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PREPARATION AND STUDY OF THE SUBSTANCE OF MULTICOMPONENT DRY EXTRACT OF BELISA AS A STAGE OF PHARMACEUTICAL DEVELOPMENT OF SEDATIVE CAPSULES

O. Shmalko, L. Vyshnevska, D. Soldatov

Мета роботи. *Науково та експериментально обгрунтувати отримання та вивчення властивостей багатокомпонентного екстракту сухого Беліса з метою формуляції капсульної суміші на його основі, враховуючи вимоги настанови ICQ 8 «Фармацевтична розробка».*

Методи. *Для визначення вологості, насипної густини та насипної густини після усадки, фракційного складу отриманого багатокомпонентного екстракту сухого Беліса та модельних сумішей з допоміжними речовинами на його основі, було використано фізико-хімічні і фармакотехнологічні методи дослідження.*

Результати. *У результаті проведених експериментальних досліджень було отримано багатокомпонентний екстракт сухий Беліса. Визначено вологість, насипну густину та насипну густину після усадки, плинність отриманого екстракту та семи модельних сумішей з ним і проведено мікроскопічний аналіз. За результатами експерименту, сухий екстракт без додавання допоміжних речовин протягом 2 діб втрачав сипкість, що спонукало до використання допоміжних речовин у подальшій його технології. Для покращення технологічних властивостей екстракту сухого Беліса виготовляли модельні зразки з різними допоміжними речовинами (аеросил у кількості 1, 2 та 3 % і мальтодекстрин у кількості 2, 3 та 4 %) та за різною технологією.*

Висновки. *Вивчено фізико-хімічні і фармакотехнологічні властивості багатокомпонентного екстракту сухого Беліса та його модельних зразків з низкою допоміжних речовин. Вивчено вологість, насипну густину та насипну густину після усадки, фракційний склад. За результатами експериментальних досліджень розроблено технологію та складено технологічну схему отримання багатокомпонентного екстракту сухого Беліса і визначено критичні параметри його виробництва*

Ключові слова: *склад, технологія, багатомпонентний екстракт сухий, допоміжні речовини, ICQ 8 «Фармацевтична розробка»*

1. Introduction

According to the World Health Organization, the rational use of medicines is their use when patients receive drugs according to clinical need, in doses that meet individual needs, for an adequate period of time and at the lowest cost to themselves and society. Currently, more than 50 % of drugs in the world are prescribed, dispensed or sold inappropriately, half of patients do not use them properly, and a third of the world's population does not have access to the necessary drugs.

Pharmaceutical development is a comprehensive study of drug development, which convincingly demonstrates that the selected dosage form, the proposed composition, primary packaging, production technology and quality control meet the intended purpose. In the process of pharmaceutical development in the creation of drugs using different approaches. One of the stages is the development of evidence-based composition of the drug and the concentration of all ingredients (APIs and excipients) given their functional purpose, safety, availability [1].

Research on obtaining and studying the pharmaco-technological properties of extracts was conducted by a whole constellation of scientists. In particular, a number of experimental studies by Gladukh E. V. and Korotkova V. A. are devoted to the extraction of the fruits of Maclura pomifera with the use of methods: maceration, extraction with variable pressure, extraction using a rotary pulsation apparatus [2, 3].

Ruban O. A. and co-authors used the methods of microscopic analysis, determination of moisture absorption, fluidity, bulk density, compressibility of the obtained dry extract of Vaccinum myrtillus leaves due to unsatisfactory performance to obtain tablets [4].

Experimental research by Shmalko O. O. et al. devoted to obtaining an extract of dry extract of urocholum and the study of its pharmaco-technological and physico-chemical properties [5].

The aim of the work was to obtain and study the properties of a multicomponent dry extract of Belisa in order to formulate a capsule mixture based on it, taking into account the requirements of ICQ 8 “Pharmaceutical Development”.

