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Study of Biopharmaceutical Properties of Recommended Capsules "Prostad" by in Vitro and in Vivo Method

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Abstract

It has been established that the dissolution test characterizes the biological availability of the drug as a first approximation, since in practice there is a very frequent correlation between the rate of dissolution and absorption. The study of the biological availability of drugs, preparations or their dosage forms usually begins with in vitro experiments and ends with in vivo experiments with further research in clinical conditions. The next series of experiments were devoted to studying the rate of release of active substances by the in vitro method from the recommended capsules "Prostad", obtained on the basis of the dry extract "Prostad". At present, there are standardized pharmacopoeial requirements for conducting the "Dissolution" test, which cover devices, dissolution media, temperature conditions, testing duration and statistical methods for processing the obtained results. In this experiment, the generally accepted "Rotating basket" method included in the State Pharmacopoeia of the Republic of Uzbekistan was used. This report presents the results of studying the pharmacological properties of the dry extract based on the narrow-leaved fireweed "Prostad" recommended for prostatitis by the in vitro and in vivo methods.

Keywords: Pharmacotechnological aspects, effective excipients, packaging materials, in vitro, in vivo, methods.

Introduction

Modern research by domestic and foreign scientists confirms the serious medicinal properties of fireweed, manifested, in particular, in gynecology and urology. And in terms of antioxidant properties, fireweed is one of the leaders among medicinal plants. It has a high protein number, i.e. the coefficient of anti-inflammatory action, because its value is used to judge the anti-

inflammatory properties of a particular substance. According to this indicator, fireweed is immediately after medical tannin and is followed by bergenia crassifolia, bearberry, oak. Moreover, whole leaves of fireweed have a relatively low protein number, while crushed ones have a significantly higher one [1,2]. Treatment with traditional medicine dates back to the appearance of man himself. Since ancient times, diseases have been treated with the help of various medicinal herbs and collections. Experience and observation of animals contributed to the expansion of human knowledge about the healing properties of medicinal plants. There are about 500 thousand species of herbs and plants in the world, but only about 5% of them have been more or less studied for pharmacological activity and are medicinal plants. In recent years, the problem of prevention and treatment of prostate hyperplasia and chronic prostate gland remains one of the most pressing issues in the field of medicine and pharmacy all over the world. Therefore, much attention is currently paid to research aimed at creating a group of dosage forms controlled by modern control methods. Much attention is paid to scientific research, such as the development of drugs based on raw materials of medicinal plants, standardization, study of factors affecting the quality of the finished product, study of pharmacotechnological aspects, and determination of shelf life. Having studied the local pharmaceutical market, the feasibility of introducing drugs into domestic pharmaceutical production was determined, which is important in reducing their import from other countries and creating convenience for the population. One of the priority tasks of modern pharmacy as a science is the development, creation and improvement of new effective drugs with increased bioavailability. Bioavailability of a medicinal substance is an objective characteristic of therapeutic effectiveness. In modern medical practice, an important place is given to medicinal products based on plant materials. In this regard, opportunities are opening up for the creation of highly effective dosed medicinal products with a targeted pharmacological effect. The solution to this complex problem is due to the requirement of a scientifically based approach to the creation of a drug [3].

It has been established that the solubility test characterizes the biological availability of the drug as a first approximation, since in practice there is a very frequent correlation between the rate of dissolution and absorption. The study of the biological availability of drugs, preparations or their dosage forms usually begins with in vitro experiments and ends with in vivo experiments with further research in clinical conditions. Pharmaceutical factors, as well as numerous other factors, affect the biological availability, i.e. technological operations, excipients, packaging materials, routes of administration of dosage forms, etc. play a special role [4,5]. Taking into account the above, the next series of experiments were devoted to studying the rate of release of active substances by the in vitro method from the recommended capsules "Prostad", obtained on the basis of the dry extract "Prostad". At present, there are standardized pharmacopoeial requirements for conducting the "Dissolution" test, which cover devices, dissolution media, temperature conditions, testing duration and statistical methods for processing the obtained results. In this experiment, the generally accepted "Rotating basket" method included in the State Pharmacopoeia of the Republic of Uzbekistan was used. This report presents the results of studying the pharmacological properties of the dry extract based on the narrow-leaved fireweed "Prostad" recommended for prostatitis by the in vitro and in vivo methods. [6].

