Study Of the Effect of a Mixture of Extracts of Medicinal Plants on the State of the Gastric Mucosa in Gastropathy Induced by Indomethacin

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ABSTRACT

In experimental animals, on the model of indomethacin-induced gastropathy, the influence of Lesbohol on the number of erosive-destructive lesions of the gastric mucosa was studied. It has been established that Lesbohol significantly reduces the number of point, strip-like and round lesions of the gastric mucosa. At the same time, Lesbohol surpasses the well-known gastroprotector misoprostol in its activity. It is believed that the mechanism of the gastroprotective activity of Lesbohol is due to the strengthening of the protective barrier of the gastric mucosa, as a result of the suppression of the intensity of free radical processes.

Keywords: NSAIDs, indomethacin, gastropathy, gastric mucosa, gastroprotectors, Lesbohol

Introduction. Non-steroidal anti-inflammatory drugs (NSAIDs) are among the drugs most often causing complications from the stomach, since this group of pharmacological agents is widely used in the treatment of diseases in the pathogenesis of which inflammation is of primary importance. According to the literature, the use of NSAIDs leads to the development of acute gastritis in a week from the start of treatment in almost 100% of cases [1,2]. Based on this, in modern conditions, the development and implementation of drugs for the prevention and treatment of NSAID gastropathy becomes very relevant. Clinical medicine currently has a number of drugs with gastroprotective properties, but their clinical efficacy does not fully meet the requirements of pharmacotherapy. It is logical to believe that in order to protect the mucous membrane of the gastrointestinal tract when using NSAIDs, specialists should have additional drugs with gastroprotective activity, which have a different mechanism of action aimed at increasing the resistance of the gastric mucosa to the effects of exogenous and endogenous aggressive factors [3]. In this regard, it seems promising to use complex multicomponent phytopreparations. Earlier, we found that a mixture of dry extracts of medicinal plants Hypericum scabrum, Ziziphora pedicellata, Mediasia macrophylla,

Glycyrrhiza glabra conventionally named Lesbochol has a distinct positive effect on gastropathy that develops under stress [4,5,10,12,13,18,19]. However, its efficacy in NSAID-induced gastropathy has remained unexplored.

Purpose of the study. The aim of this study was to study the therapeutic and prophylactic effect of a mixture of medicinal plant extracts - Lesbohol on the state of the gastric mucosa in indomethacin-induced gastropathy.

Material and methods. Experimental studies were carried out on mature male rats with an initial body weight of 160-185 g. In the first series of experiments, five groups of animals were composed of six individuals each. One day and 2 hours before the reproduction of the model of gastropathy, the animals of the first, second and third groups were intragastrically injected with Lesbohol at doses of 25, 50 and 100 mg/kg, the fourth misoprostol - 0.2 mg/kg, and the fifth group served as a control for all the rest. . Indomethacin ulcer of the gastric mucosa was reproduced by a single intragastric administration of indomethacin at a dose of 60 mg/kg in saline [14,15]. When playing "indomethacin" gastropathy, rats were deprived of food 24 hours before exposure to NSAIDs.

In the second series of experiments, the therapeutic effect of Lesbohol was studied in indomethacin gastropathy in rats. The gastropathy model was reproduced in the same way as in the first series. A day after the administration of indomethacin, the animals were divided into two groups of 6 pieces each. One group was intragastrically injected with a freshly prepared solution of Lesbohol at a dose of 100 mg/kg daily for three days, and the other with a physiological solution of sodium chloride in a similar volume. Destructive lesions of the stomach were counted after three days of treatment (animals were sacrificed by decapitation under light ether anesthesia). After slaughtering the animals, the stomach was removed and the number of formed destructions in them was counted, the number of punctate, round and strip-shaped lesions was counted.

