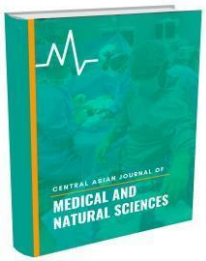

CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
https://cajmns.centralasianstudies.org/index.php/CAJMNS
Volume: 06 Issue: 01 | January 2025 ISSN: 2660-4159

Article

Kh.M. Yunusova. On The Development Of The Technology For "Prostad" Capsules Based On Natural Origin Substances

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Abstract: A promising direction in this field is the development of new preparations based on herbal medicines, such as narrow-leaved fireweed (Epilobium angustifolium). In light of the above, the search for and implementation of new, highly effective encapsulated plant-based medicinal forms is of particular interest. At the Department of Industrial Pharmaceutical Technology of the Tashkent Pharmaceutical Institute, studies are being conducted to explore the potential of extracting biologically active substances from narrow-leaved fireweed (Epilobium angustifolium) in the form of an extract, with the aim of developing an encapsulated medicinal form for the treatment of prostatitis and prostate adenoma. The article presents the results of a comparative study on the technological parameters and hygroscopicity of the dry extract and the encapsulated mass of "Prostad." During the experiments, the following technological characteristics of the dry extract were studied: moisture content, bulk density, angle of repose, and flowability coefficient. Additionally, the loss on drying, heavy metal content, and microbiological purity were determined using methods described in the literature and regulatory documentation.

Keywords: Phytotherapeutic, Capsule, Biologically, Moisture-Absorbing, Granulated, Dry Extract, Compressibility, Pressability, Gravimetric Method.

Citation: Kh.M. Yunusova. On The Development Of The Technology For "Prostad" Capsules Based On Natural Origin Substances. Central Asian Journal of Medical and Natural Science 2025, 6(1),161-168.

Received: 10th Oct 2024
Revised: 11th Nov 2024
Accepted: 24th Des 2024
Published: 27th Jan 2025

1. Introduction

In recent years, interest in herbal medicine—phytotherapy—has significantly increased. Due to the presence of biologically active substances, plant-based preparations gently affect the body as a whole and adjust altered functions. Natural bioactive substances complement and enhance each other mutually. This results not only in a phytotherapeutic effect on specific organs or systems but also in a substantial improvement in the body's overall resistance. Among natural remedies, medicinal plants and preparations derived from them hold primary value in medical practice. The development of highly effective, economically efficient, and stable dosage forms is one of the pressing tasks in pharmaceutical technology [1].

In modern medical practice, plant-based medicines hold a significant place. The flora of our country includes approximately twenty thousand plant species, many of which remain insufficiently studied and hold great potential to this day. At the beginning of the

last century, medicinal plants constituted 80% of all therapeutic agents. Over time, synthetic drugs gradually replaced them; however, plant-based medicines still occupy an important position in contemporary medicine. Recent research shows that the healing properties of medicinal plants are due to the optimal ratio and harmonious interaction of the biologically active substances they contain. These substances exhibit an evolutionary and genetic affinity with the human body, making them more compatible compared to synthetic drugs. Consequently, biologically active compounds from medicinal plants integrate more readily into vital processes and are more easily absorbed by the body.

Plant-based medicines are characterized by low toxicity, a broad spectrum of activity, a wide range of therapeutic properties, and good tolerance within therapeutic doses. When medicinal plants are used in rational combinations, their therapeutic potential expands. Furthermore, by incorporating various plant-based substances into a single formulation, a predictable pharmacological effect can be achieved. The production of galenic preparations also has the advantage of relative environmental safety, as the disposal of waste is relatively easy. Therefore, comprehensive research and the rational use of preparations derived from medicinal plant raw materials remain one of the most critical areas in pharmacy [2].

Despite the rapid development of synthetic organic chemistry, interest in natural compounds not only persists but continues to grow. Advances in high technology have made it possible to thoroughly study the composition of biologically active substances (BAS) in plants. This opens up opportunities for the development of highly effective, dosed medicinal products with targeted pharmacological effects. Addressing this complex task requires a scientifically grounded approach to drug creation.

