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Granules composition and technology development based on condensed cranberry juice for urological use

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Abstract
This work is aimed to develop granules composition and technology based on condensed cranberry juice for urological use; study their technological properties according to the requirements of the Ukraine State Pharmacopoeia. At the first stage it was composed the composition of excipients (diluents and disintegrants) to obtain granules with maximum quantity of condensed cranberry juice by wet granulation method. The greatest amount of active substance was incorporated by mixtures: glucose – guar gum (10:4), sucrose– guar gum (10:4), and lactose– guar gum (10:4) in the amount of 9, 5 and 9 parts of condensed cranberry juice respectively. The next step was to determine particle size distribution, disintegration and mechanical strength of above samples – all granules were submitted these criteria according with the Ukraine State Pharmacopoeia requirements.

Keywords: cranberry juice**,** granules, excipients, technological properties of granules.

1. Introduction
In modern pharmaceutical practice are widely used drugs based on plant raw materials. Such medicines contain various biologically active substances (BAS), providing a wide range of therapeutic action, characterized with minimum adverse reaction that allows their application for a long time.
The cranberry fruit has long been used in folk medicine for the treatment of various diseases, including urological. This plant raw materials contains a large amount of organic acids (benzoic, citric, quinic, ursolic etc.), flavonoids, pectin, vitamins, trace elements, etc. Main substances that cause the cranberry usage in urology are proanthocyanidins. These BAS belong to the group of tannins and in plants perform protective function. In humans proanthocyanidins are able to inhibit the adhesion of uropathogenic microorganisms to the epithelium tissues of the urinary system [5, 6]. The results of biological studies have enabled the European Association of Urology to recommend regular use of cranberry juice at the proanthocyanidins dose 36-72 per day for the prevention of urinary tract infectious diseases [3]. But the sour taste of cranberry juice caused that large number of patients abandoned treatment with this remedy. Considering this we have decided to develop more convenient dosage forms (DF) on the cranberry juice basis. Our choice has stopped on the granules, since the DF has a high bioavailability and disintegration, easy to use, stable during storage, their preparation does not require complicated technological process.
The purpose of the research is to develop granules composition and technology based on condensed cranberry juice, study their technological properties according to the requirements of the Ukraine State Pharmacopoeia.

2. Material and methods. The objects of the study were: standardized condensed cranberry juice, diluents (glucose, sucrose, lactose), disintegrants (sodium alginate, guar gum), granules with condensed cranberry juice. Technological properties were investigated according to the methods described in the Ukraine State Pharmacopoeia (USP) 1st edition, Supplement 2. The Fractional Composition (Particle Size Distribution) was determined using a set of sieves with holes diameter of 4 mm, 3 mm, 2 mm, 1 mm, 0.5 mm [1]. The Disintegration Test was carried out using the retort basket with DF sample of 0.5 g and size 5 mm [1]. Granules friability was tested according to the requirements of USP using drum-type friabelatore. The loss in weight obtained with a single test or the average of the three tests shall not exceed 1% [1].

Results and discussion. An important factor affecting the granules quality in the technological process of wet granulation is the type and amount of granulating fluid [2]. In our case this liquid

was the active substance – condensed cranberry juice. When selecting the diluents and disintegrants it was considered that DF should contain the maximum quantity of condensed cranberry juice with a minimum quantity of auxiliary substances. Therefore, the diluents and disintegrants were selected so that for the same their quantity granulating mass had to incorporate the maximum amount of active substance. The requirement to granulating mass was its plasticity and the lack of adhesive properties. Also at the same time it must easily go through the granulator holes. For determination of the granulating mass quality was used the organoleptic test – a small amount of mass squeezed between the fingers, the obtaining "cake" should not stick to fingers (excessive wetting) and crumble when dropped from a height of 15-20 cm (inadequate wetting) [4].

We have prepared 12 series of granules with the condensed cranberry juice, the compositions of which are presented in the table.1.

