MEDICINAL AND PLANT RAW MATERIALS AS THE BASIS FOR CREATING THE MOST EFFECTIVE ULTRA-HEALING MEDICINES

Mamatmusaeva Nilufar Erkinovna

PhD, doctoral student of the DSc of the Tashkent Pharmaceutical Institute

Abdugafurova Dilnoza Gulyamovna

PhD in biological Sciences, Senior Researcher Laboratory of Chemistry of Proteins and Peptides of the Institute of Bioorganic Chemistry named after acad. A.S. Sadykova AS RUz

Vypova Natalia Leonidovna

PhD in biological Sciences, Senior Researcher Laboratory of Pharmacology and Screening of Biologically Active Substancesof the Institute of Bioorganic Chemistry named after acad. A.S. Sadykova AS RUz

Annotation: The Institute of Bioorganic Chemistry, on the basis of existing dosage forms, developed Megosin enteric capsules for the treatment of ulcerative colitis and conducted histological studies, which proved the ulcer-healing effect of the new Megosin dosage form. Megosin is the original gossypol derivative. Previously, the drug was obtained by condensation of gossypol with β-aminoethylsulfate sodium and used as an immunosuppressive agent, which belongs to the V class of practically non-toxic compounds and contributed to a longer engraftment of skin flaps in mice, kidneys and lungs in dogs. Further, it was used as an antiherpetic agent, in the form of a 3% ointment.

Key words: Ulcerative colitis, antiulcer activity, necrosis, tissue, hyperemia, enteric capsules.

The relevance of scientific work. One of the priorities is the search and creation of the most effective, ulcer-healing agents. It is known that products based on plant materials have low toxicity, mild therapeutic effect, and the ability to comprehensively influence various parts of the pathological process [1, 2, 3].

All over the world, various biologically active substances of plant origin are widely used in traditional medicine, pharmaceuticals and in various sectors of the national economy. One such substance is gossypol, which is secreted from the bark, stems, and seeds of the cotton plant. Its derivatives have antiproliferative, anti-inflammatory and antiulcer activity. Megosyn is one such gossypol derivative that has been developed in several dosage forms for the treatment of a number of pathologies.

Megosin belongs to the group of interferon inducers, with antiviral activity and a pronounced immunomodulatory property. The immunomodulatory effect of Megosin is based on the launch, induction of the body's own interferons, which is why it was classified according to the classification to the group of immunomodulators of endogenous (internal) origin, i.e. its use leads to the induction, launch, stimulation of the internal components of the immune system - cytokines, which structurally, they are classified as small secreted proteins. Cytokines - IL-1, TNF, IL-6, chemokines, primarily regulate the development of local defense reactions in tissues involving various types of blood cells, endothelium, connective tissue and epithelium. These

cytokines are synthesized in the focus of inflammation, mainly by macrophage cells, and cause activation of the endothelium, leading to an increase in permeability, an increase in the expression of adhesion molecules, and an increase in procoagulant activity, which leads to the removal of the inflammatory response of the body at the local level [4, 5].

Thus, due to the release of the immune system's own cytokines, which stimulates the interferon inducer Megosin, the focus of inflammation is removed at the local level. In this connection, we set up an experimental model of UC, with pronounced foci of inflammation, necrosis, and treatment of the induced pathology of UC with the help of a substance, enteric and gastro-soluble capsules of Megosin.

Aim of the study. The study of the specific pharmacological (antiulcer) activity of Megosin in the form of enteric and gastro-soluble capsules of Megosin in the therapeutic and prophylactic route of administration in a model of experimental ulcerative colitis in rats.

Material and methods. An experimental model of ulcerative colitis was reproduced by introducing 1.0 ml of 4% acetic acid into the large intestine of anesthetized rats to a depth of 8 cm [1]. Throughout the experiment, rats were kept in vivarium conditions with free access to water and food. Previously, rats were anesthetized by intraperitoneal administration of sodium etaminal at a dose of 30 mg/kg. Laboratory rats weighing 175-185 gr. were divided into 3 groups: the 1st group - intact animals (without UC), the 2nd group - animals with UC, the 3rd group - animals with UC that received Megosin substance orally at a dose of 5 mg/kg for 9 days selected empirically.