According to WHO data, approximately 10-20% of the world's population primarily uses natural-origin medications. In Europe, leading countries in sales include Italy, France, and Germany, where herbal medicines account for over 25% of the pharmaceutical register. In the United States, there was a decline in herbal medicine production during the 1950s-1970s. However, by 2000, herbal medicines accounted for about 32% of the pharmaceutical market, and by 1994, this figure reached approximately 45% of total sales. In the Russian Federation, over 600 plant-based medicinal products are approved for medical use, representing roughly 40% of the drug nomenclature. According to the State Register of Medicines of Uzbekistan, unrefined or galenic preparations make up about 11.3%, with extracts accounting for 4.3%. Since gaining independence, the Republic of Uzbekistan has undergone significant changes in all spheres, including pharmaceuticals. The country has begun to establish its own system for regulating the circulation of medicines, medical devices, and equipment. It has also developed its own regulatory framework, carving out its independent path [2-3].

Research in the development of medicinal substances based on local raw materials is highly relevant, as it addresses issues related to providing the population with affordable and safe drugs. In recent years, the use of natural-origin medicines, particularly those derived from plant materials, animal organisms, and others, has gained increasing importance. Prolonged use of synthetic drugs often leads to various side effects, adverse impacts on the body’s organs and systems, and the emergence of resistant forms of pathogenic microorganisms. This justifies the growing interest of medical professionals in natural-origin medicines [3-5].

A promising direction in this field is the development of new preparations based on herbal medicines, such as narrow-leaved fireweed (Epilobium angustifolium). In light of the above, the search for and implementation of new, highly effective encapsulated plant-based medicinal forms is of particular interest. At the Department of Industrial Pharmaceutical Technology of the Tashkent Pharmaceutical Institute, studies are being conducted to explore the potential of extracting biologically active substances from narrow-leaved fireweed (Epilobium angustifolium) in the form of an extract, with the aim

of developing an encapsulated medicinal form for the treatment of prostatitis and prostate adenoma [1].

The aim of this study was to examine the technological and qualitative parameters of the dry extract obtained from narrow-leaved fireweed (Epilobium angustifolium) under the recommended methods and conditions, as well as the encapsulated masses—granulated masses based on it. The study of medicinal plants as a source of biologically active substances enables the development and introduction of new therapeutic drugs into medical practice. Experiments on the production of solid dosage forms from various materials have shown that the parameters of the technological process, as well as the properties of the finished product, depend on the entire set of physicochemical and technological properties of the starting materials. Physicochemical indicators significantly influence the technological properties of powdered medicinal substances. For optimizing production, it is crucial to study the relationship between the physicochemical and technological properties of materials, justify approaches to selecting optimal excipients, and develop an appropriate technological scheme for obtaining dosage forms [4-6].

2. Materials and Methods

In subsequent experiments, the influence of surface area on the moisture absorption kinetics of the proposed granules was studied. These experiments were conducted using the gravimetric method. Determination of the moisture content of the dry result using a device from the Japanese company "KETT".

This study develops encapsulated dosage forms from Epilobium angustifolium (narrow leaved fireweed) extract utilizing an experimental, analytical, and comparative methodology which integrates an approach designed to address the potential pharmaceutical use of this extract to treat prostatitis and prostate adenoma. The extract was evaluated systematically in terms of physicochemical and technological properties including moisture content, bulk density, flowability and compressibility. The moisture absorption kinetics of the dry extract and encapsulated mass were analyzed using advanced gravimetric techniques in response to varied environmental humidity conditions. Excipients were selected in order to improve technological parameters of the extract and thus optimize the formulation process by the achievement of higher flowability, compactness and diminished hygroscopicity.

The encapsulated mass was compared to the dry extract, and demonstrated significantly better performance maintaining their technological properties when exposed to high humidity, indicating enhanced stability. Dry extract's hygroscopicity tests showed that the limitations of dry extracts can only be addressed with optimized excipients. For moisture absorption, gravimetric analysis was used, with validated procedures to determine heavy metal content and microbiological purity employed. Taking a synthetic, comprehensive approach, a stable bioavailable and effective encapsulated formulation was created which is suitable for mass production. The results highlight the need for technology tailored development in pharmaceuticals, and represents a useful guide for development of therapeutic applications based on plant extracts. This methodology rigorously evaluates and refines material properties through the creation of a robust framework for the development of natural origin medicines in modern pharmaceutical engagements

3. Results and Discussion

Since the selection of the type and amount of excipients during the development of a dosage form is aimed at improving the properties of the substance, this study presents the results of a comparative analysis of the technological parameters and hygroscopicity of the dry extract and encapsulated mass of "Prostad." During the experiments, the following technological characteristics of the dry extract were examined: moisture content, bulk density, angle of repose, and flowability coefficient. Additionally, loss on drying,

heavy metal content, and microbiological purity were determined using methods described in the literature and regulatory documentation [7-10].

