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Development of composition and technology of capsule drug form extracted based on "cobalt-30 neo" substance

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Abstract: The fractional composition, dispersibility, bulk density, and residual moisture of the γ-cyclodextrin derivative of Cobalt-30, the "Cobalt-30 neo" substance, were determined according to the applicable regulations. In developing the composition and technology of the capsules, the type and number of excipients were selected, taking into account the technological properties of the mass. The composition and technology of the "Cobalt-30" capsule were developed, and all these aspects were thoroughly studied in the article.

Keywords: "Cobalt-30 Neo", dispersibility, bulk density, residual moisture, capsule drug form, excipients.

Introduction: One of the urgent and important issues of the modern pharmaceutical industry is to increase the solubility of drugs, control the concentration and rate of release of active substances from the drug form. In order to solve this problem, various excipients are used, as well as methods of incorporating drugs into nano-sized materials are being used. In particular, the cyclodextrin (CD) complex is increasingly attracting the attention of scientists among many nanoscale agents. Nowadays, cyclodextrin molecules are widely used by scientists to create various drug forms. The use of cyclodextrin and its derivatives makes it possible to increase the stability of substances, reduce side effects, active substances to easily pass through biological barriers, and to achieve high effectiveness in small doses. Today, a derivative of cyclodextrins with high solubility and drug solubilizing activity - hydroxypropyl-γ-cyclodextrin (HP-γ-CD) is also widely used. In this regard, Cobalt-30, a substance used in leukopoiesis and hepatitis diseases, was synthesized as a supramolecular complex compound with HP-γ-CD.

The purpose of the work: to develop a capsule drug form with optimal composition and scientific basis based on the complex combination of Cobalt-30 with HP-γ-CD.

Relevance of the topic. Currently, among ready-to-use drugs produced on an industrial scale, capsule drugs take the leading place. The capsule form of the drug is precisely dosed, has a rapid effect on the body and is highly bio-efficient, and has the ability to prolong and control the action of the active substance.

When choosing the composition and technology of certain capsules, it is of great practical importance to study the technological properties of the mass to be placed inside the capsule. Also, the technological properties of the substance "Cobalt-30 Neo" have a significant impact on the choice of the type of drug, the composition of excipients and the technology of obtaining the drug. If the technological features of the substance, such as fractional composition, dispersibility, bulk density, and residual moisture, are within the standard limits, the capsule fills evenly with the substance, ensuring a consistent average capsule weight. Moreover, the quantitative analysis meets the required standards, ensuring the stability of the capsule.

Experience part. The experiments were based on determining the physicochemical features and

technological properties of the mass to be encapsulated. The structural - mechanical properties of the substance, specifically, the shape and size of the particles, were determined according to the methods given in the section 2.9.37 "Optical microscopy" of the State Pharmacopoeia of the Republic of Uzbekistan. The size and shape of the particles are one of the main indicators that directly affect the technological properties of the mass to be encapsulated. Physicochemical properties of particles were determined using an ADF U300P microscope with a magnification of 10 to 600 times (Figure 1).

