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ANTI-INFLAMMATORY ACTIVITY OF DRY EXTRACT OF MEDICINAL PLANTS

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ABSTRACT

It was determined in sexually matured white male rats that the preventive administration of dry extract of medicinal plants (DEMP) has a distinct antiexudative action in aseptic arthritis. By its anti-inflammatory activity, DEMP is superior relatively to the known drug LIV-52 and is not inferior to the reference non-steroidal anti-inflammatory drug diclofenac sodium. Using DEMP for the treatment of inflammatory diseases might be recommended.

KEYWORDS: Dry extract of medicinal plants, inflammation, exudation, antioxidants.

INTRODUCTION

It is unthinkable to increase the effectiveness of pharmacotherapy of human diseases without using an active etiotropic, pathogenetic treatment. Since inflammation is a common reaction of the body to the action of various exogenous and endogenous damaging factors, it lies at the base of many diseases of various clinical manifestations, and is one of the central problems of pathologies in the history of study of diseases.[1] The non-steroidal anti-inflammatory drugs (NSAID) play an important role in the suppression of this pathological process. However, their use is associated with a risk of developing severe side effects, not only in the form of gastropathy, but also in the pathology of the kidneys, liver, clotting system and etc.[2,3,4,5,6] Therefore, currently the search for new anti-inflammatory drugs with few side effects remains one of the most urgent tasks of pharmacology. Unfortunately, we need to recognize that in recent times, synthetic anti-inflammatory drugs are most often used in the treatment of diseases, which are very characteristic to cause quite serious complications. There is no doubt the perspectiveness of searching for the medicines with antipyretic, anti-inflammatory and analgetic activity among compounds of natural origin - multicomponent extracts of medicinal plants and their collections.[7]

Interest in such compounds is expressed due to their relatively high biological activity and low toxicity for the human body. In this regard, our attention was drawn to the sum of dry extracts of medicinal plants - mediazia macrophylla, Glycyrrhizin glabra L., Hipericum scabrum L. and Ziziphora pedicellata Pazij Vved.

The purpose of this work was to study the anti-inflammatory activity of the dry extract of these medicinal plants.

MATERIALS AND METHODS

The influence of DEMP from local medicinal plants to the course of aseptic arthritis were conducted on white adult male rats with body weight of 160-175 g in experiment, in which the inflammation was reproduced by introducing 6% dextran solution in a volume of 0.1 ml subplantarly. Measurement of the volume of the right hind paw of animals was performed with a plethysmometer[8] before and 1, 2, 3 and 4 hours after the introduction of the flagogen agent. The value of the anti-inflammatory activity (VAA) of the drugs was calculated according to the formula VVA = V_{con}-V_{exp} / V_{con} x 100 =%.[9] DEMP was administered prophylactically intravenously at doses of 10, 25, 50 and 100 mg/kg. A separate group of animals was administered diclofenac sodium orally at a dose of 10 mg/kg, and another LIV-52 at a dose of 100 mg/kg[10] 2 hours before the administration of the flagogen agent.

All experiments were performed in compliance with the requirements of the European Convention "On Protection of vertebrate animals used for experimental and other scientific purposes" (Strasbourg 1986) and in accordance with the Russian Federal Law "On protection of animals from cruel treatment" (01.01.1997).

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 criteria were used to test statistical hypotheses about the difference between the

groups. Statically significant changes were taken at a probability level of 95% or more ($p < 0.05$).

RESULTS AND DISCUSSION

The results of the conducted studies showed that under the influence of dextran, the volume of the paws increased more than three times in control animals. In this case, the greatest increase in the volume of the paws was noted 1 hour after the introduction of dextran, which statically significantly remained for the next four hours. In contrast, in animals that received DEMP at a dose of 10 mg/kg, the maximum increase in the volume of the paw was 240%, while the it was statistically significantly less than 77%, in comparison with results of control animals. Calculation of anti-inflammatory activity of the drug showed that in this dose it was 22.1% (table 1).

Table 1: Comparative study of the influence of DEMP, diclofenac sodium and LIV-52 to dextran induced paw edema.

Groups	Dose, mg/kg	Volume of paw, ml				
		Initial	1 hour	2 hour	3 hour	4 hour
Control	-	0,45±0,01	1,41±0,06*	1,37±0,05*	1,25±0,07*	1,18±0,06*
Diclofenac sodium	10	0,49±0,02	1,11±0,04*	1,02±0,07*	0,93±0,04*	0,84±0,05*
DEMP	10	0,53±0,02	1,27±0,08*	1,15±0,07*	1,17±0,06*	0,99±0,06*
DEMP	25	0,54±0,02	1,22±0,05*	1,12±0,04*#	1,06±0,04*	0,97±0,04*#
DEMP	50	0,51±0,02	1,11±0,06*#	1,08±0,04*#	0,99±0,03*#	0,91±0,04*#
DEMP	100	0,53±0,03	1,19±0,06*#	1,11±0,06*#	1,03±0,04*#	0,93±0,05*#
LIV-52	100	0,52±0,02	1,39±0,04*	1,23±0,03*	1,17±0,04*	1,05±0,04*

Note: *-in comparison with initial index; **#**- in comparison with control group respectively to the same hours.

