



## PHARMACOTHERAPEUTIC EFFECTIVENESS OF HERBAL MEDICINE "YAZVANOL" IN THE EXPERIMENTAL INDOMETHACINE GASTROPATY MODEL

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### Abstract:

"Yazvanol" has been found to have a clear gastroprotective effect in indomethacin-induced gastropathy, preventing damage to the gastric mucosa, reducing lipid peroxidation (LPO) and increasing the activity of the antioxidant system.

**Keywords:** gastropathy, lipid peroxidation, antioxidant system, herbal medicine Yazvanol.

**INTRODUCTION.** Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the main groups of drugs widely used to relieve pain and inflammation in the treatment of arthritis, arthrosis, and inflammatory systemic diseases[1,2]. One of the most important problems associated with the use of NSAIDs is their harmful effect on the gastrointestinal tract (GI) is gastropathy[3,4]. Erosive and ulcerative lesions of the stomach and duodenum occur in 40% of patients receiving long-term NSAIDs and are often complicated by bleeding [5,6]. This is due to the fact that NSAIDs, when taken orally, cause epithelial dystrophic changes, microcirculation and epithelial regeneration in the surface parts of the mucous membrane are disturbed [7,8]. Therefore, the search for drugs that can increase the resistance of the gastrointestinal tract to the harmful effects of NSAIDs is an urgent problem [9,10]. In the world, special attention is now being paid to natural remedies, which are usually characterized by a wide range of therapeutic effects, low toxicity, and the absence of side effects in long-term use [11,12,13]. Accordingly, a dry extract prepared from the raw materials of six types of medicinal plants, conventionally called "Yazvanol", a complex herbal remedy was developed: Aloe arborescens. (leaf); (Glycirhiza glabra L. (root); Inula helenium L. (roots); Calendula officinalis L. (flower); Hippophae rhamnoides L. (fruit); Ziziphora pedicellata Pazij Vved. (leaves); It was found that it has a clear gastroprotective effect on the damage caused by it.

**THE PURPOSE OF THIS WORK.** The aim is to evaluate the pharmacotherapeutic efficacy of the herbal medicine "Yazvanol" in the model of experimental gastropathy induced by indomethacin.

**MATERIALS AND METHODS.** Experiments were performed on white male rats of the same sex weighing

180-200 g. An animal model of acute ulceration was induced by a single intragastric injection of 60 mg/kg indomethacin after a 24-hour fast [14,15]. Rats of the first experimental group were administered intragastrically with an aqueous solution of "Yazvanol" at a dose of 50 mg/kg, 10 ml/kg, for 5 days (1 time per day) and 3 hours before administration of the ulcerogenic agent. Glyceram drug was used as a comparative drug. The comparative drug was used in a dose of 75 mg/kg. Control rats were given an equivalent amount of distilled water. The gastroprotective effect of the test drug was evaluated 24 hours after indomethacin administration. For this, damage to the gastric mucosa (GM) was determined, which were divided into small hemorrhages, erosions and linear ulcers. The mean number of each lesion type was calculated for 1 animal per group. Pauls index (PI) was calculated for each injury type [16,19,23]. For pathomorphological studies, the material was fixed in 10% neutral formalin, the slices were stained with hematoxylin-eosin. In preparations stained with hematoxylin and eosin, the thickness of the mucous membrane and the depth of erosion were determined using the Motic Ima GES 2000 computer program. "Yazvanol" affects the state of the body's antioxidant system and the intensity of lipid peroxidation (LPO) processes in the homogenate of the gastric mucosa, the activity of catalase [3,22] and superoxide dismutase (SOD) [12,22] enzymes, as well as Malondialdehyde [MDA] and Acetylhydroperoxidase (AtsG) [12,20,22 ] amount was determined. The significance of differences between these parameters between experimental groups was evaluated using the non-parametric Mann-Whitney test. Differences were considered significant at  $p \leq 0.05$  [10].

