American Journal of Medicine and Medical Sciences 2019, 9(8): 307-310
DOI: 10.5923/j.ajmms.20190908.07

Study of the Influence of Dry Extract of Medicinal Plants on the Course of Carrageenan-Induced Inflammation

Z. Z. Khakimov, A. Kh. Rakhmanov*, Sh. R. Mavlanov

Pharmacology and Toxicology Department, Tashkent Medical Academy, Tashkent, Uzbekistan

Abstract The anti-inflammatory activity of dry extract of medicinal plants consisting local medicinal plants such as *Hipericum scabrum L., Ziziphora pedicellata Pazij Vved., Mediazia macrophylla* and *Glycirhiza glabra L.* was studied in carrageenan-induced inflammation model. Experimental studies were carried out on adult male rats weighing 145-160 g. The experimental model of aseptic arthritis was reproduced by subplantary administration of a 1% carrageenan aqueous solution into the hind paw of rats in a volume of 0.1 ml. The preventative efficiency of various doses of dry extract of medicinal plants (10, 25, 50 and 100 mg/kg) was studied in comparison with diclofenac sodium (10 mg/kg) and LIV-52 (100 mg/kg). The suppression of the intensity of aseptic inflammation under the influence of dry extract of medicinal plants was observed particularly in doses of 50 mg/kg and 100 mg/kg. It was determined that dry extract of medicinal plants is superior to LIV-52 in its anti-inflammatory activity in aseptic arthritis induced by carrageenan and is not inferior to diclofenac sodium.

Keywords Dry extract of medicinal plants, Carrageenan, Inflammation, Aseptic arthritis, Diclofenac sodium

1. Introduction

The development of medicines with anti-inflammatory activity is an actual task of pharmacology, since this typical pathological process forms basis of the pathogenesis of many human diseases. Despite the large number of medicines used in the treatment of acute and chronic inflammatory diseases, the effectiveness of their pharmacotherapeutic action is desired to make better, since the development of a number of side effects pose the lives of patients to the serious threat and reduce their value. For this reason, the modern range of anti-inflammatory medicines does not solve the problem of successful treatment of inflammatory diseases and their relapses, the frequency of which, after the abolition of this group of drugs can reach 100% [1]. There is no doubt that the prospect search of new anti-inflammatory drugs is promising, among compounds of natural origin - multicomponent extracts of medicinal plants and their collections [2].

The experience of developing new safe anti-inflammatory drugs convinces that great success can be achieved by searching for nonsteroidal anti-inflammatory medicines among the components of plant raw materials or by combining low toxic chemical compounds with the diverse mechanisms for restoring pathogenetic disorders during inflammatory processes [3-11]. According to the requirements of preclinical studies of new medicines, anti-inflammatory properties should be tested in experiments on models of inflammation induced by various compounds. Earlier, we established the efficacy of dry extract of medicinal plants (DEMP) in some models of aseptic arthritis [4,12-14]. However, the anti-inflammatory activity of DEMP in carrageenan-induced inflammation remained unexplored. This circumstance determined the purpose of this work.

* Corresponding author:
dr.ali.fl@mail.ru (A. Kh. Rakhmanov)
Published online at http://journal.sapub.org/ajmms

2. Material and Methods

2.1. Plant Material and Preparation of Dried Extract

Dry extract of medicinal plants was obtained from plants: Hipericum scabrum L., Mediazia macrophylla, Glycyrrhiza glabra L. and Ziziphora pedicellata Pazij Vved. Aerial parts of Hypericum perforatum L., Ziziphora pedicellata Pazij et Vved. and Mediazia macrophylla as well as root and rhizome parts of Glycyrrhiza glabra L. were obtained in summer of 2017 from foothills to medium zones of mountains of Tashkent region, Fergana, Samarkand and Surkhandaryo regions of Uzbekistan. Plant material was dried under dark conditions at room temperature for 10 days. Taking into account that the soil is contained various bacterial spores, raw material of plants were treated with special methods.

The dry material was milled, obtaining 4-6 mm particles and mixed in proportion 1,25:1,0:1,25:1,5 (productivity of dried extract was higher than other proportions) then extracted by water at 93-95°C temperature for 3 hours. The extract was then separated from the sample residue by filtration through filter paper. The resulting extracts were concentrated in vacuum until remaining a crude solid extract, which was then dried in a thermostat at temperature of 60°C.

