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DEVELOPMENT OF TABLET TECHNOLOGY QUALITY CONTROL BASED ON GERANIUM COLLINA (*GERANIUM COLLINUM* STEPH.)

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ABSTRACT
The article presents scientific studies of dosage forms obtained on the basis of a plant growing on the Uzbekistan Geranim collina - (Geranium collinum Steph.) Studied obtaining a dry extract from a plant Geranium collina with different extractants, methods for its preparation, the optimal method for obtaining a dry extract is substantiated. The article also describes the phators that influence the production of dry extracts such as the choice of extractant, hydromodule, degree of grinding of raw materials, quality assessment and standardization. Based on the obtained dry extract of Geranium collina, a solid dosage form - tablets, was obtained. Their technological parameters were studied, as well as quality assessment and expiration dates.

KEYWORDS: *extractant, Geranim collina, dry exstrakt, tablets, percolation, tannins, hydromodule.*

INTRODUCTION

With the aim of treating various pathologies around the world, much attention is paid to scientific research on the development of highly effective and safe medicinal products derived from medicinal plants. In this regard, the creation of technologies for the production of dosage forms based on medicinal plants used in inflammatory diseases and hypoxia, a decrease in the share of drugs imported from foreign countries, as well as an increase in the number of products manufactured at domestic pharmaceutical enterprises, occupies an important place.

With the aim of treating various pathologies around the world, much attention is paid to scientific research on the development of highly effective and safe medicinal products derived from medicinal plants. In folk medicine, a decoction from the underground organs of Geranium collina. Is used by the local population for gastric diseases as a hemostatic agent in the postpartum period and hemoptysis, as well as an astringent and fixing agent [6].

In Uzbekistan, growing in natural thickets, hill geraniums are found from the foothills to the middle zone of the mountains of Tashkent, Andijan, Ferghana, Samarkand and Surkhandarya regions of our Republic [9].

A complete pharmacognostic study of hill geranium shows that the underground parts of the plant contain high-quality biologically active substances, tannins up to 23%, as well as carbohydrates, monosaccharides, water-soluble polysaccharides, pectins, hemicelluloses of organic acids, amino acids, vitamin C and flavonoids with antihypoxic and anti-inflammatory actions in medical practice [3, 9].

MATERIALS AND METHODS

The indicators affecting the process of obtaining a dry extract were studied: the concentration of the extractant, the degree of grinding of the raw material, the influence of the process hydromodule, determination

of the drying temperature, as well as the results of qualitative and quantitative indicators of the dry extract. Each stage was analyzed from a scientific point of view, the most optimal method, extractant, water module and the degree of grinding of the raw material were selected, their quality and standardization were evaluated [1, 7].

Considering the complexity of the technological process for obtaining dry extracts of tannins enriched with tannins from hill geranium using various extractants, the high cost of the extractor and a small percentage of yield, dry extracts were obtained from the underground part of hill geranium using official methods: maceration, repercolation and percolation, factors were studied, affecting the process of obtaining dry extracts [5].

The advantages of the official percolation method in contrast to other methods were the simplicity of the method, the low cost of the extractant, the convenience of production in industry, and the high yield of dry extract [10].

Qualitative and quantitative indicators of the dry extract obtained by percolation were determined by the methods given in the State of Pharmacopoeia(SPh)-XI edition [7, 8].

RESULTS AND DISCUSSION

Dry extract of geranium hill in terms of qualitative and quantitative indicators meets the requirements of the general pharmacopeia article of the State of Pharmacopoeia of the XI-th edition of "Extracts". When determining tannins on 5 series of dry extract of geranium collina, an average value of 61.65% was established [7, 8] (Table 1).

Table 1
The results of qualitative and quantitative indicators of dry extract of *Geranium collina*

Defined indicators	Norm on ND	Results	Determination methods
Appearance	Hygroscopic brown powder, with a peculiar smell, astringent taste	Meets ND requirements	Organoleptic
Authenticity: tannins	With iron-ammonium alum, the sediment is black and green.	Satisfactorily	Qualitative reaction to tannins
Humidity, %	Should not exceed 5%	4.9	SPh XI 2-vol. 161.
Heavy metals	Should not exceed 0.01%	Less than 0.01%	SPh XI 2-vol. 161.
Microbiological purity	In 1 g of the drug, the total number of aerobic bacteria did not exceed 10 CFU, the total number of fungi was 10 CFU, the bacteria Esherichia coli were not observed.	Meets ND requirements	Change No. 2 SPh XI 2-edition, category 4A
The amount of tannins, %	Not less than 51%	61.65%	Permanganato-metric titration

Preclinical studies of dry extract of geranium collina were carried out, its low toxicity and a single therapeutic dose of 0.1 g were determined.

