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STUDY OF ANTI-INFLAMMATORY EFFECT OF COMPARATIVE DRUGS BY METHOD "COTTON PELLET"

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ABSTRACT

This report presents the results of a study to determine the anti-inflammatory properties of the recommended Ortof-S tablets in comparison with its ingredients in separate dosage forms according to the Cotton pellet method. The preparation combines a non-steroidal anti-inflammatory drug with an antiulcer, an inhibitor of H +, K + -ATPase.

Key words: *tablets, diclofenac, omeprazole*

I. Introduction

Nonsteroidal anti-inflammatory drugs are widely used around the world to treat various rheumatic diseases. Most patients tolerate these medications well, but a number of patients develop gastroenterological side effects, sometimes requiring discontinuation of the drug as well. Therefore, the development of non-steroidal anti-inflammatory drugs that do not have side effects is of great importance in the pharmaceutical industry [1,2].

Currently, there is a great deal of research around the world to reduce the side effects of painkillers in order to develop high-performance, harmless drugs. Today, the development and comprehensive study of combined drugs that protect the gastric and duodenal mucosa, stimulate trophic and regenerative processes, in combination with proton pump inhibitors, nonsteroidal anti-inflammatory drugs used as analgesics, is of great importance[2].

Nonsteroidal anti-inflammatory drugs — a group of drugs with painkillers, antipyretic and anti-inflammatory effects that reduce pain, fever and inflammation. The use of the term “non-steroidal” in the name emphasizes their difference from glucocorticoids, which have not only anti-inflammatory effect, but also other, sometimes undesirable, properties of steroids. Drugs of this group are usually used for acute and chronic diseases, accompanied by pain and inflammation [1,3,4].

Most commonly, NSAIDs are prescribed for the following conditions: rheumatoid arthritis, osteoarthritis, inflammatory arthropathies (ankylosing spondylitis, psoriatic arthritis, Reiter’s syndrome), gout, dysmenorrhea, bone metastases accompanied by pain, headache and migraine, postoperative pain syndrome,

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mild or moderate pain severity with inflammatory changes or trauma, fever, renal colic. The treatment of most of the above diseases requires prolonged use of NSAIDs [5,6].

However, NSAIDs have side effects, especially with prolonged use, which include damage to the mucous membrane of the stomach and duodenum with the formation of ulcers and bleeding. In this regard, together with NSAIDs, a means is prescribed to protect the mucous membrane of the stomach and duodenum. Omeprazole is a drug that belongs to the proton pump inhibitor, or pump (PPI). The action is based on the blockade of the N / K-ATPase enzyme. It is needed to complete during the last phase of the formation of hydrochloric acid by the lining cells of the stomach. It is prescribed for damage to the mucous membrane of the organ with gastritis, peptic ulcer, taking medications (antibiotics, non-steroidal anti-inflammatory drugs) [7,9].

Based on this, the administration of Diclofenac with Omeprazole is prescribed in order to prevent the formation of defects of irritation of the gastric mucosa. Also, proton pump inhibitors do not affect the concentration of anti-inflammatory drugs in the blood [8,9].

Due to the fact that the drug substance accumulates in the tubules of the gastric glands and blocks the enzyme, the production of hydrochloric acid is inhibited until secretory cells are restored. In the case of omeprazole, this time is 20-23 hours. Throughout the action of the drug, the stomach is protected from the negative effects of diclofenac on the mucosa. Despite the effectiveness of this technique, prolonged therapy according to this scheme will be economically disadvantageous, and also creates inconvenience when taking medications.

The combination of Diclofenac sodium and Omeprazole in one tablet allows you to create convenience for patients when taking the drug and provide economic benefits.

II. Experimental

2.1. Materials and Methods

“Ortof-S” - tablets, an original drug developed at the Tashkent Pharmaceutical Institute by Professor H.M. Yunusova with co-authors. These tablets contain active ingredients like diclofenac sodium and omeprozole. It is an anti-inflammatory drug of a combined composition.

