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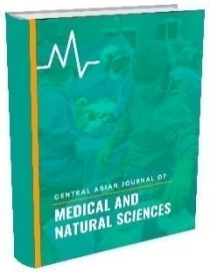

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Development of Technology of Combined Capsule on the Basis of Cholecalciferol and Ascorbic Acid Substances

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Annotation: Previous studies have studied the technological properties of cholecalciferol and ascorbic acid substances and have proven that they are negative. Therefore, the wet granulation approach was used to develop the combined capsule dosage form using the number of excipients. Based on the study of the technological parameters of the encapsulated masses, the optimal composition was chosen and a combined capsule technology containing cholecalciferol and ascorbic acid was industrialized.

Keywords: cholecalciferol, ascorbic acid, combined capsule, technological indicators, capsule size.

Vitamins are organic compounds necessary for the vital activity of a living organism and normal metabolism. In recent years, scientific research has been accompanied to prove the importance of vitamins in the normal functioning of the human body, the treatment and prevention of diverses diseases [1,3,6].

It is known that cholecalciferol and ascorbic acid belong to the group of vitamins and are necessary for the normal growth, development and normal functioning of every human being. It also ensures the general health of the human body, bone strength, blood coagulation, protection against ARVI, elimination of toxins from the body. In addition to replenishing the body's need for vitamins with natural nutrients, it is also necessary to use chemicals[4,5,7].

Taking into account the above, the development of new drugs based on cholecalciferol and ascorbic acid substances, the development of combined capsule drug form technology to provide medical practice with vitamin drugs and determine compliance with the requirements of regulatory documents is one of the pressing issues.

Our previous research was aimed at determining the technological parameters of cholecalciferol and ascorbic acid, which proved to be negative. Hence, it is necessary to utilize excipients to improve these performance of the substances. Excipients aid to give the drug not only the required dosage form, but also a set of physicochemical properties necessary for its proper distribution in the body.

The aim of the research. Development of technology for the selection of a moderate composition for a combined capsule drug type based on cholecalciferol and ascorbic acid substances.

Research methods and tasks. In the selection of the composition of the combined capsule on the basis of cholecalciferol and ascorbic acid substances, from the excipients widely used in the pharmaceutical industry today: corn starch as a filler, microcrystalline cellulose, lactose, titanium dioxide, calcium phosphate, potato starch, talc, potato starch, antifungal calcium stearate, purified water as a moisturizer, alcohols of various concentrations were used, and the capsule masses were prepared by the wet granulation method.

In the literature on the study of the technological properties of the ingredients (friability, friability density, natural deflection angle, fragmentation, fraction size from 0.2 to 0.5 mm, frictional hardness and residual moisture) in the formation of a combined capsule drug form based on cholecalciferol and ascorbic acid substances the approachs described were used.

Summary of suggestions and conclusions. The analysis of the literature and the recommendation of pharmacologists regulated that the amount of the active substance in the combined capsule cholecalciferol and ascorbic acid was 500 mg**.** In the first stage of the revision, the capsule size should be chosen. It is known today that capsules come in 8 sizes, which are 000, 00, 0, 1, 2, 3, 4 and 5 sizes. They differ in size. Based on the scattering density of the substances, it was found expedient to use sizes 0 and 00 of the capsules. However, in order to improve the friability of the substance, it is planned to use not only the addition of excipients, but also the method of wet granulation. Therefore, 0-size capsules were selected for further study.

About 10 sample mixtures based on cholecalciferol and ascorbic acid substances were developed, 5 of which gave satisfactory results, the table of contents and their technological parameters are given in Table 1.

