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The Effect of Oils Extracted from The Seeds of Althea Officilanis and Nigella Sativa Plants on Inflammation

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KEYWORDS

Althaea, Nigella, ASXUM, ASQARAXUM, in vivo, carrageenan, apaneurosis, probe, kupen, oncometric, exudation.

ABSTRACT:

In this article, the anti-inflammatory activity of Althaea and Nigella plant oils and ASXUM and ASQARAKHUM food supplements prepared on their basis was determined in vivo. The anti-inflammatory activities were compared with synthetic drugs Kupen (India) tablet and ENDNIL EKS-PRESS (Belarus) capsule.

I. INTRODUCTION

It is known that inflammatory disease is a disease that occurs as a result of an attack of the body's own tissues by the immune system. Cardiovascular diseases, rheumatoid arthritis, crohn's, colitis, kidney, inflammation, thyroid diseases are examples of inflammatory diseases.

Despite the increasing development of pharmaceuticals used in the treatment of inflammatory diseases, the development of harmless drugs has not been fully explored. It is an urgent problem to develop food supplements containing natural biologically active compounds, which are safe for medicinal plants, which are safe for treating and preventing inflammatory diseases, and to determine their chemical composition and mechanism of action on the body. Based on these data, we aimed to study the effect of the product obtained from the complex of these two medicinal plants with pharmacological properties on inflammation in rats [1].

According to information, the main component of Nigella oil is nigellon, which is a mixture of dithymoquinone and thymoquinone.

These substances are biologically active substances against internal and external inflammation of the body [2].

Results from various animal models show that nigella oil has anti-inflammatory potential. This activity is related to the reduction of NO production, interleukin-1 (IL-1), cyclooxygenase-1 (COX-1), cyclooxygenase-2 (COX-2), histone deacetylase (HDAC) and other pro-inflammatory mediators. Also, Nigella oil is considered to inhibit COX, 5-LPO in arachidonate metabolism pathways in rats. It has been shown to reduce nuclear translocation and DNA binding of nuclear factor-kappa-B (NF-kB) in mice through

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blockade of phosphorylation and subsequent degradation of IkBa [3].

Althaea - The expectorant, softening and anti-inflammatory effect of Althaea preparations has been determined by modern science, and this effect depends on the presence of mucilaginous substances in its composition. These substances have enveloping properties and protect the nerve cells in the mucous membrane of the upper respiratory tract and gastrointestinal tract from various effects, allowing for slower absorption of various drugs and a slightly longer local effect. promotes healing of tissues, for this reason Althaea root powder is used mainly in the form of tincture, liquid and thick extracts and juice, mainly in catarrhal conditions of the respiratory tract, gastrointestinal tract (gastritis, peptic ulcer disease, enteritis, colitis and others) is widely used as an anti-inflammatory drug [4].

Althaea root, seed and oil have many pharmacological effects in vitro and *in vivo*, such as antitussive, anti-inflammatory, anti-oxidative, anti-bacterial and anti-fungal activities.

Anti-inflammatory effect- US scientists Bonaterra et al studied the anti-inflammatory effect of Althaea root extract on macrophages (Mph) *in vitro* using the THP-1 (human acute monocytic leukemia) cell line. The results of the enzyme-linked immunosorbent assay showed that the extracts had a strong inhibitory effect on the induction of tumor necrosis factor-alpha (TNF-a) and interleukin-6 (IL-6) by LPS. Extracts have also been found to protect human Mph from H_2O_2-induced cytotoxicity and cellular reactive oxygen species production, in addition to improving cell migration [5].

Carrageenan is a way to detect inflammation by swelling the rat's paw. For anti-inflammatory activity, it is a fast-used, simple and routine animal model method [6].

Mouse hindpaw tumors are increasingly being used to test new anti-inflammatory drugs, as well as to study mechanisms involved in inflammation. In this regard, about 400 articles have been published in scientific journals [7]. Carrageenan swelling in rats is usually achieved by intraplantar injection of 1-3% saline solution of freshly prepared carrageenan in doses of 50-150 µl into the apaneurosis of the hind paw [8,9].

