**1,3,7-TRIMETHYLXANTHINE – KNOWN ADJUVANT OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS OF DIFFERENT CHEMICAL STRUCTURES**

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The development of a combination of drugs, the pharmacological effects of which are achieved through a rational combination of ingredients, is an urgent problem. It is known that caffeine enhances the analgesic effect of non-narcotic analgesics (NSA) and non-steroidal anti-inflammatory drugs (NSAIDs).

The aim of the study was to achieve a stronger pharmacological action from the drug composition compared with each individual component.

NSAIDs of different chemical structures were selected for research: diclofenac sodium (2-[(2,6-dichlorophenyl)-amino]-phenylacetic acid sodium salt), piroxicam (4-hydroxy-2-methyl-N-2-pyridinyl-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide) and their known adjuvant – caffeine (1,3,7-trimethylxanthine).

The anti-exudative effect of NSAIDs and their pharmaceutical compositions with caffeine was studied using an experimental model of formalin edema. Experiments were carried out on rats of WAG line. These NSAIDs, their combination with caffeine, starch mucus (control group) were administered 1 hour before maximum edema. Exudative inflammation was modeled by sub-planar introduction into the hind limb of a rat of 0.1 ml of a 2 % solution of formalin. The volume of the paw was measured before the beginning of the experiment and at the time of maximum development of edema – 4 hours after the introduction of the flogogen. The animals were divided into 6 groups of 6 animals in each group.

Analysis of the results of the experiment shows that the modeling of formalin edema contributed to a 34% increase in rat paw volume. The administration of diclofenac sodium assisted in suppressing edema by 33.00%, piroxicam by 44.44%, and caffeine by 18.33%.

The addition of caffeine to NSAIDs that have been studied has contributed to an increase in their anti-exudative activity. The composition of diclofenac sodium with caffeine probably reduced formalin edema by 47 % compared with control. The activity of the composition of diclofenac sodium and caffeine significantly differed from the activity of pure diclofenac sodium in 1,3 times, which leads to the conclusion that caffeine is able to enhance the anti-exudative activity of diclofenac sodium. The composition of piroxicam with caffeine was most effective – it showed a suppression of edema by 61.11%, which significantly exceeded the anti-exudative activity of piroxicam by 1.4 times, that is, caffeine potentially potentiated the anti-exudative activity of piroxicam.

The results of the research showed that after suppression of formalin edema in caffeine rats, experimental NSAIDs and their compositions with caffeine were located in a row: caffeine (18.33 %), diclofenac sodium (33 %), piroxicam (44.44 %), diclofenac sodium + caffeine (47 %), piroxicam + caffeine (61.11 %).

The comparative analysis carried out makes it possible to conclude that piroxicam (44.44 %) was the mono-leader in this study, and the most effective among the studied compositions was its composition with caffeine (61.11%). The role of caffeine as an adjuvant relative to anti-exudative activity is established, probably due to the vasoconstrictive effect observed in previous studies of NSAIDs of different chemical structures.

Thus, the paper presents an experimental substantiation of the feasibility of the creation of new domestic pharmaceutical compositions with anti-exudative effects containing NSAIDs of different chemical structures (diclofenac sodium or piroxicam) and their adjuvant caffeine.