Increasing of the dose of DEMP to 25 mg/kg led to an increase of the effect. At the same time, the anti-inflammatory activity of the medicine was 27.4%. the administration of DEMP in a dose twice high then the previous one led to a more significant suppression of the process of exudation, in which the anti-inflammatory activity was 35.8%. It was shown from the obtained data that the increasing of the dose of the medicine led to an increase of the anti-exudative effect of DEMP. However, despite of increasing of doses five times, the increase of the anti-inflammatory activity of the medicine was only 13,7%. Further increasing of the dose of compound to 100 mg/kg showed a distinct anti-inflammatory effect, the degree of which was slightly less than doses of 25 and 50 mg/kg. The value of anti-inflammatory activity was 26.3%. Consequently, the studied compound, which consisting sum of dry extracts from local medicinal plants, has a distinct anti-exudative effect indicating its anti-inflammatory activity. It is known that if the level of anti-inflammatory activity of the studying substance exceeds 30%, it is considered that it has a expressed anti-inflammatory action.[11] For recommendation to practical application, it is important to establish an effective dose of new compounds. It is seen from the given data that the effective dose of the studied compound is 50 mg/kg in this model of experimental aseptic arthritis. As long as, the compound is the extract of several medicinal plants, phyto-preparation LIV-52 was chosen for comparison of the anti-inflammatory activity.

It is important to note that a literature data about the specific studies on the anti-exudative activity of this medicine is not enough. Thereby, the study of the anti-exudative action of LIV-52 on the model of dextran inflammation was conducted in a separate series of experiments. LIV-52 was administered in a dose of 100 mg/kg, which is effective as a hepatoprotector by literature data.[10]

The results of the conducted studies showed that LIV-52 has substantial anti-exudative action. Its degree of activity was equal to the effect of DEMP (10 mg/kg), where the anti-inflammatory activity of LIV-52 was 23%. Consequently, the investigated DEMP with respect to its anti-exudative activity exceeds the known drug - LIV-52 even in a ten-time small dose. In the treatment of human diseases (in the pathogenesis of them lies inflammation process) are widely used NSAID from various groups of chemical compounds not selectively blocking cyclooxygenase. Among these NSAID-diclofenac sodium is considered a reference drug. Therefore, we studied the anti-inflammatory activity of diclofenac sodium using its effective dose in a separate group of animals.[12]

The results of the experiments showed that diclofenac sodium strongly suppressed the development of exudation with a maximum manifestation of anti-inflammatory activity after 1 hour from the beginning of the experiment. At the same time, the calculation of anti-inflammatory activity showed that it was equal to 37.9%. It can be seen that the effect of diclofenac sodium is insignificant (by 3.4%) higher than the effect of DEMP in a dose of 50 mg/kg.

Thus, the results of this series of experiments showed that DEMP emerges a distinct anti-exudative effect, which in twice low dose exceeds LIV-52 at anti-inflammatory activity and it is not significantly inferior the reference NSAID-diclofenac sodium. It is believed that the development of aseptic inflammation induced by dextran is due to the release of histamine and serotonin from mast cells which are considered main inflammatory mediators.[9]

It is possible to consider that DEMP has such properties which probably lead to the strengthening of membranes

of mast cells and prevent the release of inflammatory mediators. It is known that such membrane-stabilizing effect is characteristic to compounds with antioxidant effect. Since, they suppress the intensity of free radical processes that prevent damage of cells membrane and subcellular structures. Earlier, we showed that DEMP reduces the level of malonic dealdehyde in the blood, which is an intermediate product of lipid peroxidation.[13]

In our opinion, this action of DEMP is due to a large number of flavonoids in content of it, which has an antioxidant activity.[13,14,15] Antioxidants interfere the release of arachidic acid- a precursor of prostaglandins from phospholipids by the suppressing of free radical oxidation of lipids. Probability of an inhibitory effect of DEMP on cyclooxygenases is very low. However, it cannot be excluded that glycyrrhizinic acid (triterpenoid glycoside) possesses anti-inflammatory properties, provides an expression of the pharmacodynamic effect of DEMP.[14]

Thus, DEMP has a distinct anti-exudative effect, which is not inferior in its activity to diclofenac sodium and clearly superior to LIV-52 - dry extract from number of medicinal plants. So that DEMP is a non-toxic compound and has sufficient anti-inflammatory activity and it can be recommended as an agent for the treatment of diseases, in the pathogenesis of which lies inflammation process.

CONCLUSIONS

1. DEMP-extracted from Mediazia macrophylla, Glycyrrhiza glabra L., Hipericum scabrum L., and ziziphori pedicellata Pazij Vved., distinctly suppresses the process of exudation in dextran induced inflammation in experimental animals.
2. DEMP with its anti-inflammatory activity is superior to LIV-52 and is not inferior to the reference non-steroidal anti-inflammatory drug- diclofenac sodium.
3. The mechanism of anti-inflammatory activity of DEMP is associated with its antioxidant property.
4. DEMP can be recommended as a pathogenetic agent in the treatment of inflammatory diseases.

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