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# ANTI-INFLAMMATORY, MEMBRANEPROTECTIVE AND CAPILLARY STRENGTHENING PROPERTIES OF SWEET FLAG LEAF EXTRACTS

Kalko K. O.[1], Derimedvid L. V.[1], Korang L. A.[1],
Toziuk O. Yu.[2], Okipniak I. V.[3], Domar N. A.[1], Zhurenko, D. S.[1]
[1]National University of Pharmacy, Kharkiv, Ukraine
[2]National Pirogov Memorial Medical University, Vinnytsya, Ukraine
[3]Bukovinian state medical university, Chernivtsi, Ukraine
ketrin27kalko@gmail.com

**Abstract**

Despite significant advances in the treatment of inflammatory diseases of the gastrointestinal tract, the problem of pharmacological correction of this pathology remains quite relevant. Many drugs used in the pharmacotherapy of inflammatory pathology are characterized by several adverse reactions, which limits their use in polymorbid patients. A promising way to solve this problem is the use of herbal remedies that affect some inflammatory patterns, reduce manifestations of oxidative stress, have a polymodal effect, have a sufficient raw material base, and are characterized by efficiency and safety. The aim of this work was a comparative study of anti-inflammatory, membrane-protective, and capillary-strengthening properties of Acorus calamus extracts.

**Materials and methods.** Anti-inflammatory activity was studied in models of carrageenan and zymosan paw edema in rats. Investigation of capillary-strengthening activity of Acorus calamus leaf extracts was carried out by the method of P. Golikov and the study effect of extracts on the vascular permeability of the skin of rats without the participation of phlogogenic agents (McClure-Aldrich test) by the rate of resorption of saline papules. The study of membrane-stabilizing properties of Acorus extracts was carried out by the method of Jager F. C., which is based on determining the degree of spontaneous peroxide destruction of erythrocyte membranes.

**Results and Discussions.** In models of carrageenan, histamine, and zymosan edema of the paw in rats, the presence of dose-dependent antiexudative action of Acorus leaf extracts has been established. According to the degree of antiexudative effect in carrageenan (79.5%) and histamine (50%) edema, the maximum activity was shown by LHAEAL, in the model of zymosan edema - DEAL (43.5%). In terms of this type of activity, the extracts were not inferior to quercetin comparison drug and were somewhat inferior to sodium diclofenac. Acorus leaf extracts have a capillary-strengthening and membrane-stabilizing effect, which is confirmed by a significant decrease in vascular permeability by 1.2-1.4 times. Membrane-stabilizing activity of Acorus leaf extracts in the model of spontaneous hemolysis of erythrocytes was 31.3% –40.7%. In this type of activity, they reliably exceeded the effect of comparison drugs of quercetin and sodium diclofenac. The maximum activity was observed when using DEAL at a dose of 1 mL/kg, which should be used for further research as a conditionally therapeutic.

**Conclusions.** The obtained results determine the prospects for further research of Acorus leaf extracts to develop a new effective anti-inflammatory phytomedicine for the prevention and complex therapy of human diseases.

**Keywords**: anti-inflammatory activity, membraneprotective activity,

## Introduction

Despite significant advances in the treatment of inflammatory diseases of the gastrointestinal tract, the problem of pharmacological correction of this pathology remains quite relevant. Many drugs used in the pharmacotherapy of inflammatory pathology are characterized by several adverse reactions, which limits their use in polymorbid patients [1, 2, 3].

A promising way to solve this problem is the use of herbal remedies that affect some inflammatory patterns, reduce manifestations of oxidative stress, have a polymodal effect, have a sufficient raw material base, and are characterized by efficiency and safety [4, 5, 6, 7, 8].

After analyzing the phytochemical composition of Acorus calamus leaves and the obtained liquid hydroalcoholic extract of Acorus leaves (LHAEAL) and dealcoholized extract of Acorus leaves (DEAL), it can be stated of the presence of a pronounced antioxidant, anti-inflammatory, antiulcer, hepatoprotective capacity of BAS in their compositions, and the creation of drugs based on these extracts will expand and optimize phytotherapy of inflammatory diseases of the gastrointestinal tract and other diseases caused by oxidative stress. Also, in our previous studies, the presence of antiulcer, hepatoprotective, antidepressant, and neuroprotective properties inherent in the studied extracts under conditions of their favorable safety profile has been established [9, 10, 11, 12, 13, 14].