Lesions in the experimental model of UC were evaluated in points on a scale: no visible damage - 0 points; edema - 1 point; hyperemia - 2 points; hemorrhages: pinpoint - 3 points; merged - 4 points; erosion: single, each erosion - 5, erosion with bleeding - 6 points; ulcer - 7 points. The sum of points was calculated for each animal under the influence of the following drugs: Megosyn (substance) - 5 mg/kg, Megosyn (gastric soluble capsules) - 40 mg/kg, Megosyn (enteric capsules) - 40 mg/kg, Sulfasalazine (comparator drug) - 140 mg / kg, Altan (comparator drug) - 30 mg / kg. The macroscopic examination of the SOTC was carried out using a magnifying glass. Next, the large intestine was placed in a 10% solution of neutral formalin. Paraffin sections 5 μm thick were stained with hematoxylin-eosin. Microscopic evaluation of the colon using a microscope.

Statistical processing of the obtained results was carried out with the calculation of the mean value M and the error of the mean value m, at a significance level of $p < 0.05$ (https://medstatistic.ru).

Results. During a macroscopic study of areas of the colon mucosa (CM) of experimental and control animals, pronounced morphological differences were noted, confirming the reproduction of experimental UC. As shown by the experimental data in the figures (see Table 1), macroscopic examination of the large intestinal mucosa in animals of the control group on the 3rd day shows pronounced hyperemia and swelling of the mucous membrane, intense hemorrhages, numerous areas of necrosis, the severity of the inflammatory process was 8, 79 points. On the 6th day of the experiment, the animals of the control group continued to have signs of inflammation.

In animals treated with the Megosin substance, which, on macroscopic examination, significantly differ from control animals: the severity of the inflammatory process on the 9th day

in the treatment with the substance was 3.55 points, gastro and enteric forms of Megosin, respectively, 1.8 and 1.5 points. Comparator drugs Sulfasalazine and Altan - 1.8 and 2 points, respectively

Thus, as a result of the study of the ulcer-healing effect of the substance at a dose of 5 mg/kg and gastric and enteric forms of Megosin at a dose of 40 mg/kg, an improvement in the destructive state of treatment was revealed, the severity of damage to the colon mucosa (SDCM) was 2.5-3.5 times less than in animals of the control group and 1.2-1.6 times compared with the reference drugs, which indicates a decrease in the inflammatory process. On the 10th day of treatment with the substance and dosage forms of Megosin in animals, necrotic changes in the mucosa were practically not expressed, i.e. regenerative processes occurred that were comparable or superior to the comparators.

These data are confirmed by histological studies. Comparative histological analysis revealed the following changes: under the influence of the substance and lek. forms of megosyn at a dose of 40 mg/kg, a sharp decrease in interstitial edema was revealed, in which the activity of reparative regeneration, necrotic and inflammatory infiltration in such labile cells of the mucous membrane as in the prismatic epithelium, connective cells, enterocytes and components of mesenchymal cells was stopped. Dosage forms of Megosin at a dose of 40 mg/kg showed the appropriate therapeutic effect, i.e., it has a high activity of anti-inflammatory and antiulcer action comparable to that of reference drugs. Based on the results obtained, the following **conclusions** are formulated:

1. Megosin substance and drug forms of gastro- and enteric-soluble capsules at a dose of 40 mg/kg have a pronounced anti-inflammatory and anti-ulcer effect on the model of acute experimental colitis in rats, which manifests itself in a decrease in the area of ulcers and the degree of damage to the mucous membrane of the colon and is not inferior in efficiency, and in some indicators is superior to drugs comparison Sulfasalazine and Altan.

2. The pronounced therapeutic and prophylactic effect of Megosin in the form of gastro- and enteric-soluble capsules at a dose of 40 mg/kg on the model of ulcerative lesions of the large intestine allows us to recommend the study drug for use in the complex therapy of inflammatory diseases of the large intestine.

References:

1. M. V. Osikov, E. V. Simonyan, A. V. Bakeeva, A. E. Bakeeva, et al., *Modern Problems of Science and Education*, № 4, 60-71 (2016). URL: https://scienceeducation.ru/ru/article/view?id=25072/
2. N. V. Derkach, L. N. Maloshtan, F. Anas, *Medicine and Education in Siberia*, № 3, 1-10 (2015). eLIBRARY ID 26027195
3. Ya. S. Zimmerman, *Classification of the main gastroenterological diseases and syndromes*, 3rd ed., Perm: PGMA (2012).
4. http://propionix.ru/citokiny#immun.
5. Mamatmusaeva N.E., Abdugafurova D.G., Vypova N. L., Ziyaev H.L., Tagayalieva N. A.Abrekova N. N., Sagdullaev B.T. Anti-ulcer effect of megosin in a model of acute experimental colitis in RATS. International Journal of Health Sciences, (2022). *6*(S7), 47349–47356.