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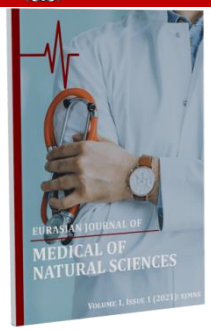

RESEARCH ON THE DEVELOPMENT OF CAPSULE COMPOSITION AND TECHNOLOGY BASED ON DRY EXTRACT FROM WALNUT LEAVES

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ABSTRACT
This article presents the results of research aimed at selecting the optimal composition and developing the technology of capsules based on dry extract obtained from walnut leaves. For this purpose, encapsulated masses were prepared using widely used fillers and moisturizing agents, and their pharmaco-technological indicators were evaluated. As a result, it was established that the most optimal filler for a biologically active additive in the form of a capsule containing a dry extract of walnuts as an active substance is a 1:1 ratio of microcrystalline cellulose and aerosil, a moisturizing agent is a 10% starch solution. Based on this composition, the technology of capsules based on dry walnut extract was developed.

ИССЛЕДОВАНИЯ ПО РАЗРАБОТКЕ СОСТАВА И ТЕХНОЛОГИИ КАПСУЛ НА ОСНОВЕ СУХОГО ЭКСТРАКТА ИЗ ЛИСТЬЕВ ГРЕЦКОГО ОРЕХА

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ABSTRACT
В данной статье представлены результаты исследований, направленных на выбор оптимального состава и разработку технологии капсул на основе сухого экстракта, полученного из листьев грецкого ореха. С этой целью были приготовлены инкапсулированные массы, с использованием широко применяемых наполнителей и увлажняющих агентов и оценены их фармакотехнологические показатели. В результате установлено, что наиболее оптимальным наполнителем

вещества, фармако-технологические показатели, технология.

для биологически активной добавки в виде капсул, которые в качестве активного вещества в своём составе содержат сухой экстракт грецкого ореха, является соотношение микрокристаллической целлюлозы и аэросила 1:1, увлажняющим агентом является 10% раствор крахмала. На основе этого состава, была разработана, технология капсул на основе сухого экстракта грецкого ореха.

Introduction. Walnut (*Juglans regia* L.) is a medicinal plant widely used in folk medicine and homeopathy and belongs to the Walnut family (*Juglandaceae*). Today, almost all parts of the plant are used as medicinal raw materials: leaves, lateral roots, bark of branches, green bark at the time of fruit collection, raw fruits at the milky stage [1-5].

The great physicians of their time, Abu Ali ibn Sina, Farabi, al-Aqimi and others, noted these advantages of walnuts in their works. Among the 1400 medicines mentioned in Ibn Sina's works and derived from plants, one of the most widely used is walnut (*Juglans regia* L.). According to the "Canon of Medicine," the great physician used freshly harvested and fried walnuts, walnut peel, oil, and freshly squeezed juice as a astringent, hemostatic, drying, wound healing, and anti-inflammatory remedy.

Information is also provided on the anthelmintic effect of walnuts consumed in large quantities. At the same time, this plant was also used as an antidot [1].

Abu Ali ibn Sina used the fruit, bark, roots, and branches of walnuts to treat nervous system, weakness, cardiovascular system, splenic inflammation, stomach, gallbladder, rheumatism, goiter, teeth, and throat pain [6,7].

Analysis of the literature on the study of the chemical composition of various parts of walnuts, the development, standardization and pharmacological properties of medicinal preparations based on plant raw materials shows that all parts of the plant have a rich chemical composition, which determines its multifaceted pharmacological effect. [2,3,4,8,9,10,11,12,13].

Purpose of the study: Selection and development of a technology for the composition of a biologically active additive in capsule form based on a dry extract obtained from walnut leaves.