Therefore, the aim of this work was a comparative study of anti-inflammatory, membrane-protective, and capillary-strengthening properties of Acorus calamus extracts.

## Methods

Anti-inflammatory activity was studied in models of carrageenan and zymosan paw edema in rats [15]. The choice of these inflammation models is due to the fact that the development of the exudative stage of inflammation involves biogenic amines, kinin system, prostaglandins, leukotrienes, and other biologically active substances [16, 17]. Therefore, the study of the effectiveness of drugs for edema of different genesis will determine the most optimal tools for the treatment of inflammatory processes of various genesis.

Carrageenan edema was reproduced by subplantar administration of 0.1 mL of 1% carrageenan (Fluka, Switzerland) in the right hind paw of rats [15]. As a sign of inflammation swelling was assessed, the development of which was observed in the dynamics after 30; 60; 90; 120; 180 and 240 minutes, as well as after 24 hours, for which measured 'paw volume in $cm^3$ using a digital plethysmometer Panlab (Spain) model LE 7500 version V29/10/2014. Animals were divided into 6 groups of 6 rats: I - control pathology (animals that were injected carrageenan solution subplantarly and administered 0.5 mL/ kg distilled water intragastrically); II-III - animals that were subplantarly injected with a solution of carrageenan and intragastrically administered the studied 70% LHAEAL, respectively, at a dose of 1 and 0.5 mL/kg; rats of IV-V groups on the background of the administration of carrageenan intragastrically received DEAL, at a dose of 1 and 0.5 ml/kg respectively; VI and VII groups of rats against the background of carrageenan received reference drugs: diclofenac sodium at a dose of 8 mg/kg (capsules of 25 mg manufactured by LLC "Kharkiv Pharmaceutical Enterprise "People's Health" Ukraine) [15] and quercetin at a dose of 11 mg/kg (2 g granules manufactured by BCPP, Ukraine), respectively [18]. Group VI consisted of intact animals, which were injected subplantarly 0.1 mL of saline. The studied extracts and reference drugs were used in the treatment-and-prophylactic mode: intragastrically once daily for 5 days before the simulation of inflammation, the last time 1 hour before the injection of carrageenan [15]. The development of edema was observed in the dynamics after 30, 60, and 90 minutes, for which the paws volume was measured'in $cm^3$ using Panlab digital plethysmometer (Spain) model LE 7500 version V29/10/2014.

The treatment and prevention mode of administration of LHAEAL, DEAL, and comparison drug [15] was chosen because the basic drugs for the treatment of inflammatory processes are NSAIDs [19]. Herbal remedies, including study extracts, contain polyphenols and other biologically active substances that have anti-inflammatory properties [12, 18, 20, 21]. The mechanism of their

anti-inflammatory action is associated with inhibition of the synthesis and activity of inflammatory mediators, inhibition of the processes of destruction induced by free radical oxidation, cytolysis, etc. [18, 21].

Zymosan edema was simulated by subplantar administration of 0.1 mL of 2% solution in the right hind paw [15]. The mechanism of zymosan edema (in the first hour of its development) mainly involves inflammatory mediators - leukotrienes. This model allows determining whether this anti-inflammatory mechanism is involved in the pharmacological action of the studied extracts [15, 22]. Animals were divided into groups of 6 rats: I - control pathology (animals which were subplantarly injected with 0.1 mL of 2% zymosan solution and administered 0.5 mL/kg distilled water intragastrically); Groups II and III - rats with zymosan edema, which were administered the subject LHAEAL at a dose of 0.5 and 1.0 mL/kg, respectively; IV and V groups - animals with zymosan edema, which were administered the subject DEAL at a dose of 0.5 and 1.0 mL/kg, respectively; VI - rats with zymosan edema treated with quercetin at a dose of 11 mg/kg [18].

The anti-exudative effect of the studied extracts and comparison drugs under conditions of carrageenan and zymosan edema was calculated by the formula [15]:

$$AA = (V_{CP} - V_D) / V_{CP} \bullet 100, (\%) \quad (2.2)$$

where AA - antiexudative activity, %;

$V_{CP}$ ($cm^3$) - median paw volume in animals from the group of control pathology;

$V_D$ ($cm^3$) - median paw volume in animals from the group of the studied product.

