1983.

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## STRESZCZENIE

Badania przeprowadzono na myszach szczepu Albino Swiss, samcach, którym przez 3 miesiące podawano w różnych dawkach, dootrzewnowo, preparat o działaniu cytotoksycznym — Ukrain (7). U wszystkich zwierząt doświadczalnych stwierdzono zmiany morfologiczne w obrębie błony śluzowej żołądka. Wystąpiła też powierzchowna martwica rozplywna nabłonka pokrywającego. Stwierdzono zmiany zwyrodnienia wodniczki komórek. Liczne jądra komórkowe miały nietypowy wygląd, inne uległy kariolizie. Zmiany destrukcyjne żołądka były najbardziej zaawansowane po dawce preparatu  $1/20 LD_{50} = 9,5 \text{ mg/kg c.c.}$ . Mniejsze efekty obserwowano zarówno po dawce maksymalnej:  $1/10 LD_{50} = 19 \text{ mg/kg c.c.}$ , jak i po minimalnej:  $1/40 LD_{50} = 4,75 \text{ mg/kg c.c.}$



Fig. 1. Control group. Rat'sstomach. H+staining. Magn. 10 ×

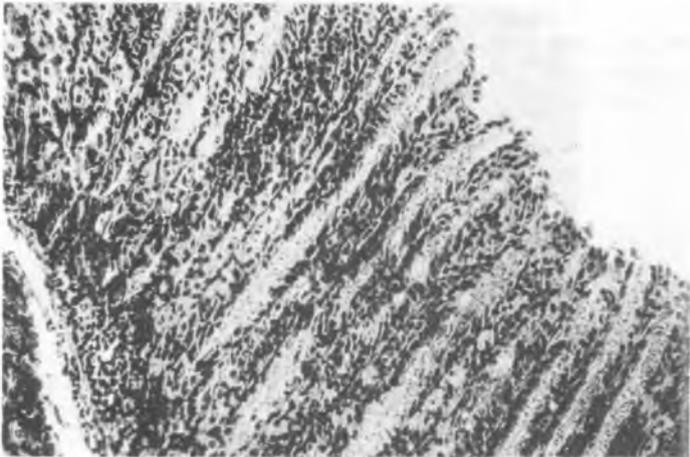


Fig. 2. Experimental group I. The light of glands widened and filled with acidophilic substance.  
H+E staining. Magn. 10 ×

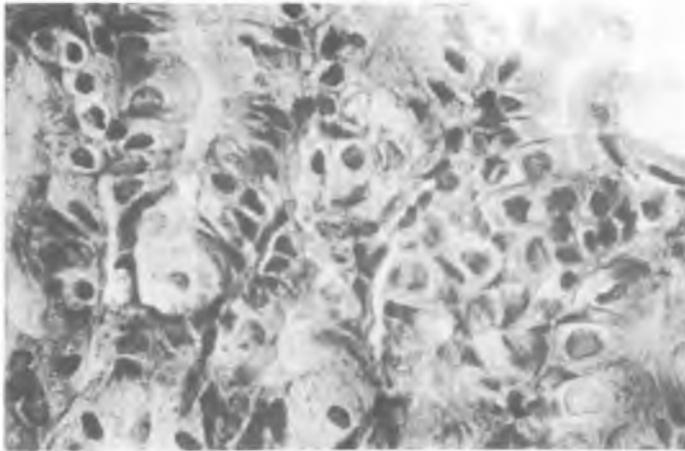


Fig. 3. Experimental group I. Vacuolar degeneration changes. Accompanying morphological changes of cellular nuclei. Magn. 40 ×



Fig. 4. Experimental group II. Destruction changes of epithelium and of cells of stomach mucous membrane. H + E staining. Magn. 10 ×

