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Original Research Article

Study of the Biological Activity and Acute Toxicity of the Dry Extract of Rheum Tataricum L

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Abstract: ***Objective***: The purpose of the work was to study the acute toxicity and biological activity of the dry extract of Rheum tataricum L. ***Methods***: Acute toxicity was studied according to generally accepted methods on outbred white mice of both sexes, with a body weight of 18–22 g. Each group consisted of 6 animals, with a total of 18 mice used. The tested extract was administered to the experimental animals once orally as a 10% solution at doses of 1250 mg/kg (0.25 ml/20 g), 2500 mg/kg (0.5 ml/20 g), and fractionally (0.5 ml/20 g) at 10-minute intervals up to 5000 mg/kg (1.0 ml/20 g). The maximum permissible volume of oral administration for mice was 0.5 ml, with the total number of administrations not exceeding three times per day. The study of the anti-inflammatory activity of the dry extract was carried out using the formalin-induced paw edema method in mice. The experiments were conducted on 15 outbred white mice weighing 18–21 g, which were then divided into groups of 5 animals each. For 7 days, the animals received a single daily oral administration of the dry extract in solution form (prophylactic dose of the preparation): 1. Control group (control) – animals without exposure to the dry extract. 2. "Rheum tataricum L." – animals received the dry extract at a dose of 250 mg/kg, in a volume of 0.2 ml/20 g. 3. "Biomol" – animals received "Biomol" capsules (Shrey Nutraceuticals & Herbals Pvt. Ltd., India) at a dose of 250 mg/kg, in a volume of 0.2 ml/20 g body weight. On the last day, one hour after drug administration, the animals of each group were injected subplantarly with 0.02 ml of a 2% aqueous formalin solution into the left hind paw. The paw edema size was measured using a plethysmometer at 1, 2, and 4 hours, and the data obtained at the peak of the inflammatory response were used to assess anti-inflammatory activity. Similar experiments were conducted using carrageenan- and histamine-induced edema models. ***Results***: In the study of acute toxicity, due to the absence of mortality in animals after oral administration of the dry extract of Rheum tataricum L., it was not possible to determine the lethal dose, which indicates the absence of toxicity within the dose range of 1250–5000 mg/kg; therefore, the LD_{50} is assumed to be greater than 5000 mg/kg. Further, the anti-inflammatory activity of the preparations was studied using the formalin-induced edema model. In the experiments, the dry extract of Rheum tataricum L. demonstrated the most pronounced anti-inflammatory effect, whereas "Biomol" showed a moderate effect, limited mainly to reducing the inflammatory response at the early stage. In the carrageenan-induced edema model, the dry extract of Rheum tataricum L. showed a tendency to reduce the inflammatory response at an early stage (1 hour); however, no statistically significant difference from the control group was recorded ($p > 0.05$). "Biomol" demonstrated a moderate anti-inflammatory effect in the initial phase, which was diminished at later observation periods. The obtained data suggest that both studied preparations are capable of exerting some influence on the dynamics of carrageenan-induced edema;

however, no pronounced and statistically significant anti-inflammatory effect was observed under the conditions of the present experiment. Further experiments examined the effectiveness of the dry extract of Rheum tataricum L. using the histamine-induced edema model. In this model, the extract exhibited an anti-inflammatory effect at the early stage of the inflammatory process, as evidenced by a significant reduction in edema volume as early as 1 hour after administration ($p < 0.001$). At later time points (2–4 hours), the differences from the control group were less pronounced; however, a tendency toward reduction of the inflammatory response compared to the control group was still observed. Under these conditions, "Biomol" did not demonstrate a significant anti-inflammatory effect. ***Conclusion***: The results of the study demonstrated that the dry extract of Rheum tataricum L., at the investigated doses, is a low-toxic substance. In a series of experiments employing three inflammation models (formalin-, carrageenan-, and histamine-induced paw edema), it was established that the dry extract of Rheum tataricum L. exhibits anti-inflammatory activity, most pronounced in the formalin-induced edema model. In this model, the extract significantly reduced edema volume at 1 and 2 hours of observation ($p < 0.05$). In the carrageenan-induced edema model, only a tendency toward inflammation reduction was observed, with no statistically significant differences from the control group. "Biomol" exhibited a moderate effect, limited predominantly to the early phase of inflammation, and did not demonstrate a significant influence on edema dynamics at later stages.

