
The Importance of Plant Extract in Improving the Microflora of the Gastrointestinal Tract in the Treatment of Diseases of the Stomach and Duodenum

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Abstract: *The paper presents the results of studying the anti-ulcer activity of a combination of complex plant extracts on experimental models of stress and acetylsalicylic gastric ulcers when administered per os extract at a dose of 150 mg/ kg to laboratory animals. The experiments were performed on nonlinear male rats and mongrel male mice. Determination of the Pauls index, the anti-ulcer action index (AUE) - the main criteria for evaluating the anti-ulcer activity of drugs. It is shown that in stress ulcers, the effectiveness of the extract is characterized by a decrease in large, point, stripe-shaped ulcers, a decrease in the number of ulcerative lesions in mice, the AUE index = 4.6. It was found that in the acetylsalicylic model of gastric ulcers against the background of the introduction of the extract, ulcers were detected only in 70% of animals, less pronounced damage to the gastric mucosa was observed, the AUE index is 4.5.*

Keywords: *Ulcerative Damages, Plant Extract, Microflora of the Gastrointestinal Tract, Pauls Index.*

1. INTRODUCTION

Peptic ulcer of the stomach and duodenum is characterized by a wide prevalence, including about 4-6% of the adult population in all countries, and with full medical screening of patients, this percentage increases by more than 20%. It is known from the literature data that the peak incidence occurs at the age of 30-45 years and mainly in men aged 35-50 years, peptic ulcer of the stomach and duodenum occurs 3-4 times more often. Peptic ulcer of the stomach and duodenum is a seasonal recurrent disease with the severity of the course and a tendency to chronization, leading to disability and mortality of patients. These disorders occur against the background of destabilization of nervous and humoral mechanisms in the human body, which regulate secretory-reparative processes in the stomach and duodenum. In the pathogenesis of the disease, the main role is assigned to the imbalance between the factors



of aggression and protection of the mucous membrane of the stomach and duodenum against the background of changes in neuroendocrine and immune regulation of the gastroduodenal zone. The main factors of aggression are hydrochloric acid, pepsin, bile acids, *Helicobacter pylori* (*H. pylori*), and mucus, bicarbonates, epithelial hydrophobicity, proper blood supply, cell renewal of the epithelial layer, as well as produced prostaglandins and other mediators protect the mucous membrane directly [1-8]. It is known that today, with peptic ulcer of the stomach and 12 duodenum, the main 3 and 4 secret combined therapeutic measures are used. At the same time, as part of these therapeutic measures, along with antibiotics, antacids and gastroprotectors, agents with the ability to improve the microflora are also used. It has been noticed that this facilitates the course of the disease and reduces the recovery time. In this regard, the extract obtained on the basis of local medicinal plants was used in experimental conditions as part of a combination used in the treatment of gastric ulcer and duodenal ulcer [9 -13].

2. MATERIAL AND METHODS OF RESEARCH

The object of research was a dry extract obtained from the following types of plant raw materials: *Plantago major* L. leaves, *Achillea millefolium* L. grass, and *Polygonum Hydropiper* L, *Radix Glycyrrhizae* roots, *Matricaria chamomilla* L. flowers, *Polygonum aviculare* L grass [12-13]. The resulting extract contains carotenoids, polysaccharides, flavonoids, tannins, triterpene saponins, steroids, proteins, sesquiterpene lactones, mucus, resins, organic acids, vitamins, macro- and microelements, essential oils and other natural compounds. Standardization of the extract was carried out according to the amount of flavonoids. The presence of this spectrum of biologically active substances suggests the potential probiotic activity of the resulting extract. The work was carried out in accordance with the "Guidelines for conducting preclinical studies of medicines". The experiments were performed on nonlinear male rats with an initial weight of 180-220 g and on white mongrel male mice with an initial weight of 20-22 g. The animals were obtained and kept in a vivarium with free access to feed and water. Pharmacological studies were carried out according to the "Rules of work using experimental animals" [14, 15, 16].