2.2. Experiments

All experimental studies were carried out on adult male rats weighing 145-160 g, which were obtained from the vivarium of the Sanitary-Epidemiological Surveillance Department of the Chief Medical Administration under the Administration of the President of the Republic of Uzbekistan. Before the start of the experiment, all laboratory animals were carefully examined, weighed as well as their age, gender, and motor activity were taken into account. During the whole period of preparation for the experiment and its holding, all laboratory animals were kept in a vivarium at temperature 20-25°C, humidity not less than 50%, in a well-ventilated room and light mode day/night as well as by 6 animals in standard plastic cages with a standard diet. The daily requirement for food is compiled according to the age of the animals. Before the beginning of the experiment all laboratory animals had a healthy appearance and were active.

Inflammatory edema of the rat paws was modeled by the subplantational administration of the carrageenan, which are widely used to evaluate the anti-inflammatory activity of new potential drugs [15]. The experimental model of aseptic arthritis was reproduced by subplantary administration of a 1% carrageenin aqueous solution into the hind paw of rats in a volume of 0.1 ml. The preventative efficiency of various doses of DEMP (10, 25, 50 and 100 mg/kg) was studied in comparison with diclofenac sodium (10 mg/kg) and LIV-52 (100 mg/kg) [16]. The above drugs were administered intragastrically with a metal cannula 2 hours before the introduction of carrageenan. Measurement of the volume of paw of animals was performed by plethysmometer before and 1, 2, 3, 4 and 5 hours after the introduction of the carrageenan. The value of the anti-inflammatory activity (VAA) of the drugs was calculated according to the formula:

$$VAA = Vcon\text{-}Vexp/Vcon \times 100 = \%.$$

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).

2.3. Statistical Analysis

The received results were subjected to the statistic processing with the using of standard software package Biostat 2009 on well-known method of variation statistics with an estimation of the statistical significance of indicators (M±m) and differences between groups were analyzed using the Student's t-test. $P<0.05$ was considered significant.

3. Results and Discussion

The obtained results (table 1) showed that in healthy animals under the influence of carrageenan, there was an expressed increase of the paw volume by 62.1% after one hour, and more than twice after three and four hours from the injection of carrageenan compared to the initial paw volume. At the same time, the volume of the paw even after 24 hours remained increased by 26.4%. It is considered that in the first hours of the inflammation process induced by carrageenan determines by the action of kinins, and in later periods (after three and four hours) - prostaglandins [17].

It is seen from the data given in table 1 that the increase of paw volume under the influence of carrageenan was noticeably low in animals, which were administered reference nonsteroidal anti-inflammatory drug, diclofenac sodium. After one hour, it increased to 41.1%, and after two hours - 46.6%, after three hours - 53.4% and by the end of the fourth hour - 37.0% compared to the initial volume of paw. At the same time, after one day from the start of the experiment, the paw volume of rats administered diclofenac sodium did not practically differ from the initial values.

The anti-inflammatory activity of diclofenac sodium in the first phase of carrageenan action was 33.3%, and in the second phase 50.6 - 60.3%. It is seen that diclofenac sodium has a more expressed influence on the prostaglandin than the kinin system. Similar in character of directionality of action, we found in rats preventively received LIV-52 - a preparation representing the sum of medicinal plants with an antioxidant effect [18,19]. However, its anti-inflammatory activity was noticeably low in carrageenan-induced inflammation compared with diclofenac sodium.

It is seen in table 1 that the suppression of the intensity of aseptic inflammation under the influence of DEMP was observed particularly in doses of 50 mg/kg and 100 mg/kg. At the same time, the paw volume decreased under the influence of the last doses of the preparation by the end of the 24 hours of the experiment and paw volume of animals did not practically differ from the initial values. It is characteristic that DEMP at a dose of 50 mg/kg was rather superior to diclofenac sodium by its influence on the kinin system, and in the second phase, the effect of the compared preparations is not significantly different.

Consequently, dry extract of medicinal plants is superior to LIV-52 in its anti-inflammatory activity in aseptic arthritis induced by carrageenan and is not inferior to diclofenac sodium. The modern concept of inflammation considers inflammation - a pathophysiological phenomenon from the standpoint of the decisive participation of oxidative stress in it [20].

It is notable that DEMP and diclofenac sodium have the same type of effect on both phases of carrageenan-induced inflammation. We have previously shown the low toxicity of DEMP [21], which has hepatoprotective [22], choleretic [23] activity and the mechanism of which is probably related to the inhibition of free radical processes [24]. Based on this, we assumed that using DEMP as a medicine for treatment a

number of diseases, which the inflammation processes has significance in their pathogenesis, might be promising. This gives the right to raise the question of the possibility of including DEMP in complex traditional therapy of inflammatory diseases, after conducting adequate clinical studies.

As noted, obtained results by the authors, DEMP has both a high choleretic, hepatoprotective, anti-inflammatory activity and has an advantage over the known non-steroidal anti-inflammatory drug, since it is a compound with low toxicity and availability of plant raw materials in Uzbekistan.

