American Journal of Medicine and Medical Sciences 2023, 13(2): 39-42
DOI: 10.5923/j.ajmms.20231302.01

Antiexudative Activity of a New Phytocomposition Consisting from the Flora of Central Asia

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Abstract Anti-exudative activity of a new phytocomposition conventionally named Soyaktop was studied on male white rats weighing 180-200 g. It has been established that the preparation clearly suppresses the development of dextran and histamine induced paw edema in rats, especially at a dose of 50 mg/kg. the preventive administration of the phytocomposition Soyaktop-2 did not lead to a further increase in the antiphlogogenic activity of the studied mixtures. However, the combination of extracts of medicinal plants in a different ratio, conditionally named as a phytocomposition Soyaktop-3 showed a higher pharmacological activity. In the studied periods of observation in dextran-induced inflammation, its AIA was 27.7; 41.1; 45.1 and 49.3% respectively. Such an effect of Soyaktop-3 is also observed in histamine-induced aseptic arthritis, which indicates an important role for the antihistamine activity of the test compound.

Keywords Phytocomposition, Medicinal plants, Inflammation, Exudation, Antihistamine activity

1. Introduction

Liver One of the important problems of pharmacology is the discovery and development new, affordable, effective medicines from local raw materials that suppresses the process of exudation, alteration and proliferation in pathological conditions. Therefore, the search for new medicines obtained from local raw materials with the appropriate type of action, and the study of the possibility of using them in pathologies which the inflammation plays an important role in the pathogenesis of them, is an urgent task of modern theoretical medicine.

Considering the literature data, it seems logical to study the anti-inflammatory activity (AIA) of dry extracts of the following medicinal plants: root of Glycyrrhiza glabra, Alhagi pseudalhagi, Stigma maydis, Uvae Ursi folia, and Fructus petroselini [1,2]. At the same time, their combination in various ratios, in our opinion, would allow to determine the new phytocompositions with an expressed anti-inflammatory effect.

For this purpose, a mixture of medicinal plants was developed conventionally called "Soyaktop", which differ each other in their composition and the ratio of extracts in the mixture (table 1).

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Received: Jan. 8, 2023; Accepted: Feb. 3, 2023; Published: Feb. 13, 2023
Published online at http://journal.sapub.org/ajmms

Table 1. The composition of the mixture "Soyaktop" (ratios in grams)

№	Name of medicinal plants	Soyaktop-1	Soyaktop-2	Soyaktop-3
1	root of *Glycyrrhiza glabra*	1,0	1,0	0,5
2	*Alhagi pseudalhagi*	1,0	0,5	1,0
3	*Stigma maydis*	1,0	1,0	0,5
4	*Uvae Ursi folia*	1,0	0,5	1,0
5	*Fructus petroselini*	1,0	1,0	0,5

The aim of current work was to study the anti-exudative activity of Soyaktop in the model of aseptic arthritis induced by various flogogens on experimental animals.

2. Material and Methods

2.1. Experiments

Experimental studies were carried out on male white rats weighting 140-160 g. After quarantine for two weeks, all laboratory animals were carefully examined, weighed and their age, sex, and motor activity were taken into account. Each experimental and control group consisted of six animals. During the entire period of experiment, laboratory animals were kept in a vivarium in standard plastic cages at a temperature of 20-24℃, humidity of at least 50%, in a

well-ventilated room and day/night light regimen. Animal feeding diet was calculated according to their age.

The dry extracts of medicinal plants was studied which were prepared by scientists of the Research Institute of Chemistry and Pharmaceutics of the Republic of Uzbekistan.

LIV-52 (Himalaya Drug Co., India) and Canephron (Bionorica SE., Germany) were used as a reference drug, which also consist a mixture of dry extracts of medicinal plants. The classical models of experimental aseptic arthritis induced by solutions of various phlogogenic agents, such as dextran (6%) and histamine (0.1%) were used to study the anti-exudative activity of compositions of dry extracts of medicinal plants [3,4,5,6]. Phlogogen solutions were 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 volume and was taken as 100%. One day and 1 hour before the reproduction of aseptic arthritis, the animals of the experimental groups were intragastrically administered Soyaktop in various compositions at doses of 25, 50 and 100 mg/kg, and LIV-52 and Canephron - 100 mg/kg and the rats of the control group were administered water an equivolume amount. The volume of the paws of the animals was measured by the oncometric method using a plethysmometer before and after the administration of dextran and histamine. 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 preparations was calculated according to the formula:

AIA = Vcontrol – Vexperiment / Vcontrol x 100 = %,

Where, Vcontrol - average increase in paw volume of control group, sm3,

Vexperiment – average increase in paw volume in the experimental group, sm3.