Experimental therapeutic doses of the extract obtained using the Pauls anti-ulcer index were determined on the model of stress ulcers, which corresponded to 100-150 mg/kg. Therefore, all subsequent experiments were carried out using a dose of 150 mg/kg. The anti-ulcer activity of an aqueous solution of a complex plant extract at an experimental therapeutic dose of 150 mg/kg and used together with the drug in effective doses of amoxicillin (25/kg), ranitidine (50 mg/kg) and metronidazole (25/kg) was carried out on models of stress in mice and "acetylsalicylic" ulcers in rats [2, 14]. Stress ulcers in rats were caused by hanging them by the cervical skin fold for 24 hours, and then the effect of drugs was evaluated with the calculation of the anti-ulcer effect. Previously, the mice were divided into groups: intact (10 mice); control (10 mice), experimental 1 (10 mice); experimental 2 (10 mice). Experimental animals 1 were injected into the stomach through a probe with the studied extract at an experimental therapeutic dose of 150 mg / kg and doses of amoxicillin (25 / kg), ranitidine (50 mg / kg) and metronidazole (25 / kg) 1 time a day for 7 days beforehand and 1 hour before stress exposure. mice of experimental 2, was administered reference drugs in is



effective doses of amoxicillin (25/kg), ranitidine (50 mg /kg) and metronidazole (25/kg), according to a similar scheme. Animals of the control group were injected with an equi-volume amount of purified water according to a similar scheme. The animals of the intact group served as an additional control. Animals of all groups, except for mice of the intact group, were deprived of food, water and litter 1 day before immobilization.

A model of experimental acetylsalicylic ulcer in rats was created by administration of acetylsalicylic acid per os to control and experimental animals at a dose of 150 mg/kg 1 time per day for 3 days. The experiments were carried out on white rats, which were divided into groups: intact (10 rats); control (10 rats); experimental 1 (10 rats); experimental 2 (10 rats); experimental 3 (10 rats). Experimental 1 was injected with an extract in the form of an aqueous solution at an experimental therapeutic dose of 150 mg / kg and amoxicillin (25 / kg), ranitidine (50 mg / kg) and metronidazole (25 / kg), 1 time per day for 3 days from the beginning of the experiment; experimental 2 in an isoeffective dose of amoxicillin (25 / kg), ranitidine (50 mg / kg) and metronidazole (25 / kg), control group of rats – purified water in an equi-volume amount and according to a similar scheme. The interval of administration of acetylsalicylic acid and medicinal substances, as well as water, was 4-5 hours. Intact rats served as an additional control. Determination of the anti-ulcer activity of the studied extract and reference agents was carried out 18 hours after their last administration.

The pharmacotherapeutic efficacy of the extract was evaluated at the end of the experiments. The animals were euthanized in a CO₂ chamber, their stomachs were opened, the mucous membrane was washed with saline solution and the nature and number of destructive lesions on the gastric mucosa were determined macroscopically using a magnifying glass. The Pauls Index (IP) was calculated by the formula: $IP = A \cdot B / 100$, where A is the average number of ulcers per animal; B is the number of animals with ulcers in the group. The anti-ulcer effect (AUE) of the extract was judged in relation to the IP in the control to the IP in the experimental group of animals ($PD = IP_k / IP_o$), with AU/E 2 or more, it was believed that the extract, as well as reference drugs, have an anti-ulcer effect. Statistical processing of the obtained data was carried out using the Statistica 6.0 software package (USA). The data obtained during the experiments were processed by statistically generally accepted methods for a small sample with the determination of the average value (M) and the standard error of the average (m) using the formula $M \pm m$. The reliability of the results (P) was evaluated using the Student's t-test [17]. The differences were considered significant at $P \leq 0.05$.

3. RESEARCH RESULTS AND THEIR DISCUSSION

The effect of the extract on the course of stress ulcers in the stomach in white mice was studied. The data obtained are presented in Table 1.

Table 1. Effect of the obtained extract on the course of stress ulcers in the stomach of white mice ($M \pm m$)

| № | Animal groups | Number of mice | Average number of ulcers | | | Number of ulcers | Number of erosion | IP/AUE |
|---|---------------|----------------|--------------------------|---------|-------|------------------|-------------------|--------|
| | | | Large | Striped | Point | | | |
| | | | | | | | | |

| | | with ulcers, % | | | | per 1 mouse | s | |
|----|----------------|----------------------|------------|------------|----------|----------------|----------|---------|
| 1. | Intact | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2. | Control | 100 | 1,2±0,24 | 0,8±0,24 | 6,9±0,11 | 8,7±0,12 | 6,6±0,11 | 8,5/0 |
| 3. | Experimental 1 | 50 | 0,24±0,01* | 0,24±0,01* | 3,1±0,20 | 3,3±0,1* | 3,1±0,24 | 1,8/4,1 |
| 4. | Experimental 2 | 75 | 0,48±0,01* | 0,24±0,01* | 4,1±0,40 | 4,6±0,60* | 4,4±0,24 | 4,1/2,4 |

Note: * - means here and further that the differences compared to the control are significant at $P \leq 0,05$.

