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RESEARCH ARTICLE

Experimental substantiation of anti-inflammatory activity of a gel containing *Convolvulus arvensis* extract in carrageenan-induced aseptic arthritis

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ABSTRACT

Background: Despite the huge number of drugs used for the treatment of inflammatory diseases, the modern assortment of this group of drugs does not solve the problem of their successful therapy and relapses, the frequency of which after stopping the administration can reach high values. **Aim and Objective:** The aim of this work was to study the anti-inflammatory activity of a gel containing *Convolvulus arvensis* in aseptic arthritis induced by carrageenan. **Materials and Methods:** Experimental studies were carried out on sexually mature white males' rats with an initial weight of 155–180 g. A 5% *C. arvensis* extract containing gel and 5% ibuprofen gel was applied to the surface of the right hind paw of the animals 1 h before the injection of flogogen and after each measurement of the paw volume. Measurement of the paw volume of animals was carried out using a plethysmometer **Results:** A more expressed antiexudative effect was observed when used *C. arvensis* extract-containing gel. Hence, after 1, 2.3, and 4 h from the beginning of the action of carrageenan, the volume of the rat paws increased compared to the initial by 45.5; 51.9; 59.7; and 51.9%, respectively. An almost twofold inhibition of the development of the exudation process was observed under the influence of *C. arvensis* extract containing gel in comparison with the control group. **Conclusions:** The gel containing the extract of *C. arvensis* has an expressed antiexudative effect in aseptic arthritis induced by carrageenan. In terms of its antiexudative activity, the preparation containing the extract of *C. arvensis* is not inferior to ibuprofen when applied locally in the form of a gel.

KEY WORDS: Inflammation; Carrageenan; Anti-exudative activity of *Convolvulus arvensis* extract

INTRODUCTION

Despite the huge number of drugs used for the treatment of inflammatory diseases, the modern assortment of this group of drugs does not solve the problem of their successful therapy and relapses, the frequency of which after stopping the administration can reach high values. It is necessary to note that the development of a number of side effects (gastro-, nephro-, cardio-, hemato-, and hepatotoxicity) aggravating the course of the underlying disease poses a serious threat to the life of patients.[1-4] Based on this, it seems logical to use antiphlogogenic drugs locally, in which their resorbtive and, accordingly, side effects practically do not develop.[5-9] Earlier, it was experimentally proven high anti-exudative effect of *Convolvulus arvensis* extract when it administered orally.[10-12] However, the anti-inflammatory activity of the gel form of the preparation has not been sufficiently

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studied. In this regard, it seems important to study the anti-inflammatory activity of the gel containing *C. arvensis* extract on the course of carrageenan-induced aseptic arthritis. It is known that carrageenan is a phlogogen, which induces aseptic inflammation and this model of inflammation is widely used to study new anti-inflammatory drugs.[13] The aim of this work was to study the anti-inflammatory activity of a gel containing *C. arvensis* in aseptic arthritis induced by carrageenan.

MATERIALS AND METHODS

Experimental studies were carried out on sexually mature white males rats with an initial weight of 155–180 g. Before the experiment, the animals were quarantined for 12–14 days. All animals were kept in vivarium conditions (with natural lighting, at a temperature 22–24°C; relative humidity 40–50%) using a standard diet. Each experimental group consisted of 6 individuals. The antiexudative effect of the drugs was studied on a model of acute inflammation in animals by subcutaneous injection of 2% solution of carrageenan (0.1 ml/animal) into the right hind extremity of rats. This model of inflammatory edema is widely used to assess the anti-inflammatory activity of new potential drugs.[14,15] Measurement of the volume of the paws of animals was carried out by the oncometric method using a plethysmometer[16] before and hourly for 6 h after the injection of the flagogen. The value of anti-inflammatory activity (VAA) of drugs was calculated according to the formula VAA = $V_{control}–V_{experiment}/V_{control} \times 100$ =%.[14] A 5% *C. arvensis* extract containing gel and 5% ibuprofen gel was applied to the surface of the right hind paw of the animals 1 h before the injection of flogogen and after each measurement of the paw volume. The approval of National Ethics Committee for experimental research on animals was taken before the onset of the experiment. Experimental studies were carried out in accordance with the rules of good laboratory practice when conducting preclinical studies in the Republic of Uzbekistan, as well as the rules and International Recommendations of the European Convention for the Protection of Vertebrate Animals used in Experimental Research (1986).

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

RESULTS

The obtained results were given in Table 1.