Despite the evidence of the presented results, in our opinion, it is premature to declare about its clinical demand. Further, it is necessary to investigate the ability of DEMP to interfere to the course of various inflammatory processes in-depth studies not only in the experiment, but also in clinical studies.

Table 1. Comparative study of the influence of dry extract of medicinal plants, LIV-52 and diclofenac sodium on course of aseptic arthritis induced by carrageenan

Groups	Volume of paw, sm^3					
	Initial	1 hour	2 hours	3 hours	4 hours	24 hours
Control	0,72 ± 0,02	1,17 ± 0,05	1,35 ± 0,05	1,51 ± 0,07	1,40 ± 0,05	0,91 ± 0,04
Increasing of paw, %		62,5	87,5	109,7	94,4	26,4
Diclofenac sodium (10 mg/kg)	0,73 ± 0,03	1,03 ± 0,04	1,07 ± 0,03	1,12 ± 0,04	1,01 ± 0,04	0,77 ± 0,04
Increasing of paw,%		41,1	46,6	53,4	37,0	5,5
VAA, %		33,3	46,0	50,6	60,3	78,9
DEMP (10 mg/kg)	0,73 ± 0,02	1,10 ± 0,09	1,22 ± 0,07	1,35 ± 0,08	1,25 ± 0,09	0,83 ± 0,05
Increasing of paw,%		50,7	67,1	84,9	71,2	13,7
VAA, %		17,8	22,2	21,5	23,5	47,4
DEMP (25 mg/kg)	0,75 ± 0,02	1,11 ± 0,06	1,23 ± 0,05	1,33 ± 0,04	1,24 ± 0,04	0,82 ± 0,05
Increasing of paw,%		48,0	64,0	77,3	65,3	9,3
VAA, %		20,0	23,8	26,6	50,0	63,1
DEMP (50 mg/kg)	0,78 ± 0,02	1,05 ± 0,06	1,13 ± 0,05	1,20 ± 0,04	1,09 ± 0,03	0,79 ± 0,02
Increasing of paw,%		34,6	44,9	53,8	39,4	1,3
VAA, %		40,0	44,4	46,8	54,4	94,7
DEMP (100 mg/kg)	0,80 ± 0,02	1,13 ± 0,06	1,19 ± 0,06	1,26 ± 0,05	1,17 ± 0,05	0,83 ± 0,02
Increasing of paw,%		41,2	48,7	57,5	46,2	3,7
VAA, %		26,7	38,1	41,8	45,6	84,2

Note: *- in comparison with initial indexes (P<0,05); #- in comparison with control group (P<0,05).

4. Conclusions

1. The determined suppression of the exudative stage of inflammation by dry extract of medicinal plants indicates its effectiveness in aseptic inflammation.
2. The studied dry extract is not inferior to the reference non-steroidal anti-inflammatory drug- diclofenac sodium by its anti-exudative activity, especially at a dose of 50 mg/kg.
3. The studied dry extract of medicinal plants surpasses diclofenac sodium by the effect on the kinin system.
4. Dry extract of medicinal plants after further relevant in-depth studies can be recommended into practical medicine as an effective anti-inflammatory medicine.

ACKNOWLEDGEMENTS

The work was supported by national grant PZ -20170926458.

REFERENCES

[1] Drogovoz S.M., Zupanets M.V., Kononenko A.V., 2013, Prospects for the creation of anti-inflammatory drugs based on D - (+) - ammonium glucosyl salts of 3-oxamoyl-substituted N-phenyl-anthranilic acids and extract of Syrbus aucupбria leaves, Scientific and Production Journal "Drug Development and Registration", 3(2), p.64–67.

[2] Polukonova N.V., Navolokin N.A., Raikova S.V. et al., 2015, Anti-inflammatory, antipyretic and antimicrobial activity of flavonoid - containing extract of the Aurvine (Gratiola officinalis. l), Experimental and Clinical Pharmacology, 78(1), p.34-38.

[3] Khakimov Z.Z., Mirzokhidov Kh.A., Musaev U.N., 2000, Pharmacological activity of the dry extract from the field bindweed plant, Chemistry and pharmacy, 3(4), p.117-119.

[4] Khakimov Z.Z., Rakhmanov A.Kh., Mavlanov Sh.R., Abduvaliev A.A., Allayeva M.J., Botiralieva G.K., 2018, Influence of flavonoids containing extract from medicinal

plants to the course of aseptic inflammation, American Journal of Medicine and Medical Sciences, 8(11), p. 291-294.

[5] Khakimov Z.Z., Mustanov T.B, Mirzohidov Kh.A., 2013, The study of anti-inflammatory activity konvena with its local application, Medical Journal of Uzbekistan, 5, p. 99-105.