Materials and methods: A dry extract from walnut leaves was chosen as the active substance. Various auxiliary substances were used to select the composition of the biologically active additive in capsule form based on it. In this case, microcrystalline cellulose (State Pharmacopoeia of the Republic of Uzbekistan I ed., Ph. Eur.), aerosil (CAS:9005-84-9), lactose monohydrate (Ph. Eur.); as a moisturizing agent - purified water (FS 42 Uz 0511-2022), ethyl alcohol (State Pharmacopoeia of the Republic of Uzbekistan I ed.), potato starch solutions (State Pharmacopoeia of the Republic of Uzbekistan I ed., Ph. Eur.) was used.

In this case, the dose of the active substance (dry extract) was set at 0.15 g. Based on the bulk density of the dry extract, the expediency of using "1" size gelatin capsules was determined.

Pharmaco-technological indicators of encapsulated masses prepared as models were determined according to the methods given in the State Pharmacopoeia of the Republic of Uzbekistan I ed. and the State Pharmacopoeia of the Russian Federation XIV ed. [14,15].

Results and discussion. To determine the joint mass-forming ability of the active substance, filler, and moisturizing agent, 20 samples of compositions were prepared, which are presented in Table 1.

Table 1

Samples of mixtures of dry walnut extract with various fillers and moisturizing agents

Fillers	Humidifying agent			
	purified water	70% ethyl alcohol	40% ethyl alcohol	10% starch paste
microcrystalline cellulose	1	2	3	4
aerosil	5	6	7	8
lactose monohydrate	9	10	11	12
microcrystalline cellulose + aerosil (1:1)	13	14	15	16
microcrystalline cellulose + lactose (1:1)	17	18	19	20

The masses obtained from these samples were granulated and analyzed according to the following indicators: ease of technological processes such as mixing, wetting, granulation, as well as positive indicators such as flowability and angle of natural deviation. In this case, it turned out that the dispersibility with vibration should be greater than $5.0*10^{-3}$ kg/s, and the angle of natural deviation should be in the range of 25-45 degrees.

In this case, when 70% and 40% ethyl alcohol were used as a moisturizing agent, the masses formed easily, did not stick to the hand, but the granules formed after granulation were brittle, which led to an increase in the proportion of fine fractions. When using purified water as a moisturizing agent, regardless of the type of filler used, the masses were viscous, ductile and the granulation process was difficult.

Taking the above into account, for the next stage of research, samples of the mass formed by the moisturizing agent with 10% starch paste were selected: compositions №4,8,12,16,20. The technological indicators of the masses prepared according to these compositions (fractional composition, friability with vibration, angle of repose, bulk density after compaction, granule decomposition, and residual moisture content) were determined. The obtained results are presented in Table 2.

Table 2

Technological indicators of encapsulated masses prepared using a 10% starch solution as a moisturizing agent

Indicator	Unit of measurement.	Samples				
		№4	№8	№12	№16	№20
Fractional composition -1000 μm + 500 μm -500 μm + 355 μm -355 μm + 250 μm -250 μm + 180 μm -180 μm + 63 μm -63 μm	%	30,61 27,34 23,95 10,87 5,56 1,67	18,92 23,15 27,38 19,96 6,71 3,88	13,37 17,20 28,34 25,33 10,60 5,16	36,14 26,60 20,38 13,74 2,06 1,08	31,8 24,29 21,25 14,73 5,29 2,64
Vibro-oscillation scattering	10^{-3} kg/s	8,43 ±0,96	7,14 ±0,83	6,11±0,62	9,22 ±1,05	7,86 ±1,18
Natural angle of deviation	degree	34,0±2,0	38,0±2,0	44,0±3,0	31,0±2,0	37,0±2,0
Bulk density after compaction	kg/m^3	629,59±37,16	520,07±26,49	482,34±44,09	676,41±24,59	566,80±56,02
Granule decomposition	min.	5,50±0,40	6,05±0,35	7,25±0,30	5,15±0,20	6,55±0,35
Residual moisture	%	2,49±0,26	2,38±0,41	1,76±0,28	2,46±0,12	1,97±0,48

