PHARMACEUTICAL SCIENCES

STUDY OF ANTIEXUDATIVE ACTIVITY OF A NEW PHARMACEUTICAL COMPOSITION OF N-(4-NITRO-2-PHENOXYPHENYL) METHANESULFONAMIDE WITH 1,3,7-TRIMETHYLXANTHINE IN EXPERIMENT

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The effectiveness and continuous development of medical science requires the search for new medicines, as well as research to expand the therapeutic capabilities of known pharmaceutical drugs. An important problem at the current stage of development of medicine and pharmacy is the creation of new domestic combination medicines, the pharmacological effects of which are achieved through a rational combination of components. It is known that a pharmaceutical composition containing multiple components in a single medicinal product can expand its pharmacological spectrum of action, and the combination of ingredients in a multicomponent pharmaceutical composition may contribute to the enhancement of their pharmacological effects. Experimental studies have confirmed the advantages of combined medicinal products over monocomponents for the pharmacotherapy of pain syndromes and inflammatory processes. This can be explained by the fact that such

pharmaceutical compositions are more effective than each individual component. This approach allows the inclusion of active pharmaceutical ingredients in lower doses than the average therapeutic ones, thereby reducing toxicity and negative side effects. At present, there is an arsenal of modern nonsteroidal anti-inflammatory drugs (NSAIDs) used for the treatment of many diseases, ranging from fever to severe autoimmune processes. However, the wide variety of anti-inflammatory drugs does not solve the problem of successfully treating inflammatory diseases and their recurrences, which occur in many cases after drug discontinuation. Moreover, their use is complicated by a significant number of undesirable effects.

Therefore, despite the saturation of the pharmaceutical market with NSAIDs, the search for new, safe, domestically produced medicinal products for the treatment of inflammatory processes that would be more effective and less toxic remains a pressing issue today. Considering the above, our study aimed to develop a new two-component pharmaceutical composition based on N-(4-nitro-2-phenoxyphenyl)methanesulfonamide (nimesulide) and 1,3,7-trimethylxanthine (caffeine) and to investigate the anti-exudative activity (AEA) of the developed pharmaceutical composition in comparison with the individual administration of its components and the reference drug 2-[(2,6-dichlorophenyl)amino]phenyl]sodium acetate (diclofenac sodium). The AEA of the developed pharmaceutical composition and its components was studied in WAG rats with an average weight of 200-230 g using the experimental model of "formalin-induced edema" (f.e.) compared with the reference drug. The edema was induced by subplantar injection of 0.1 ml of a 2% formalin solution into the rat's hind paw. The paw volume was measured using a plethysmometer (IITC Life Science, USA) before the modeling injection of formalin and 4 hours after the administration of the phlogogen (formalin, f.e.) at the peak of edema development. The rats were divided into 6 groups, with 6 animals in each group. The animals in the 1st group served as the control and were administered a single intragastric dose of 3% starch mucus (2 ml per 200 g of rat body weight). The animals in the 2nd group underwent f.e. modeling and were also administered a single i.g. dose of 3% starch mucus (2 ml per 200 g of rat body weight).

The animals in groups 3 to 6, against the background of f.e., received a single intragastric administration of the tested medicinal substances and their pharmaceutical composition as a suspension in 3% starch mucus. Specifically, the experimental animals in group 3 received nimesulide (15 mg/kg of body weight), group 4 received caffeine (0.6 mg/kg), group 5 received a combination of nimesulide (15 mg/kg) with caffeine (0.6 mg/kg), and group 6 received the reference drug diclofenac sodium (8 mg/kg). It is known that the peak development of f.e. occurs 4 hours after its induction. The 3% starch mucus, the tested medicinal substances and their pharmaceutical composition, and the reference drug, were administered 1 hour before this time, taking into account their pharmacokinetic characteristics.

The induction of f.e. (group 2) led to a 36.84% increase in paw volume compared to the control group. The administration of nimesulide (group 3) in the context of f.e. contributed to inflammation suppression, with an AEA of 63.6%. The monoadministration of caffeine (group 4) also reduced inflammation, showing an AEA of 22.7%. The addition of caffeine to nimesulide enhanced the AEA of nimesulide: the developed two-component composition (nimesulide + caffeine) demonstrated an AEA of 72.7% (group 5), which exceeded the AEA of the reference drug diclofenac sodium (45.5%). This indicates that caffeine potentiated the AEA of nimesulide. The comparative analysis of AEA allows us to conclude that the leader of our experimental study on laboratory rats is the newly developed domestic pharmaceutical composition of nimesulide (15 mg/kg of rat body weight) with caffeine (0.6 mg/kg of rat body weight). Based on AEA values, the components, pharmaceutical composition, and reference drug formed the following series:

AEA caffeine (22.7%) < AEA diclofenac sodium (45.5%) < AEA nimesulide (63.6%) < AEA nimesulide + caffeine (72.7%).

In the f.e. model, it was experimentally proven that the pharmaceutical composition of nimesulide with caffeine effectively reduces exudation processes and is promising for further study. The role of caffeine as an adjuvant to nimesulide in modulating exudation processes has been experimentally confirmed.