[6] Rakhmanov A.Kh., Khakimov Z.Z., Tadjibaev AB, Mavlanov Sh.R., 2016, Features of the course of aseptic arthritis under influence of dopamine receptor agonist, Pharmaceutical Bulletin of Uzbekistan,3, p.91-94.

[7] Khakimov Z.Z., Rakhmanov A.Kh., Asadov N.N., 2017, Influence of calcium antonogonists to the course of exudative and proliferative phase of aseptic inflammation, Science of Europe (Praha, Czech Republic), 2(17), p.21-24.

[8] Khakimov Z.Z., Rakhmanov A.Kh., Tadzhibaev A.B., 2017, Experimental studies of the effect of dopamine precursor on the course of aseptic inflammation, Reports of the Academy of Sciences of the Republic of Uzbekistan, 1, p.81-83.

[9] Khakimov Z.Z., Rakhmanov A.Kh., Kasimova G.E., Anvarov A.A., 2017, The effect of kinase inhibitors –II on the course of aspetic inflammation, Pharmaceutical Bulletin of Uzbekistan, 1, p.77-79.

[10] Yuldasheva Sh.A., Khakimov Z.Z., 2000, The study of anti-inflammatory activity and toxicity of the CTM drug, Physicians work, 6, p.41-44.

[11] Yuldasheva Sh.A., Khakimov Z.Z., Radjapova Sh.D., 2000, Some aspects of the mechanism of the anti-inflammatory action of the dry extract from the field Convolvulus plant, Chemistry of natural compounds, special edition, p.128-129.

[12] Khakimov Z.Z., Rakhmanov A.Kh., Mavlanov Sh.R., Yakubov A.V., 2018, Study of the anti-flagogenic effect of a dry extract of medicinal plants in case of formalin-induced inflammation, Medical Journal of Uzbekistan, 5, p.85-88.

[13] Khakimov Z.Z., Rakhmanov A.Kh., Mavlanov Sh.R., Abduvaliev A.A., Allaeva M.J., 2018, Investigation of influence of the collection of flavonoids on the course of histamine induced inflammation, Scientific journal "Fundamentalis scientiam", 21, p.45-47.

[14] Rakhmanov A.Kh., Khakimov Z.Z., Mavlanov Sh.R., Abduvaliev A.A., Botiralieva G.K., 2018, Allaeva M.J. Anti-inflammatory activity of medicinal plants, European journal of pharmaceuticals and medical research, 5(8), p.55-57.

[15] Mironov A.N., 2012, Guidelines for conducting preclinical studies of drugs. Part One, Moscow, Grief and K., p. 944.

[16] Kushwaha Sh., Semwal Bh., Upadhayay P.K., 2017, Hepatoprotective activity of ethanolic extract of Euphorbia royleana linn in carbon tetrachloride treated guinea pig. Innovations in Pharmaceuticals and Pharmacotherapy, 4(1), p.22-32.

[17] Necas J., Bartosikova L., 2013, Carrageenan: a review, Veterinarni Medicina, 58(4), p.187-205.

[18] Singh K. K., Singh Y. K. et al., 1979, Liv.52 in the treatment of cirrhosis of liver- certain observations, Antiseptic, 7, p.393.

[19] Sandir R., Gill K.D., 1999, Hepatoprotective effect of LIV-52 on ethanol induced liver damage in rats, Indian journal of experimental biology, 37, p.762-766.

[20] Novikov V.E., Ilyukhin S.A., 2013, The effect of hypoxane on the effectiveness of acetylsalicylic acid in acute inflammation, Experimental and Clinical Pharmacology, 76 (4), p.32-35.

[21] Khakimov Z.Z., Rakhmanov A.Kh., Mavlanov Sh.R., Gildiyeva M.S., 2017, Preclinical toxicological study "Lesbokhol" - a mixture of dry extracts from the local flora, Pharmaceutical Bulletin of Uzbekistan, 2, p.74-81.

[22] Khakimov Z.Z., Rakhmanov A.Kh., Mavlanov Sh.R., 2016, The effect of Lesbohol on some biochemical blood parameters in acute intoxication with carbon tetrachloride in rats, Infection, Immunity and pharmacology, 6, p.180-183.

[23] Khakimov Z. Z., Rakhmanov A. Kh., Mavlanov Sh. R., Khodzimatov O. K., 2015, The Importance Dry Extract from Plants of Central Asia for Eliminating Alterations of Functional State of Liver in Its Alcoholic Lesion, American Journal of Medicine and Medical Sciences, 5(5), p. 260-263.

[24] Mavlanov Sh.R., Khakimov Z.Z., Rakhmanov A.Kh., 2017, The influence of Lesbohol on the content of glycogen in the liver in its acute toxic damage, Infection, immunity, pharmacology, 1, p.129-134.