All technological parameters of the encapsulated mass are important, but according to the literature, the bulk density indicator is the main parameter that allows obtaining a product of the same dosage and quality. According to the results presented in Table 2, when lactose was used as a filler (sample №12), the proportion of fine fractions was greater, and the flowability indicator was lower than that of other masses (6.11±0.62*10^{-3} kg/s). Similar results were also observed when using aerosil as a monofiller and the vibration dispersibility of this mass was 7.14±0.83*10^{-3} kg/s. In the remaining samples, when using microcrystalline cellulose itself (Sample №4) and aerosil and lactose (Samples №16 and №20), this technological indicator was significantly higher and amounted to 8.43 ±0.96*10^{-3} kg/s, 9.22 ±1.05*10^{-3} kg/s, 7.86 ±1.18*10^{-3} kg/s.

It is known that the angle of natural deviation is in the range of 25-45 degrees, which is the reason why the bulk density of the mass is characterized as good. All analyzed masses met this requirement, but this indicator of the lactose-prepared composition was equal to 44.0±3.0 degrees and had a limiting value. The natural deviation of the samples prepared from aerosil and a mixture of microcrystalline cellulose and lactose was close to each other and was 38.0±2.0 degrees and 37.0±2.0 degrees, respectively. The most positive natural

deviation angle was observed in samples №4 (34.0±2.0 degrees) and №16 (31.0±2.0 degrees).

Taking the above into account, a sample prepared according to composition №16 with the highest flowability indicator was selected for further research. Another reason for this is that the proportion of fractions smaller than 0.2 μm in granulated masses should not exceed 5%. And it is the composition №16 that meets this requirement (3.14%).

Determination of the bulk density indicator after compaction made it possible to divide the encapsulated masses from which the fillers were prepared into two groups: namely, samples №8, №12 and №20 - light powders (520.07±26.49 kg/m^3, 482.34±44.09 kg/m^3, 566.80±56.02 kg/m^3), samples №4 and №16 (629.59±37.16 kg/m^3, 676.41±24.59 kg/m^3) - medium powders.

The granule decomposition time was in the range of 5.15±0.20 - 7.25±0.30 minutes, with the best indicator observed when using microcrystalline cellulose itself and a mixture with aerosil in a 1:1 ratio. However, the decomposition time of the granules in other samples meets the requirements of regulatory documents. The residual moisture content did not exceed the established 3% and was found to be in the range of 1.76±0.28 - 2.46±0.12%.

As a result of a comparative study of the technological indicators of the sample masses, it was established that the most optimal filler for a biologically active additive in the form of a capsule containing dry walnut extract as an active substance is a 1:1 ratio of microcrystalline cellulose and aerosil, and the moisturizing agent is a 10% starch solution.

The technological process of obtaining capsules is shown in picture 1 and is proposed in the following sequence: the required amount of dry walnut extract, microcrystalline cellulose, aerosil, and potato starch are sifted and weighed through a sieve with a hole diameter of 150 μm. A 10% potato starch solution is prepared according to the technology described in the VII ed. of the State Pharmacopoeia.

According to the general rules for preparing powders, microcrystalline cellulose and aerosil are mixed, then dry extract is added and mixed until a homogeneous mass is obtained. Then, while constantly stirring, it is moistened with a 10% potato starch solution, and the prepared mass is dried in a drying oven at a temperature of 40-50°C to a residual moisture content of 10-15%. Then the mass is granulated by grinding and continued to dry in the drying cabinet until optimal moisture content (2-3%) is obtained. The obtained granulated mass is packaged in capsules numbered "1" in the amount of 0.25 g.

