PHARMACOLOGICAL EVALUATION OF THE ANTI-INFLAMMATORY ACTIVITY OF CELAGRIP IN AN EXPERIMENT ON PREPUBERTAL ANIMALS

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Introduction. The inflammatory response is a multistage biological process involving vascular, cellular, and humoral mechanisms. One of the characteristic manifestations of acute inflammation is increased vascular permeability, which leads to the extravasation of the fluid component of blood into the surrounding tissues and the formation of edema. The severity of this response is determined by the nature of the triggering factor, the activity of inflammatory mediators, and the functional state of the organism [1,2]. The study of these processes is of considerable importance for the experimental evaluation of pharmacological agents with potential anti-inflammatory properties.

Particular importance is attached to the investigation of inflammatory responses in animals during the early postnatal period, when the maturation of organs and physiological systems is still ongoing. Specifically, in one-month-old rats, the immune system and physiological adaptation mechanisms are still developing, which may account for age-related differences in the characteristics of the inflammatory response. Furthermore, the age of experimental animals may influence drug metabolism and the magnitude of pharmacological effects. Therefore, investigating the anti-inflammatory activity of drugs in young rats makes it possible to assess the specific features of their action against the background of postnatal development [3,4].

Histamine is a key mediator of acute inflammation and is involved in the regulation of vascular tone and microvascular permeability. Its interaction, primarily

with H_1 receptors on endothelial cells, contributes to disruption of the vascular barrier, plasma extravasation into the interstitial space, and edema formation. In experimental pharmacology, the histamine-induced edema model is used to evaluate the anti-inflammatory effects of substances, particularly their effects on the early vascular phase of inflammation. However, this model does not allow a comprehensive characterization of all the mechanisms underlying the inflammatory process; therefore, the results obtained should be interpreted in conjunction with data from other experimental models [5,6].

In this regard, investigating the anti-inflammatory properties of CelAgrip in one-month-old rats from a herd-bred population under conditions of experimentally induced histamine-mediated inflammation is of particular relevance. Assessing the dynamics of the inflammatory response will make it possible to determine the potential effect of the drug on the severity of edema and obtain data for further investigation of its pharmacological effects, taking into account the age-related characteristics of the experimental animals.

Aim of the Study — to evaluate the anti-inflammatory activity of CelAgrip in one-month-old rats from a herd-bred population under conditions of experimentally induced histamine-mediated inflammation.

Materials and Methods. To assess the antiexudative activity of CelAgrip and Ibuprofen, a model of experimental aseptic inflammation induced by a 0.1% histamine solution was used. The phlogogenic agent was administered subplantarly into the right hind paw of the rats at a volume of 0.1 mL. The initial paw volume was taken as 100%.

The drugs were administered intragastrically using a metal gavage tube 1 day and 1 hour before the induction of inflammation, at doses of 10, 25, and 50 mg/kg. The control group received an equivalent volume of water. Paw volume was measured using a digital plethysmometer (Ugo Basile Srl, Italy) before administration of the phlogogenic agent and subsequently at 30, 60, 90, and 120 minutes. In the dextran-

and carrageenan-induced inflammation models, measurements were performed at 1, 2, 3, and 4 hours.

Antiexudative activity was assessed based on the increase in paw edema volume, the degree of edema inhibition, and the anti-inflammatory activity of the drugs.

Results. Following histamine administration, paw volume in the rats increased 2.1-fold within the first 30 minutes. Subsequently, the severity of edema gradually decreased; however, after 2 hours, its volume remained 1.8 times higher than the baseline value. According to the data presented in Table 1, CelAgrip and Ibuprofen demonstrated dose-dependent anti-edematous effects. At doses of 10 and 25 mg/kg, the effects of the drugs were less pronounced, whereas a more substantial suppression of edema was observed at a dose of 50 mg/kg. This may indicate the involvement of different mechanisms in mediating the anti-inflammatory effects of the investigated agents. Despite differences in the magnitude of their effects, both drugs significantly reduced the intensity of edema.

Table 1. Effect of CelAgrip and Ibuprofen on the Severity of Histamine-Induced Paw Edema in Rats (M ± m, n = 6)

Groups	Dose (mg/kg)	Baseline	30 min	60 min	90 min	120 min
Control	—	0.72 ± 0.03	1.51 ± 0.11*	1.42 ± 0.10*	1.36 ± 0.11*	1.30 ± 0.10*
CelAgrip (ST, %)	10	0.66 ± 0.02	1.34 ± 0.09* (5.5)	1.28 ± 0.08* (8.1)	1.19 ± 0.08* (9.8)	1.13 ± 0.08* (11.0)
CelAgrip (ST, %)	25	0.76 ± 0.04	1.40 ± 0.11* (22.9)	1.32 ± 0.08* (24.0)	1.26 ± 0.08* (26.1)	1.21 ± 0.08* (26.0)
CelAgrip (ST, %)	50	0.73 ± 0.03	1.35 ± 0.07* (22.1)	1.27 ± 0.06* (23.7)	1.22 ± 0.07* (24.6)	1.17 ± 0.06* (24.7)
Ibuprofen (ST, %)	10	0.77 ± 0.03	1.43 ± 0.10* (21.4)	1.35 ± 0.09* (22.3)	1.29 ± 0.08* (24.1)	1.23 ± 0.07* (25.3)
Ibuprofen (ST, %)	25	0.70 ± 0.02	1.33 ± 0.09* (17.4)	1.25 ± 0.08* (19.0)	1.20 ± 0.07* (19.4)	1.15 ± 0.07* (19.6)
Ibuprofen (ST, %)	50	0.73 ± 0.03	1.34 ± 0.10* (23.3)	1.26 ± 0.09* (25.1)	1.24 ± 0.08* (21.5)	1.19 ± 0.07* (21.2)

Note: * — statistically significant differences compared with baseline values; ST — degree of edema inhibition (%).

Conclusion. The results of the present study indicate that CelAgrip and Ibuprofen exhibit anti-edematous activity in a rat model of histamine-induced inflammation. Both drugs contributed to a reduction in the severity of the exudative response, with the observed effects demonstrating a dose-dependent pattern. The most pronounced inhibition of edema was observed following administration of the drugs at a dose of 50 mg/kg, whereas their effects at lower doses were less substantial. The persistence of an increased paw volume even 2 hours after histamine administration indicates the sustained nature of the inflammatory response and provides an opportunity to assess the ability of the investigated agents to limit its progression. The observed reduction in edema severity suggests that CelAgrip and Ibuprofen are involved in modulating the early exudative phase of the inflammatory process.

Thus, the findings confirm the dose-dependent nature of the anti-edematous effects of CelAgrip and Ibuprofen in histamine-induced inflammation. The hypothesis that additional mediator-related mechanisms may be involved requires further experimental confirmation. For a more comprehensive characterization of the anti-inflammatory properties of these drugs, it would be appropriate to compare the findings obtained with data from other experimental models of inflammation and to evaluate the dynamics of their effects in relation to dose and observation time.

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