Investigation of capillary-strengthening activity of Acorus calamus leaf extracts was carried out by the method of P. Golikov [23]. Anesthetized experimental animals were fixed on the operating table in a supine position. The femoral vein was exposed on the right hind limb and 1% solution of trypan blue was administered intravenously at a rate of 2 mg/kg. 10 minutes after intravenous administration of trypan blue in the shaved area of the abdomen, phlogogenic substances were injected intradermally. As phlogogens used: 0.1% solution of zymosan; 1% solution of histamine; egg white; formalin 3%. The time of onset of staining of papules caused by the introduction of phlogogenic agents was taken into account. The experiments were performed on 30 white outbred male rats weighing 170-210 g. Preparations of Acorus leaf extracts and comparison drugs diclofenac sodium (8 mg/kg) and quercetin (11 mg/kg) administered intragastrically once daily for 3 days and on day 4 1 hour before the introduction of phlogogens. The vasoconstrictive properties of the extracts were evaluated by the difference in the time of staining of papules in the control group of animals and in the experimental.

The next stage of our research was to study the effect of LHAEAL and DEAL on the vascular permeability of the skin of rats without the participation of phlogogenic agents (McClure-Aldrich test) by the rate of resorption of saline papules [24]. The experiments were performed on 25 white outbred rats, 5 animals per group. Preparations of Acorus leaf extracts and comparison drugs - diclofenac sodium (8 mg/kg) and quercetin (11 mg/kg) were administered intragastrically once a day for 3 days and on day 4 for 1 hour before the introduction of saline [24].

The study of membrane-stabilizing properties of Acorus extracts was carried out by the method of Jager F. C., which is based on determining the degree of spontaneous peroxide destruction of erythrocyte membranes. To do this, spectrophotometrically at a wavelength of 540 nm determined the extinction of extra-erythrocyte hemoglobin, which enters the blood as a result of spontaneous lysis of erythrocyte membranes [25, 26]. The study was performed on 25 white outbred rats weighing 220-230 g. The animals of the experimental groups were intragastrically injected with the studied objects: extracts of Acorus leaves and comparison drug for 3 days. Control animals received water. On the fourth day, blood was taken from the tail vein of animals and determined the degree of hemolysis of erythrocytes in the experimental and control groups.

Statistical processing was performed using Statistica 6.0 (StatSoft, Inc., USA), the normality of the distribution was determined using the W-Shapiro-Wilk test. Under normal distribution, ANOVA analysis of variance was used, data were expressed as M ± m. In the absence of normal distribution, the nonparametric Mann-Whitney U-

test was used, the results were presented as median (Me) and interquartile range (25-75 percentile) [27].

All studies, except for cytotoxicity studies, were conducted based on the Educational and Scientific Training Center for Medical and Biological Research of the Educational and Scientific Institute of Applied Pharmacy of the National University of Pharmacy (NUPh). During the experiment, the animals were in the vivarium of the NUPh training center at an air temperature of 20-22 ° C, natural light regime "day and night", in standard ventilated cages, on a standard diet.

All manipulations with animals were carried out following the requirements of GLP, the recommendations of the SEC of the Ministry of Health of Ukraine, the National General Ethical Principles of Animal Experiments (Ukraine, 2001), Law of Ukraine No. 3447-IV dated 21.02.2006, as amended. "On the protection of animals against cruel treatment", the decision of the First National Congress on Bioethics (Kyiv, 2007) and the "European Union Directive 2010/63 / EU on the protection of animals used for scientific purposes" (Directive 2010/63 / EU of the European Parliament) [28].

## Results and Discussions

As a result of experiments, it was found that within 3 hours of the experiment the anti-exudative effect of LHAEAL and DEAL increases and becomes reliable as compared to CP from the 2nd hour of the experiment (Table 1).

The maximum anti-edematous effect of Acorus leaf extracts - LHAEAL and DEAL falls for 3rd hour of the experiment. Antiexudative activity of LHAEAL at carrageenan-induced edema at the maximum inflammation (180 min) was 79.5% ($p < 0.05$), DEAL - 70.1% (Fig. 4.1).

The maximum antiexudative activity in the model of carrageenan edema in rats throughout the study period was when using diclofenac sodium - 78.9-81%. According to the degree of suppression of exudative processes (average for 3 hours of the experiment), LHAEAL (53%) and DEAL (51%) were slightly inferior to diclofenac sodium (63.4%).

Such changes indicate a probable decrease in the intensity of the inflammatory process during the use of LHAEAL, DEAL, and diclofenac sodium.

According to the degree of exudative processes suppression with carrageenan edema throughout the study period, LHAEAL and DEAL at the dose studied, are slightly inferior to diclofenac sodium (table. 1 and Fig. 1).