Table 1: Compositions of granules with condensed cranberry juice

Ingredients	№1	№2	№3	№4	№5	№6	№7	№8	№9	№10	№11	№12
Condensed cranberry juice	3,0	3,0	3,0	3,0	2,0	1,0	3,5	3,0	4,0	9,0	5,0	9,0
Glucose	14,0			7,0	7,0		10,0			10,0		
Sucrose		14,0		7,0		7,0		10,0			10,0	
Lactose			14,0		7,0	7,0			10,0			10,0
Sodium alginate							4,0	4,0	4,0			
Guar gum										4,0	4,0	4,0

These components were weighed, crushed and mixed, and then humidified with condensed cranberry juice. The granulating mass was pushed through a granulator with a hole diameter of 4 mm and left to dry in natural conditions at a temperature of 18-20 ^{0}C for 1 day. Obtained samples №1, №2, №3, №4, №5, №6 did not possess satisfactory granulating properties, №7, №8 and №9 have incorporated a small amount of condensed cranberry juice. In this regard, for next research we have selected series of granules №10, №11 and №12. These samples were analyzed by the following technological parameters: particle size distribution, friability, disintegration test. The study result of the granules particle size distribution is presented in the table. 2.

Table 2: The study result of the granules particle size distribution

Sample number	Particle size, mm	Fraction content in overall granules mass	
		g	%
10	3,0-2,0	24,084	48,1
	2,0-1,0	25,329	50,7
	1,0-0,5	0,587	1,2
11	3,0-2,0	22,149	44,3
	2,0-1,0	26,831	53,7
	1,0-0,5	1,021	2,0
12	3,0-2,0	21,801	43,6
	2,0-1,0	24,088	48,2
	1,0-0,5	4,111	8,2

The studied samples, presented in the table 2, were positively evaluated because their particle size was in the range of 0.5 – 3.0 mm which submitted the USP requirements. Quantity of smaller and larger fractions did not exceed 5%.

The results obtained in the study of the granules disintegration are presented in table 3.

Table 3: Study results of the granules disintegration

Sample number	Time of granules disintegration, min				Average value	
№10	1,25	1,0	1,0	1,3	1,25	1,16±0,066
№11	2,73	2,7	3,1	2,8	2,7	2,08±0,076
№12	1,15	1,07	1,08	1,13	1,09	1,10±0,015

From table 3 it's evidenced that the investigated samples submitted the USP requirement – time of granules disintegration was no more than 15 minutes [1].

These samples were also tested for friability (mechanical strength), which serves as important criteria for excipients selection. The loss in granules weight did not exceed 1%, so all three samples were positively tested.

4. Conclusions

1. It was composed the composition of excipients to obtain granules with condensed cranberry juice by wet granulation method. The greatest amount of active substance was incorporated by mixtures: glucose – guar gum (10:4), sucrose– guar gum (10:4), and lactose– guar gum (10:4) in the amount of 9, 5 and 9 parts of condensed cranberry juice respectively.
2. It was selected granules samples with maximum content of condensed cranberry juice - №10, №11, №12 which were submitted the USF requirements: the particle size distribution, disintegration and mechanical strength.

To determine the final granules composition we additionally will carry out the whole complex of physical, chemical and technological studies with selected samples.

5. References

1. Державна Фармакопея України 2008, 618.
2. Латыпова ГМ, Давленшина РЯ, Катаев ВА, Романова ЗР. Получение гранул на основе экстракта травы первоцвета весеннего. Известия Самарского научного центра Российской академии наук 2011; 5(13):64-67.
3. Сычев ДА. Применение препаратов клюквы в урологической практике: взгляд клинического фармаколога. Урология 2011; 6:97-103.
4. Хаджиева ЗД. Изучение возможности медицинского применения фитокомплексов крапивы и солодки в форме гранул. Научные ведомости. Серия Медицина. Фармация 2010; 16:114-119.
5. Ofek I, Hasty DL, Sharon N. Anti-adhesion therapy of bacteriai diseases: prospects and problems. Immunology and Medical Microbiology 2003; 38:181-191.
6. Ronald L Prior, Ellen Fan, Hongping Ji. Multi-laboratory validation of a standard method for guantifying proanthocyanidins in cranberry powders. J Sci Food Agric. 2010; 90:1473-1478.