2. Research planning (methodology)

Within one of the stages of pharmaceutical development of the drug in the form of capsules, our task was to obtain a multicomponent dry extract and study of its properties.

On the domestic pharmaceutical market there are Belisa oral drops obtained by extraction of a mix-

ture of medicinal plant raw materials (Passiflora herba, Tiliae flores, Origani herba, Salviae officinalis folia, Melissae herba) with 40 % ethanol in a ratio of 1:3. Belisa has a sedative, antihypertensive, antispasmodic and anti-inflammatory effect, causes increased urinary and biliary excretion, regulates metabolism (carbohydrates and fats), improves the overall condition of the body. Used in the complex therapy of diseases of the nervous system (neurasthenia, headache, sleep disorders, asthenic condition).

The task was to obtain capsules from Belisa liquid extract. For this purpose it was necessary to dry Belisa liquid extract, to determine its physico-chemical and pharmaco-technological parameters, depending on the obtained data to choose excipients and experimentally confirm their concentration.

Thus, the problem of stability of physico-chemical and pharmaco-technological parameters of the multicomponent dry extract of Belisa and its model samples with excipients that play a key role in capsule technology remained unresolved.

3. Materials and methods

The objects of the study were model samples of multicomponent dry extract of Belisa, a number of excipients, as well as mixtures thereof.

The weight loss during drying was determined in the developed laboratory model samples (using an express moisture meter Sartorius MA-150). Sample of 3–5 g was used; fluidity (according to SPHU 2.0 2.9.16); bulk density and bulk density after shrinkage (according to SPHU 2.0 2.9.34); microscopy was performed in transmitted light on a Lumam P1 microscope [6–9].

4. Research results

For experimental studies took a fraction of multicomponent plant dry extract of Belisa with a particle size of less than 0.25 mm in appearance, the resulting extract is a loose powder from reddish-brown to brown, a specific odour, which was stored in a plastic container with a plastic lid to study its properties during storage. Studies have shown that after 2 days of storage under normal conditions, the dry Belisa extract turns into a lumpy mass that loses fluidity and cannot be used in further work to obtain a capsule mass.

To improve the technological properties of the dry Belisa extract, model samples were made with different excipients (Aerosil in the amount of 1, 2 and 3 % and maltodextrin in the amount of 2, 3 and 4 %) and by different technology.

The following technological methods were used to improve the flowability and prevent the adhesion of the dried extract particles [10].

According to the first scheme, Aerosil was added to the dry, crushed and sieved extract in the amounts of 1, 2 and 3 % – model samples No. 1, No. 2 and No. 3, respectively (Tabl. 1). According to the second scheme, maltodextrin was added to the liquid Belisa extract in the amount of 2, 3 and 4 % in terms of dry matter – model samples No. 4, No. 5 and No. 6, respectively. Next, the liquid extract was evaporated on a laboratory rotary vacuum evaporator to obtain a thick extract, which was dried in a vacuum oven, crushed and sieved (Table 1). According to the third scheme, maltodextrin in the amount of 5 % in terms of dry matter was added to the liquid Belisa extract. The liquid extract was then evaporated on a laboratory rotary vacuum evaporator to obtain a thick extract, which was dried in a vacuum oven, crushed and sieved. To the obtained crushed and sieved dry extract was added 5 % of Aerosil and stirred for 5–10 min to obtain a homogeneous mass and obtained a model sample No. 7 (Table 1).

Next, we studied the organoleptic properties of the obtained samples No. 1–7 (Table 2) after storage for 2 days and 5 days in a plastic container with a plastic lid. The research results are given in Table 2.

As can be seen from the Table 2, model samples No. 1–5 after 2 days lumped and lost fluidity, after 5 days the particles completely adhered to a solid mass, which makes it impossible to study their technological properties and precludes further use in obtaining capsules.

Samples No. 6 and 7 (with a maltodextrin content of 4 % in terms of dry matter of dry extract and maltodextrin and Aerosil of 5 %, respectively) after 5 days remained fluid, did not stick together and did not clump.