In our opinion, the slight difference in anti-exudative action of LHAEAL and DEAL is due to the presence of a minimal amount of β-azarone in the LHAEAL, which is characterized by anti-inflammatory activity.

The next stage of our research was to study the antiexudative effect of extracts of sweet flag leaves on the course of zymosan edema in rats (table. 2).

In the model of zymosan edema in rats, it was found that the prophylactic administration to animals of both extracts of sweet flag leaves inhibited the development of zymosan edema in the studied period. Thus, 0.5 h after administration of zymosan to animals, in rats injected with the studied extracts, edema was significantly lower than in the control pathology group - when using quercetin, 11 mg/kg - 1.46 times, LHAEAL, 1 ml/kg - 1.71 times, DEAL, 0.5 mL/kg - 1.67 times, DEAL, 1 mL/kg 1.81 times, 1.64 times when using LHAEAL, 1 mL/kg and 1.14 times when using sodium diclofenac (table. 2).

The anti-edematous activity of the test compounds in the model of zymosan edema was for LHAEAL, 0.5 mL/ kg - 39.1%, LHAEAL, 1 mL/ kg - 41.6% ($p < 0.05$), DEAL, 0.5 mL/ kg - 38.5% ($p < 0.05$), DEAL, 1 mL/ kg - 46% ($p < 0.05$), with the introduction of quercetin - 31.7% ($p < 0.05$) and diclofenac sodium - 12.4% (table. 2). With zymosan edema (table. 2), in the pathogenesis of which the leading role belongs to leukotrienes, the activity of DEAL at a dose of 1 mL/kg was 9.1% higher than LHAEAL and significantly higher than that of quercetin (19.4%) and diclofenac sodium (33.6%). %). The ability of sweet flag leaf extracts to inhibit the development of zymosan edema is associated with the action of flavonoids, which can inhibit the activity of LOG [18, 21, 29, 30].

It is known that plant flavonoids that are part of the extracts of sweet flag leaves have capillary-strengthening properties [29, 30]. Therefore, further research aimed to study the effect of sweet flag leaf extracts on vascular permeability of rat skin

by the method of PP Golikov. The results of the experiment are presented in Fig. 2

As a result of the research, it was found that in animals of the control group the most rapidly stained is the papule, caused by zymosan 54.8 sec, then papule at the histamine injection site is stained (115.6 sec), then - egg white - 123.4 sec, and later formalin papule is stained - 228 sec.

The introduction of sweet flag leaf extracts delayed the staining of papules and, consequently, reduced vascular permeability caused by the injection of phlogogens.

Thus, against the background of the use of zymosan, the use of LHAEAL (0.5 mL/kg) increased the time of staining of papules in comparison with CP in 1.38 times, LHAEAL (1 mL/kg) - 1.53 times, DEAL (0.5 mL/ kg) - 1.38 times, DEAL (1 mL/ kg) -1.58 times, the introduction of diclofenac sodium increased the staining time by 1.1 times, and quercetin - 1.3 times, respectively.

Against the background of the use of histamine, the introduction of LHAEAL (0.5 mL/kg) increased the time of papules staining by 1.2 times, LHAEAL (1 mL/ kg) - 1.33 times, DEAL (0.5 mL/ kg) - by 1.22 times, DEAL (1 mL/ kg) - 1.5 times, the introduction of diclofenac sodium increased the staining time by 1.1 times, and quercetin - 1.26 times, respectively.

Against the background of the use of egg white, the introduction of the studied extracts and the comparison drug increased the staining time of papules by 1.5; 1.6 times; 1.8 times; 1.6 times, 1.45, and 1.4 times, respectively.

Against the background of the introduction of formalin, the studied compounds and reference drugs diclofenac sodium and quercetin, increased the staining time of papules in 1.3; 1.36 times; 1.4 times; 1.5 times, 1.18 times, and 1.13 times, respectively. It should be noted that the degree of increase in the staining time of papules, the effectiveness of DEAL (1 mL/kg) was significantly higher than the effectiveness of LHAEAL at the same dose.

Given the above, according to the degree of reduction of the effect on vascular permeability caused by the introduction of various phlogogens, the studied drugs can be arranged in the following sequence: DEAL, 1 mL/kg > LHAEAL, 1 mL/ kg > DEAL, 0.5 mL/ kg > LHAEAL, 0.5 mL/ kg > quercetin > sodium diclofenac.