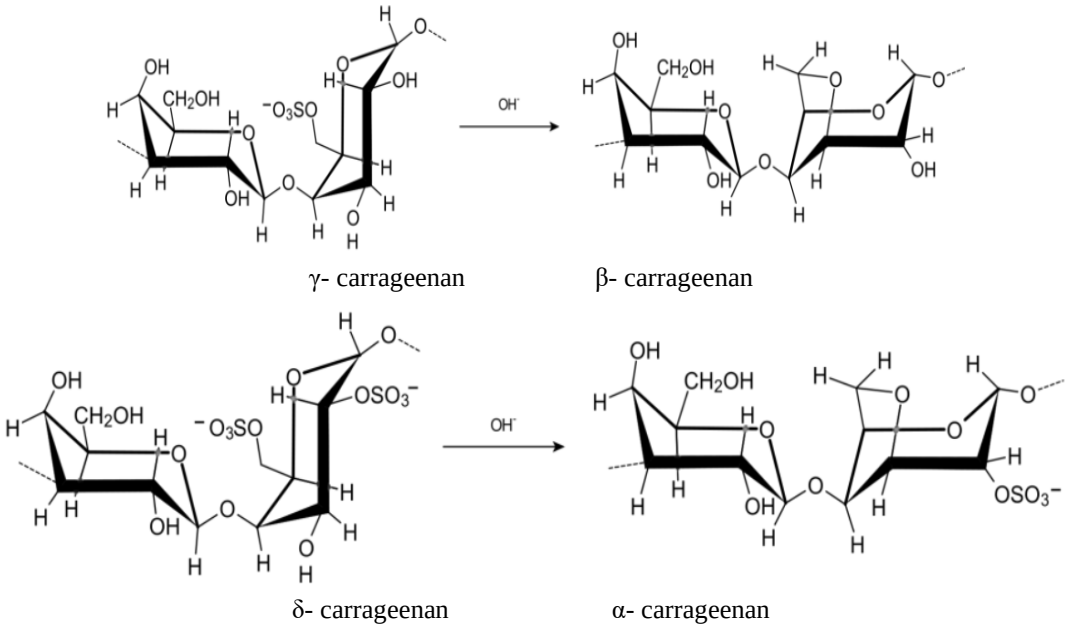

Figure 1. Conversion of γ-carrageenin to β-carrageenan under alkaline conditions and d-carrageenin to α-carrageenan under alkaline conditions

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A biphasic, age-dependent phenomenon following carrageenan injection has been described in mouse hindpaw swelling. In it, various mediators cause an inflammatory reaction as a result of sequential action [10]. There are a number of drugs that participate in the inflammatory process of the body, among which we can cite substances such as histamine, serotonin and bradykinin [11].

We investigated the anti-inflammatory activity of locally grown Althaea and Nigella seed oils and the food supplement ASXUM and ASQARAXUM based on them using an *in vivo* carrageenan swelling model.

II. EXPERIMENTAL PART

The studies were carried out in the model of acute exudative inflammation induced by subplantar injection of classic phlogogen - carrageenin. The experiment was carried out in male mice with a body mass of 20±2.0 g. The experiment consisted of 7 groups, and 5 mice were taken from each group. Kupen (Avison Pharmaceuticals Pvt. Ltd., India) tablet form and ENDNIL EXPRESS (Belarus) capsule were used as comparative pharmacopoeia drugs and administered to mice at a therapeutic dose of 55 mg/kg. As research groups, freshly prepared Althaea and Nigella oils and biologically active ASXUM and ASQARAXUM food supplements prepared on their basis were injected into the stomach in a volume of 0.04 ml during the 5th day using a special probe, and 1 hour after the introduction on the 5th day, the back of the mice a 1% solution of carrageenan in a volume of 0.05 ml was injected into the aponeurosis area of the left paw [12]. The same volume of distilled water was administered to the animals of the control group. In the experimental and control groups, before carrageenan injection, the initial volumes of the hind legs of the animals were measured oncometrically. The anti-inflammatory effect of the drugs was noted 3.5 hours after the induction of inflammation. Swelling volume was estimated based on the difference between non-inflamed and inflamed hindpaw volumes.