The results of the studies were subjected to statistical processing using the Biostat 2009 software package according to the method of variation statistics with an assessment of the significance of the characteristics M ± m and differences in the considered samples according to Student's t-test. Differences in the compared groups were considered significant at a significance level of 95% ($p<0.05$

All experiments were carried out in accordance with the rules of a qualitative laboratory (GLP) for preclinical studies, as well as the rules and International recommendations of the European Convention for the Protection of Vertebrate Animals used in experimental studies (ETS No. 123, Strasbourg, 1986), the requirements of the National Guidelines for maintenance and use of laboratory animals.

Results and discussion. The results of the experimental studies of the first series showed that under the influence of indomethacin there was significant damage to the gastric mucosa with a destruction area in the control group equal to 107.42 ± 5.65 mm2, which consisted of erosion and ulcers with a total of 42.15 ± 1.99 pieces. At the same time, the number of punctate lesions was 63.3%, round - 19.3%, and strip-like - 17.4%. In contrast, in animals treated with Lesbohol at a dose of 25 mg/kg, the area of the affected surface was 34.0% less compared to the control, and the total number of ulcers was 26.8% less. At the same time, the number of strip-like, round and punctate ulcers decreased by 25.0; 18.5 and 41.1% respectively. We also noted a positive effect in animals treated with Lesbohol at a dose of 50 mg/kg. Thus, the area of the ulcerative surface and the number of ulcers decreased almost to the same extent - 51.2%, and the number of strip-like, round and small-dotted, respectively, by 45.4; 42.7 and 58.1%. As can be seen from the data in Table 1, a more pronounced positive effect is observed when Lesbohol is used at a dose of 100 mg/kg. In animals treated preventively with the drug at this dose, the area of the ulcerative surface compared with the control was 59.8% less, and the total number of ulcers by 62.4%. The

decrease in the number of band-shaped ulcers was 56.7%, and round and small punctate ulcers by 59.2 and 65.6%, respectively. In another group of animals treated with the reference gastroprotector - misoprostol, the decrease in the area of the ulcerative surface compared to the control was 55.7%, and the total number of ulcers was 57.8%. The decrease in the number of strip-like, round and small-point ulcers was 49.9; 57.1 and 59.4% respectively.

Therefore, based on the results of the experiments performed, it can be concluded that the various doses of Lesbohol studied have a distinct preventive effect on the gastric mucosa when exposed to indomethacin, especially at a dose of 100 mg/kg.

The results of the second series of experiments showed that three days after the cessation of the administration of the ulcerogen, the number of ulcers formed in the stomach was 11.17 ± 1.01. Of these, 9.85% were strip-shaped, 7.43% round and 83.5% small-dotted. The total area of the ulcerative surface was 19.08±1.64 mm2. After the experimental therapy with Lesbohol, a significant decrease in the number of gastric ulcers formed in rats is observed. Thus, the total area of the ulcerative surface decreased by 59.0% compared with the control. At the same time, the number of strip-like ulcers decreased by 54.5%, and round and small-pointed ulcers by 60.2 and 64.3%, respectively.

Therefore, under the influence of indomethacin, pronounced erosive-destructive damage develops in the gastric mucosa, which clearly persist in the following days from the onset of NSAID action. The use of Lesbohol for prophylactic and therapeutic purposes significantly reduces the quantitative and qualitative manifestations of erosive - ulcerative lesions of the gastric mucosa. At the same time, the studied collection of medicinal plants in terms of its pharmacological activity is not inferior to the reference gastroprotector misoprostol.

Table 1

Investigation of the influence of the gasprotective action of Lesbohol in gastropathy induced by indomethacin.

