

UDK:615.276**EVALUATION OF THE ANTI-EXUDATIVE AND ANTI-PROLIFERATIVE
EFFECTS OF A GEL CONTAINING CONVULVULUS ARVENSIS EXTRACT****Kadir Shukurlaevich Shukurlaev**

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Abstract: The anti-exudative and anti-proliferative effects of a gel containing *Convolvulus arvensis* extract were studied in experiments on male white rats. In models of acute exudative (dextran-induced) and proliferative (granulomatous) inflammation, a gel containing *Convolvulus arvensis* demonstrated pronounced anti-inflammatory activity comparable to that of the nonsteroidal anti-inflammatory gel ibuprofen.

Keywords: inflammation, exudation, proliferation. *Convolvulus arvensis*.

Introduction. Modern medicine is increasingly focusing on the development of new, highly effective and safe medications. The use of drugs, whether chemically synthesized or derived from animals or plants, is often associated with side effects, which often limits their clinical use. The search for new potential therapeutic agents, including those based on natural ingredients, remains a pressing issue. In this case, it is important to search for agents that exhibit a multifaceted effect (including anti-inflammatory, wound healing, anti-burn, antihemorrhagic, anticoagulant) when applied topically to treat injuries at home, in emergency situations, in sports medicine, etc. [6]. In recent years, great importance has been attached to the local use of anti-inflammatory agents in the form of soft dosage forms [3, 4, 5, 8]. An aqueous extract of the aerial part of Field Bindweed (*Convolvulus arvensis*), when administered orally to experimental animals, exhibits a distinct anti-inflammatory effect, which is associated with its antagonism with respect to inflammatory mediators, a decrease in vascular permeability and suppression of hyaluronidase activity [9]. One

of the effective ways to prevent the development of adverse drug reactions is their local use in the form of gels, creams, ointments, etc. In this case, their action is limited to the site of application and does not allow the development of a systemic effect. Gels, due to the special composition of auxiliary substances, promote the accelerated onset of a local anti-inflammatory effect [1,2]. Therefore, gels are currently the most common "modification" of NSAIDs for topical use.

The aim of this study was to investigate the antiexudative and antiproliferative effects of a gel containing *Convolvulus arvensis* extract applied topically.

Materials and methods.

Experimental studies were conducted on mature male albino rats with an initial weight of 155-180 g. Each experimental group consisted of 6 rats. The antiexudative effect of the drugs was studied using a model of experimental aseptic arthritis induced by subplantar administration of a 6% dextran solution (0.1 ml). This model of inflammatory edema is widely used to evaluate the anti-inflammatory activity of new potential drugs [10, 11]. Paw volumes were measured using an oncometric method using a plethysmometer before and hourly for four hours after administration of flagogen. A gel containing 5% *Convolvulus arvensis* extract and 5% ibuprofen gel was applied to the surface of the animals' right hind paws one hour before the flagellant injection and after each paw volume measurement. The anti-inflammatory activity (AIA) of the drugs was calculated using the formula:

$$PBA = \frac{V_{\text{KOH}} - V_{\text{OH}}}{V_{\text{KOH}}} \times 100\% .$$

A gel containing *Convolvulus arvensis* extract and ibuprofen gel were applied to the right hind paw of the animals one hour before the injection of flagellant and after each measurement.

To study the effect of the drugs on the proliferative phase of inflammation, a cotton pellet technique was used. Sterile cotton pellets weighing 15 mg were implanted into the subcutaneous tissue of the interscapular region of the back of rats under ether anesthesia. The drugs were applied to the skin surface in the area of the cotton pellet for 7 days. On the 8th day, the animals were sacrificed, the cotton pellets containing the formed granulation tissue were removed, their wet weight was determined, and then, after drying to a constant weight at 70°C, their dry weight was determined. The mass of the resulting granulation tissue was determined by the difference between the masses of the dried granuloma and the implanted cotton pellet.

The results of all experimental series were statistically processed using the Biostat 2009 software package. Data are presented as mean (M) and standard error of the mean (m). A difference at a probability level of 95% or greater ($p < 0.05$) was considered statistically significant.