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2. Experimental Section

2.1. Materials and Methods

This report presents the results of a study of the pharmacological properties of the dry extract based on narrow-leaved fireweed "Prostad" recommended for prostatitis using the in vitro and in vivo methods. Study of the dry extract "Prostad" specific activity using the in vivo method. The object of the study was the capsules "Prostad" recommended by us. As is known, the rate of release of the active substance is affected by various factors such as: the used excipients, the volume and pH of the dissolving medium, the speed of rotation of the basket. Object of research: "Ivan tea": Dry extract of narrow-leaved fireweed and the comparison drug "Prostamol® UNO", manufactured by Berlin-Chemie AG (Menarini Group), Germany.

3. Results and Discussions

To select the optimal pH value of the dissolving medium, the following dissolving media with different pH values were used. Purified water was used as a neutral medium, 0.1 N hydrochloric acid as an acidic medium, and 0.1 N sodium hydroxide as an alkaline medium.

In the experimental studies, the volume of the dissolving medium was 500 and 1000 ml. Figure 1 shows the results of studying the effect of the pH of the dissolving medium on the dissolution rate of Prostad capsules. The results obtained showed that the pH of the medium directly affects the dissolution rate of the recommended tablets. Since at a neutral pH, acidic and alkaline, the concentration of active substances that passed into solution in 45 minutes from the recommended capsules is 89.11%, 54.340% and 64.31%, respectively. However, at a neutral pH from the recommended tablets, the concentration of active substances that passed into solution in 45 minutes is higher, which in turn meets the requirements of the State Pharmacopoeia of the Republic of Uzbekistan.

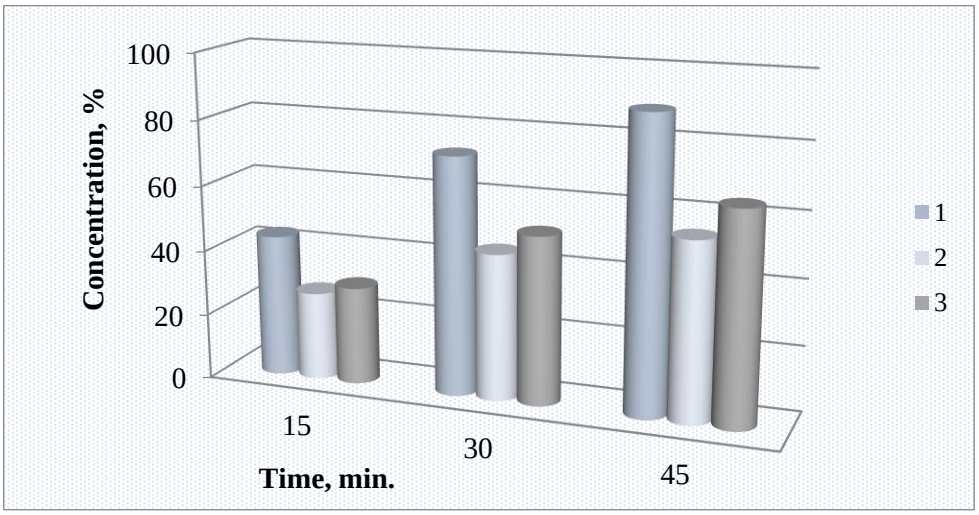

Fig. 1. Results of the study of the effect of the pH of the dissolving medium on the dissolution rate of the Prostad capsule

1 - neutral medium (purified water)
2 - acidic medium (0.1 N HCl solution)
3 - alkaline medium (0.1 N NaOH solution)

Based on the above and on the obtained data on the study of the effect of pH on the dissolution rate of the recommended Prostad capsules, we have determined the use of a neutral medium - purified water - for further research. At the second stage of the study, when developing the "Dissolution Test", the intensity of the release of biologically active substances, studies were conducted to establish the optimal speed of rotation of the basket. The experiments were carried out at basket rotation speeds of 50, 100, 150 and 200 rpm. Figure 2 shows the results of the experiment. From Figure 2 it is evident that the release of the active substance from the Prostad capsule at different basket rotation speeds occurs intensively.

