

Department of Histology and Embryology with the Lab of Experimental Cytology
Skubiszewski Medical University of Lublin

ALICJA ZARĘBSKA, DARIA HERNIK, JANUSZ MATUSIEWICZ,
KRYSTYNA CZERNY

*The influence of experimental administration of ethanol
and cephalixin on stomach mucous barrier of rat*

In consideration of lack of precise data available relating to influence of cephalosporins on stomach mucosa, investigations we took up are interesting in clinical respect. It is known that ethanol reduces absorption of oral β -lactam antibiotics (2), on the other hand increases toxic action of many drugs.

The performed experiment aimed at displaying the effect of cephalixin on the activity of gastric gland mucous cells and the activity change influenced by simultaneous administration of ethanol and cephalixin.

MATERIAL AND METHODS

The investigations were carried out on white male Wistar rats weighing approximately 200 g. The animals were divided into three experimental groups and one control group. Each group included five animals.

The rats in control group were fed standard granulated feed and had unlimited access to drinking water. The animals in experimental group I except standard feed were given 20% ethanol *ad libitum* instead of water during 10 days. The animals in experimental group II were administered cephalixin (Lilly, Florence, Italy) in one dose 42 mg per day. This dose corresponds to tenfold minimum daily therapeutic dose for humans. The drug was administered by intragastric bougie every morning before feeding in the form of suspension in physiological saline. The animals in experimental group III were administered cephalixin in identical way to the animals of group II. Moreover, the animals received 20% ethanol *ad libitum* instead of water. On average, each animal in experimental group I drank about 20 ml of ethanol, and in experimental group II about 15 ml in the course of the day.

After 10 days the animals were decapitated. Specimens of the stomach were taken from the major curvature, fixed in 10% formalin, dehydrated in alcohols and immersed in paraffin. 7μ thick sections were stained by Mc Manus's PAS reaction. Pictures were taken under the optic microscope and the Carl Zeiss Jena photographic camera.

RESULTS AND DISCUSSION

Each of gastrointestinal tract sections co-operate together closely and they are dependent on each other because of abundant innervation and local secreted hormones (GEP system). Stomach has numerous polyneuric junctions with intestine and pancreas (5). Thus chemical stimuli influenced intestine (cephalexin absorption takes place in the duodenum) can cause modulation of histamine and gastrin secretion – hormones affected gastric glands secretion in essential means. In contradistinction to cephalixin ethanol is absorbed into the blood for the most part through stomach mucosa. This alcohol elicits a number of changes in the course of metabolic processes in different organs (1, 2, 3, 10). It was proved that alcohol reduces secretion of gastric juice decreasing cAMP level – intracellular secretion regulator – through adenyl cyclase. Alcohol administered in 20% concentration inhibits completely digestive activity of pepsin (7, 9).

In the conducted experiment we found that ethanol also completely inhibited secretory activity of cervix mucous cells and decreased activity of superficial mucous cells and orifice mucous cells of gastric glands (Fig. 1 and 2). Authors engaged in investigation of ethanol influence on different organs notify of cells activity inhibition through ribosomes disintegration (8), smooth endoplasmic reticulum proliferation (4) and mitochondria lesion (6, 10).



Fig. 1. Proper gastric mucosa of a rat from control group. Strong reaction on neutral mucopolysaccharides in superficial mucous cells and orifice mucous cells of gastric glands, and less intensive reaction in cervix mucous cells are visible. PAS reaction. Magn. 200x

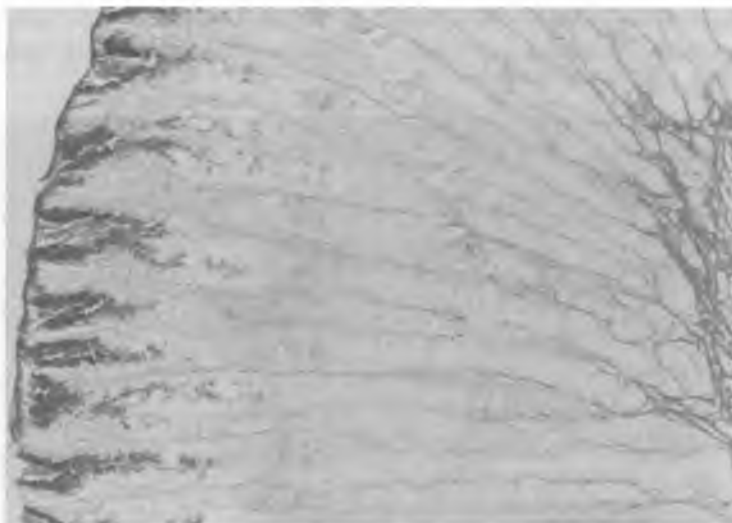


Fig. 2. Proper gastric mucosa of a rat from experimental group I (ethanol). Weaker reaction on neutral mucopolysaccharides in superficial mucous cells and orifice mucous cells of gastric glands, and no reaction in cervix mucous cells are visible. PAS reaction. Magn. 200x