Study Results and Discussion

The results of the studies showed that subplantar administration of a dextran solution resulted in a nearly twofold increase in rat paw volume within the first two hours of the experiment, which remained unchanged for the next four hours (Figure 1). This fact once again convincingly demonstrates the high activity of dextran as a flagellant. In the group of animals, the use of 5% ibuprofen gel resulted in a significant reduction in the level of dextran-induced paw edema in rats. Thus, compared with the initial paw volume, its increase after 1 hour was 61.0%, after 2 hours - 63.0%, and after 3 and 4 hours - 52.6 and 44.2%. At the same time, the PVA values of the drug at the specified time points of the study were 34.8; 36.2; 38.3 and 40.0%, respectively. It is evident that ibuprofen gel exhibits distinct anti-inflammatory activity when applied locally. Further studies showed that the gel containing *Convolvulus arvensis* extract also has antiexudative activity. Thus, the PVA values when using 1% gel of *Convolvulus arvensis* extract were 10.1 and 9.6% in the first two hours of the experiment. Increasing the gel concentration to 3% led to an increase in the degree of antiexudative effect of *Convolvulus arvensis* extract. Thus, after 1 hour of dextran administration, paw volume increased by 67.0%, and after 2 hours, by 68.1%. This effect, with minor fluctuations, persisted at subsequent observation periods. Calculation of the PVA value using 3% gel showed that at the indicated experimental times, it was 31.4, 34.0, 35.8, and 37.1%, respectively. A gel containing *Convolvulus arvensis* extract and ibuprofen gel were applied to the surface of the right hind paw of the animals one hour before the injection of dextran and after each measurement.

To study the effect of the drugs on the proliferative phase of inflammation, a cotton pellet technique was used. Sterile cotton pellets weighing 15 mg were implanted into the subcutaneous tissue of the interscapular region of the back of rats under ether anesthesia. The drugs were applied to the skin surface in the area of the cotton pellet for 7 days. On day 8, the animals were sacrificed, the cotton balls containing the formed granulation tissue were removed, and their wet weight was determined. Their dry weight was then determined after drying to a constant weight at 70°C. The mass of the resulting granulation tissue was determined by the difference between the masses of the dried granuloma and the implanted cotton ball.

The results of all experimental series were statistically processed using the Biostat 2009 software package. Data are presented as the mean (M) and standard error of the mean (m). A difference at a probability level of 95% or greater ($p < 0.05$) was considered statistically significant.

Thus, in experimental animals using a dextran model of aseptic inflammation, *Convolvulus arvensis* extract gel and ibuprofen gel exhibit a distinct antiexudative effect. However, the

differences between the results were statistically insignificant, suggesting that the concentrations used have the same PVA. However, in our opinion, the gel containing 5% *Convolvulus arvensis* extract is the most effective.