To develop a scientifically-based composition and technology for the production of solid dosage forms - tablets for oral administration, convenient for transportation, dosage, having high performance, and resistant to environmental influences, the technological parameters of the dry extract of geranium hillum were studied, taking into account the hygroscopic properties of the dry extract for the selection of species and the amount of excipients used.

Despite the fact that the bulk density (520,0 kg/m3) and the humidity (4,9%) of the dry extract of hill geranium meet the requirements, flowability ($4{,}6\times10^{-3}$ kg / s), compressibility factor (3,0 K) and compressibility, unsatisfactory for obtaining tablets by direct compression. And this, in turn, indicates that to obtain tablets by wet granulation, it is necessary to use loosening, antifriction and binders from auxiliary substances.

In the following experiments, to study the technological parameters of tablet masses of dry extract of geranium hillock, various compositions were prepared by wet granulation using 96% ethanol as granulating substance, as well as excipients such as fillers, disintegrants, and antifriction substances (Table 2).

According to the results of a comparative study of the technological parameters of tablet masses obtained by 7 compositions, it was shown that tablets prepared according to composition No. 3 had positive technological properties and met the requirements (Table 3).

Table 2
The composition of the tablets of dry extract of *Geranium collina* 0.1 g obtained by wet granulation

№	Ingredients	Compositions, (g.)						
		№1	№2	№3	№4	№5	№6	№7
1.	Dry extract of *Geranium collina*	0.100	0.100	0.100	0.100	0.100	0.100	0.100
2.	Potato starch	-	0.0284	0.0284	0.03	-	0.3	0.0268
3.	Lactose	-	0.03	0.03	-	0.03	-	-
4.	Sodium bicarbonate	0.0284	-	-	-	0.0276	-	0.0284
5.	MCC	0.03	-	-	0.0284	-	0.0284	-
6.	Calcium stearate	0.0016	-	0.0016	0.0016	-	0.0016	-
7.	Talc	-	0.0016	-	-	0.0024	-	0.0048
	Average weight, g	0.16	0.16	0.16	0.16	0.16	0.16	0.16

Table 3
The results of a study of the technological properties of tablet masses of dry extract of geranium collina

The studied indicators	The composition of the tablet masses						
	№1	№2	№3	№4	№5	№6	№7
Fractional composition: -1000+500- -500+310- -310+250 -250	 18.0 20.8 35.8 25.4	 10.45 42.4 37.10 10.05	 8.75 35.4 49.37 6.48	 30.4 25.7 34.9 9.0	 50.2 10.4 37.2 2.2	 5.6 36.7 31.4 11.3	 40.1 37.0 5.0 7.9
Friability, 10-3kg / s	4.8	3.5	8.5	5.0	3.8	7.2	6.4
Bulk density, kg / m3	435.0	550	615.0	395.0	580.0	470.0	450.0
Compressibility, N	35	55	50	40	50	30	35
The compressibility factor, K	2.4	3.5	1.9	5.4	2.2	5.7	6.8
Residual humidity,%	4.9	6.1	7.5	6.4	8.3	6.9	11.5

A technology was developed for producing tablets of dry extract of geranium by the hill method of wet granulation using excipients according to the scientifically sound composition No. 3, which showed positive technological properties, the tablets are given the conventional name “Geratan”.

The composition and technology of tablets "Geratan". Composition per 1 tablet, g:

Dry extract of geranium collina-0.100
Lactose -0.03
Starch – 0.0284
Calcium Stearate – 0.0016

Average tablet weight 0.16g

Technology. Sifted separately through a sieve with a hole diameter of 150 μm, dry extract of *Geranium collina* and auxiliary substances (lactose and 5% starch previously dried to a moisture content) are thoroughly mixed, moistened with 96% ethyl alcohol until an optimum wet mass is formed. The wet mass is passed through a sieve with a hole diameter of 2000 μm and dried in an oven at 30-40 ° C to a residual moisture content of 7,5-8,0%. The mass is re-passed through a sieve with a hole diameter of 1000 μm, dry granulation is carried out. The mass is dusted with pre-sieved calcium stearate and get tablets "Geratan" with a diameter of 7 mm, an average weight of 0,16 g on a tablet machine.

In the development of tablet technology, quality assessment is considered one of the final stages of importance. The quality assessment of "Geratan" tablets was carried out in accordance with the requirements of the general pharmacopoeial article “Tablets” (SPh XI edition) and current regulatory documents (ND), the quantitative content of tannins was determined by the permanganometric method and standardized (Table 4).