Therefore, in further studies, samples No. 6 and No. 7 were used. Technological indicators of the obtained model samples after 5 days of storage are given in Tabl. 3.

As can be seen from the Tab. 3, the humidity of the model sample No. 6 was 3.16 and No. 7 – 4.07 %, which meets the requirements of SPhU. The bulk density and the bulk density after shrinkage of both samples are within acceptable limits. However, the fluidity of samples No. 6 and No. 7 was 2.25 and 1.30 g / s, respectively, which is insufficient for uniform dosing of the capsule mixture, and this parameter needs to be improved.

The micrographs of the model samples of the obtained dry extract No. 6 and No. 7 are shown in Fig. 1, 2.

Table 1

Model samples of multicomponent dry extract of Belisa with excipients

Ingredient, amount	Model samples						
	No. 1	No. 2	No. 3	No. 4	No. 5	No. 6	No. 7
Dry extract, in terms of dry matter, %	99.0	98.0	97.0	98.0	97.0	96.0	90.0
Aerosil, %	1.0	2.0	3.0	–	–	–	5.0
Maltodextrin, %	–	–	–	2.0	3.0	4.0	5.0

Table 2

Organoleptic properties of model samples during storage

Sample number	Organoleptic properties		
	Start of storage	Storage for 2 days	Storage for 5 days
1	Powder from reddish-brown to brown, specific odor. Loose	The powder particles clump and lose their fluidity	The powder particles stick together into a solid mass
2		The powder particles clump and lose their fluidity	The powder particles stick together into a solid mass
3		The powder particles clump and lose their fluidity	The powder particles stick together into a solid mass
4		The powder particles clump and lose their fluidity	The powder particles stick together into a solid mass
5		The powder particles clump and lose their fluidity	The powder particles stick together into a solid mass
6		Powder particles do not stick together, loose	Powder particles do not stick together, loose
7		Powder particles do not stick together, loose	Powder particles do not stick together, loose

Table 3

Technological indicators of model samples during storage

Technological indicators, dimension	Results	
	Sample No. 6	Sample No. 7
Fluidity, g / s	2.25	1.30
Bulk density, g / ml	0.526	0.398
Bulk density after shrinkage, g / ml	0.606	0.481
Weight loss during drying, %	3.16 %	4.07

