

# Multicomponent Photocomposition as A Source for Development New Anti-Inflammatory Medicines

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**Abstract.** The results of experimental studies on mature white male rats showed that phytocompositions 1, 2 and 3 containing various extracts of medicinal plants have a distinct antiphlogogenic activity. Among the studied phytocollections, composition 3 showed a higher anti-inflammatory activity compared to other studied phytocollections. The studied new mixtures of medicinal plants have a higher antiphlogogenic activity than canephron, especially phytocomposition 3, and in terms of their pharmacological activity, it is not inferior to the gold standard non-steroidal anti-inflammatory drug - sodium diclofenac.

**Key words:** aseptic arthritis, phytocomposition, medicinal plants, anti-inflammatory agents.

**Introduction.** Currently, there is no doubt that the use of non-steroidal anti-inflammatory drugs (NSAIDs) is fraught with the development of various adverse side effects. At the same time, lethality from adverse effects of drugs ranks fifth in the world. Exactly, drugs cause to the death of 0.1% of therapeutic patients [1]. The risk of such side effects are higher than in young people in the elderly is 5-7 times as well as the severe reactions occur in elderly and senile people in 64.0% of cases, which is largely due to polypharmacy [2]. Considering the prevalence of inflammatory processes, especially in the elderly people, the use of NSAIDs is quite large, since they have different properties (anti-inflammatory, antipyretic, analgesic, antiplatelet). Therefore, they are one of the most popular over-the-counter drugs in the world [3,4]. However, using of them, as mentioned above, is accompanied by multiple side effects, sometimes life-threatening [3,4,5]. Based on this, it is important to develop new drugs with anti-inflammatory properties. In this regard, it seems most effective to develop multicomponent mixtures from medicinal plant raw materials, since they have valuable advantages over other herbal remedies: the main pharmacological effect on the patient's body provides as a whole in combination with a complex effect, mildness of action and the absence of undesirable side effects [6]. This is due to the fact that at this time the life expectancy of a people have increased, and at the same time, various pathologies have become widespread, the treatment of which requires a combination of several medicines [7].

**The purpose of this work** was to select the most effective anti-inflammatory compositions consisting of various medicinal plants.

**Materials and methods.** For the study, we have chosen the following medicinal plants containing biologically active substances that affect the main links of the inflammatory process: *Alhági*, *Stigmata Maydis*, *Uvae Ursi folia*, *Glycyrrhizae radices*, *Fructus Petroselini*, *Juniperi fructus*, *Fructūs Rosae*, *Equiseti arvensis herba*, *Chamomillae flores* and *Aerva lanata*. There were three compositions: №1 consisting from *Glycyrrhizae radices*, *Alhági*, *Stigmata Maydis*, *Uvae Ursi folia* and *Fructus Petroselini*, №2 consisting from *Juniperi fructus*, *Fructūs Rosae*, *Equiseti arvensis herba*, *Chamomillae flores* and *Aerva lanata* №3 consisting from *Alhági*, *Uvae Ursi folia*, *Fructūs Rosae*, *Glycyrrhizae radices* and *Chamomillae flores*.

Experimental studies were carried out on adult white male rats weighing 140-160 g, obtained from the vivarium of the Department of Sanitary and Epidemiological Surveillance of the Main Medical Department under the Administration of the President of the Republic of Uzbekistan. Prior to the start of the experiment, all animals were examined, weighed after a two-week quarantine. Age, sex, physical activity and skin condition of animals were taken into account. Each experimental and control group consisted of six individuals. During experimental studies, laboratory animals were kept in a vivarium in plastic cages, bedding

of sawdust at a temperature of 20-24°C, in a well-ventilated room and day/night light regimen. Humidity was at least 50%.

Feeding of animal was calculated according to their age. Diclofenac sodium (Belmedpreparaty) and Canephron (Bionorica SE., Germany), which is a mixture of dry extracts of medicinal plants, were used as a reference drugs. To study the anti-exudative activity of the above compositions of dry extracts of medicinal plants was used by using the classical model of experimental aseptic arthritis induced by a 6%- solution of dextran [8]. The phlogogen solution was injected (0.1 ml per animal) subplantarly (under the plantar aponeurosis) into the hind right paw of rats. The volume of paws of rats before the injection of the phlogogen was considered initial and was taken as 100%. One day and 1 hour before the reproduction of aseptic arthritis, rats of the control group were administered intragastrically an equivolume amount of water as well as animals of the experimental groups were administered the phytocomposition 1, 2 and 3 in various doses of 25, 50 and 100 mg/kg, canefron - 100 mg/kg and sodium diclofenac - 10 mg/kg. The volume of the paws of the animals was measured by the oncometric method using a plethysmometer (Ugo Basile Srl, Italy) before and after the injection of dextran. The anti-inflammatory activity of the studied compounds was judged by the difference in paw volume before the start of the experiments and at the moment of maximum development of edema. The value of anti-inflammatory activity (AIA) of the preparations was calculated according to the formula (5):

$$AIA = \frac{V_{\text{con}} - V_{\text{exp}}}{V_{\text{con}}} \times 100 = \%$$

where;

$V_{\text{con}}$  - average increase in paw volume in control group,  $\text{cm}^3$ ,

$V_{\text{on}}$  - average increase in paw volume in experimental group,  $\text{cm}^3$ .