The next stage of our research was to study the effect of DEAL on the vascular permeability of the skin of rats without the participation of phlogogenic agents (McClure-Aldrich test) by the rate of resorption of saline papules. The result of the experiment is shown in Fig. 3

It was found that the use of DEAL, LHAEAL, and quercetin showed a significant prolongation of the retention time of the papule. Thus, the time of disappearance of clear edges of the papule when using DEAL increased 1.8 times, LHAEAL- 1.37 times, quercetin - 1.26 times. The above drugs significantly increased the time of complete disappearance of papules (Fig. 3). The comparison drug sodium diclofenac slightly increased the time of disappearance of clear edges of the papule and the time of complete disappearance of papules, but these changes were not reliable. In our opinion, the effectiveness of the use of Acorus extracts is due to the presence of bioflavonoids in their composition, which can reduce their permeability and strengthen the walls of capillaries. In terms of vasoconstrictive activity, the efficiency of DEAL was higher than LHAEAL by an average of 20.8%.

Thus, it was established that by the vasoconstrictive activity the extract-leader is DEAL at a dose of 1 mL/kg.

It was found that in the membrane-stabilizing effect the activity of drugs changed in the following sequence - DEAL, 1 mL/kg, 40.7%> LHAEAL, 1 mL/kg, 31.3% > DEAL, 0.5 mL/kg, 29.6%> LHAEAL, 0.5 mL/kg 31.4%> quercetin, 25.9% (table. 3).

Thus, the results of the study indicate that the extracts of sweet flag leaves can stabilize the membrane in all studied doses. According to the degree of membrane stabilizing activity, all extracts of Acorus leaves exceeded the effect of the reference drug - quercetin. For DEAL at a dose of 1 mL/ kg, this difference was 15% ($p < 0.05$).

Given the above, we consider it appropriate to conduct further studies of Acorus leaf extracts at a dose of 1 mL/kg, which was selected as conditionally therapeutic.

The presence of anti-exudative action of the studied extracts, in our opinion, is due to the composition and synergistic effect of BAS (most of them are strong antioxidants) of the extracts. Based on own and literature data, we can assume that the anti-inflammatory effect of Acorus leaf extracts is

mainly due to the inhibitory effect of polyphenols on the release of inflammatory mediators: histamine, kinins, and prostaglandins [10, 12, 29, 30, 31]. This is confirmed by the significant antiexudative activity of the extracts from 2nd hour of the experiment. In leukotriene-induced edema caused by zymosan administration, DEAL activity was higher than LHAEAL. The membrane-stabilizing properties of Acorus leaf extracts, the effect of which exceeded the effect of comparison drug quercetin, were also experimentally proved.

In our opinion, due to flavonoids, flavonols, and oxycinnamic acids that are part of the extracts, the process of adhesion and migration of leukocytes, the formation of prostaglandins E1, F2, and thromboxane A2 is reduced; also reduced is capillary permeability induced by inflammatory mediators and microtraumas [30, 31].

These same BAS contribute to reducing the intensity of the processes of proteolysis, lipolysis in the inflammatory focus. Polyphenolic compounds that are part of the leaf extract can inhibit the activity of hyaluronidase, reduce the intensity of free radical oxidation. It is known that the receptor site of COX-2 (as opposed to physiological COX-1) has an additional lateral hydrophilic cavity, through which the interaction of COX-2 with flavonoids and similar compounds can take place [32]. All this explains the anti-exudative properties of Acorus leaf extracts.

Also, anti-inflammatory and membrane-stabilizing activity are inherent in oxycinnamic acids, primarily rosmarinic, ferulic, caffeic, and p-coumaric acids, for which antioxidant, membrane-stabilizing, anti-inflammatory, cerebroprotective activities have been established [33, 34, 35, 36].

The universality of the action of the components of Acorus leaf extract was proved in the model of vascular permeability caused by the introduction of various phlogogens (formalin, zymosan, histamine, and undiluted egg white). It is known that one of the factors damaging the membrane structures of cells, mitochondria, endoplasmic reticulum, etc. is the excessive activation of FRO processes [37, 38, 39]. The degree and severity of inflammatory and destructive processes depend on the depth of damage to the membrane apparatus of cells [40, 41]. Due to the high content of flavonoids, hydroxycinnamic acids, and other compounds with proven antioxidant activity in the extracts of Acorus leaves [10, 12, 20, 29], the intensity of FRO processes decreases, cytodestruction decreases, which leads to a decrease in vascular permeability.