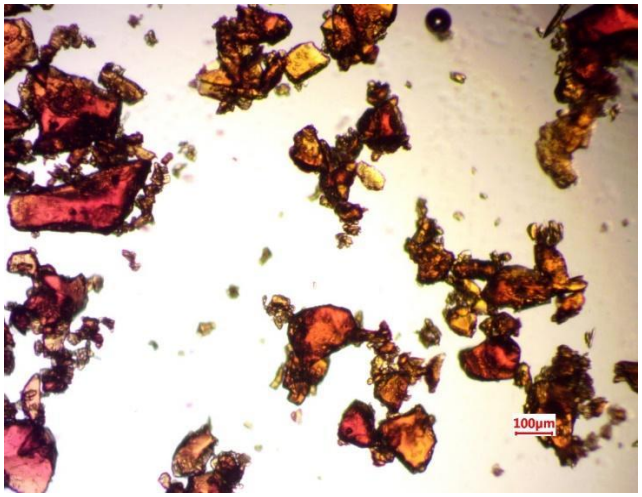

Fig. 1. Microphoto of a model sample of dry extract No. 6

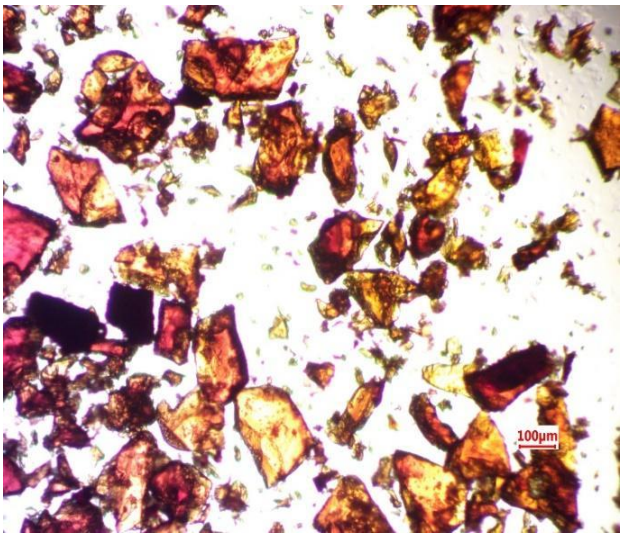

Fig. 2. Microphoto of a model sample of dry extract No. 7

As can be seen from Fig. 1, the particles of the dry extract are fragments of irregular shape, in transmitted light small in size particles of dark yellow color, large particles – from light brown to dark brown with a reddish tinge. The bulk of the particles have sizes from 60 to 250 microns. Particles larger than 250 μm are absent because this sample is obtained by sieving through a sieve with a hole size of 0.25 mm.

As can be seen from Fig. 2, the particles of the obtained dry extract in the sample No. 7 are fragments of irregular shape with a bulk particle size of from 80 to 250 μm. The particles of the extract are transparent in transmitted light, dark yellow and from light brown to dark brown with a reddish tinge. Against the background of the obtained results, for further work we chose a model sample of dry extract No. 7, the technological scheme of production of which is shown in Fig. 3.