It should be noted that at a basket rotation speed of 100 rpm, the concentration of active substances that passed into solution in 45 minutes is more than 75% (88.96%), which meets the requirements of the State Pharmacopoeia of the Republic of Uzbekistan. Thus, based on the above, for further study of the quality of the Prostad capsule from a biopharmaceutical point of view, a basket rotation speed of 100 rpm is recommended. Based on the obtained results on studying the effect of pH on the dissolution rate of Prostad capsules, the use of a neutral medium - purified water - is recommended for further studies. In the experiments, the volume of the dissolving medium was set at 1000 ml, which was chosen taking into account the sensitivity of the method we developed for the quantitative determination of active substances. The above results of biopharmaceutical studies are summarized in Tabl 1 and 2.

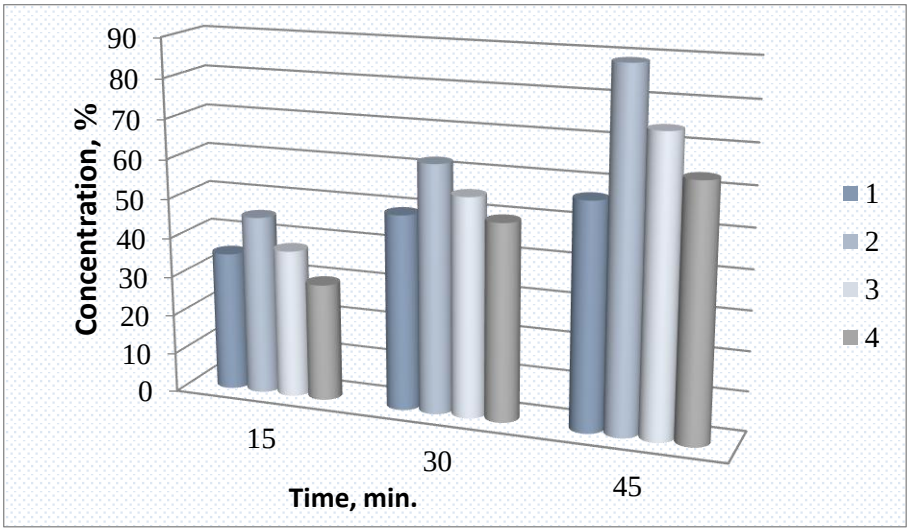

Fig. 2. Results of the study of the influence of the basket rotation speed on the intensity of the release of the active substance from the Prostad capsule

1- basket rotation speed 50 rpm
2- basket rotation speed 100 rpm
3- basket rotation speed 150 rpm
4- basket rotation speed 200 rpm

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Table 1 **Generalized results of the study of the effect of the pH of the dissolving medium on the dissolution rate of the Prostad capsule (n=5)**

№ Experiments		Time, min. 15	30	45	Average value, 45 minutes	Norm of the State Fund of the Republic of Uzbekistan - <, =75%
		pH of the environment				
		Neutral environment (purified water)				
1	Concentration, %	45,11	61,76	82,95	85,60	> 75%
2		44,87	64,62	88,37		
3		38,43	56,59	85,96		
4		28,84	49,99	83,85		
5		37,09	48,87	86,89		
Acidic environment (0.1N HCl solution)						
1	Concentration, %	25,74	37,42	59,33	57,63	< 75%
2		31,49	44,28	57,35		
3		26,38	29,43	69,12		
4		21,08	25,98	49,48		
5		25,64	37,26	52,86		
Alkaline medium (0.1N NaOH solution)						
1	Concentration, %	23,32	36,92	49,97	58,38	< 75%
2		28,76	48,89	62,43		
3		25,59	38,99	55,84		
4		23,51	41,85	58,37		
5		24,57	45,85	65,31		