Keywords: dry extract of Rheum tataricum L, acute toxicity, anti-inflammatory effect, histamine-induced edema model, formalin-induced edema model, carrageenan-induced edema model.

INTRODUCTION

It is well established that the rich flora of Uzbekistan is a source of various phytopreparations and dietary supplements. One such plant is *Rheum tataricum* L., a perennial ephemeroid, a desert and desert-steppe species that forms thickets on heavily compacted and saline gray-brown and sierozem soils. The rhizome is vertical with dark brown sheaths. The stems, numbering two or three, are hollow, sturdy, grooved, up to 45–50 cm in height, and branch profusely from the middle, forming a broad inflorescence. The leaves are large, rounded, rugose, with a cordate base and three prominent veins. The flowers are small and cream-colored. The fruits are three-angled, heart-shaped, finely wrinkled, dark brown, dull winged nutlets with narrow dark reddish-brown wings. Flowering occurs in April–May, and fruiting takes place in May–early June. The species is widespread in plains and deserts and has industrially significant raw material reserves in the Republic of Uzbekistan [1].

Rheum tataricum, growing in the territory of Karakalpakstan, contains carbohydrates, organic acids, phenols, catechins, anthraquinones, and higher aliphatic hydrocarbons, and differs from other species of this plant by the highest content of tannins (ranging from 20.61% to 25.74%) in all parts of the plant. The presence of such a high amount of tannins in the plant makes it possible to use *Rheum tataricum* as an anti-inflammatory agent. The rhizomes of *Rheum tataricum* also contain anthracene derivatives, with particularly high levels during the fruiting phase, amounting to 1.71 ± 0.04% in terms of chrysophanic acid. The presence of anthracene derivatives in the plant allows its use as a bactericidal, spasmolytic, and anti-inflammatory agent [2].

Objective. Based on the above, the purpose of the study was to examine the acute toxicity and biological activity of the dry extract of *Rheum tataricum* L.

MATERIALS AND METHODS:

Study of Acute Toxicity

The experiments were conducted on healthy animals that had undergone a quarantine period of no less than 10–14 days [6, 7].

Acute toxicity was studied according to generally accepted methods on outbred white mice of both sexes, weighing 18–22 g. Each group consisted of 6 animals, with a total of 18 mice used.

The tested extract was administered to the experimental animals once orally as a 10% solution at doses of 1250 mg/kg (0.25 ml/20 g), 2500 mg/kg (0.5

ml/20 g), and fractionally (0.5 ml/20 g) at 10-minute intervals up to 5000 mg/kg (1.0 ml/20 g). The maximum permissible volume of oral administration for mice was 0.5 ml, with the total number of administrations not exceeding three times per day [8].

After administration of the dry extract, the animals were distributed into groups in separate cages and continuously observed during the first hour. Thereafter, monitoring was carried out hourly during the first 24 hours, and subsequently once daily over the next 13 days of the experiment (the total observation period was 14 days). The general condition of the animals was assessed, including their behavioral characteristics, the intensity and nature of motor activity, the presence and severity of convulsions, coordination of movements, skeletal muscle tone, response to external stimuli, respiratory rate and depth, heart rhythm, condition of the fur and skin, coloration of the mucous membranes, tail position, quantity and consistency of feces, food and water intake, as well as other indicators reflecting possible toxic effects. In addition, the timing of the appearance of signs of intoxication was recorded [10].

Throughout the experiment, all animals were maintained under standard vivarium conditions, receiving a balanced diet and free access to water.

Methods for Studying the Biological Activity of the Dry Extract of *Rheum tataricum* L.

The study of the anti-inflammatory activity of the dry extract was carried out using the **formalin-induced** paw edema method in mice [6, 7]. The experiments were conducted on 15 outbred white mice weighing 18–21 g, which were then divided into groups of 5 animals each.