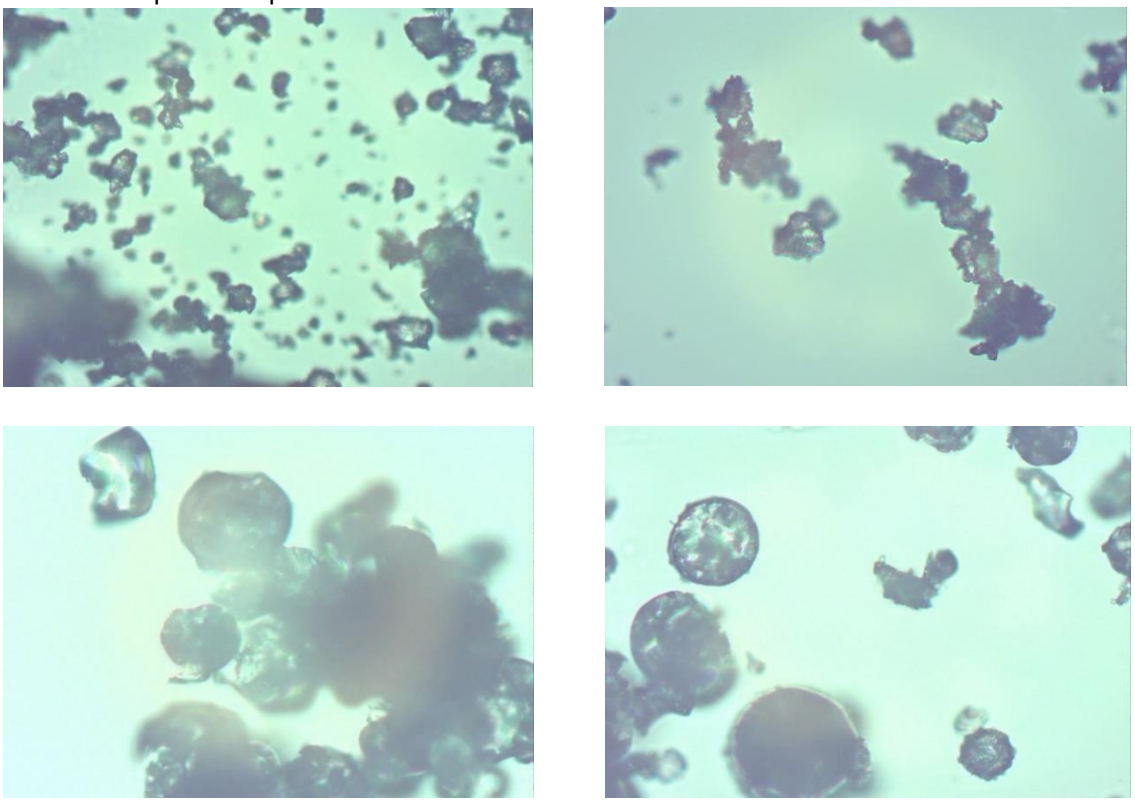

Figure 1. Magnified images of the substance "Cobalt-30 Neo" under an electron microscope

Looking at Figure 1, it can be seen that the substance "Cobalt-30 Neo" is a polydisperse powder composed of various particles, and it is mainly composed of plate-shaped irregular particles of similar length and width. At the next stage of the research, the technological properties of the substance "Cobalt-30 Neo" were studied, and the results of the fractional composition analysis are presented in Table 1. The fractional composition of the substance was determined according to the method presented in the scientific literature. To determine the fractional composition, 100 g of substance was placed in a set of sieves of different diameters and then sieved. For this purpose, 100 g of mass was placed on the uppermost sieve and a mechanical oscillatory motion was created for 5 minutes. Then the sieves were opened, the masses on the sieve were weighed individually with an accuracy of 0.01g, and the obtained results were written in the form of Table 1. The ones that remained on the sieve were marked with (+), and the ones that passed through the sieve were marked with (-). Fractional composition was expressed in µm, %.

Table 1

Results of determining the fractional composition of the substance "Cobalt-30 Neo" (n=5)

Fractional composition:	Units of measure	Obtained results
	µ km, %	
+1000		54,75
-1000 +500		25,7
-500 +355		11,7
-355 +250		3,71
-250 +180		2,35

-180		1,79

Based on the obtained results, it can be concluded that 54.75% of the substance consists of particles larger than +1000 µm. The proportion of -1000+500 µm particles is 25.7%, while the -500+355 µm fraction accounts for 11.7%. Additionally, -355+250 µm particles make up 3.71%, -250+180 µm particles represent 2.35%, and particles smaller than 180 µm constitute 1.79%, as shown by the experimental results. It is known that if the particles of the substance and the mass to be encapsulated are of the same size or the difference between their sizes is not large, the amount of the active substance in the capsules filled during the encapsulation process and the average weight of the capsules will be the same and there will be minimal deviations from it.

For the development of capsule drug forms, residual moisture, dispersibility and bulk density of the substance "Cobalt-30 Neo" were determined. The results are presented in Table 2.

Table 2

Results of determination of technological properties of "Cobalt-30 Neo" substance (n=5)

Examined parameters	Units of measure	Obtained results
Dispersibility	g/s	3,4
Bulk density	kg/m^3	450
Natural deviation angle	degree	43
Residual moisture	%	4.45

According to the results of determining the physicochemical features and technological properties of the substance "Cobalt-30 Neo", it is necessary to improve the fractional composition, dispersibility and bulk densities. Various excipients were used for this purpose, which are widely employed in the pharmaceutical industry today. When choosing the composition of the "Cobalt-30 Neo" capsule, corn starch and microcrystalline cellulose were used as fillers, sodium croscarmellose and sodium starch glycolate as lubricants and dissolution enhancers, while calcium stearate and magnesium stearate were used as anti-friction agents. Taking into account the humidity of the substance, it was first dried at 60°C for 1 hour and then ground in a mill. 6 different compositions were prepared with ground substance and various excipients approved for use in medical practice (Table 3).