The anti-exudation activity of the products was determined in percentages by the difference in the reduction of tumors on the hind paws of the experimental animals compared to the control.

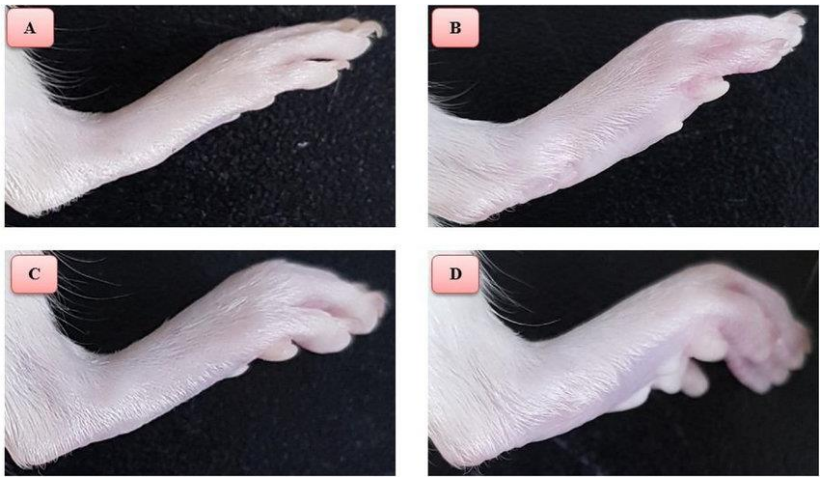

Figure 2. Macroscopic images of carrageenan-induced hindpaw edema in mice (A) Normal; (B) control; (C) when 1% carrageenan is included; (D) 3.5 hours after administration of 1% carrageenan

The anti-exudation activity of the products was determined in percentage by the difference in the reduction of swellings in the hind paw of the experimental animals compared to the control.

The anti-exudation activity is calculated by the following formula:

$EQF=\Delta V_{exp}-\Delta V_n / \Delta V_n \times 100\%$;

When the anti-exudative activity is compared to the control group, the following formula is used;

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100% – ($\Delta V_{exp} – \Delta V_n / \Delta V_{n\ (exp.)}$ / $\Delta V_{exp} – \Delta V_n / \Delta V_{n\ (cont.)}$) x 100% here,

EQF – anti-exudation activity, in percent;

ΔV_n and ΔV_{exp} – control and experimental group hind paw size.

In this experiment, the second method was used to determine the anti-inflammatory activity. In this case, the hind legs of the same mice were cut below the knee, and the weight of each leg was measured separately, and the anti-exudation activity was determined according to the above formula [13]. The results of the study were statistically processed using the Microsoft Excel program to determine the average value (M) and the average error (m); differences - $p<0.05$ were considered statistically significant.

III. RESEARCH RESULTS.

In studies, acute exudative inflammation induced by carrageenan was measured 3.5 hours after the introduction of phlogogen, the size and weight of swelling of the hind limbs in mice. The results of the study were compared to the control and comparative Kupen pharmacopoeia drug and ENDNIL EXPRESS (Belarusian) capsule groups of mice and are presented in Table 1 below.

Table 1: Effects of Althaea and Nigella oils and ASXUM and ASQARAXUM food supplements based on them on carrageenan-induced inflammation in mice,
(M±m; n=5)

Groups	Dose, mg/kg	After 3.5 hours			
		Swelling size, %	EQF, %	Swelling severity, mg, %	EQF, %
Control	0,2 ml	82,0±8,4	-	36,5±1,6	-
Kupen	55 mg/kg **(p=0,009)**	44,0±4,0	56,0	30,7±1,5 (**p=0,05**)	15,9
ELDNIL EXPRESS capsule	0,2 ml **(p=0,0096)**	47,2±4,3	60,0	32,9±1,6 (**p=0,054**)	17,0
Nigella oil	0,2 ml **(p=0,02)**	52,6±6,5	47,4	31,1±3,0	14,8
Althaea oil	0,2 ml **(p=0,01)**	48,8±5,3	51,2	28,5±3,5 (**p=0,09**)	21,9
ASXUM food additive	0,2 ml **(p=0,002)**	36,4±3,0	63,6	26,8±2,0 (**p=0,01**)	26,6
ASQARAKHUM food supplement	0,2 ml (**p=0,001; (p_1=0,01**	25,0±4,3	75,0	18,0±2,5 **(p=0,001; (p_1=0,004)**	50,7