For 7 days, the animals received a single daily oral administration of the dry extract in solution form (prophylactic dose of the preparation):

1. Control group (control) – animals without exposure to the dry extract.
2. "Rheum tataricum L." – animals received the dry extract at a dose of 250 mg/kg, in a volume of 0.2 ml/20 g.
3. "Biomol" – animals received "Biomol" capsules (Shrey Nutraceuticals & Herbals Pvt. Ltd., India) at a dose of 250 mg/kg, in a volume of 0.2 ml/20 g body weight.

On the last day, one hour after administration of the preparation, the animals of each group were injected subplantarly with 0.02 ml of a 2% aqueous formalin solution into the left hind paw. The paw edema size was measured using a plethysmometer at 1, 2, and 4 hours, and the data obtained at the peak of the inflammatory response were used to assess anti-inflammatory activity.

The criterion for evaluating the pharmacological activity of the preparations was the reduction of paw edema in the experimental animals compared to the control group.

Statistical analysis of the results was performed using ANOVA at a significance level of $p = 0.05$ with GraphPad Prism software, version 8.0.0 for Windows (GraphPad Software, San Diego, California, USA, www.graphpad.com) [9].

The results are presented as arithmetic means (M), standard deviations (SD), and sample sizes (n).

The study of the anti-inflammatory activity of the dry extract was carried out using the carrageenan-induced paw edema method in mice [6, 7]. The experiments were conducted on 15 outbred white mice weighing 18–21 g, which were then divided into groups of 5 animals each.

For 7 days, the animals received a single daily oral administration of the dry extract in solution form (prophylactic dose of the preparation):

1. Control group (control) – animals without exposure to the dry extract.
2. "Rheum tataricum L." – animals received the dry extract at a dose of 250 mg/kg, in a volume of 0.2 ml/20 g.
3. "Biomol" – animals received "Biomol" capsules (Shrey Nutraceuticals & Herbals Pvt. Ltd., India) at a dose of 250 mg/kg, in a volume of 0.2 ml/20 g body weight.

On the last day, one hour after administration of the preparation, the animals of each group were injected subplantarly with 0.02 ml of a 0.1% aqueous carrageenan solution into the left hind paw. The paw edema size was measured using a plethysmometer at 1, 2, and 4 hours, and the data obtained at the peak of the inflammatory response were used to assess anti-inflammatory activity.

The criterion for evaluating the pharmacological activity of the preparations was the reduction of paw edema in the experimental animals compared to the control group.

Statistical analysis of the results was performed using ANOVA at a significance level of $p = 0.05$ with GraphPad Prism software, version 8.0.0 for Windows (GraphPad Software, San Diego, California, USA, www.graphpad.com) [9].

The results are presented as arithmetic means (M), standard deviations (SD), and sample sizes (n).

The study of the anti-inflammatory activity of the dry extract was carried out using the histamine-induced

paw edema model in mice [6, 7]. The experiments were conducted on 15 outbred white mice weighing 18–21 g, which were then divided into groups of 5 animals each.

For 7 days, the animals received a single daily oral administration of the dry extract in solution form (prophylactic dose of the preparation):

1. Control group (control) — animals without exposure to the dry extract.
2. "Rheum tataricum L." — animals received the dry extract at a dose of 250 mg/kg, in a volume of 0.2 ml/20 g body weight.
3. "Biomol" — animals received "Biomol" capsules (Shrey Nutraceuticals & Herbals Pvt. Ltd., India) at a dose of 250 mg/kg, in a volume of 0.2 ml/20 g body weight.

On the last day, one hour after administration of the preparation, the animals of each group were injected subplantarly with 0.02 ml of a 0.1% aqueous histamine solution into the left hind paw. The paw edema size was measured using a plethysmometer at 1, 2, and 4 hours after injection. The data obtained at the peak of the inflammatory response were used to assess anti-inflammatory activity.

The criterion for evaluating the pharmacological activity of the extract was the reduction of paw edema in the experimental animals compared to the control group.

Statistical analysis of the results was performed using analysis of variance (ANOVA) at a significance level of $p = 0.05$ with GraphPad Prism software, version 8.0.0 for Windows (GraphPad Software, San Diego, California, USA, www.graphpad.com) [9].

The results are presented as arithmetic means (M), standard deviations (SD), and the number of observations (n).