A number of authors indicate that if the AIA value exceeds 30%, then, as is commonly believed, the drug has a expressed anti-inflammatory effect [7].

2.2. Statistical Analysis

The data obtained were processed by the method of variation statistics using the paired Student's test and one-way analysis of variance using the standard software package BIOSTAT 2009 with an assessment of the significance of indicators (Mean±Std error). Differences in the compared groups were considered significant at a significance level of 95% $p < 0.05$, in the case of $0.05 < p < 0.10$, the differences were assessed as a trend.

3. Results and Discussion

The results of the experimental studies have shown the presence of a certain anti-exudative activity of the mixture of phytocomposition Soyaktop. So, in control group of animals under the influence of a subplantar injection of dextran after 1, 2, 3 and 4 hours from the start of the injection of phlogogen, the volume of the paws of rats increased by 154.1; 129.5; 114.7 and 106.5% respectively compared to the initial volume. In contrast, the intensity of edema development was noticeably lower under the influence of various phytocompositions of Soyaktop. It can be seen from the data in table 2 that the phytocomposition of medicinal plants has a distinct anti-inflammatory activity. So, if the subplantar injection of dextran leads to an increase in the volume of the paws of rats in the first hours of the experiment by almost 2.5 times, which persists with small fluctuations over the next four hours. After 1, 2, 3 and 4 hours from the moment of dextran injection, The volume of edema was less in the groups of rats that received preventive Soyaktop-1 phytocomposition, and the paw volume increased respectively by 108,7; 64.2; 84.0 and 75.4% in comparison with the initial volume of the paws of rats. At the same time, the value of AIA of the medicines was respectively 25.7; 27.8; 29.3 and 30.7% in the indicated periods of observation. As shown by the analysis of the results shown in table 2, the preventive administration of the phytocomposition Soyaktop-2 did not lead to a further increase in the antiphlogogenic activity of the studied mixtures. However, the combination of extracts of medicinal plants in a different ratio, conditionally named as a phytocomposition Soyaktop-3 showed a higher pharmacological activity. In the studied periods of observation, its AIA was 27.7; 41.1; 45.1 and 49.3% respectively.

Table 2. Study of the influence of various phytocompositions of a mixture of extracts of medicinal plants Soyaktop to course of aseptic arthritis induced by dextran (Mean±Std error, n=6)

Groups	dose mg/kg	Volume of paw, sm^3 (hours of experiments)				
		initial	1 hour	2 hours	3 hours	4 hours
Control	-	0,68 ± 0,02	1,69 ± 0,07*	1,58 ± 0,06*	1,50 ± 0,06*	1,43 ± 0,06*
Soyaktop -1	50	0,69 ± 0,03	1,44 ± 0,07*	1,34 ± 0,09*	1,27 ± 0,08*	1,21 ± 0,07*
Soyaktop -2	50	0,70 ± 0,02	1,53 ± 0,07*	1,43 ± 0,06*	1,35 ± 0,06*	1,28 ± 0,06*
Soyaktop -3	50	0,66 ± 0,03	1,39 ± 0,06*	1,19 ± 0,05*	1,11 ± 0,05*	1,04 ± 0,06*
LIV-52	100	0,61 ± 0,02	1,29 ± 0,07*	1,18 ± 0,06*	1,11 ± 0,06*	1,06 ± 0,06*
Conephron	100	0,68 ± 0,02	1,46 ± 0,04*	1,38 ± 0,05*	1,32 ± 0,05*	1,26 ± 0,04*

Note: * - statistically significant in comparison with initial paw volume of the corresponding groups of animals.

Table 3. Study of the influence of Soyaktop on the course of aseptic arthritis induced by histamine (Mean±Std error, n=6)

Groups	Dose, mg/kg	Volume of paw, sm^3 (minutes of study)				
		Initial	30 minute	60 minute	120 minute	180 minute
Control	-	0,57 ± 0,02	1,54 ± 0,09*	1,47 ± 0,06*	1,40 ± 0,06*	1,32 ± 0,09*
mixture-1	50	0,55 ± 0,02	1,30 ± 0,08*	1,23 ± 0,10*	1,16 ± 0,08*	1,08 ± 0,07*
mixture -2	50	0,60 ± 0,01	1,39 ± 0,10*	1,31 ± 0,10*	1,24 ± 0,08*	1,16 ± 0,09*
mixture -3	50	0,58 ± 0,02	1,27 ± 0,07*	1,18 ± 0,08*	1,07 ± 0,09*	0,99 ± 0,09*

Note: * - statistically significant difference in comparison with initial volume P<0.05.