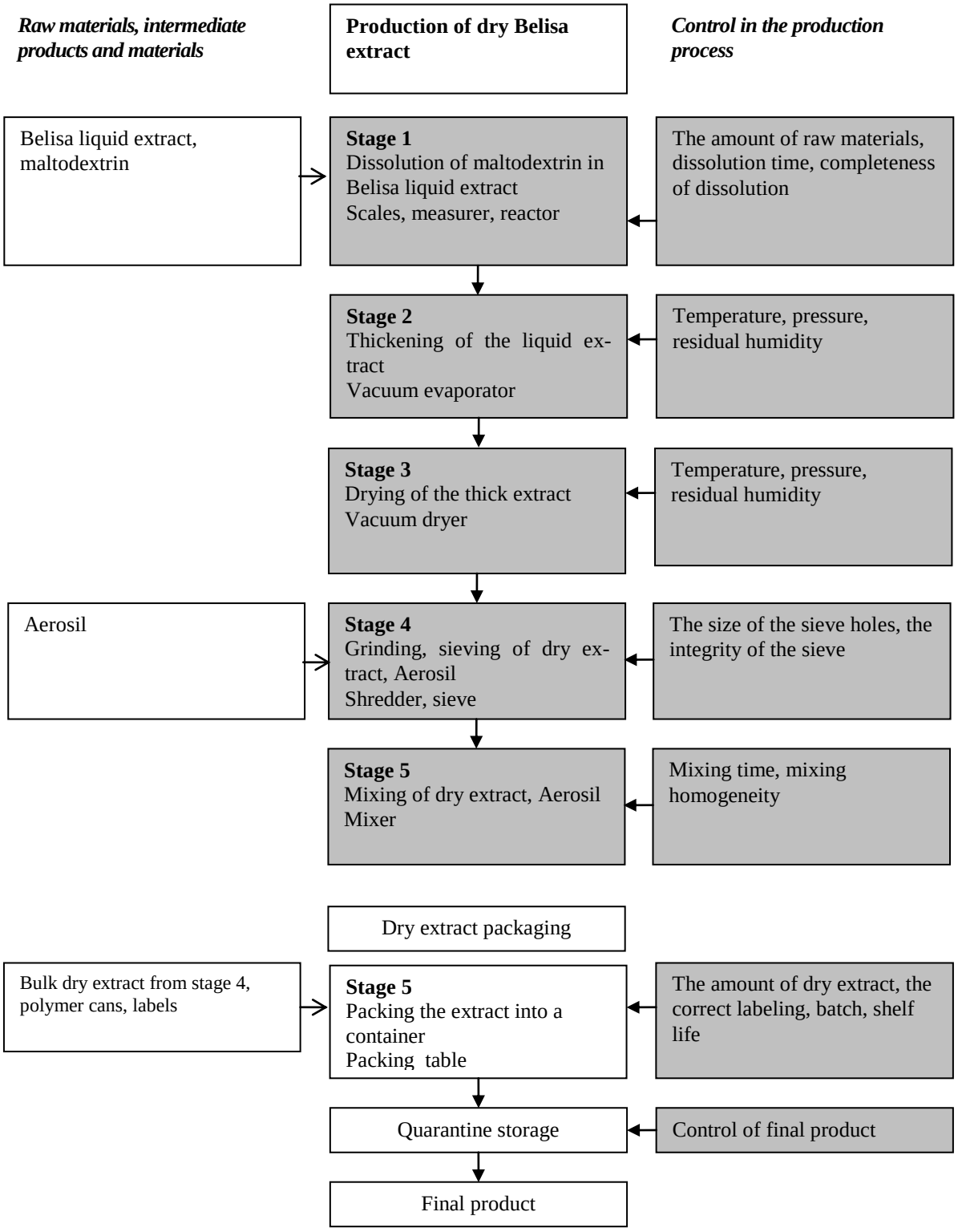

Fig. 3. Technological scheme of production of dry Belisa extract (sample No. 7)

The critical parameters of obtaining dry Belisa extract and subject to control are the amount of raw material, dissolution time, completeness of dissolution, temperature, pressure, residual moisture, hole size and sieve integrity, time and homogeneity of mixing ingredients, amount of obtained dry extract, labeling, series, shelf life.

5. Discussion of research results

It is proposed to use a model sample of dry extract No. 7 in further studies, against the background of microscopic analysis and pharmacotechnological parameters (humidity, bulk density and bulk density after shrinkage), which after 5 days of storage met the requirements of SPHU. According to our analysis, the flowability of the obtained model sample of dry extract No. 7 is maintained due to the use of the excipient Aerosil. It is its individual transparent unstained particles can be distinguished between colored particles of the extract (Fig. 2). It can be assumed that the hydrophobic Aerosil particles do not allow the extract particles to press tightly together and stick together. The developed technological scheme of production will allow to receive Belisa dry extract, and the specified critical parameters - to control its quality.

In previous works, experimental research by Shmalko O. O. et al. devoted to obtaining a dry extract of urocholum also proved the need to use excipients to improve its flowability and fluidity in order to obtain a capsule mass.

Study limitations. Given the multicomponent nature of the dry extract, the contribution to the overall result of each individual active pharmaceutical ingredient, which is of interest for further work, remains unexplored.

Prospects for further research are the selection of excipients to improve the fluidity of the selected model sample of dry extract of Belisa, capsule formation and capsule production.

6. Conclusions

Physico-chemical and pharmaco-technological properties of multicomponent dry extract of Belisa and its model samples with excipients Aerosil and maltodextrin in different concentrations were studied. Humidity, bulk density and bulk density after shrinkage, fractional composition were studied. Microscopic analysis of samples was performed. Based on the results of experimental research, the technology is developed and the technological scheme of obtaining the multicomponent dry extract of Belisa is made and the critical parameters of its production are determined.

Conflict of interest

The authors declare no conflict of interest.

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Liliia Vyshnevska, Doctor of Pharmaceutical Science, Department of Pharmaceutical Technology of Drugs, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: liliiavyshnevska@gmail.com

Oleksandr Shmalko, Department of Pharmaceutical Technology of Drugs, National University of Pharmacy Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: shmalko.a@gmail.com

Dmytro Soldatov, PhD, Department of Industrial Pharmacy, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002
E-mail: soldatovdp@gmail.com