RESULTS AND DISCUSSIONS:

Results of the Acute Toxicity Study

After oral administration of the dry extract, no signs of intoxication, changes in general condition, or other effects indicating toxic action of the preparation were observed (Table 1).

Table 1 Results of the Registration of the Toxic Effects of the Dry Extract of *Rheum tataricum* L.

Dose	Result
1250 mg/kg	After administration of the dry extract, no signs of intoxication were observed in the animals.
2500 mg/kg	After administration of the dry extract, no signs of intoxication were observed in the animals.
5000 mg/kg	After administration of the dry extract, no signs of intoxication were observed in the animals.

Calculation of acute toxicity indicators was not possible due to the absence of mortality in animals after oral administration of the dry extract of *Rheum tataricum* L. (TashPharmi, Uzbekistan), which indicates the absence of toxicity within the dose range of 1250–5000 mg/kg. Therefore, the LD_{50} is assumed to be greater than 5000 mg/kg (Table 2).

Table 2 Results of the Study of Acute Toxicity Indicators of the Dry Extract of *Rheum tataricum* L.

"Rheum tataricum L.", TashPharmi, Uzbekistan	
Doses, mg/kg	Number of mice deceased/total
1250 mg/kg	0/6
2500 mg/kg	0/6
5000 mg/kg	0/6
LD_{50} > 5000 mg/kg	

Therefore, the studied dry extract of *Rheum tataricum* L. (TashPharmi, Uzbekistan) does not exhibit toxicity within the dose range of 1250–5000 mg/kg according to acute toxicity indicators following oral administration, and even at the maximum dose it does not cause animal mortality.

Formalin-induced edema model

In the conducted study, the anti-inflammatory activity of the preparations was examined using the formalin-induced edema model. In the control group, a gradual increase in paw edema volume was observed, from the baseline level of 0.11 ± 0.01 ml to 0.26 ± 0.01 ml after 1 hour and 0.29 ± 0.02 ml after 2 hours, followed by a slight decrease to 0.24 ± 0.02 ml by the 4th hour. In the animals treated with *Rheum tataricum* L., the initial edema volume was 0.13 ± 0.02 ml, and it showed a statistically significant reduction compared to the control group after 1 hour (0.23 ± 0.02

ml; $p < 0.05$) and after 2 hours (0.21 ± 0.02 ml; $p < 0.05$), indicating an anti-inflammatory effect. In the "Biomol" group, the initial value was 0.14 ± 0.01 ml; after 1 hour, a significant reduction in edema to 0.22 ± 0.02 ml was observed ($p < 0.05$ compared to the control), but by the 2nd hour, the differences with the control group had leveled off (0.29 ± 0.02 ml), and by the 4th hour, only a tendency toward reduction remained (0.23 ± 0.02 ml). Thus, the dry extract of *Rheum tataricum* L. demonstrated the most pronounced anti-inflammatory activity, while "Biomol" exhibited a moderate effect, limited mainly to reducing the inflammatory response at the early stage (Table 3 and Figure 1).

Table 3 Results of the Study of the Anti-inflammatory Activity of the Dry Extract of *Rheum tataricum* L. (TashPharmi, Uzbekistan) in the Formalin-induced Edema Model

(M±SD; p=0,05; n=5)

Group	Paw edema volume (ml) after			
	0 h.	1 h.	2 h.	4 h.
Control	0,11 ± 0,01	0,26 ± 0,01	0,29 ± 0,02	0,24 ± 0,02
«Rheum Tataricum L»	0,13 ± 0,02	0,23* ± 0,02	0,21* ± 0,02	0,20 ± 0,02
«Biomol»	0,14 ± 0,01	0,22* ± 0,02	0,29 ± 0,02	0,23 ± 0,02

Note: * – statistically significant difference at $p < 0.05$ compared with the control group