Summarizing the results of experimental research, it can be concluded about the prospects for their further in-depth study to develop a new effective anti-inflammatory phytomedicine for the prevention and complex treatment of human diseases.

## Conclusions

1. In models of carrageenan, histamine, and zymosan edema of the paw in rats, the presence of dose-dependent antiexudative action of Acorus leaf extracts has been established. According to the degree of antiexudative effect in carrageenan (79.5%) and histamine (50%) edema, the maximum activity was shown by LHAEAL, in the model of zymosan edema - DEAL (43.5%). In terms of this type of activity, the extracts were not inferior to quercetin comparison drug and were somewhat inferior to sodium diclofenac.

2. Acorus leaf extracts have a capillary-strengthening and membrane-stabilizing effect, which is confirmed by a significant decrease in vascular permeability by 1.2-1.4 times. Membrane-stabilizing activity of Acorus leaf extracts in the model of spontaneous hemolysis of erythrocytes was 31.3% –40.7%. In this type of activity, they reliably exceeded the effect of comparison drugs of quercetin and sodium diclofenac. The maximum activity was observed when using DEAL at a dose of 1 mL/kg, which should be used for further research as a conditionally therapeutic.

3. The obtained results determine the prospects for further research of Acorus leaf extracts to develop a new effective anti-inflammatory phytomedicine for the prevention and complex therapy of human diseases.

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**Table 1.** Study of the antiexudative properties of LHAEAL and DEAL in a model of carrageenan edema in rats (n = 6, Median (Q25; Q75)

| Experimental conditions | $V_{30\ min} - V_i$ | $V_{60\ min} - V_i$ | $V_{120\ min} - V_i$ | $V_{180\ min} - V_i$ |
|---|---|---|---|---|
| Carrageenan 1% -0.1 mL (CP) | 0.30 (0.26; 0.37) | 0.45 (0.41; 0.59) | 0.90 (0.59; 0.95) | 1.51 (1.4; 1.55) |
| Carrageenan 1% -0.1 mL + LHAEAL, 0.5 mL/kg | 0.27 (0.19; 0.39) | 0.39 (0.26; 0.70) | 0.28* (0.20; 0.52) | 0.30* (0.06; 0.48) |
| Carrageenan 1% -0.1 mL + DEAL, 0.5 mL/kg | 0.27 (0.19; 0.39) | 0.38 (0.24; 0.72) | 0.26* (0.19; 0.50) | 0.33* (0.25; 0.48) |
| Carrageenan 1% -0.1 mL + diclofenac sodium, 8 mg/kg | 0.17 (0.14; 0.31) | 0.31 (0.17; 0.47) | 0.19* (0.17; 0.32) | 0.30* (0.30; 0.46) |

Note: * - valuable in relation to the CP group, p <0.05.

**Table 2.** Antiexudative effect of LHAEALand DEAL on a model of zymosan edema in rats

| Experimental conditions | The amount of edema, Δ V, Units | AIA, % |
|---|---|---|
| CP | 26.83±1.17 | |
| LHAEAL, 0.5 mL/ kg | 16.33±0.76 * | 39.1 |
| LHAEAL, 1 mL/ kg | 15.66±0.67 * | 41.6 |
| DEAL, 0.5 mL/ kg | 16.5±0.56 * | 38.5 |
| DEAL, 1 mL/kg | 14.8 ±0.47 * | 46.0 |
| Quercetin, 11 mg/kg | 18.33±0.67 | 31.68 |
| Diclofenac sodium, 8 mg/kg | 23.5±0.82 | 12.4 |

Note: * - valuable in relation to the CP group, p <0.05.

**Table 3.** Influence of Acorus leaf extracts on spontaneous hemolysis of erythrocytes in intact animals by the method of F. C. Jager, M ± m (n = 6)

| Experimental conditions | The severity of hemolysis, % | Membrane stabilizing activity, % |
|---|---|---|
| IC | 10.8±0.8 | |
| DEAL, 0.5 mL/kg | 7.6 ± 0.24 * | 29.6 |
| LHAEAL, 0.5 mL/kg | 7.8±0.31 * | 27.7 |
| DEAL, 1 mL/kg | 6.4±0.4 */** | 40.7 |
| LHAEAL, 1 mL/ kg | 7.4±0.8 * | 31.4 |
| Quercetin, 11 mg/kg | 8.0±0.31 * | 25.9 |

Notes:

1. * - deviations are significant relative to the values of IC, p <0.05;
2. ** - deviations are significant relative to the values of quercetin, p <0.05;
3. n is the number of animals in the group.