Conclusion. The optimal composition of capsules based on dry extract from walnut leaves was selected. In this case, based on the bulk density of the active substance, the expediency of using gelatin capsules with the number "1" has been proven. It was established that the optimal filler for the biologically active additive in capsule form is a 1:1 ratio of microcrystalline cellulose and aerosil, and the moisturizing agent is a 10% starch

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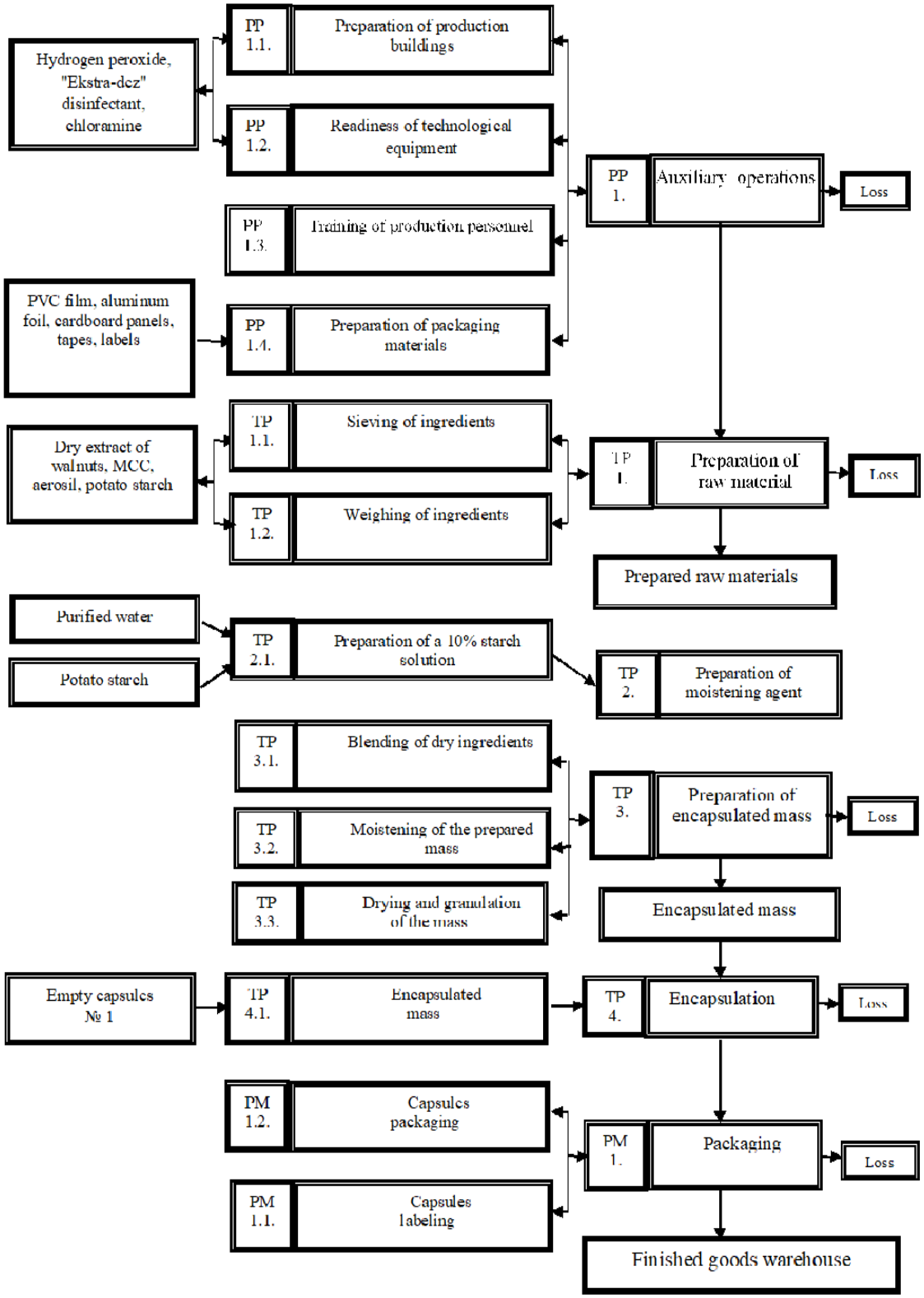

Picture. 1. Technological scheme for obtaining capsules containing dry walnut extract

solution. The technology of capsules based on dry walnut extract according to this composition was developed based on the wet granulation method.

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