Группы	Dose, mg/kg	Stripe-like ulcers (pcs)	Round ulcers (pcs)	Small punctate ulcers (pcs)	Total number of ulcers (pcs)	Total ulcer surface area (mm2)
Контроль	-	7,33 ± 0,59	8,16 ± 0,68	26,66 ± 1,89	42,15 ± 1,99	107,42 ± 5,65
Lesbohol P	25	5,50 ± 0,41 < 0,05	6,65 ± 0,59 > 0,05	15,70 ± 1,29 < 0,01	27,81 ± 1,10 < 0,002	78,61 ± 2,58 < 0,01
Lesbohol P	50	4,00 ± 0,35 < 0,01	4,67 ± 0,47 < 0,01	11,17 ± 0,72 < 0,001	19,83 ± 1,01 < 0,001	52,42 ± 3,67 < 0,001
Lesbohol P	100	3,17 ± 0,29 < 0,01	3,33 ± 0,41 < 0,002	9,16 ± 0,72 < 0,001	15,82 ± 0,77 < 0,001	43,17 ± 1,37 < 0,001

Misoprostol P	0,2	3,67 ± 0,32 < 0,01	3,50 ± 0,21 < 0,002	10,83 ± 0,58 < 0,001	17,80 ± 0,81 < 0,001	47,58 ± 2,12 < 0,001

Note: P - differences, statistically significantly different from the control.

An analysis of the results of experimental studies suggests that the mechanism of the gastroprotective action of Lesbohol is in many respects similar to the latter. Since misoprostol is a synthetic analogue of prostaglandin E, which causes an increase in the protective mucous membrane of the stomach, given the uniformity of the pharmacological effect, it can be assumed that Lesbochol has the properties characteristic of prostaglandin E. Indeed, under the influence of Lesbochol, in gastropathy induced by indomethacin, the content of soluble and insoluble glycoproteins, as well as protein and indicating an increase in the protective barrier of the stomach. At the same time, Lesbochol was statically significantly superior to misoprostol in its activity and was not inferior to Mucogen [12]. Violation of the structural and functional state of organs and systems in pathological conditions, as is known, is due to increased processes of free radical oxidation of lipids in biological membranes of cells and subcellular structures [13,14,16,17]. Based on this, it seems pulmonary to believe that Lesbohol has an antioxidant property. Separate biochemical studies have confirmed this assumption. So, in case of indomethacin-induced gastropathy, Lesbohol, like misoprostol and mukonen, reduced the amount of acyl hydroperoxides and malonic dialdehyde in the gastric mucosa against the background of an increase in the activity of the enzymes of the antioxidant system catalase and superoxide dismutase [12,13].

Table 2
Study of the therapeutic effect of Lesbohol in gastropathy induced by indomethacin.

Группы	Доза, мг/кг	Полосовидные язвы (шт)	Круглые язвы (шт)	Мелкоточечные язвы (шт)	Общее количество язв (шт)	Общая площадь язвенной поверхности ($мм^2$)
Контроль	-	1,10 ± 0,07	0,83 ± 0,19	9,33 ± 0,69	11,17 ± 1,01	19,08 ± 1,64
Lesbohol P	50	0,50 ± 0,04 < 0,01	0,33 ± 0,09 < 0,01	3,33 ± 0,27 < 0,001	4,16 ± 0,38 < 0,001	7,83 ± 0,84 < 0,001

Note: P - differences, statistically significantly different from the control.

Thus, Lesbohol, which is a mixture of extracts of medicinal plants, has a pronounced gastroprotective activity, the mechanism of therapeutic and prophylactic action of which is associated with an increase in the state of the gastric mucosal barrier, as a result of a decrease in the intensity of free radical lipid oxidation processes due to an increase in AOS activity.

Conclusions:

1. In indomethacin-induced gastropathy, Lesbohol significantly reduces the degree of erosive-destructive lesions of the gastric mucosa and is not inferior to misoprostol in its activity.
2. The mechanism of gastroprotective activity of Lesbohol is largely due to an increase in the state of the protective mucous barrier.
3. At the heart of the therapeutic and prophylactic action of Lesbohol is a decrease in

the intensity of free radical lipid oxidation processes due to an increase in the activity of enzymes in the antioxidant system.

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