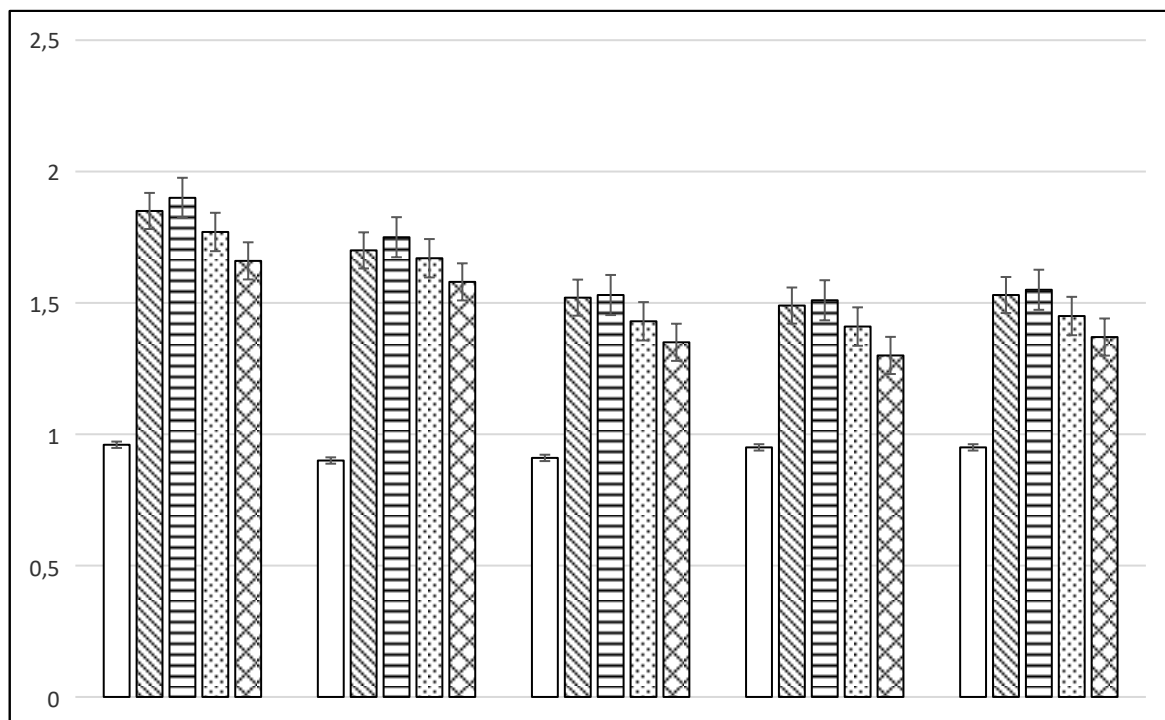


Figure 1. Effects of a gel containing *Convolvulus arvensis* extract and ibuprofen on the course of dextrin-induced inflammation

Inflammatory processes of various etiologies are known to occur with the simultaneous occurrence of three processes: exudation, alteration, and proliferation. It has been noted that the exudative stage of inflammation, with increased permeability of various capillaries, culminates in the proliferation of mesenchymal cells [7]. Since the studied gel containing *Convolvulus arvensis* extract has a distinct inhibitory effect on exudation processes, it was of interest to study its effect on the proliferative phase of inflammation.

In this series of experiments, the effect of a gel containing *Convolvulus arvensis* extract on the course of the proliferative phase of inflammation was compared with that of ibuprofen gel. Experimental studies showed that in healthy rats, the weight of 15-mg cotton balls reached 333.83 mg by the beginning of the 8th day after implantation. The dry mass of the resulting granulomas was 64.01 mg. Therefore, sterilized cotton balls implanted subcutaneously resulted in the development of granulation tissue significantly exceeding their initial mass. At the same time, the

dry mass of granulomas increased more than fourfold, objectively indicating the magnitude of the proliferation process. In contrast, in animals treated for 7 days of the experiment, the increase in the mass of both wet and dry granulomas significantly decreased. Thus, while the mass of wet granulomas in the group of rats treated with 5% *Convolvulus arvensis* extract gel was 31.4% lower, in the group of animals treated with 5% ibuprofen gel, it was only 21.4% lower. It is evident that both drugs suppress exudation when applied topically, which objectively confirms the experimental results presented in the previous sections and indicates a distinct anti-exudative effect of the gel containing *Convolvulus arvensis* extract. Furthermore, as the table shows, the topical preparations tested exhibit distinct antiproliferative activity when applied topically. It is evident that the gel containing dry *Convolvulus arvensis* extract reduced dry granuloma weight by 31.3%, while in the group of animals treated with 5% ibuprofen gel, it was only 24.0%.

Consequently, the topical preparations tested in the "cotton wool granuloma" model exhibited a single-target anti-exudative and anti-proliferative effect. Moreover, the pharmacological activity of the gel containing *Convolvulus arvensis* extract was somewhat superior to that of ibuprofen gel. It can be assumed that the topical preparations tested positively influence the main phases of inflammation.

Conclusions

A gel containing *Convolvulus arvensis* extract exhibits a distinct antiexudative effect in a dextran-based aseptic arthritis model and as a potential anti-inflammatory drug. In an experimental animal model of cotton wool granuloma, a gel containing *Convolvulus arvensis* extract and ibuprofen gel exhibit a distinct antiproliferative effect. *Convolvulus arvensis* extract in gel form can be proposed as a treatment for inflammatory conditions of the musculoskeletal system.

References

1. Abramova, S., "Principles for Selecting Topical NSAID Formulations," Pharmaceutical Bulletin "September," 2015, No. 26, pp. 111-114.
2. Aleeva, G.N., Zhuravleva, M.V., Khafizyanova, R.Kh. The Role of Excipients in Ensuring Pharmaceutical and Therapeutic Properties of Drugs // Pharmaceutical Chemistry Journal. - 2009. - Vol. 43, No. 4. - Pp. 51-56.]
3. Ivanova E. A., Matyushkin A. I., Voronina T. A. Effect of Hemontan in a Dosage Form for External Use on the Inflammatory Process Induced by Freund's Complete Adjuvant in Rats // Experimental and Clinical Pharmacology, - 2019, - Vol. 82, No. 4. - Pp. 23-27.