Tablet 4
Results of quality assessment and quantitative analysis
"Geratan" tablets

The studied indicators	Indicators according to the requirements of ND	Results
Appearance	Brown color, the edges are smooth, rounded in shape, with a smooth surface	Compliant
Authenticity: tannins	With iron-ammonium alum, the sediment is black and green.	Compliant
Diameters mm	Must be within 2,1-3,3mm	2.5 mm
The ratio of height to diameter,%	Must be between 30-40%	34%
The average mass and deviations from it, g,%	Not more than ± 7.5%	0.162+3.0 0.162-2.8
Disintegration, min	Up to 15 minutes	8-10 min
Breaking Strength, N	Must be at least 30.0 N	55.0
Abrasion resistance	97.0-100	98.6
Dissolution, 45 min	Must be at least 75%	86.02
Microbiological purity	Change No. 2 to the State Parmacop. XI 2-volume, category 4A	Satisfactorily
The amount of tannins, g	Must be between 0,051 g and 0,065 g	0.0586

When conducting one of the biopharmaceutical studies using the in vitro method to determine the rate of release of the active substance from tablets, the studies were carried out using the official method on the Rotating Basket instrument at rotation speeds of 50, 100, 150 and 200 revolutions.

The solubility of the "Geratan" tablets corresponded to the requirements and at a basket rotation speed of 100 revolutions per minute fit straight, the possibility of dissolving the tablet at a given rotation speed was proved. The amount of active substance released from the tablet after 45 minutes was 86.02% and it became possible to reliably evaluate the bioefficiency of the tablet (Figure 1).

A number of experiments were conducted to select the excipients that make up the "Geratan" tablets: loosening, binders and antifriction substances, their scientifically sound choice was confirmed by the evaluation of the quality of the tablets.

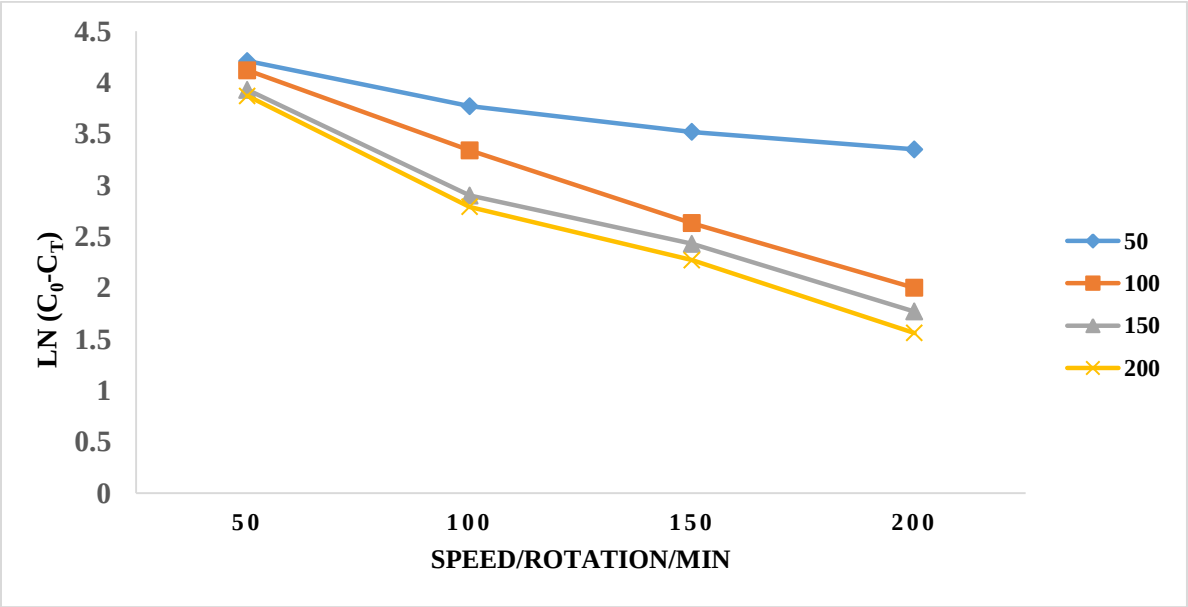

Figure 1. Antilogorim under the curve of the pill "Geratan"

CONCLUSION

Dry extracts were obtained from the underground part of hill geranium (*Geranium collinum* Steph.) growing in Uzbekistan, factors affecting the process of obtaining dry extracts were studied and quality assessment was carried out.

Dry extract of geranium collinal in terms of qualitative and quantitative indicators meets the requirements of the general pharmacopoeial article of the State pharmacopoeia of the XI-th edition of "Extracts".

A technology was developed for producing tablets of dry extract of geranium by the hill method of wet granulation using excipients of a scientifically sound composition.

Quality indicators and results of the quantitative analysis of "Geratan" tablets, the proposed technology met the requirements of the general pharmacopoeial article "Tablets" of the State pharmacopoeia of the 11th edition.

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