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**THE INFLUENCE OF CAFFEINE ON ANTIEXUDATIVE ACTIVITY OF
MELOXICAM UNDER THE CONDITIONS OF FORMALIN-INDUCED EDEMA**

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The relevance. The combined drug therapy is frequently put into practice to increase the efficiency of medication. According to literature data combined nonsteroidal anti-inflammatory drugs (NSAIDs) often include caffeine, and meloxicam is NSAID of oxicams. However, there are no data on the pharmacological composition of meloxicam with caffeine in the literature. Experimental data obtained in preliminary studies showed the feasibility of such a their combination.

Aim: to create and investigate new compositions comprising caffeine and meloxicam and to substantiate pharmacologically their suitability for anti-exudative activity under the conditions of formalin-induced edema.

Materials and methods. Exudative inflammation serves as a classic example of an acute one. Experimental researches have been conducted in order to study anti-exudative activity of composition of the investigated compound with caffeine. Exudative action of examined compounds and combinations was studied on 30 white male rats of the WAG strain weighing 210-230 g using an experimental model of formalin edema. All the experiments were performed in accordance with the modern recommendations. First group was the control one, 3% starch mucilage was once orally intragastrically administered to animals of this group (2 ml per 200 g of rat). Exudative inflammation was modeled by subplantar injection of 0,1 ml of 2 % formalin solution in the rat hind paw. Paw volume was measured using plethysmometer before the experiment and at the moment of maximal swelling i.e. 4 hours after administration of flogogenic agent (formalin). Animals were divided into 5 groups, 6 animals in each group. The anti-exudative effect was studied by comparison 3-5 groups on the condition of formalin edema (3th group – caffeine (0,6 mg/kg), 4th group – meloxicam (0,63 mg/kg), 5th group – combination of meloxicam (0,63 mg/kg) and caffeine (0,6mg/kg)) with positive control (group 1th) and with negative control (group 2nd – 3 % starch mucilage, 2 ml for 200g of rat on condition of formalin edema) also 4 hours after injecting a formalin. Examined drugs, their composition with caffeine and starch mucilage (control group) were administered 1 hour before the maximal experimental edema. The percent of inhibition of inflammation was calculated by the formula:

$$\% \text{ inhibition of inflammation} = \frac{\Delta V_k - \Delta V_r}{\Delta V_k} \cdot 100\% .$$

The study was carried out in accordance with the methodological recommendations of the State Pharmacological Center MoH Ukraine. Number of animals and their distribution in groups were in accordance with economical approach, bioethical rules and statistics requirements. Recalculation of the human doses for rats was done by using the ratio of species sensitivity by Rybolovlev Yu. R. Laboratory animals employed in the study were kept in experimental biological clinic of KhNMU following the norms of the storage, care and feeding approved by the principles of "European Convention for the Protection of Vertebrate Animals used for experimental and other scientific purposes" (Strasbourg, 1986) and the decision of the First national Congress on Bioethics (Kyiv, 2007). Received data were processed using generally accepted methods of statistical analysis (mean, error of mean, F-test) with the help of MS Excel and StatGraphics Plus 2.1.

Results and their discussion. The analysis of experimental research has showed that caffeine (anti-exudative activity 18,33%) potentiates anti-exudative activity of meloxicam (anti-exudative activity 40,56%), so that their pharmacological composition has more intense anti-exudative activity 50,56%.

Conclusion. Pharmacological composition of meloxicam with caffeine is expedient and is perspective for the study of the central component of analgesic action.