Note: - reliability of $p<0.05$ compared to control; - reliability of $p_1<0.05$ compared to Kupen drug and ELDNIL EXPRESS capsule;

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In this experiment, mice in all groups in the carrageenan swelling model had 82.0±8.4% of the control group's hindpaw swelling volume measured oncometrically. This indicator was 44.0±4.0% in the comparative preparation Kupen (India) and 47.2±4.3% in ELDNIL EXPRESS (Belarus) capsule. In comparison with the comparative preparation Kupen (India) by 1.76 times, and in capsule ELDNIL EXPRESS (Belarus) by 1.25 times, and statistically significant differences were achieved (p=0.009). Anti-exudation activity in the control group was 56% compared to the drug Kupen (India) and 60% compared to the ELDNIL EXPRESS (Belarus) capsule. The swelling volume of the carrageenan-infused mice group with 0.2 mL of Nigella seed oil was 52.6±6.5% after 3.5 hours, and the anti-exudation activity was 47.7%, with a statistically significant difference compared to the control. achieved (p=0.02). In the group of mice that received Althaea seed oil in a volume of 0.2 ml, the swelling volume was 48.8±5.3%, and the anti-exudation activity was 51.2% compared to the control, and a statistically significant difference was noted (p=0, 01). At a dose of 0.2 ml of ASXUM food supplement, the swelling volume of the hind paw of mice was on average 36.4±3.0%, and the anti-exudation activity was 63.6%, and a statistically significant difference was noted (p=0.002). In the anti-inflammatory carrageenan swelling model of ASQARAKHUM food supplement, the paw size of mice was 25±4.3, the swelling volume was reduced by 3 times compared to the control group animals, the anti-exudation activity was 75%, and statistically significant differences were observed (p=0.001).

In the second part of our experiments, 3.5 hours after the introduction of carrageenan to all animal groups, the hind paws were cut from the lower area of the knee, and the weights of the right and left legs were measured, the right leg as a control, the left as an experiment (flagogen included) mean tumor volume for each group relative to leg volumes and anti-exudate activity relative to the control group was determined. In this case, the weight of the hind legs of mice of the control group was 36.0±1.6%. Average leg weights of mice were 30.7±1.5% when the drug of the comparative Kupen pharmacopoeia was administered, and 32.9±1.6% when administered in the ELDNIL EXPRESS (Belarusian) capsule, and the volume of exudation compared to the control group was 15.9 % and 17 % and statistically significant differences were achieved (p=0.05). Nigella seed oil 0.2 ml carrageenan injected leg swelling weights measured after 3.5 hours were 31.1±3.0%, anti-exudation activity compared to control 14 was 8%. In this case, the paw weights of mice in this group increased compared to the control group, but no statistically significant difference was noted. In the group of mice that received Althaea seed oil in a volume of 0.2 ml, the tumor weight was 28.5±3.5%, and the anti-exudation activity increased by 21.9%, compared to the control group, the tumor volume was reduced in the mice of this group. tended, that is, a trend was observed, but it was not statistically reliable (p=0.09). The swelling weight in the ASXUM-supplemented animal group was 26.8±2.0%, and the anti-exudation activity was 26.6% compared to the control group, which was statistically significant (p=0.01). The average swelling weight of the hind legs in the ASQARAKHUM food additive group was 18±2.5%, and the anti-exudation activity was 50.7% compared to the control group, a statistically significant result was recorded (p =0.001).

IV. CONCLUSION

The anti-inflammatory activity of bioactive food additives prepared from mixtures of oils extracted from Althaea and nigella seeds was studied in the carrageenan swelling model. The anti-inflammatory activity of these new food additives is 7.6%-19% higher than that of the synthetic preparations Kupen (India), and 3.6%-15% higher than that of ELDNIL EXPRESS (Belarus) capsule. proved to be high. It is important in the treatment of this disease with the help of folk medicine methods, as well as in the further study of scientific research.

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