DISCUSSION

Subplantary injection of carrageenan in healthy animals, as shown by the analysis of the results of experimental studies, leads to an expressed increase of the volume of the paws by 85.9% after 1 h, 98.6% – 2 h, 115.3% –3 h, and 107.0% after 4 h compared to the initial measurement, while the observed effect persists even by the 6th h of the experiment with small fluctuations. The obtained results prove the high phlogogenic activity of carrageenan, which persists for a rather long period. It is believed that the inflammatory effect of carrageenan is due to the action of kinins in the 1st h, and in later periods, that is, at 3 and 4 h and further, it is related to prostaglandins.[17,18]

Preventive treatment of rat paws with 5% ibuprofen gel caused a distinct inhibition of the exudation process. Thus,

Table 1: Study of the influence of the gel containing the extract of *C. arvensis* and ibuprofen on the course of aseptic arthritis induced by carrageenan when its preventative application

Groups	Volume of paw,cm^3						
	Initial value	After 1 h	After 2 h	After 3 h	After 4 h	After 5 h	After 6 h
Control	0.71±0.02	1.32±0.06 0.61±0.06	1.41±0.06 0.70±0.07	1.53±0.06 0.82±0.07	1.47±0.05 0.76±0.05	1.41±0.04 0.70±0.04	1.33±0.04 0.62±0.04
P		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
C. arvensis	0.77±0.02	1.12±0.06 0.35±0.05	1.17±0.04 0.40±0.04	1.23±0.05 0.46±0.04	1.17±0.04 0.40±0.03	1.10±0.03 0.33±0.03	1.03±0.02 0.26±0.02
P		<0.01	<0.002	<0.001	<0.001	<0.001	<0.002
P_1		<0.05	<0.02	<0.01	<0.002	<0.001	<0.001
Ibuprofen	0.76±0.04	1.23±0.08 0.47±0.06	1.28±0.07 0.52±0.05	1.32±0.07 0.56±0.05	1.24±0.07 0.48±0.05	1.17±0.06 0.41±0.05	1.11±0.04 0.35±0.04
P		<0.01	<0.002	<0.001	<0.002	<0.01	<0.01
P_1		>0.05	>0.05	<0.05	<0.01	<0.01	<0.01

The numerator is the paw volume, the denominator is the difference in paw edema in rats of the corresponding measurement period. P - significant difference in relation to the initial volume of the paws. P1 - significant difference in the difference in edema of the paws by hours in relation to the control group.
C. arvensis: *Convolvulus arvensis*

compared with the initial volume of the paws in the group of rats using ibuprofen, the increase of paw volume was by 61.8% after 1 h, by 68.4% after 2 h, by 73.7% after 3 h, and 63.2% after 4 h. The calculation of the value of anti-inflammatory activity of the drug in the indicated periods of observation showed that it was 22.9; 25.7; 31.7; and 36.8%, respectively. It can be seen from the data in Table 1, a more expressed antiexudative effect was observed when used *C. arvensis* extract containing gel. Hence, after 1, 2, 3, and 4 h from the beginning of the action of carrageenan, the volume of the rat paws increased compared to the initial by 45.5; 51.9; 59.7; and 51.9%, respectively. It can be seen that an almost twofold inhibition of the development of the exudation process was observed under the influence of *C. arvensis* extract containing gel in comparison with the control group.

Consequently, the gel containing the extract of *C. arvensis* has a distinct anti-exudative activity and in its pharmacological activity is not inferior to the non-steroidal anti-inflammatory drug ibuprofen. It is noteworthy that the investigated gel containing the extract of *C. arvensis* and ibuprofen has a unidirectional effect on both phases of inflammation in the model of carrageenin-induced aseptic arthritis. In earlier studies, an anti-exudative, antiproliferative,[12] analgesic and antipyretic effects,[19] as well as low toxicity of *C. arvensis* extract[11] were determined where extract was administered orally. The mechanism of anti-inflammatory action of the *C. arvensis* extract is due to its antagonism in relation to the effects of inflammatory mediators as well decrease of vascular permeability and suppression of hyaluronidase activity and its activity is not associated with the effect on the adrenal cortex.[12]

Since the studied gel as a pharmacological substance contains only a dry extract of the plant *C. arvensis*, it can be assumed that the mechanism of its antiexudative action is associated with suppression of the kinin system activity, hyaluronidase activity,[12] a decrease of the vascular permeability, as well as suppression of the intensity of free radical processes.[20,21]

CONCLUSIONS

The gel containing the extract of *C. arvensis* has a expressed antiexudative effect in aseptic arthritis induced by carrageenan. In terms of its antiexudative activity, the preparation containing the extract of *C. arvensis* is not inferior to ibuprofen when applied locally in the form of a gel. The mechanism of antiexudative action of the gel containing *C. arvensis* extract is multidirectional and this is mainly associated with suppression of the kinin system activity, hyaluronidase activity, decrease of vascular permeability, as well as suppression of the intensity of free radical processes

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