The study of the physicochemical properties of the dry extract of narrow-leaved fireweed (Epilobium angustifolium) revealed that the extracts are dry, hygroscopic, fine powders of dark brown color with a specific odor. The loss on drying was 3.56%, the heavy metal content was 0.0092%, and the moisture content of the dry extract, as measured using a "Kett" device from Japan, was 10.77%. The quantitative content of biologically active substances was 91.78%.

Further investigation into the technological properties of the dry extract showed that developing the technology for solid dosage forms would require the use of a complex of excipients and technological operations.

The study of technological parameters (particle size distribution, bulk density, flowability, angle of repose, compressibility coefficient, compactability coefficient, porosity, residual moisture, etc.) predicted unsatisfactory values for almost all technological properties.

Since the dry extract is characterized by hygroscopicity, poor compressibility, and insufficient flowability, it is not possible to obtain granules (for the preparation of tablets, for example, or encapsulated dosage forms) without incorporating excipients that enhance the technological characteristics of the mass [11-14].

The obtained data are presented in Table 1.

Table 1

Results of the Study on the Physicochemical Properties of the Dry Extract of Narrow-Leaved Fireweed (Epilobium angustifolium)

Properties	Indicators
◎ **Appearance**	The extracts are dry, hygroscopic, amorphous powders ranging in color from red to dark brown with a specific odor.
◎ **Authenticity**	Complies
◎ **Loss on drying, %**	3,56
◎ **Heavy metals, %**	less 0,0092
◎ **Moisture content, %**	10,77
◎ **Microbiological purity**	Complies
◎ **Quantitative content, %**	91,78

The above data indicate that this method of raw material extraction is the most rational, as it ensures maximum extraction of active substances and allows for the creation of a standardized finished product.

Alongside technological properties, the quality of the dosage form, storage conditions, and shelf life are significantly influenced by its ability to absorb moisture from the environment, i.e., hygroscopicity [2, 3, 21].

Given this circumstance, we also studied the moisture absorption properties of the dry extract compared to the encapsulated mass. The gravimetric method of determination (as recommended by Nosovitskaya and co-authors) was employed, which involved measuring the amount of absorbed moisture depending on the humidity of the surrounding environment [2, 15].

The gravimetric method determined the increase in absorbed moisture over time. Every 24 hours for 7 days, the samples in desiccators were removed, covered with lids,

and weighed on analytical scales with an accuracy of ±0.0001 g. The desiccators were thermostatted at a temperature of 22 ± 1°C.

The moisture absorption (W, %) was calculated using the formula:

B = (m-m0) / m0) x 100

Where:

- m is the mass of the sample at specific time intervals, g.
- m0 is the initial mass of the sample, g.

In this study, as recommended by the method, moisture absorption properties were examined in specialized climatic chambers with relative air humidity levels of 58%, 79%, 90%, and 100%. The humidity was artificially created using purified water (100%), saturated solutions of zinc sulfate (90%), ammonium chloride (79%), and sodium bromide (58%).

The obtained results confirm the rationality of the selected excipient complex in the development of the encapsulated dosage form. For instance, significant improvements were observed in indicators such as flowability ($5.91 \cdot 10^3$), bulk density (594 kg/m³), angle of repose (37°), compactness coefficient (2.02), and compressibility (85 N). At the same time, the encapsulated mass exhibited lower hygroscopicity compared to the dry extract. At 100% environmental humidity, the dry extract absorbed 17.39% moisture, losing its flowability properties by the end of the first day of observation, whereas the encapsulated mass absorbed a similar amount only by the fourth day. At 90% humidity, the dry extract lost its flowability by the third day of the experiment, while the encapsulated mass retained this property until the end of the study. In other cases, these properties were preserved.

The results of the study on the moisture absorption properties of the dry extract obtained from narrow-leaved fireweed indicate strongly pronounced hygroscopic characteristics of the dry extract samples.

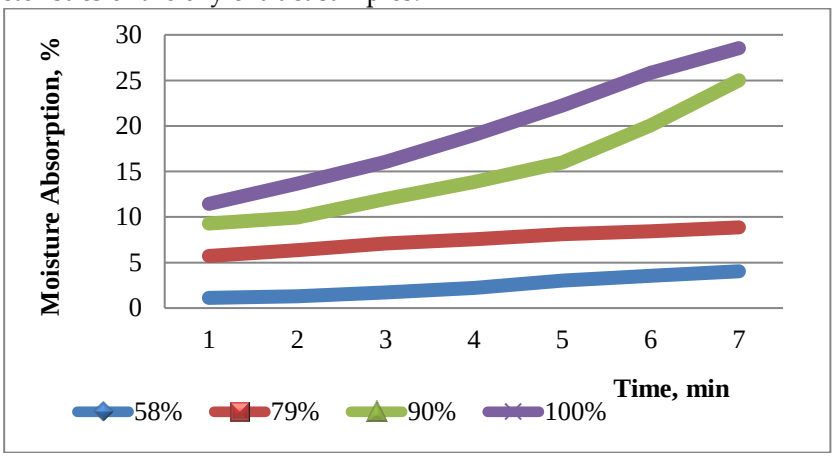

Fig. 1. Results of the Study on the Moisture Absorption Properties of the Dry Extract of Narrow-Leaved Fireweed (Epilobium angustifolium)

