

**FEATURES OF CYTOPROTECTION IN THE STOMACH AND SOME ASPECTS  
OF THE PHARMACOLOGICAL ACTION OF BISMUTH PREPARATIONS**

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**Abstract:** The article presents the historical development of ideas about the protective mucous barrier in the stomach, provides a modern understanding of cytoprotection in the stomach and describes the capabilities of pharmacological cytoprotective drugs. The cytoprotective properties of drugs based on bismuth salts are presented.

**Keywords:** stomach, mucus, cytoprotection, tripotassium bismuth dicitrate.

## **INTRODUCTION**

The participation of the gastric mucosa in the digestive process is associated with its ability to synthesize and secrete proteolytic enzymes that function optimally in an acidic environment. The pH values in the lumen of the stomach required for this are achieved through the active functioning of the parietal cells in the main glands of the stomach, which produce hydrochloric acid [1]. The presence of acid in the stomach was first suggested by Paracelsus at the beginning of the 16th century, believing that acid appears when drinking acidic water.

## **MATERIALS AND METHODS**

The first ideas about the structural and functional mechanisms of cytoprotection appeared in the time of I.P. Pavlov, when it was assumed that there were mechanisms for the secretion of alkali in the stomach, in addition to acid and pepsin.

The assumption about the protective function of mucus was made by B.P. Babkin, who wrote: "The physiological role of mucus is reduced, apparently, to the following:

- 1) protection of the gastric mucosa from mechanical and chemical irritants and
- 2) neutralization of gastric acid."

At that time, the presence of bicarbonates in the mucus layer was not yet known. Attention was attracted only to the mucous barrier [3].

Further development of scientific ideas about the protective mucous barrier system of the stomach underwent evolutionary development. Secretion of bicarbonates by the intact mucous membrane of the stomach, and then the duodenum, was proven. Bicarbonates are secreted by superficial and intermediate epithelial cells, released into the cavity, enter the supraepithelial mucous layer, and create a pH gradient: on the surface facing the lumen of

the stomach, the environment is acidic, and in the epithelial cells it is neutral or slightly alkaline.

## RESULTS AND DISCUSSION

The mechanisms that ensure the protection of the gastric mucosa have numerous internal connections that are coordinated by a variety of messengers. Mucus and bicarbonates make up the first, so-called pre-epithelial, level of protection of the mucosa. In fact, this factor performs the protective function, and all the others ensure its existence. Therefore, it seems important to us to dwell in more detail on its structural and functional features and interaction with other cytoprotective components.

The gastric mucosa is covered with a continuous layer of mucus. It largely determines the structure and properties of this supraepithelial layer, which is why it is also called the supraepithelial mucous layer (SML) [2]. This mucous layer consists of two components: a) a layer of attached, or more precisely, stuck, mucus (adherent mucus gel) - a gel, the main components of which are:

- water - about 95% of the mass;
- mucins - 3%;
- free proteins, nucleic acids and lipids (phospholipids) – 0.5–2%;
- salts and other components – 1%;

b) cavity mucus, which can be washed from the

surface of the mucous membrane and contains mucous gel at different stages of degradation.

Mucus is a viscous, elastic secretion that does not dissolve in either water or saline. The thickness of the mucus varies depending on the organ and the state of the body. Thus, in the human stomach, the thickness of the mucus is 180  $\mu\text{m}$ .

The main structural and functional component of mucus is mucins (from the Latin mucus - mucus), or mucoproteins, a special class of high-molecular glycoproteins containing acidic polysaccharides.

About 19 genes are responsible for the synthesis of mucins in humans. The following mucins are expressed in normal gastric mucosa: MUC1, MUC5AC and MUC6. Mucin genes are highly polymorphic. For a long time, the role of mucus in the body was not given importance. Currently, intensive work is being carried out to study the expression of mucin genes. It has been established that the course of many diseases is manifested by changes in the properties of mucus. Thus, with the development of gastric cancer (GC), the composition of mucins changes qualitatively and quantitatively. A relationship has been shown between the expression of intestinal mucin MUC2 and the mucinous type of cancer and poor survival. Expression of MUC13 is characteristic of intestinal cancer and is not detected in normal mucosa.

Simultaneously with the secretion of prostaglandins, the production of bicarbonates increases, which occupy a key position in the protective mucous barrier of the stomach. The increase in bicarbonate secretion is prostaglandin-dependent. However, the increase in prostaglandin synthesis and bicarbonate secretion against the background of bismuth preparations occurs simultaneously, which does not exclude the presence of a mechanism of direct stimulating effect of bismuth on bicarbonate secretion.

An important property of bismuth-containing preparations is the suppression of pepsin activity, both basal and stimulated by pentagastrin.

The effects of colloidal bismuth subcitrate (CBS) on porcine pepsin were studied in laboratory conditions. It turned out that the inhibition of pepsin activity by bismuth compounds is a pH-dependent process. CBS had no effect on pepsin activity at pH 4.0, but inhibited pepsin activity at pH 1.0 ( $IC_{50}$ :  $2.3 \pm 0.09$  mmol/L) and pH 2.0 ( $IC_{50}$ :  $8.9 \pm 0.7$  mmol/L). From these data, it can be concluded that the negatively charged bismuth salts derived from CBS bind at pH 2.0 and 1.0 via ionic interaction with the positively charged groups of pepsin, thereby inactivating the enzyme [4].

## CONCLUSION

A modern approach to the treatment of stomach diseases is to use drugs that affect all links in the pathogenesis of the disease. Elimination of aggressive factors (HP infections, etc.), the ability to stimulate the synthesis of prostaglandins, increase the secretion of mucus and bicarbonates, improve blood flow in the mucous membrane, antioxidant effect, preservation of the epidermal growth factor - these are the capabilities of bismuth preparations. However, it is necessary to take into account that differences in the production technology of various bismuth preparations can have a significant impact on the implementation of these effects.

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