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STUDIES OF THE ANTI-INFLAMMATORY ACTIVITY OF CELAGRIP IN PREPUBERTARY RATS

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Abstract: To identify the antiphlogistic activity of CelAgrip on the model of aseptic inflammation induced by dextran, a study was conducted on growing animals of the prepubertal period. It was found that CelAgrip has a distinct anti-inflammatory effect on the model of acute inflammation induced by dextran. In its pharmacological activity, CelAgrip is slightly superior to the well-known non-steroidal anti-inflammatory drug - Ibuprofen.

Key words: aseptic inflammation, dextran, CelAgrip, Ibuprofen.

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Introduction.

Today, nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used worldwide to treat various pathologies in the genesis of which inflammation occupies a leading place. However, despite sufficient evidence of the beneficial effects of NSAIDs on children and adolescents, there are no comprehensive data on infants. Various NSAIDs are used in infants: ibuprofen, dexibuprofen, ketoprofen, flurbiprofen, naproxen, diclofenac, ketorolac, indomethacin, niflumic acid, meloxicam, celecoxib, parecoxib, rofecoxib, acetylsalicylic acid and nimesulide [1, 2]. NSAIDs have been shown to be effective for a variety of conditions such as inflammation, fever and pain, and are also the mainstay of anti-inflammatory treatment, for example, in childhood inflammatory rheumatic diseases [3-6]. It is known that limited data are available on the safety of most NSAIDs for infants. Adverse drug reactions may be renal, gastrointestinal, hematological or immunological, etc. [7-11]. Since NSAIDs are among the most commonly used drugs in the pediatric population, safety and efficacy studies can be conducted in routine clinical practice even in small infants. To increase the safety of NSAIDs in infants, treatment should be initiated with the minimum dose appropriate for age or weight. The duration of treatment and the amount of drug used should be regularly assessed, and maximum dose limits and other recommendations of the manufacturer or expert committees should be observed. Treatment of non-chronic conditions such as fever and acute (postoperative) pain should be as short as possible. In this regard, the development and creation of new less toxic and more effective antifungal drugs is of great interest. The aim of this experimental study was to evaluate the anti-inflammatory activity of CelAgrip in prepubertal rats.

Materials and research methods.

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Experimental studies were conducted on two month-old rat pups of both sexes weighing 75-90 g. Before the experiment, all laboratory animals were carefully examined, weighed, their age and motor activity were taken into account. During the entire preparation period for the experiment, the laboratory animals were kept in a vivarium at a temperature of 20-25 ° C, humidity of at least 50%, in a well-ventilated room and day / night light mode, in standard plastic cages with 6 individuals in each, with a standard diet, the daily requirement is compiled in accordance with the age of the animals. All laboratory animals participating in the experiment before the experiment had a healthy appearance and were active.

Inflammatory edema of the paw in rats was modeled by subplantar administration of dextran, which is widely used to assess the anti-inflammatory activity of new potential drugs [12, 13]. Experimental models of aseptic arthritis were reproduced by subplantar injection of 0.1 ml of 6% aqueous dextran solution into the hind paw of rats. The prophylactic effect of CelAgrip at a dose of 10 mg/kg was studied in comparison with the "gold standard" Ibuprofen - 10 mg/kg [14]. The above-mentioned drugs were preventively administered intragastrically with a metal tube 1 hour before the introduction of phlogogen. The paw volume of the animals was measured using a plethysmometer (Ugo Basile Srl, Italy) [13] before and 1, 2, 3 and 4 hours after the introduction of phlogogen. The increase in limb volume and the index of inflammation inhibition were used as criteria for assessing the anti-inflammatory efficacy [15,16]. The increase in paw edema was calculated using the formula:

$$P = O - I / I \times 100,$$

where, P is the increase in paw edema by the hour; O – paw volume after administration of the inflammation inducer;

I – paw volume before administration of the inflammation inducer.

The degree of inflammation inhibition was calculated using the formula:

$$100\% - [O - I / I(O) \div O - I / I(C)] \times 100,$$

where, O – experimental animals (treated);

C – control group (without treatment)

The experiments were conducted in accordance with the “Rules for conducting work using experimental animals”, as well as the rules adopted in the European Convention for the Protection of Vertebrate Animals used for experimental research or other scientific purposes (ETS No. 123, Strasbourg, 18.03.1986).

The obtained results of the experimental studies were processed statistically using the standard software package StatPlus 2009 by well-known methods of variation statistics with an assessment of the significance of indicators (M±m) and differences in the samples under consideration by Student's t-test. A difference at a probability level of 95% or more ($P<0.05$) was considered reliable.

Research results and their discussions

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Inflammation as a central link in the pathogenesis of many human pathologies is an urgent problem of modern medicine, because despite the introduction of a huge number of drugs of steroid and non-steroid structure in the treatment of inflammatory diseases, especially chronic ones, it is a large, unsolved problem. In this regard, pharmacologists are faced with the task of creating new effective drugs with a different mechanism of anti-inflammatory action. Therefore, in-depth studies of drugs from other groups of drugs could solve the problem of creating new anti-inflammatory drugs. According to the requirements of preclinical studies of new drugs, anti-inflammatory properties should be tested in an experiment on models of inflammation induced by various phlogogens. The results of the studies showed that with subplantar administration of dextran, statistically significant swelling of the paws was observed in animals in all groups, indicating the development of inflammation. In the group of animals preventively receiving CelAgrip and Ibuprofen, a certain modeling effect on the exudation process during aseptic inflammation was noted. Thus, if in control rats after subplantar administration of dextran the paw volume increases after 1 hour by 137.0%, after 2 hours - by 120.3%, after 3 hours - by 107.4% and after 4 hours - by 96.2% from the beginning of the experiment, then in rats receiving CelAgrip at a dose of 10 mg / kg it was 89.1, 74.5, 63.6 and 52.7%, respectively. It is evident that under the influence of CelAgrip the increase in the paw volume of rats was less than in the control. At the same time, the degree of inflammation inhibition at the indicated study times was 35.0, 38.3, 41.1 and 44.8%, respectively. A classic representative of non-steroidal anti-inflammatory drugs – ibuprofen in a similar dose – 10 mg/kg statistically significantly suppressed the exudative phase of inflammation induced by dextran and its degree of inflammation inhibition was 29.9, 32.5, 33.6 and 37.5%, respectively, in the above-studied hours (Table 1). It should be noted that the anti-inflammatory effect of CelAgrip, although higher compared to Ibuprofen, however these indicators between the groups were statistically insignificant.

Table 1

Indices of anti-inflammatory activity of CelAgrip and Ibuprofen in the model of acute exudative inflammation in prepubertal rats

Groups	Volume of paws, cm3		Increase in edema, %	Inflammation inhibition,%
	Before dextran administration	1 hour after administration of dextran		
Control	0,54 ± 0,02	1,28 ± 0,08*	137,0	-
CelAgrip	0,55 ± 0,02	1,04 ± 0,10*	89,1	35,0
Ibuprofen	0,53 ± 0,02	1,03 ± 0,07*	94,3	30,9

Note: * - reliable difference in relation to the original corresponding groups

Thus, CelAgrip and Ibuprofen in experimental animals have an anti-flagogenic effect manifested in a decrease in the exudation process on the effect of dextran

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