**Figure 1.** Anti-inflammatory activity (%) of LHAEAL, DEAL, diclofenac sodium in carrageenan edema in rats

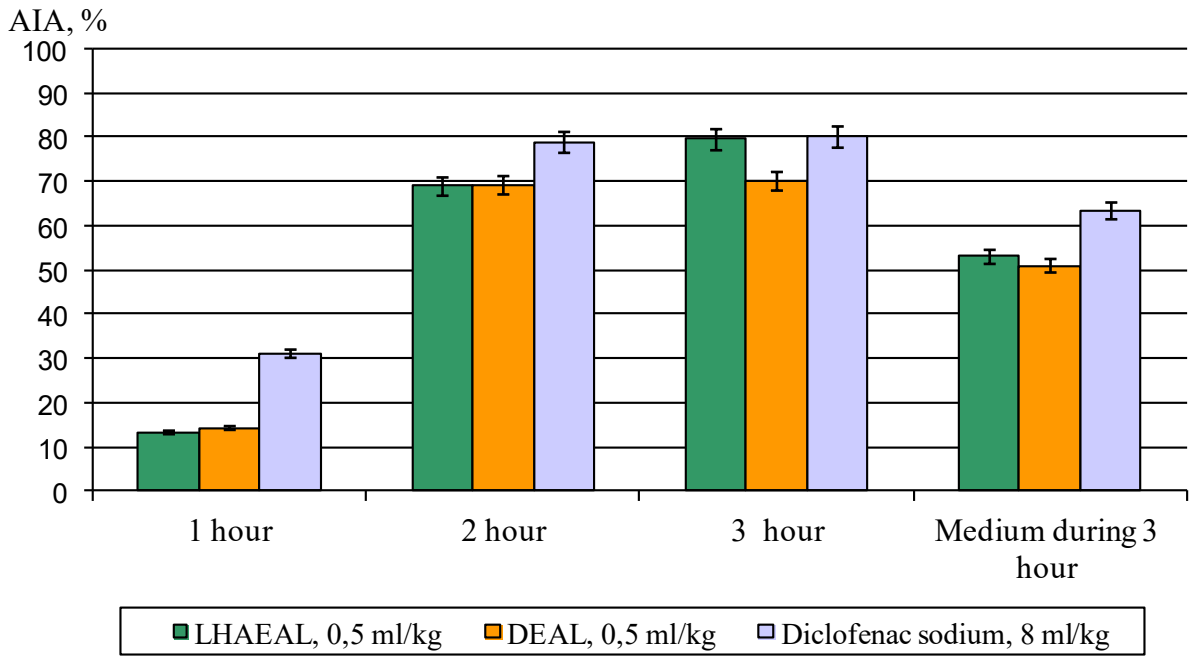
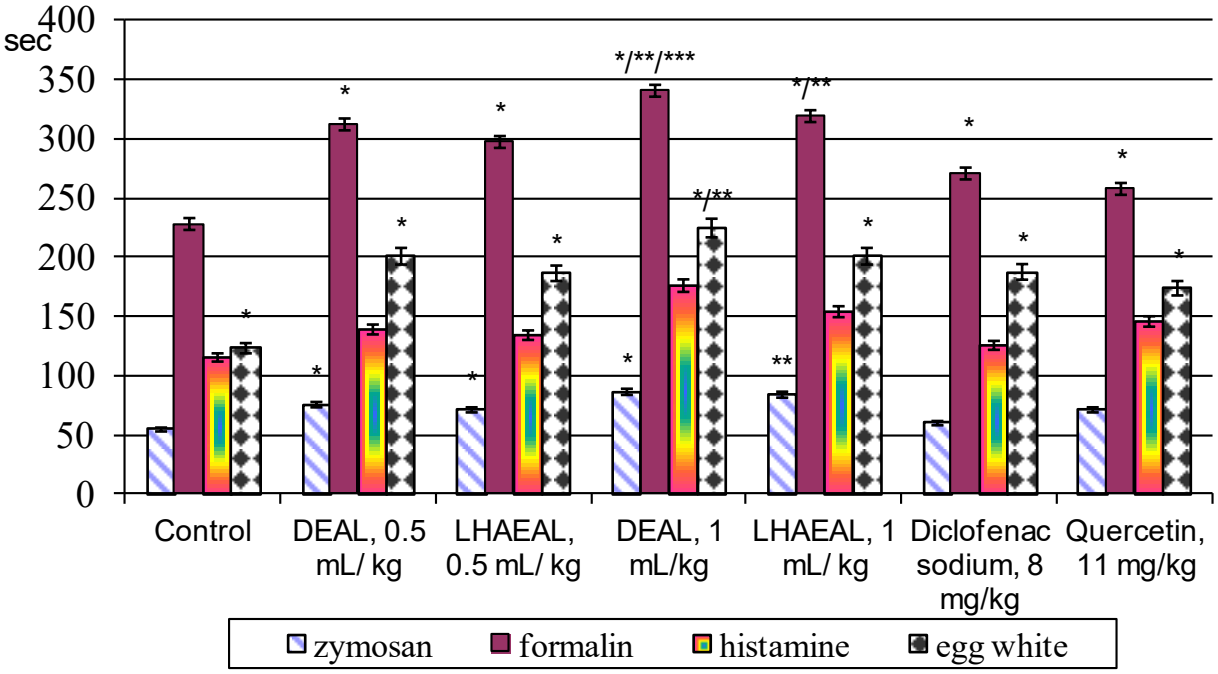