Thus, the results of the study on the moisture absorption properties of the dry extract indicate highly pronounced hygroscopic characteristics of the analyzed dry extract samples. These findings demonstrate their unsatisfactory properties for encapsulation and underscore the necessity of considering this factor when determining the storage conditions and shelf life of dosage forms prepared from the dry extract obtained using the recommended technology for narrow-leaved fireweed (Epilobium angustifolium) [23-25].

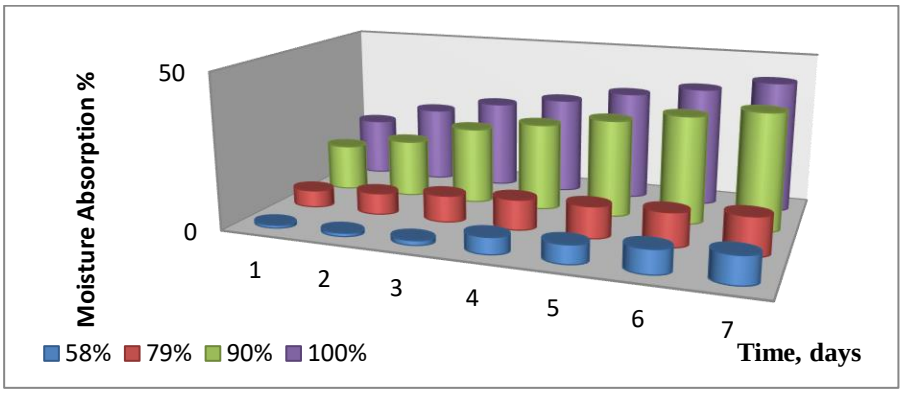

Fig. 2. Moisture Absorption of Granulated Mass at Different Relative Humidity Levels of the Environment

The study results showed that at 100% relative humidity, the granulated mass lost its flowability within 5 days, absorbing 22.16% moisture. By the end of the 7th day, it had absorbed 29.42% moisture and turned into a wet mass. At 58% and 79% relative humidity, the granulated mass absorbed 4.02% and 9.44% moisture, respectively.

In subsequent experiments, the influence of surface area on the moisture absorption kinetics of the proposed granules was studied. These experiments were conducted using the gravimetric method at 58% relative humidity.

Samples placed in all three containers retained their flowability until the end of the experiments, absorbing between 1.06% and 1.21% moisture. Based on the results, it can be concluded that increasing the surface area of the sample slightly enhances the moisture absorption properties of the studied mass [16-18].

The obtained results are presented in Table 2.

Table 2

Conditions for Conducting Studies on the Moisture Absorption Properties of the Granulated Mass

Study of Moisture Absorption Depending on:						
Relative Humidity of the Environment				Surface Area of the Sample		
No.	Initial Mass of the Sample m0, g	Relative Humidity of the Environment, %	Diameter of the Container *d*, cm	Initial Mass of the Sample m^0, g	Diameter of the Container d, см	Surface Area of the Sample S, g/m^2
1	0,4976	100	2,5	0,4988	3,5	8,61
2	0,4949	90	2,5	0,4979	3,0	5,45
3	0,4955	79	2,5	0,5131	2,5	3,22
4	0,5101	58	2,5	0,4979	3,0	3,11

4. Conclusion

Thus, the above results indicate a rational approach to selecting the excipient complex during the development of encapsulated dosage form technology. The study results showed that at 100% relative humidity, the granulated mass lost its flowability within 5 days, absorbing 22.16% moisture. By the end of the 7th day, it had absorbed 29.42% moisture and turned into a wet mass. At 58% and 79% relative humidity, the

granulated mass absorbed 4.02% and 9.44% moisture, respectively. Samples placed in all three containers retained their flowability until the end of the experiments, absorbing between 1.06% and 1.21% moisture. Based on the results, it can be concluded that increasing the surface area of the sample slightly enhances the moisture absorption properties of the studied mass.

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