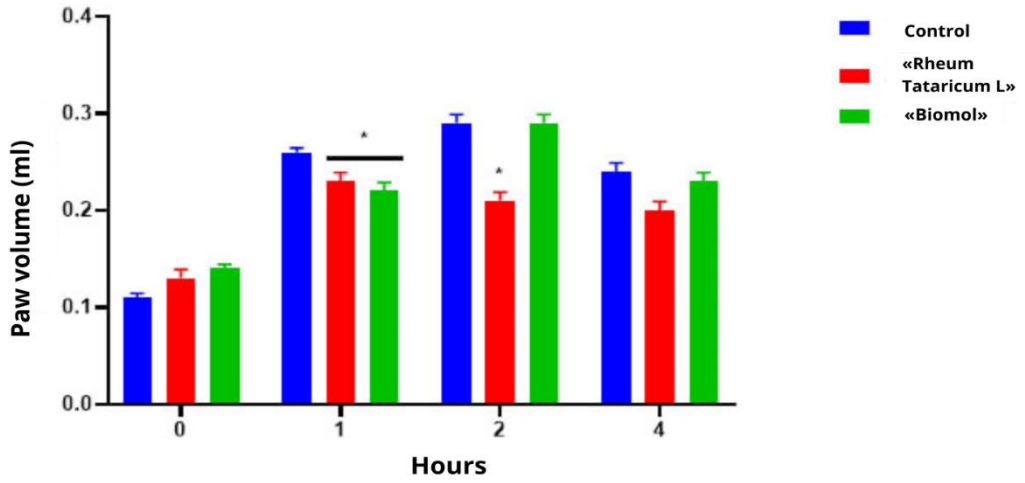

Figure 1. Results of the study of the anti-inflammatory activity of the dry extract of *Rheum tataricum* L. (TashPharmi, Uzbekistan) in the formalin-induced edema model (M ± SD; p = 0.05; n = 5).

Note: * – statistically significant difference at $p < 0.05$ compared with the control group.

Carrageenan-induced edema model

In the conducted study, the anti-inflammatory activity of the dry extract of *Rheum tataricum* L. (TashPharmi, Uzbekistan) was evaluated using the carrageenan-induced paw edema model. In the control group, paw edema volume increased from 0.13 ± 0.02 ml at the beginning of the experiment to 0.24 ± 0.02 ml after 1 hour and remained at the same level after 2 hours (0.24 ± 0.02 ml), followed by a slight decrease to 0.22 ± 0.02 ml by the 4th hour. In the animals treated with *Rheum tataricum* L., the initial value was 0.14 ± 0.02 ml; after 1 hour, the edema volume was lower than in the control group (0.18 ± 0.04 ml), and remained at 0.24 ± 0.03 ml after 2 hours and 0.23 ± 0.03 ml after 4 hours. In the "Biomol" group, the baseline value was 0.16 ± 0.02 ml; after 1 hour, the edema volume decreased to 0.18 ± 0.02 ml, but by 2 and 4 hours the values were comparable to the control group (0.24 ± 0.01 ml and 0.24 ± 0.03 ml, respectively).

Thus, the dry extract of *Rheum tataricum* L. demonstrated a tendency to reduce the inflammatory response at an early stage (1 hour); however, no statistically significant difference from the control group was recorded ($p > 0.05$). The "Biomol" preparation also exhibited a moderate anti-inflammatory effect in the initial phase, which was leveled off at later observation points. The obtained data suggest that both tested preparations may exert some influence on the dynamics of carrageenan-induced edema; however, a pronounced statistically significant anti-inflammatory effect was not observed under the conditions of this experiment (Table 4 and Figure 2).

Table 4 Results of the study of the anti-inflammatory activity of the dry extract of *Rheum tataricum* L. (TashPharmi, Uzbekistan) in the carrageenan-induced edema model (M ± SD; p = 0.05; n = 5).

Group	Paw edema volume (ml) after			
	0 h.	1 h.	2 h.	4 h.
Control	0,13 ± 0,02	0,24 ± 0,02	0,24 ± 0,02	0,22 ± 0,02
«Rheum Tataricum L»	0,14 ± 0,02	0,18 ± 0,04	0,24 ± 0,03	0,23 ± 0,03
«Biomol»	0,16 ± 0,02	0,18 ± 0,02	0,24 ± 0,01	0,24 ± 0,03