According to the literature, the scattering and scattering density of the encapsulated mass depends on the percentage of fractions from 0.2 to 0.5 mm relative to the total amount, and it is recommended that this figure not be less than 85%. In the mixtures obtained for compositions 1 and 5, the amount of this fraction was less than 85% and was 80.12 ± 1.65% and 89.8 ± 0.64%, respectively. At the same time, the content of the above fractions in the mixtures of components 2, 3 and 4 was 93.12 ± 1.38%, 97.71 ± 1.04% and 86.32 ± 0.71%. Proof of this view was shown in the results of determining the fragility: when the proportion of fractions of 0.2-0.5 mm was more than 85%, the fragility was also high, for example, 6.69 ± 1.06 mm (2 content), 4.88 ± 0.77 mm (content 4), 6.18 ± 1.29 mm (content 5).

In the next stage, the scattering densities of the 1st, 3rd and 5th compositions also showed high performance and were 0.422 ± 20.82kg / m^3, 0.674 ± 22.31 kg / m^3 and 0.802 ± 17.70 kg / m^3, respectively. In all analyzed compositions, the natural deflection angle was positive and ranged from 31.04 ± 1.67 degrees to 34.2 ± 1.61 degrees.

In XIV DF and according to the normative documents the disintegration of granules should not exceed 15 minutes. All contents met the requirement for this indicator, and their decomposition ranged from 6.13 ± 0.31 minutes to 7.75 ± 1.33 minutes, i.e, no more than the specified 15 minutes. However, the residual moisture of drugs should not exceed 5%. Of the analyzed components, only 2 and 3 components met the demand and their moisture content was 4.4 ± 0.32 and 3.2 ± 0.10%, respectively. However, the moisture content in the 1.4 and 5 compositions exceeded the specified amount and was 7.3 ± 0.22%, 5.8 ± 0.62% and 6.7 ± 0.31%, respectively.

In view of the above, the most moderate masses for the capsule were 2 and 3 ingredients. However, since the scattering index was of great importance during capsule filling, 3 ingredients with this index were selected.

The mass obtained according to this composition was prepared according to the following technology: Pre-ground and sifted through a sieve with a hole diameter of 150 μm, mixed with corn starch filling with cholecalciferol. This mass was moistened with 40% ethyl alcohol. The resulting mass was dried at 40-50 0S, ascorbic acid was pulverized into the prepared granules. The prepared mass is from 0.5 g to 0-size capsules.

Figure 1 shows the technological process of a combined capsule containing cholecalciferol and ascorbic acid.