**RESULTS AND THEIR DISCUSSION.** The results of the research showed that 24 hours after the

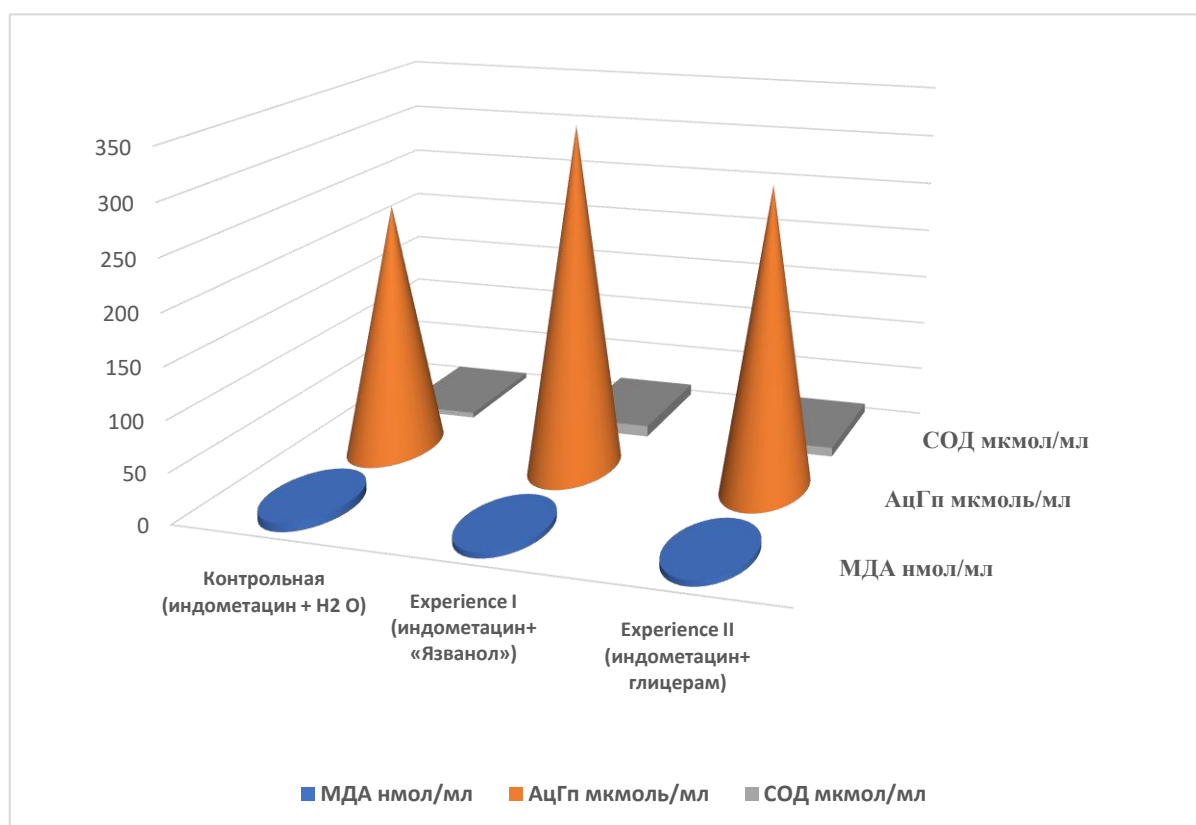


introduction of indomethacin, all animals of the control group had clear hyperemia of the mucous membrane, as well as the presence of various disorders in the form of small hemorrhages, erosion and linear wounds, Pauls index 10.7; 2.7 and 3.7 respectively. The pathomorphological study revealed a significant amount of superficial and deep erosions in the MECs of animals in the control group against the background of clear dystrophic changes. Superficial erosions are characterized by necrosis and rejection of the surface epithelium, deep erosions penetrate into the gastric

mucosa. The lower part of such erosions is necrotic, impregnated with fibrin and infiltrated with leukocytes with polymorphous nuclei. Morphometric analysis of microsections of animals in the control group showed that the depth of such erosions was on average  $0.54 \pm 0.034$  mm, which is 87% ( $0.62 \pm 0.023$ ) of the thickness of the gastric mucosa (Fig. 1). The surrounding erosion, covering the pit and the glandular epithelium underwent dystrophic processes: vacuolization of the cell cytoplasm, pyknosis of the nuclei, expansion of the gland space