After administration of cephalixin we ascertained increase in the activity of superficial mucous cells and orifice mucous cells of gastric glands. However, positive reaction on mucopolysaccharides was observed in cervix mucous cells only close by orifice mucous cells of gastric glands (Fig. 3). Superficial mucous cells and orifice mucous cells of gastric glands are of essential importance in mucous barrier formation. Increase in their activity accompanied increased activity of principal cells and parietal cells after administering cephalixin (11).

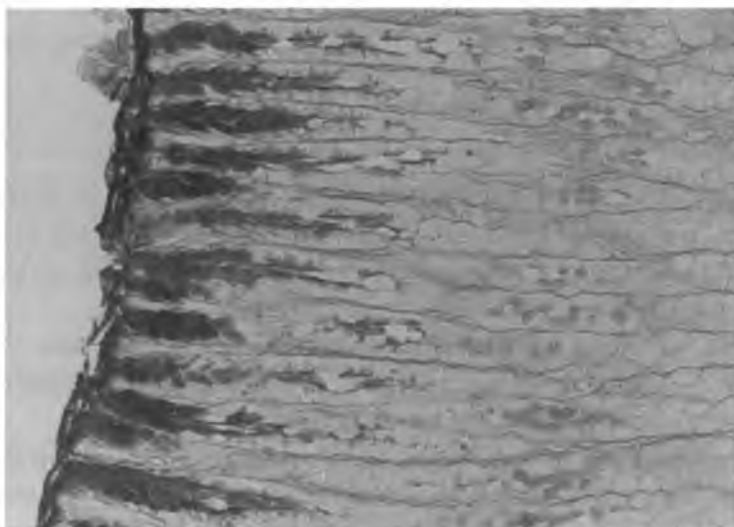


Fig. 3. Proper gastric mucosa of a rat from experimental group II (cephalexin). A little stronger reaction on neutral mucopolysaccharides in superficial mucous cells and orifice mucous cells of gastric glands than in control group, weaker reaction within cervix glandulae. PAS reaction. Magn. 200x

After simultaneous administration of cephalexin and ethanol reaction on mucopolysaccharides was very weak in superficial mucous cells and orifice mucous cells of gastric glands whereas negative in cervix mucous cells (Fig. 4).

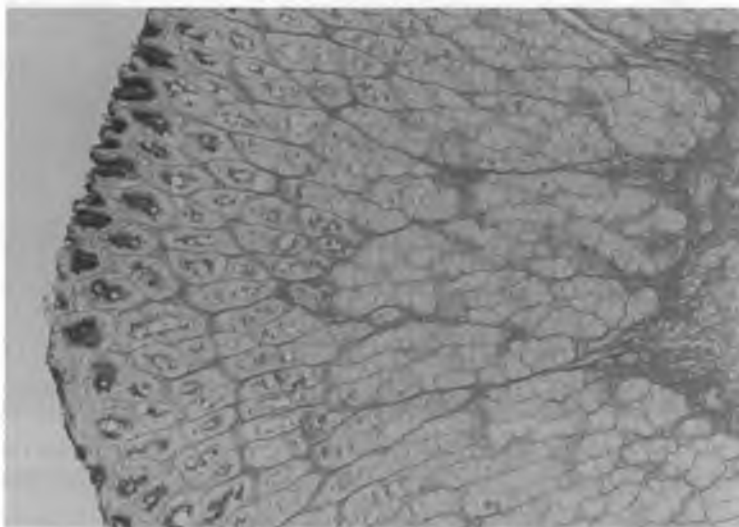


Fig. 4. Proper gastric mucosa of a rat from experimental group III (cephalexin and ethanol). Very weak reaction on neutral mucopolysaccharides in superficial mucous cells and orifice mucous cells of gastric glands, and no reaction in cervix mucous cells. PAS reaction. Magn. 200x

If after administering only ethanol functional decrease in secretion of mucous cells was observed, after simultaneous administration of antibiotic and ethanol very weak reaction to mucopolysaccharides was caused by mucous barrier damage and degenerative changes in gastric glands.

Comparing reactions of three mucous cell types on cephalexin and ethanol effect it can be ascertained that most sensitive cells are cervix mucous cells.

CONCLUSIONS

1. 10-day administration of 20% ethanol *ad libitum* causes in gastric glands: a) functional inhibition of the secretory activity of cervix mucous cells, b) functional decrease in the secretory activity of superficial mucous cells and orifice mucous cells of gastric glands.