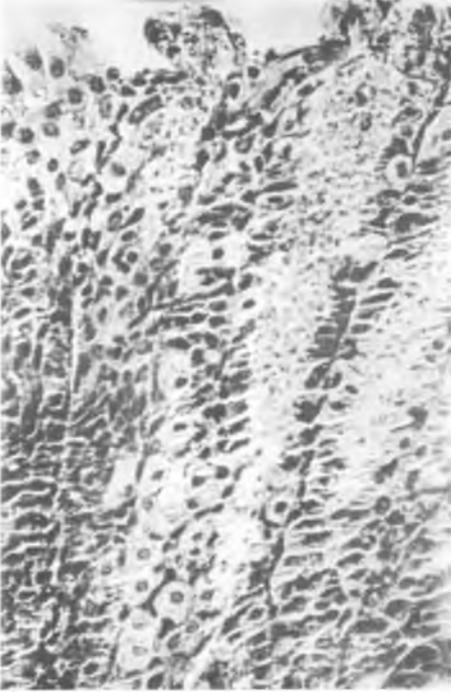


Fig. 5. Experimental group II. Very wide openings of stomach glands, filled with coagulated secretion. Magn. 20 ×

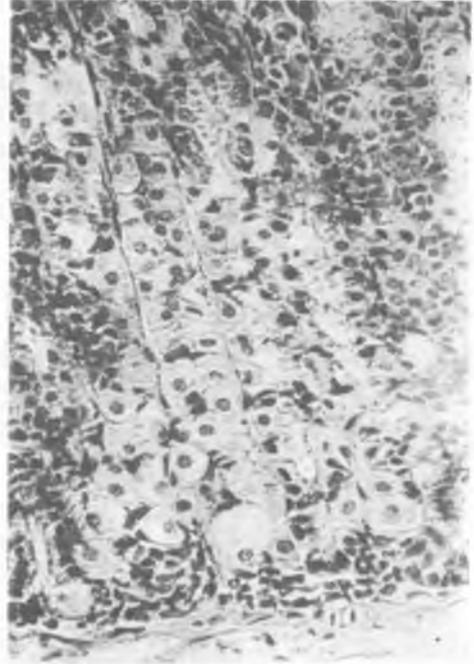


Fig. 6. Experimental group II. Increased number of parietal cells in proper gastric glands. Magn. 20 ×

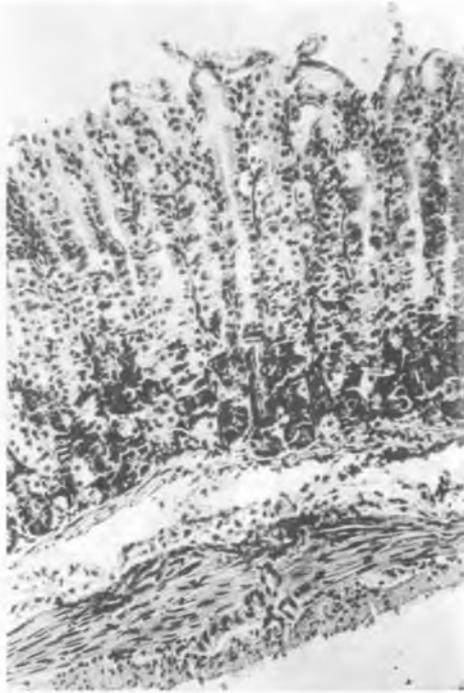


Fig. 7. Experimental group III. The width of mucous membrane of the stomach approximates the control one. Superficial epithelium locally damaged. H + E staining. Magn. 10×

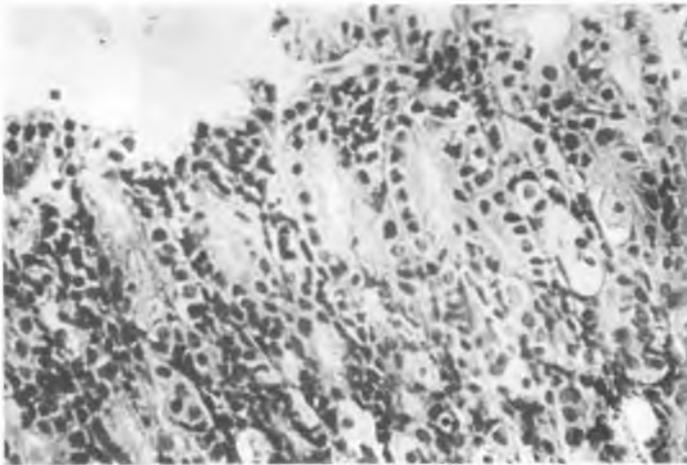


Fig. 8. Experimental group III. Visible erosion of mucous membrane and morphological changes of cellular nuclei of proper gastric glands. Magn. 20×

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