Table 2 **Generalized results of the study of the effect of basket rotation speed on the intensity of release of the active substance from the Prostad capsule**

Basket rotation speed		*Time, min. 15*	*30*	*45*	*Norm of the State Fund of the Republic of Uzbekistan - <, =75%*
		pH of the environment			
		Neutral environment (purified water)			
50	*Concentration, %*	*35,27*	*49,32*	*56,81*	*< 75%*
100		*45,38*	*62,47*	*88,96*	*> 75%*
150		*37,57*	*55,19*	*74,12*	*< 75%*
200		*29,73*	*49,67*	*63,58*	*< 75%*
Acidic environment (0.1N HCl solution)					
50	*Concentration, %*	*25,87*	*36,78*	*49,75*	*< 75%*
100		*31,12*	*42,86*	*54,38*	*< 75%*
150		*19,97*	*28,91*	*39,75*	*< 75%*
200		*15,34*	*25,73*	*43,89*	*< 75%*
Alkaline medium (0.1N NaOH solution)					
50	*Concentration, %*	*23,54*	*33,42*	*45,52*	*< 75%*
100		*29,91*	*38,95*	*39,22*	*< 75%*
150		*24,58*	*35,87*	*42,28*	*< 75%*
200		*21,09*	*31,46*	*39,53*	*< 75%*

Thus, based on the above, the conditions of the dissolution test were selected for further study of the quality of the Prostad capsule.

For further research, it is recommended to use a neutral medium - purified water, the volume of the dissolving medium is set at 1000 ml and the basket rotation speed is selected at 100 rpm.

Specific activity. In this study, we evaluated the therapeutic effect of Dry extract of Fireweed "Ivan tea" in non-bacterial prostatitis caused by the introduction of carrageenan.

The experiment was conducted on 24 white male rats weighing 200 - 250 g. All experimental animals were divided into four groups (N = 6): 1-intact group, which did not receive carrageenan; 2-control group, non-bacterial carrageenan-induced prostatitis was reproduced without treatment; 3-experimental group reproduced non-bacterial carrageenan-induced prostatitis + extract of fireweed “Ivan tea” at a dose of 100 mg/kg, orally for 5 days; 4-experimental group reproduced non-bacterial carrageenan-induced prostatitis + “Prostamol® UNO” at a dose of 100 mg/kg, orally for 5 days;

To reproduce experimental non-bacterial prostatitis, experimental animals were anesthetized with urethane (1 g/kg, i.p.), and a small incision was made along the midline of the lower abdomen while maintaining asepsis. The urinary bladder and prostate were carefully exposed from the surrounding tissues. Carrageenan (Sigma, USA) was dissolved in sterile saline at a concentration of 1% and 50 µl was injected into the left and right ventral lobes of the prostate using a 27G needle. The wound was closed in layers, and antibacterial cream was applied to the wound [7,8].

The animals were treated with Dry extract of Fireweed “Ivan tea” at a dose of 100 mg/kg and “Prostamol® UNO” at a dose of 100 mg/kg, orally for 5 days after the injection of the carrageenan solution. The prostatic index (PI) of all rats was estimated as the ratio of prostate mass (mg) (mg/g) to rat body mass [9]. The obtained data were processed using the Excel software package. All data are presented as the mean value M±m standard deviation, the reliability of differences was estimated using the Student's criterion, the difference between groups was considered statistically reliable at $P<0.05$.

Results obtained: the results obtained in studying the effect of drugs on non-bacterial inflammation of the prostate gland of rats caused by carrageenan showed that in intact animals the absolute weight of the prostate averaged 289.1 ± 21.7 mg, and the prostatic index was 1.36 ± 0.07 (Table 2).

In control animals, with the introduction of carrageenan, the absolute weight of the prostate statistically significantly increased by 57.9% and the prostatic index was greater by 67.6% compared to the intact group.