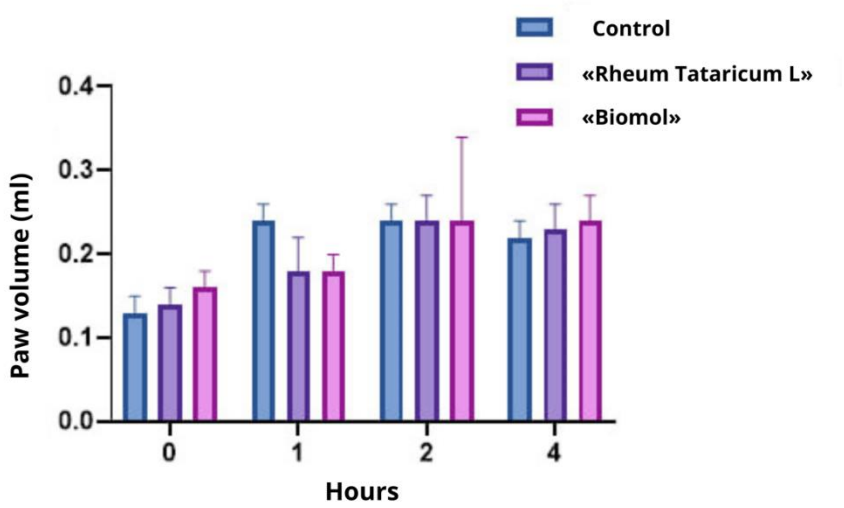

Figure 2. Results of the study of the anti-inflammatory activity of the dry extract of *Rheum tataricum* L. (TashPharmi, Uzbekistan) in the carrageenan-induced edema model (M ± SD; p = 0.05; n = 5).

Histamine-induced edema model

The anti-inflammatory activity of the dry extract of *Rheum tataricum* L. (TashPharmi, Uzbekistan) was evaluated in the histamine-induced paw edema model. In the control group, paw edema volume increased from 0.11 ± 0.01 ml at the beginning of the experiment to 0.26 ± 0.02 ml after 1 hour, reached 0.28 ± 0.02 ml after 2 hours, and decreased to 0.19 ± 0.02 ml by the 4th hour. In the animals treated with the dry extract of *Rheum tataricum* L., the baseline value was 0.12 ± 0.02 ml. After just 1 hour, the edema volume was statistically significantly lower compared with the control group (0.20 ± 0.03 ml vs. 0.26 ± 0.02 ml; $p < 0.001$). At the 2nd hour, the edema volume was 0.26 ± 0.02 ml, comparable to the control values, whereas by the 4th hour it decreased to 0.19 ± 0.01 ml, also lower than the control values. In the "Biomol" group, the baseline value was 0.11 ± 0.01 ml; after 1 hour, it increased to 0.25 ± 0.01 ml, then gradually decreased to 0.26 ± 0.02 ml at the 2nd hour and to 0.19 ± 0.02 ml by the 4th hour, without showing significant differences from the control group.

Thus, the dry extract of *Rheum tataricum* L. exhibited an anti-inflammatory effect at the early stage of the inflammatory process, as evidenced by a significant reduction in edema volume as early as 1 hour after administration ($p < 0.001$). At later time points (2–4 hours), the differences from the control group were less pronounced; however, a tendency toward reduced inflammatory response compared with the control group persisted. Under these conditions, the "Biomol" preparation did not demonstrate a significant anti-inflammatory effect.

Table 5 Results of the study of the anti-inflammatory activity of the dry extract of *Rheum tataricum* L. (TashPharmi, Uzbekistan) in the histamine-induced edema model (M ± SD; p = 0.05; n = 5).

Group	Paw edema volume (ml) after			
	0 h.	1 h.	2 h.	4 h.
Control	0,11 ± 0,01	0,26 ± 0,02	0,28 ± 0,02	0,19 ± 0,02
«Rheum Tataricum L»	0,12 ± 0,02	0,20*** ± 0,01	0,26 ± 0,02	0,19 ± 0,01
«Biomol»	0,11 ± 0,01	0,25 ± 0,01	0,26 ± 0,02	0,19 ± 0,01

Note: *** – statistically significant difference at $p < 0.001$ compared with the control group.