Table 3

Suggested compositions for "Cobalt-30 Neo" capsules

№	The substances taken for the capsule mass, mg	Compositions, mg					
		1	2	3	4	5	6
Substance, mg							
1.	"Cobalt-30 Neo"	81.7	81.7	81.7	81.7	81.7	81.7
Excipients, mg							
2.	Magnesium stearate	2.5		2.5		2.5	
3.	Calcium stearate		2.5		2.5		2.5
4.	Sodium croscarmellose	7.5	7.5		7.5		
5.	Corn starch	158.3	158.3			158.3	
6.	Sodium starch glycolate			7.5		7.5	7.5
7.	Microcrystalline cellulose			158.3	158.3		158.3
8.	The mass quantity for per capsule	250±10	250±10	250±10	250±10	250±10	250±10

The technological properties of the prepared compositions were determined according to the above methods, and the obtained results are presented in Table 4.

Table 4

The results of determining the technological parameters of the mass contained in the "Cobalt-30 Neo" capsule

Examined parameters	Obtained results					
	T-1	T-2	**T-3**	T-4	T-5	T-6
Fractional composition, μm, %:						
+1000	2,6	2,34	**2,1**	2,8	2,2	2.95
-1000 +500	9,4	9.1	**9.8**	9.4	9,8	9,51
-500 +355	64.09	65,22	**67.73**	65,11	63,48	64,08
-355 +250	18,35	17,5	**15,8**	17,3	18,7	18,1
-250 +180	4,3	4,6	**3,4**	4,2	4.54	4.11
-180	1,26	1,24	**1,17**	1,19	1,28	1,25
Dispersibility, g/s	3,85	3,91	**4,5**	4,28	3,95	4,19
Bulk density, kg/m^3	502	512	**569**	525	528	523
Natural deviation angle, degree	43	45	**35**	42	40	37
Residual moisture, %	4,14	4,16	**4,07**	4,11	4,15	4,1
Disintegration time, min	13,33	13,33	**9,24**	10,3	11,33	9,55

From the results presented in Table 4, it can be seen that all compositions have different technological properties. The bulk density was 502-569 kg/m3, the natural deviation angle was 35-45 degrees. The residual moisture index in the mass to be encapsulated did not exceed 5% in all compositions and was found to be significantly improved compared to the initial substance and was in the range of 4.07-4.16%. However, the dispersibility of the prepared masses was relatively low in the 1,2,5-contents, and the samples containing corn starch were 3.85 g/s, 3.91 g/s, and 3.95 g/s, respectively. A mass with low dispersibility increases the likelihood of sticking to the hopper of the encapsulating machine.

The disintegration time of the capsules was determined according to the method given in State Pharmacopoeia of the Republic of Uzbekistan and did not exceed 20 minutes, as required by the pharmacopoeia.

Based on the above results, the technological properties of the studied compositions were analyzed. The number of excipients selected for composition № 3 demonstrated the most optimal indicators, including dispersibility, natural deviation angle, fractional composition, and residual moisture.

To prove the scientific justification of the selected composition for the "Cobalt-30 Neo" capsule and to preliminarily assess its compliance with ND requirements, a comparative study of the technological properties of the "Cobalt-30 Neo" substance and the selected composition was conducted. The results are recorded in Table 5.

Table 5

Comparative study of the technological properties of the substance "Cobalt-30 Neo" and the selected composition

Examined parameters	**Units of measure**	**Obtained results**	
		"Cobalt-30 Neo" substance	**Selected composition (№3)**
Fractional composition	μm, %		
+1000		54,75	2,1
-1000 +500		25,7	9.8
-500 +355		11,7	67.73
-355 +250		3,71	15,8

-250 +180 -180		2,35 1,79	3,4 1,17
Dispersibility	g/s	3,4	4,5
Bulk density	kg/m^3	450	569
Natural deviation angle	degree	43	35
Residual moisture	%	4.45	4,07

Based on the results, it was determined that the fractional composition of the substance "Cobalt-30 Neo" was 11.7% of 0.355-0.5 mm particles, and the fractional composition of the selected capsule mass was 67.73%. This shows that the result is shifted in a positive direction, leading to an improvement in the dispersibility of the mass and the possibility of obtaining a high-quality capsule increases. It was proved that the dispersibility of the mass to be encapsulated changed from 3.4 g/s to 4.5 g/s, the bulk density from 450 g/ cm3 to 569 g/ cm3, and the residual moisture from 4.45% to 4.07%.