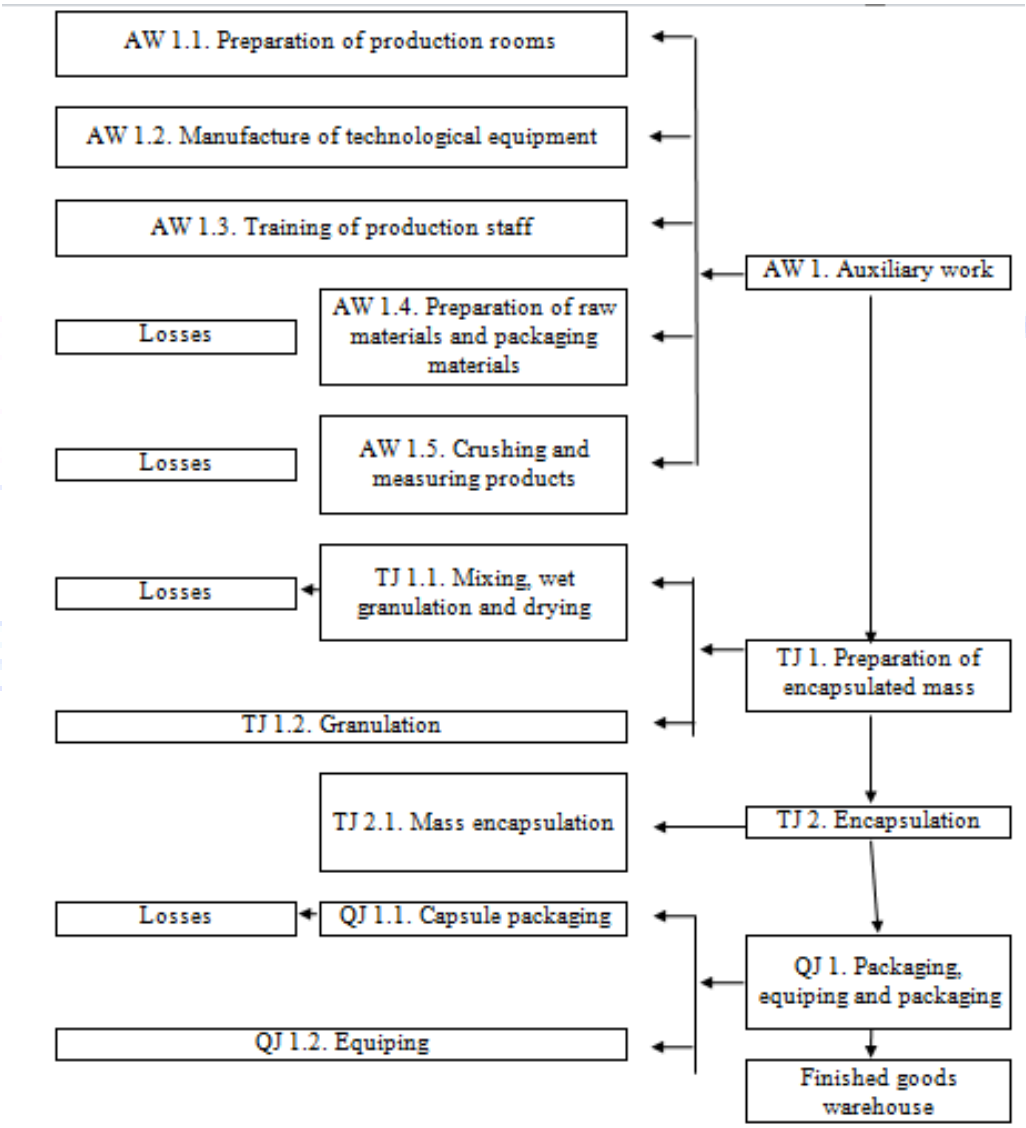

Table 1. Results of the study of technological parameters of the capsule mass based on cholecalciferol and ascorbic acid substances

№	Contents	fragility, 10^{-3} кг/с	scattering density, kg / m^3	natural angle of inclination, degrees	decomposition, min	the fractions of size 0.2-0.5 mm,%	residual moisture,%
1.	Cholecalciferol 1000 ME Ascorbic acid 100 mg Lactose 100 mg Up to 500 mg of corn starch 70% ethyl alcohol	4.51±0,89	0,422±20,82	34,07±1,02	7,75±1,33	80,12±1,65	7,3±0,22
2.	Cholecalciferol 1000 ME Ascorbic acid 100 mg Calcium phosphate 7 mg Up to 500 mg of corn starch Purified water	6,69±1,06	0,580±16,65	31,04±1,67	5,75±1,65	93,12±1,38	6,4±0,32
3.	Cholecalciferol 1000 ME Ascorbic acid 100 mg Up to 500 mg of corn starch 40% ethyl alcohol	6,72 ±0,81	0,674±22,31	34,2±1,61	4,13±0.31	97,71±1,04	3,2 ±0,10
4.	Cholecalciferol 1000 ME Ascorbic acid 100 mg microcrystalline cellulose Up to 500 mg of potato starch Purified water	4,88±0,77	0,722±18,63	37,22±1,82	7,08±0,98	86,32±0,71	5,8±0,62
5.	Cholecalciferol 1000 ME Ascorbic acid 100 mg titanium dioxide 2mg Up to 500 mg of corn starch 40% ethyl alcohol	6,18±1,29	0,802±17,70	31,03±1,38	6,08±0,84	89.8±0,64	5,7±0,31

Conclusion. Taking into account the negative technological properties of cholecalciferol and ascorbic acid substances, the composition and technology of the combined capsule drug type were selected using various excipients and wet granulation method.

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