When treating animals with Dry extract of Fireweed "Ivan tea" at a dose of 100 mg / kg, the absolute weight of the prostate and the prostatic index were significantly less by 49.2% and 61.7% compared to the untreated group, respectively. When treating animals with the drug "Prostamol® UNO" at a dose of 100 mg/kg, a positive effect was also noted, since after treatment, the absolute weight of the prostate and the prostatic index were significantly lower by 8.3% and 25.3% compared to the untreated group, respectively. "Ivan tea" and "Prostamol® UNO" in non-bacterial carrageenan-induced prostatitis. (Table 2.)

Table 2 **Study of the therapeutic effect of Dry extract of Fireweed**

Group	Absolute weight of the prostate, mg	Prostatic index, mg/g
Intact	289,1±21,7	1,36±0,07
Control	456,5±20,4 x	2,28±0,12 x
«Ivan tea», 100 мг/кг	305,9±27,1 y	1,41±0,07 y
«Prostamol® UNO», 100 мг/кг	421,7±69,7 y	1,82±0,23

Note: x - reliability of differences in comparison with the intact group at P< 0,05;
y - reliability of differences in comparison with the indicators of the control group at P< 0,05;

4. Conclusions

1. Thus, based on the above, the conditions of the dissolution test were selected for further research into the quality of the Prostad capsule. For further research, it is recommended to use a neutral medium - purified water, the volume of the dissolving medium is set at 1000 ml and the basket rotation speed is selected at 100 rpm.
2. The data obtained showed that the LD50 of the studied Dry extract of Fireweed "Ivan tea" was more than 5000 mg / kg and belongs to class V according to the classification of acute toxicity of chemical compounds.

REFERENCES

1. Nabatnikov S.A., Martirosyan L.Yu. Some aspects of the use of fireweed (Chamaenérion angustifolium). Agrarian science. 2022;(12):130-134.
2. Karomatov I. D., Turaeva N. I. Fireweed, Ivan-tea // Biology and integrative medicine. - 2016. - No. 6. - P. 160-169.
3. Yunusova H.M., Abdizhalilova Z.Kh., Ilkhamova N.B., Biopharmaceutical and pharmacological study of the properties of Ambrol tablets by in vitro and in vivo methods // Infection, immunity and pharmacology.-Tashkent-2020.- No. 3.- P.208-214.
4. Yunusova H.M., Abdizhalilova Z.Kh., Tulyaganov R.T., Pharmacological study of Ambroxol syrup // Infection, immunity and pharmacology.-Tashkent-2020.- No. 4.- P.166-171.
5. Yunusova H.M., Abdizhalilova Z.Kh., Tursunova M. Study of acute toxicity of expectorant elixir "Bronhotus forte" // Infection, immunity and pharmacology.-Tashkent-2020.-№5.- P.180-185.
6. Belenkiy M.L. Elements of quantitative assessment of pharmacological effect. L. Medgiz 1963, -152 p.
7. Polezhaeva I.V., Polezhaeva N.I., Levdansky V.A. Comparative study of the chemical composition of fireweed (chamerion angustifolium (l.) Holub). 133-138
8. Maksyutina N. P., Sereda P. I., Z. Kh., Bryuzgina T. S. Study of fatty acid composition of lipid complex of fireweed (Ivan-tea). Phytotherapy. Journal. 2010. No. 4. P. 93−95.
9. Kurkin, V.A. Modern aspects of chemical classification of biologically active compounds of medicinal plants / V.A. Kurkin // Pharmacy. - 2002. - V. 50, No. 2. - P. 8-16.
10. Alekseeva R.R. Phytotherapeutic sedative drug // International Journal of Applied and Fundamental Research. – 2016. – № 8-4. – P. 573-576.