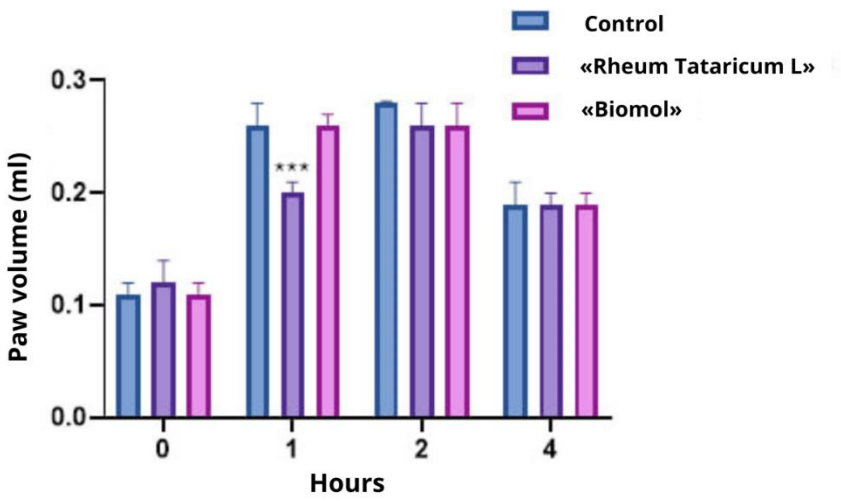

Figure 3. Results of the study of the anti-inflammatory activity of the dry extract of *Rheum tataricum* L. (TashPharmi, Uzbekistan) in the histamine-induced edema model (M ± SD; p = 0.05; n = 5).

Note: *** – statistically significant difference at $p < 0.001$ compared with the control group.

CONCLUSION:

The results of the study demonstrated that the dry extract of *Rheum tataricum* L., at the investigated doses, is a low-toxic substance.

In a series of experiments employing three inflammation models (formalin-, carrageenan-, and histamine-induced paw edema), it was established that the dry extract of *Rheum tataricum* L. exhibits anti-inflammatory activity, most pronounced in the formalin-induced edema model. In this model, the preparation significantly reduced the edema volume at 1 and 2 hours of observation ($p < 0.05$). In the carrageenan-induced edema model, only a tendency toward inflammation reduction was noted, with no statistically significant differences from the control group. The "Biomol" preparation demonstrated a moderate effect, mainly limited to the early phase of inflammation, and did not show a significant influence on the edema dynamics at later time points.

REFERENCES:

1. Pazilbekova Z.T., Aqseitov J.J. *Pharmaceutical Industry Today: Challenges and Prospects*. Proceedings of the 3rd International Scientific-Practical Conference (2022). "Bioecology and Medicinal Properties of *Rheum tataricum* L. Growing in the Conditions of Karakalpakstan."
2. Pazilbekova Z.T., Jollybekov B.B., Aqseitov J.J. *Scientific Justification of the Medicinal Properties of the Raw Material of Rheum tataricum L.* In: *Modern Achievements and Prospects of Pharmaceutical Technology*. Proceedings of the Scientific-Practical Conference (2025): 392–394.
3. Guidelines for Experimental (Preclinical) Study of New Pharmacological Substances. Edited by R.U. Khabriev. 2nd ed., revised and supplemented. Moscow: Medicine Publishing House, 2005. 832 p.
4. Guidelines for Conducting Preclinical Studies of Medicinal Products. Part One. Edited by A.N. Mironov. Moscow: Grif & K, 2012. 944 p.
5. Morton, D. B., Jennings, M., Buckwell, A., Ewbank, R., Godfrey, C., Holgate, B., Inglis, I., James, R., Page, C., Sharman, I., Verschoyle, R., Westall, L., Wilson, A. B., & Joint Working Group on Refinement (2001). Refining procedures for the administration of substances. Report of the BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on Refinement. British Veterinary Association Animal Welfare Foundation/Fund for the Replacement of Animals in Medical Experiments/Royal Society for the Prevention of Cruelty to Animals/Universities Federation for Animal Welfare. Laboratory animals, 35(1), 1–41. https://doi.org/10.1258/0023677011911345
6. Sokal, R. R., & Rohlf, F. J. (2012). Biometry: The Principles and Practice of Statistics in Biological Research (4th ed.). W. H. Freeman.
7. Stefanov A.V. *Preclinical Studies of Medicinal Products.* Kyiv, 2002: pp. 78–104.