The anti-inflammatory effect of the compared drugs was studied according to the Cotton pellet method (cotton granuloma) [5] on 24 white rats weighing 180-200 g of both sexes. Chronic proliferative inflammation was caused by the implantation of 4 sterilized felt discs weighing about 10 mg under the skin of the abdomen of rats. The operation was performed under mild ether anesthesia under aseptic conditions. On the 8th day after the operation, cotton pads with granulation tissues formed around them were removed and weighed on a torsion balance and dried to constant weight at 60 ° C. The proliferative reaction was evaluated by the difference between the dried granuloma and the initial mass of the cotton pad. The exudative reaction was evaluated by the difference between the raw dried granulomas. Compared drugs were administered daily for 7 days 2 times a day.

For the experiment, rats were divided into 4 groups of 6 animals each. The drugs were administered as follows:

1. Group - control - 1 ml of purified water;

2. Group - experimental - 0.5% aqueous solution of the drug "Diclofenac" -tablets at a dose of 50 mg / kg;

3. The group - experimental - 0.7% aqueous solution of the drug "Ortof-S" -tablets at a dose of 70 mg / kg + 0.1 ml of 2% formalin solution;

4. The group - experimental - 0.2% aqueous solution of the drug "OMES®" -capsules manufactured by Combitic Global Caplet Pvt. Ltd, India.

Anti-inflammatory effect (effect on the proliferative and exudative components of chronic inflammation) was expressed as a percentage in relation to the control.

III. Result and Discussion

The results obtained when studying the anti-inflammatory activity of the Ortof-S preparation - tablets developed at the Pharmaceutical Institute show that at a dose of 70 mg / kg it had a significant anti-inflammatory effect.

Table 1. Comparative anti-inflammatory activity of the Ortof-S tablets developed at the Pharmaceutical Institute, Diclofenac, manufactured by Ozone LLC, Russia and OMES®, Combitic Global Caplet Pvt. Ltd, India

Weight, g	**Dose**		**The mass of raw granulomas, mg**	**The mass of dry granulomas, mg**	**Inhibition of exudation,%**	**Inhibition of proliferation, %**
	mg/kg	**ml**				
Control group (purified water)						
190,7 ± 6,9	-	-	52 ± 6	16,17 ± 1,1	-	-
Ortof-S, developed at the Pharmaceutical Institute						
191,5 ± 7,3	70	2	22,8 ± 3,2	11,0 ± 0,8 P<0,05	71,4	**83,7**
Diclofenac, manufactured by Ozone LLC, Russia						
190,5 ± 6,8	50	2	25,8 ± 3,4	12,3 ± 1,01 P<0,05	68,1	**62,3**
OMES®, Combitic Global Caplet Pvt. Ltd, India						
191,3 ± 7,2	**20**	**2**	**26,5 ± 3,9**	**12,1± 0,7**	**66,2**	**65,7**

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				P<0,05		

The study of antiproliferative activity showed that in the control group of animals the weight of granulation tissue was 52 ± 6 mg. We have taken this value as 100.00%. Under the influence of the studied drugs, the size of granulation-fibrous tissue compared with the control data was 71.4% less (Orthof-S), 68.1% (Diclofenac) and 66.2% (OMES®) which led to a significant decrease in the inflammatory process. Moreover, a more pronounced antiproliferative activity was established with the introduction of the drug "Ortof-S", developed at the Pharmaceutical Institute. Against the background of taking the Ortof-S drug developed at the Pharmaceutical Institute, the weight of the granuloma was 12.1 ± 2.9 mg, i.e. the exudative effect was 71.4% and the proliferative effect was 83.7%.

IV. Conclusions

The Ortof-S preparation of tablets developed at the Pharmaceutical Institute has a significant effect on the exudation and proliferation processes in the experimental model of chronic inflammation according to the Cotton pellet method and is not inferior in comparison to the comparison drug Diclofenac tablets manufactured by Ozone LLC, Russia.

The research results are presented in the form of a scientific report on research work in accordance with the requirements of GOST a O´zDSt 276: 2013 “Good laboratory practice”, Tashkent 2013.

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