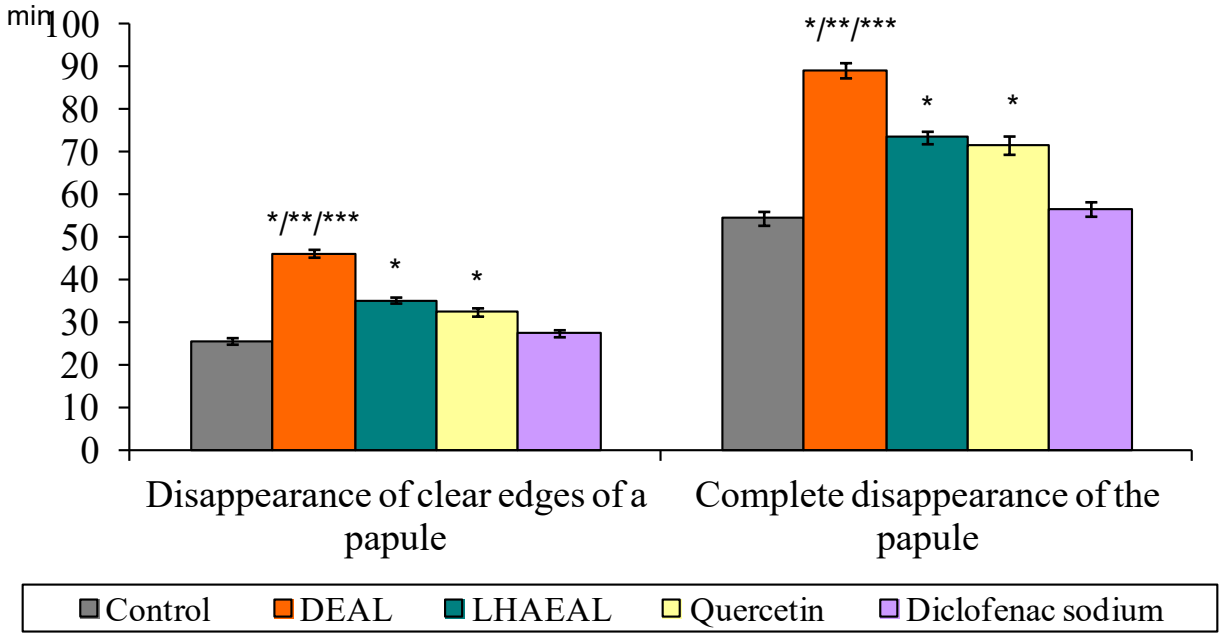
**Figure 2.** The effect of extracts of sweet flag leaves on vascular permeability in rats




Notes:

1. * - valuable in relation to the CP, p <0.05;
2. ** - valuable relative to quercetin, p <0.05
3 *** - valuable relative to sodium diclofenac, p <0.05.

**Figure 3.** Influence of Acorus leaf extracts on vascular permeability of rat skin with intradermal administration of saline (McClure-Aldrich test)




Notes:

1. * - valuable in relation to the CP, p <0.05;
2. ** - valuable relative to quercetin, p <0.05
3 *** - valuable relative to sodium diclofenac, p <0.05.