11. Yunusova Kh.M., Abdijalilova Z.H. "Research On The Choice Of 'Ambronat' Syrup Technology" // The American Journal of Medical Sciences and Pharmaceutical Research, February 13, Vol. 03, Issue 02-01, 2021.-P. 1-9.
12. Yunusova Kh.M., Abdijalilova Z.H. "Research on the Selection of a Certain Content of 'Ambronat' Juice Syrup" // International Journal of Pharmacy and Pharmaceutical Research, Vol.:20, Issue:4, 2021.-P.62-71.
13. Yunusova Kh.M., Jaloliddinova M.Sh. Biopharmaceutical aspects of capsulirine drug based on NSAIDs // International Journal of Psychosocial Rehabilitation.-Vol. 24, Issue 04, 2020.-P.2258-2265.
14. N.B. Ilkhamova, Z.A. Nazarova, Kh.M. Yunusova. "Studying the effect of relative humidity and compaction pressure on the quality of tablets and pressed mass" // World Journal of Pharmacy and Pharmaceutical Sciences. 2019.-Vol. 8.-Issue 6.-P. 35-40.
15. N.N. Sherkhadjayeva, Kh.M. Yunusova, N.B. Ilkhamova. "On the choice of the composition of soluble tablets with licorice extract" // World Journal of Pharmacy and Pharmaceutical Sciences.-2019.-Vol. 8.-Issue 6.-P. 41-47.
16. Ravshanova S.E., Yunusova Kh.M. Evaluation of biopharmaceutical and pharmacological properties of combined ternary componential analgesic tablets // International Journal of Psychosocial Rehabilitation.-United Kingdom. 2020.-Vol. 24.-Issue 02.-P.6009-6017.
17. Yunusova Kh.M., Jaloliddinova M.Sh. Studying pharmacotechnological aspects and stability of “Ortof-S” tablets // World Journal of Pharmacy and Pharmaceutical Sciences.-2019.-Vol. 8.-Issue 1.-P. 277-288.
18. Kachalina T.V. Development of technology for obtaining solid dosage forms containing plant extracts: Dissertation Abstract, Candidate of Pharmaceutical Sciences / T.V. Kachalina.-Moscow, 2005.-26 p.
19. Larry L. Augsburger, Stephen W. Hoag. Pharmaceutical dosage forms: Tablets.- Informa Health Care, 2008.-568 p.
20. Cox D.C., Druglas W.B. et al. Guidance for dissolution testing // Pharm Technol. – 2008. – Vol. 4.- №1. – P.78-90.
21. Yunusova Kh.M., Samedinova D.N. Analysis of the volume and cost of import of metoclopramide tablets in the Republic of Uzbekistan // EPRA International Journal of Multidisciplinary Research.-2021.-Vol. 7, Issue 1.-P. 97 102.
22. Yunusova K. M., Abdijalilova Z.Kh., Zaynutdinov K.S. The Peculiarities of Studies on the Stability of Ambronat // International Journal of Current Science Research and Review ISSN: 2581-8341 Volume 07 Issue 02 February 2024 DOI: 10.47191/ijcsrr/V7-i2-18, Impact Factor: 7.943. P.1043-1049.
23. Kh.M. Yunusova, Sh.Kh. Sunnatov, M.Sh. Jaloliddinova, F.Zh. Anvarova On The Development Of The Technology For "Prostad" Capsules Based On Natural Origin Substances // Central Asian Journal of Medical and Natural Science 2024, 6(1),161-168
24. Guidelines in the Manual for experimental (preclinical) study of new pharmacological substances. Under the general editorship of Corresponding Member of the Russian Academy of Medical Sciences, Professor R. U. KHABRIEV. Second edition, revised and supplemented/. M.: - 2005. - M.: OJSC "Izdatelstvo" Medicine ", 2005.- 830 p.

25. Wu ZS, Wang HJ, Lee WC, Luo HL, Lin TK, Chuang YC. Low-Energy Shock Wave Suppresses Prostatic Pain and Inflammation by Modulating Mitochondrial Dynamics Regulators on a Carrageenan-Induced Prostatitis Model in Rats. Int J Mol Sci. 2023 Feb 15;24(4):3898. doi: 10.3390/ijms24043898. PMID: 36835316; PMCID: PMC9968097.
26. Can-Feng Lu, Xiang-Hu Meng, Hui-Bing Li, Hao Wu and Zhong-Ling Dou. Effect of Phellodendron chinense Extract on CarrageenanInduced Chronic Prostatitis in Rats// Tropical Journal of Pharmaceutical Research February 2015; 14 (2): 257-262.