2. 10-day administration of cephalexin in dose 42 mg daily causes: a) increase in the activity of superficial mucous cells and orifice mucous cells of gastric glands, b) decrease in secretory activity in cervix mucous cells.

3. A simultaneous administration of ethanol and cephalexin in the above-mentioned doses causes: a) decrease in the number of mucous cells concomitant with atrophic changes, b) strong decrease in the activity of superficial mucous cells and orifice mucous cells of gastric glands, c) no activity of cervix mucous cells.

REFERENCES

1. Arkay R. A.: The effect of alcohol on carbohydrate metabolism: carbohydrate metabolism in alcoholics. 197-229. In: The Biology of Alcoholism. Ed. Kissin B., Beigleiter H.: Plenum Press, New York-London, T. 1, Biochemistry 1971.
2. Barrio-Lera J. P., Alvares A. J., Prieto J. G.: Effects of ethanol on the pharmacokinetics of cephalexin and cefadroxil in the rat. J. Pharm. Sci., 80, 6, 511, 1991.
3. Chang T., Lewis J., Galazko A. J.: Effect of ethanol on the intestinal of aminoacids. Clin. Res., 15, 230, 1967.
4. Iseri O. A., Lieber C. S., Gottlieb L. S.: The ultrastructure of fatty liver induced by prolonged ethanol ingestion. Amer. J. Pathol., 48, 535, 1966.
5. Konturek S.: Fizjologia układu trawiennego. Fizjologiczne podstawy gastroenterologii. PZWL, Warszawa 1985.
6. Lieber C. S. et al.: Differences in hepatic and metabolic changes after acute and chronic alcohol consumption. Fed. Proc., 34, 2060, 1875.
7. Puurunen J., Karppanen H.: Effect an ethanol on gastric mucosal in the rat. Life Sci., 16, 1513, 1975.
8. Rotschild M. A. et al.: Alcohol induces depression albumin synthesis reversal by tryptofan. J. Clin. Invest., 50, 1812, 1971.
9. Shanbour L. L.: Mechanism of action of alcohol on rat gastric mucosa. Gastroenterology, 62,809,1972.
10. Stiasma I., Grabowska-Hibner J., Szukalski B.: Metabolizm alkoholu etylowego w wątrobie. Post. Bioch., 26, 1, 29, 1980.
11. Zarębska A. et al.: Histologiczne badania komórek głównych i okładzinowych gruczołów właściwych żołądka szczura po doświadczalnym podawaniu cefaleksyny i etanolu (in press).

SUMMARY

The Wistar rat males weighing approximately 200 g were administered 20% ethanol *ad libitum* during 10 days, cephalexin in the dose of 42 mg/24 h, and simultaneously ethanol and cephalexin in the above-mentioned doses. After 10 days the animals were decapitated and stomach specimens were taken from the major curvature region for examinations. They were fixed in 10% formalin, dehydrated and immersed in paraffin. For the purpose of estimation changes in activity of gastric gland mucous cells Mc Manus's PAS reaction was performed on 7 μ -thick sections. It was found that ethanol causes functional decrease in the activity of mucous cells. However, cephalexin increases the activity of superficial mucous cells and orifice mucous cells of gastric glands, and inhibits the activity of cervix mucous cells. A simultaneous administration of ethanol and cephalexin causes atrophic changes in gastric glands, and thereby strong reduction of mucous cells activity.

Wpływ doświadczalnego podawania etanolu i cefaleksyny na barierę śluzową żołądka szczura

Szczurom samcom rasy Wistar o masie ciała około 200 g podawano przez 10 dni 20% etanol *ad libitum*, cefaleksynę w dawce 42 mg/dobę oraz etanol i cefaleksynę równocześnie w wyżej wymienionych dawkach. Po 10 dniach zwierzęta dekapitowano i z okolicy krzywizny większej pobierano do badań wycinki żołądka. Utrwalano je w 10% formalinie, odwadniano i zatapiano w parafinie. W celu oceny zmian aktywności komórek śluzowych gruczołów właściwych żołądka na skrawkach o grubości 7 μ wykonano reakcję PAS Mc Manusa. Stwierdzono, że etanol powoduje

czynnościowe obniżenie aktywności komórek śluzowych. Cefaleksyna natomiast zwiększa aktywność komórek śluzowych powierzchniowych i ujścia gruczołów, a hamuje aktywność komórek śluzowych szyjki. Łączne podawanie etanolu i cefaleksyny wywołuje zmiany zanikowe w gruczołach żołądka, a tym samym silne obniżenie aktywności komórek śluzowych.