4. Kakorkin P. A., Kozin S. V., Ramenskaya G. V., Pavlova L. A. Dermatotropic Activity of an Aqueous Extract from *Carana Juvenata* Shoots in a Model of Atopic Contact Dermatitis // Experimental and Clinical Pharmacology. - 2018. - Vol. 81, No. 3. - P. 28-33.
5. Mavlyanova Sh. Z., Ubaydullaeva Z. A., Fayzullaeva N. S., et al. Use of a new herbal preparation for external use in experimental contact allergic dermatitis // Medical Journal of Uzbekistan. - 2019. - No. 2. - P. 99-102.
6. Mitrokhin N. M., Efimova A. O. Study of the pharmacological properties of *hirudo medicinalis* extract, ointment and gel based on it during cutaneous application in an experiment // Modern problems of science and education. - 2017. - No. 6 <https://www.science-education.ru/ru/article/view?id=27090>
7. Physiology. Edited by Novitsky V. V. University: IATE MEPhI. 2018.- 896 p.
8. Fedosov P.A., Nikolaevsky V.A., Chernov Yu.N. et al. Modern approaches to the selection of wound healing agents// Experimental and clinical pharmacology. - 2018. - Vol. 81, No. 4. - Pp. 41-48.
9. Yuldasheva Sh.A., Khakimov Z.Z. Study of anti-inflammatory activity and toxicity of the drug CTM// *Lekarska sprava* - Kyiv, "zdorovya".- 2000.- No. 6. - Pp. 41-44.
10. Khakimov Z.Z., Rakhmanov A.Kh., Bekova, N.B. K.Sh. Shukurlaev K.Sh. Specific features of exudative and proliferative phase of inflammation when using calcium channel blockers // *American Journal of Medicine and Medical Sciences*.-2020.-Vol.10, No. 10.-R. 817-821.
11. Rakhmanov A. Kh., Khakimov Z.Z., Mavlanov Sh. R., et al. Anti-inflammatory activity of dry extract of medicinal plants // *European journal of pharmaceutical and medical research*. - 2018. - Vol. 5, No. 8. - R. 55-57.
12. Rakhimov, Bakhtiyar; Rakhimova, Feroza; Sobirova, Sabokhat; Allaberganov, Odilbek; ,Mathematical Bases Of Parallel Algorithms For The Creation Of Medical Databases,,,,,2021,InterConf
13. Saidovich, Rakhimov Bakhtiyar; Bakhtiyarovich, Saidov Atabek; Farkhodovich, Babajanov Boburbek; Ugli, Karimov Doston Alisher; Qizi, Musaeva Mukhtasar Zayirjon; ,Analysis And Using of the Features Graphics Processors for Medical Problems,Texas Journal of Medical Science,7,,105-110,2022,
14. Rakhimov, Bakhtiyar; Ismoilov, Olimboy; ,Management systems for modeling medical database,AIP Conference Proceedings,2432,1,060031,2022,AIP Publishing LLC

15. Rakhimov, BS; ,Russian “Information technologies in medical education”,METHODS OF SCIENCE Scientific and practical journal,12,,25-7,2017,
16. Rakhimov, BS; Ismoilov, OI; Ozodov, RO; ,Russian “Software and automation of forensic examination”,METHODS OF SCIENCE Scientific and practical journal,11,,28-30,2017,
17. Allaberganov, Odilbek R; Rakhimov, Bakhtiyar S; Sobirova, Sabokhat K; Rakhimova, Feroza B; Saidov, Atabek B; ,Problem for medical system with infinite zone potential in the half line,AIP Conference Proceedings,2647,1,050025,2022,AIP Publishing LLC
18. Рахимов, Бахтияр Саидович; Жуманиёзов, Сардор Пирназарович; ,Аппаратно-ориентированный алгоритм вычисления коэффициентов в базисах J-функций,Актуальные вопросы технических наук,,,59-62,2015,