**Diagram1**

**Activity of LPO products and AOT enzymes in gastric mucosa in indomethacin-induced gastropathy model**



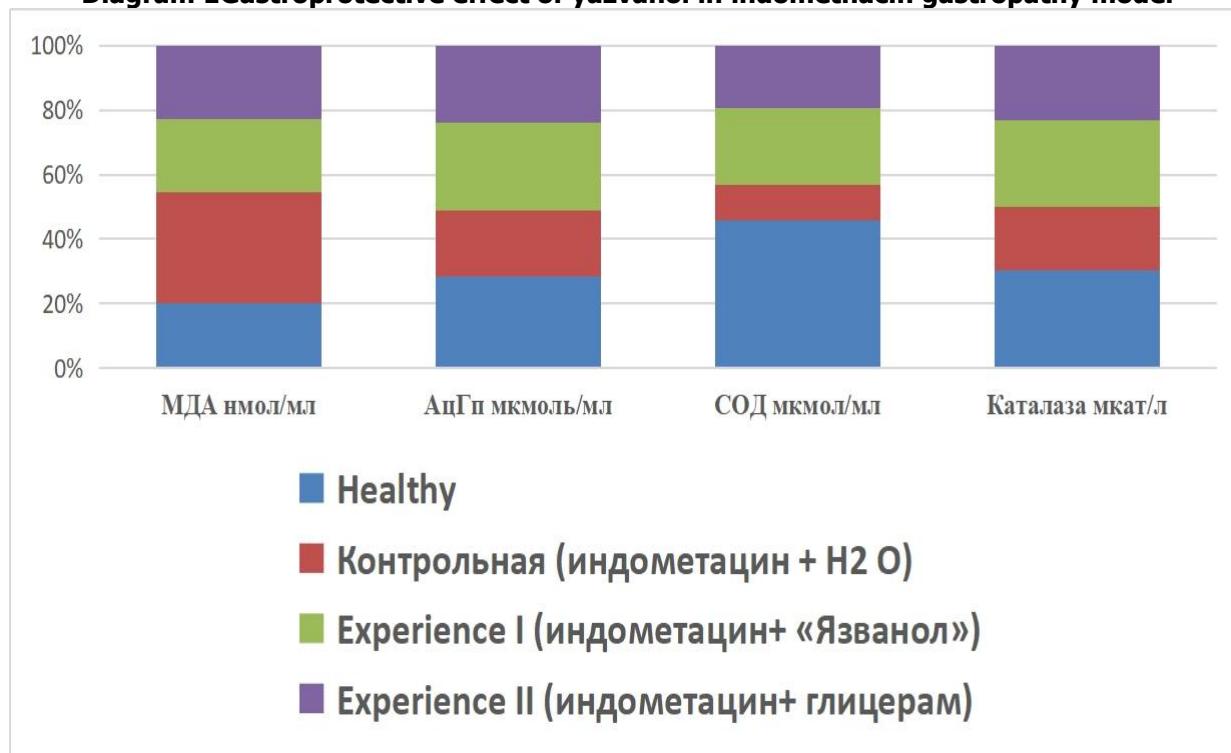
Violation of microcirculation was noted in the form of small bleeding and stagnation of erythrocytes in capillaries, as well as diffuse infiltration of the gastric mucosa by polymorphonuclear leukocytes, lymphocytes and plasma cells. The given data show that the prophylactic course of "Yazvanol" at a dose of 50 mg/kg has a clear gastroprotective effect. Thus, in rats treated with Yazvanol, the Pauls index was 2.0 for punctate hemorrhage, erosion, and linear ulceration; 8.7 is 7.4 times less than that of control group animals.

Against the background of using a course of Yazvanol, the structural changes in the gastric mucosa were superficial and mainly affected the surface deep epithelium and the layer of the mucous protective barrier. Local inflammatory infiltration of MShQ was noted. The results of morphometric studies showed that against the background of the introduction of Yazvanol, reparative processes prevail over degenerative ones, so the average depth of erosion is 78% less than that of animals in the control group (Fig. 1). The introduction



of glyceram had a less gastroprotective effect. Thus, erosions penetrated 1/3 of the gastric mucosa, and their average size was  $0.20 \pm 0.02$ .

**Diagram 1** Gastroprotective effect of yazvanol in indomethacin gastropathy model



Currently, many authors have experimentally and clinically proven the leading role of activation of LPO processes in the development of ulcerative lesions of the gastric and duodenal mucosa [16,17,18,22]. According to the data presented in Table 2, a single administration of a toxic dose of indomethacin was accompanied by an increase in LPO processes and a decrease in the strength of the body's antioxidant defense system, which indicates an increase in the content of free radical oxidation products. Active products decreased by 2 times, the level of AtsG decreased by 1.4 times, and the activity of the main enzymes of the antioxidant system - catalase and SOD decreased by 44 and 78%, respectively. Against the background of acute indomethacin damage to the stomach, it was found that the prevention of the "Yazvanol" course has a clear antioxidant effect, which is confirmed by a 36% decrease in the concentration of MDA in the blood serum, an increase in its concentration in the blood serum. The activity of SOD and catalase was 2.0 and 1.5 times, respectively, and the amount of MDA was reduced - by 37% compared to similar values in rats in the control group.

**CONCLUSION:** Thus, prophylactic use of "Yazvanol" in an experimental therapeutic dose against the background of acute indomethacin damage to white rats has a clear pharmacotherapeutic effect: it reduces the severity of dystrophic and necrotic processes in the epithelium, as well as prevents their development. The molecular-cellular mechanism of the gastroprotective action of Yazvanol is to suppress free radical oxidation processes and increase the potential of the body's endogenous antioxidant system. It should be noted that the pharmacotherapeutic effect of the tested phytoextract is comparable and superior to the effect of the comparative drug in a number of parameters. In general, the obtained data confirm the feasibility of using the complex herbal remedy "Yazvanol" with antioxidant effect in the complex treatment and prevention of gastropathy caused by NSAIDs.

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