In the conducted studies, visual studies have shown that the expressed anti-ulcer activity with the extract in the dose used is higher than the reference means without extracts (Table 1). The effectiveness of the combination with the extract is characterized by a decrease not only in large, point, stripe-shaped ulcers, but also by a decrease in the number of ulcerative lesions in mice in experimental 1. The AUE index at the introduction of the studied extract was 4.6, and in comparison drugs: in an isoeffective dose of amoxicillin (25 / kg), ranitidine (50 mg / kg) and metronidazole (25 / kg). It is obvious that under the influence of which the addition of biologically active substances available in the extract under study helps to limit the hyperactivation of stress-implementing systems of the animal body: hypothalamic-pituitary-adrenal, sympatho-adrenal with a decrease in aggression factors, along with the mobilization of protective factors of the gastric mucosa, improves microflora and stabilization of cell membranes due to the content of phenolic substances the nature of the extract [18]. The effect of the extract on the course of "acetylsalicylic" gastric ulcer in white rats was studied. The data obtained are presented in Table 2.

Table 2. The effect of the extract on the course of "acetylsalicylic" gastric ulcer in white rats (M ± m)

| № | Animal groups | Number of mice with ulcers, % | Average number of ulcers | | | Number of ulcers per 1 mouse | Number of erosions | IP/AUE |
|----|----------------|-------------------------------|--------------------------|-----------|-----------|------------------------------|--------------------|---------|
| | | | Large | Striped | Point | | | |
| 1. | Intact | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2. | Control | 100 | 1,1±0,03 | 5,7±0,1 | 8,9±0,16 | 15,7±2,24 | 7,8±0,50 | 16,3/0 |
| 3. | Experimental 1 | 70 | 0,22±0,01* | 1,7±0,22* | 3,1±0,30* | 5,3±0,50* | 3,1±0,21* | 3,9/4,9 |
| 4. | Experimental 2 | 87 | 0,44±0,01* | 2,9±0,55* | 4,4±0,11* | 7,7±1,21* | 4,2±0,22* | 6,8/2,8 |



Note: * - means here and further that the differences compared to the control are significant at $P \leq 0,05$.

Acetylsalicylic acid in the used dose irritates the gastric mucosa, causes premature peeling of the epithelium with the appearance of erosions, hemorrhagic ulcers [2]. Against the background of the introduction of the extract, less pronounced damage to the gastric mucosa was observed compared to the data of experimental 1, experimental 2. In experimental 1, the index of anti-ulcer action when the extract was administered was 4.5, and in reference agents: in an isoeffective dose of amoxicillin (25 / kg), ranitidine (50 mg / kg) and metronidazole (25 / kg). Against the background of the introduction of the extract, ulcers were detected only in 70% of animals, and in the control – in 100% of cases. The introduction of the extract to rats was accompanied by an increase in the resistance of the gastric mucosa, the restriction of aggression factors due to the biologically active substances contained in it, primarily flavonoids, mucus, tannins and other natural compounds. It is known that acetylsalicylic acid causes destruction of the mucosal barrier caused by blockade of the prostaglandin-synthetase complex due to inhibition of cyclooxygenase, as well as mucosal ischemia with microcirculation disorder and microthrombosis in the subepithelial layer [19]. The compounds contained in this extract limit damage to the gastric mucosa due to their multifaceted action, primarily its membrane-stabilizing effect due to the content of flavonoids, tannins and other compounds capable of suppressing free radical oxidation of biomacromolecules, and thereby limit the destruction of the mucosa [20].

4. CONCLUSION

In general, the data of the conducted studies indicate a pronounced anti-ulcer activity of the obtained combination with plant extracts, which to some extent exceeds the effects of an isoeffective dose of amoxicillin (25 / kg), ranitidine (50 mg / kg) and metronidazole (25 / kg) in experiments on white mice and rats with damage to the gastric mucosa. The course administration of the extract and reference drugs to animals in isoeffective doses is characterized by a natural decrease in the Pauls index and an increase in the anti-ulcer index, the main criteria for evaluating the anti-ulcer activity of drugs. It is the rich complex of biologically active substances available in the extract that accelerates the healing of the ulcerative defect due to its multifaceted effect on the main pathogenetic mechanisms of this pathology. In fact, the systemic effect of the extract is considered, balancing the factors of aggression and defense when using it, which is consistent with the literature data [21]. The results obtained indicate the anti-ulcer activity of the combination with complex plant extracts and are of great interest for clinical practice, argue for the expediency of its use as part of the technologies used for the treatment of patients with peptic ulcer disease, as well as at the recovery stage, which will increase the effectiveness of therapeutic and preventive measures.



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