The results of the study were statistically processed using the Biostat 2009 software package. The data are presented as the mean (M) and standard error of the mean value (m). Student's t-tests were used to test statistical hypotheses about the difference between the study groups. Statically significant changes were taken at a probability level of 95% or more ( $p < 0.05$ ).

### Research results.

The results of the studies showed that aseptic arthritis develops under the influence of dextran, which caused an increase in the volume of the paws of rats by 166.2-180.3% compared to the initial volume of paw. In contrast, the degree of paw edema was significantly low in animals that received phytocompositions and comparative drugs (Table 1). Thus, under the influence of phytocomposition 1 in doses of 25, 50, and 100 mg/kg, the volume of the paws of rats after 1 hour from the injection of phlogogen, respectively, decreased by 26.0, 29.1, and 31.5% compared with the control group. The obtained effect increased slightly in subsequent periods of observation. in the initial period of observation, the anti-inflammatory activity of phytocomposition 1 in the administered doses was 23.6; 30.9 and 27.3%, respectively. A low degree of edema was also determined in animals that preventively received phytocomposition 2 compared to the control group. The severity of edema was low by 27.4% at a dose 25 mg/kg, by 31.0% at a dose 50 mg/kg, and by 25.0% at a dose 100 mg/kg. The values of the anti-inflammatory activity of this phytocomposition from the studied doses were, respectively, 28.7, 34.5, and 31.7% in the indicated terms of the experiment. And in this case, the noted effect increased a little in subsequent periods of observation. Analysis of the results of studies in animals that received phytocomposition 3 showed that under the influence of this composition, the degree of edema was low by 27.8% at a dose of 25 mg/kg and by 38.1% and 37.4% at doses of 50 and 100 mg/kg, respectively. At the same time, the anti-inflammatory activity from the indicated doses was 25.7; 37.2 and 31.8% respectively. It can be seen that the most effective dose of the studied phytocompositions is 50 mg/kg. It was interesting to compare the activity of the studied phytocompositions with the phytopreparation - canefron [9], which reduced the degree of edema by 24.0%, and the anti-inflammatory activity was 28.2% in our studies. The obtained results were also compared with the effect of the gold standard NSAID - diclofenac sodium [10], which under the conditions of our experiment suppressed the development of aseptic inflammation by 42.4% compared with the control group and the value of anti-inflammatory activity was 39.8%.

Table 1

Influence of the phytocomposition, canefron and diclofenac sodium on the exudative phase of inflammation induced by dextran ( $M \pm m$ ,  $n=6$ )

Groups of animals	Dose mg/kg	Difference between volumes of inflamed and non-inflamed paws, cm <sup>3</sup>	AIV, %
<b><i>Dextran edema</i></b>			
Control	-	1,10 ± 0,05	-
Phytocomposition 1	25	0,84 ± 0,04*	23,5
	50	0,76 ± 0,04*	30,9
	100	0,80 ± 0,05*	27,3
<b><i>Dextran edema</i></b>			
Control	-	1,01 ± 0,07	-
Phytocomposition 2	25	0,72 ± 0,04*	28,7
	50	0,66 ± 0,03*	34,6
	100	0,69 ± 0,04*	31,7
<b><i>Dextran edema</i></b>			
Control	-	1,13 ± 0,06	-
Phytocomposition 3	25	0,84 ± 0,05*	25,7
	50	0,71 ± 0,03*	37,2
	100	0,77 ± 0,04*	31,8
Canefron	100	0,81 ± 0,06*	28,3
Diclofenac	10	0,68 ± 0,03*	39,8

Note: \* - significant difference in comparison with control.

Therefore, the studied new phytocompositions have distinct anti-edematous effects in the model of dextran-induced aseptic arthritis. Among the studied phytocompositions, composition 3 was more active. This phytocomposition by its antiphlogogenic activity was clearly superior than canefron and did not statistically differ from diclofenac sodium.

It is known that the mechanism of the phlogogenic effect of dextran is due to the release of biologically active substances such as histamine from mast cells, which is one of the important mediators of inflammation. Based on this, it can be assumed that the studied phytocompositions have antihistamine activity. It seems that the main mechanism of the anti-inflammatory effect of the studied mixtures of medicinal plants is due to the substances with the antioxidant properties (flavonoids, polyphenolic compounds) containing in medicinal plantsb [11,12,13,14].

### Conclusions

1. Phytocomposition 1, 2 and 3 containing various extracts of medicinal plants have a distinct anti-exudative activity.
2. Among the studied phytocompositions, composition 3 showed a higher anti-inflammatory activity compared to other studied phytocompositions.
3. The studied new mixtures consisting of various medicinal plants have a higher anti-exudative activity than canefron, especially composition 3, and in terms of their pharmacological activity, it is not inferior to diclofenac sodium.

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