Table 4. Study of the anti-inflammatory activity of various doses of Soyactop-3 in dextran-induced aseptic arthritis (Mean±Std error, n=6)

Groups	Dose, mg/kg	Volume of paw, sm^3 (hours of study)				
		Initial	1 hour	2 hour	3 hour	4 hour
Control	-	0,56 ± 0,02	1,57 ± 0,07*	1,49 ± 0,08*	1,41 ± 0,08*	1,35 ± 0,06*
Soyaktop-3	25	0,55 ± 0,03	1,27 ± 0,05*	1,20 ± 0,05*	1,12 ± 0,05*	1,07 ± 0,05*
Soyaktop -3	50	0,49 ± 0,02	1,08 ± 0,05*	1,01 ± 0,05*	0,95 ± 0,05*	0,90 ± 0,04*
Soyaktop -3	100	0,53 ± 0,03	1,17 ± 0,06*	1,11 ± 0,06*	1,05 ± 0,06*	1,01 ± 0,06*

Note: * - statistically significant difference in comparison with initial volume P<0.05.

Therefore, Soyaktop has an expressed antiexudative effect. From a pharmacological point of view, it is important to establish the effective dose of the medicine, which is also necessary for calculating the width of pharmacological action, especially in clinical trials of new drugs. Based on this, in a separate series of experiments on the model of dextran induced aseptic arthritis, we studied various doses of the phytocomposition Soyaktop-3. Soyaktop-3 was chosen by us due to its high AIA in comparison with other ratio of extracts of medicinal plants.

It should be noted that herbal medicines containing flavonoids have a expressed AIA, such as LIV-52 [3,8,9]. In this regard, it was interesting to compare the obtained results with the antiphlogogenic activity of LIV-52. As can be seen from the data in table 2, the administration of LIV-52 reduced the development of edema of the paws of rats induced by dextran and it was somewhat less than control group and AIA in the studied periods of observation was 27.6; 27.8; 28.6 and 30.6% respectively. It can be seen that LIV-52 is clearly inferior in its pharmacological activity then the studied phytocomposition Soyaktop-3.

There are lots of data about the pharmacological properties of canephron (Bionorica CE, Germany) in literature, where the anti-inflammatory properties of this drug are widely written [10]. It is known that canephron is multicomponent and contains extracts of a number of medicinal plants, it seemed important to compare the pharmacological activity of various Soyaktop-3 phytocompositions with this drug.

The results of the study of this series of experiments showed that canephron exhibits a distinct anti-exudative effect on the model of dextran-induced inflammation. At the same time, in rats that received preventive canephron at a dose of 100 mg/kg, the increase in paw volume was noticeably low and after 1, 2, 3 and 4 hours of observation, it was 114.7; 102.9; 94.1 and 85.3%, respectively compared with the initial volume of paw. On this model in the studied periods of observation, the AIA value of the drug was 30.9; 32.7; 34.0 and 34.8%, respectively.

Therefore, the results of experimental studies on the establishment of AIA phytocomposition Soyaktop indicate that this mixture has a pronounced AIA, especially Soyaktop-3, which is clearly superior in activity not only to LIV-52, but also to canephron.

According to many researchers, the phlogogenic effect of dextran is due to the stimulation of the release of biologically active substances - inflammatory mediators, such as histamine, serotonin, etc. from mast cells [3,6]. In order to study possible mechanism of the antiphlogogenic action of mixtures of extracts of medicinal plants, in a separate series of experiments, we studied the antiexudative activity of the Soyaktop phytocomposition in various ratios of their components in a model of histamine-induced aseptic inflammation.

The results of the studies showed that subplantar injection of histamine led to an increase in the volume of the paw of rats by 2.7 times after 30 minutes, which gradually decreased, but remained quite high (2.32 times) in the subsequent hours of observation (table 3). In contrast, the preventive administration of the phytocomposition of Soyaktop in various combinations led to a decrease in the intensity of exudation under the influence of histamine, which indicated a high AIA of the medicine. So, after 30 minutes from the beginning of the experiment, the value of AIA Soyaktop-1, Soyaktop-2 and Soyaktop-3 was 22.7; 18.5 and 28.8% respectively. The determined effect subsequently increased and AIA was 29.3; 25.3 and 45.3% respectively at the end of the third hour of observation.

4. Conclusions

1. Phytocomposition composed from the flora of Central Asia has a distinct anti-exudative activity.

2. The degree of anti-inflammatory activity of Soyaktop depends on the administered dose. Its effective dose is 50 mg/kg.
3. In the mechanism of the anti-exudative effect of Soyaktop, an important place is occupied by its antihistamine activity. Antihistamine activity plays an important role in the mechanism of Soyaktop's anti-exudative effect.

ACKNOWLEDGEMENTS

This scientific work was supported by national grant PZ-202102233.

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