Due to the correct selection of excipients in the selection of the composition of the "Cobalt-30 Neo" capsule, it was scientifically proven that the residual moisture of the mass decreased, its dispersibility improved and other technological indicators changed in a positive direction. The selected composition was recommended for further research on the development of capsule technology.

Thus, the composition of the drug "Cobalt-30 Neo" for 1 capsule was selected:

"Cobalt-30 Neo" 81.7mg

Sodium starch glycolate 7.5mg

Magnesium stearate 2.5mg

Microcrystalline cellulose 158.3mg

The average mass is 250mg

Technology: To prepare the capsule mass, residual moisture in "Cobalt-30 Neo" was dried to the optimum level at a temperature of 60ºC, ground and sieved using a 0.5 µm sieve. The excipients listed above were also sieved using a 0.5 µm sieve and thoroughly mixed with the substance. Capsules were filled by direct encapsulation method in UXF-300 type mechanical encapsulation equipment. The technological scheme of obtaining "Cobalt-30 Neo" capsules is presented in figure 2.

When filling the "Cobalt-30 Neo" capsule mass into hard gelatin capsules, № 2 gelatin capsules were used. The description of the technological process is presented in Figure 2.

It is known that the direct encapsulation method of the mass to be encapsulated without granulation is practically economical and has the following advantages: it does not require additional equipment (granulator, mixer), reduces energy consumption, and increases work efficiency. The composition of the capsule offered on the basis of "Cobalt-30 Neo" shows good technological properties and allows direct filling of the capsule. The proposed capsule composition based on "Cobalt-30 Neo" exhibits good technological properties, allowing for direct capsule filling. In the development of the above technology, the shape of the powder particles and losses during grinding were taken into account. The quality parameters of the hard № 2 dark yellow gelatin capsules obtained according to formulation 3 were determined. The results are presented in Table 6.

Table 6
Results of evaluation of the quality of "Cobalt-30 Neo" capsules

External parameters	**Average weight and its deviation g, % (±10%)**	**Solubility, % (not less than 75%)**	**Disintegration, minutes (not less than 20 minutes)**	**Quantitative analysis, Cobalt-30 mg (13,5-16,5 mg)**
Dark yellow hard gelatin capsules № 2	-7,35%; +9.8%	90%	9,24 min	15.3 mg

The obtained capsules complied with the requirements specified in State Pharmacopoeia of the Republic of Uzbekistan in terms of appearance, deviation from average weight and dissolution time.

CONCLUSION

According to the results of the experiment, by studying the technological properties of the "Cobalt-30 neo" capsule, an alternative composition suitable for the preparation of the capsule medicine was selected and its technology was developed.

REFERENCES

Ushakova L.S. Obtaining, studying, and using inclusion complexes of cortisone acetate, dexamethasone, and sinaflan with cyclodextrins: dis. ... Candidate of Pharmaceutical Sciences — Pyatigorsk, 1996.

Ramazonova K.R., Khodjaeva I.A. Preparation of cyclodextrin derivatives of the cobalt-30 substance and their properties. //The current state of the pharmaceutical industry: problems and prospects, materials of the international scientific-practical conference. - Tashkent, 2020. P. 258-259.

Alekseev, K.V. Pharmaceutical technology. Solid dosage forms / K.V. Alekseev, S.A. Kedik, E.V. Blynskaya; edited by Prof. S.A. Kedik. - Moscow: IFT, 2011. P. 298-305.

Industrial Drug Technology: [Textbook. In 2 volumes. Volume 2] edited by Prof. V.I. Chueshov; Nova Book, 2014.

Turaboev Sh.M., Ziyaev H.L., Sagdullaev B.T. Development of Gozalidone Capsule Drug Type Technology // Journal of Pharmacy. - Tashkent, 2018. - № 3. P. 65-71.

State Pharmacopoeia of the Republic of Uzbekistan. - Vol. I.: Tashkent, 2021. P. 429-510.

Alekseev K.V., Blynskaya E.V., Suldin A.S., Sizyakov S.A., Alekseeva S.K., Ditkovskaya A.G. Excipients in the technology of hard capsules // Pharmacy. – 2009, № 5. P. 31-36.