DEVELOPMENT OF TECHNOLOGY AND DETERMINATION OF CRITICAL PARAMETERS OF THE PRODUCTION PROCESS OF OROMUCOSAL DRUG FOR THE TREATMENT OF HELMINTHIASES IN CHILDREN

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Introduction.

Oromucosal drugs combine a large group of drugs that are introduces into the oral cavity or throat in various aggregate states for local or systemic action [1].

Recently, the range of Oromucosal medicines such as troches and lozenges is actively expanding. Troches and lozenges are solid, single-dose, sucking or chewing drugs, usually for topical action in mouth or throat, containing one or more sweet flavorings with active ingredients, intended for slow dissolution or decay in the mouth [1, 2].

Today, the nomenclature of troches on the pharmaceutical market of Ukraine is represented by hard lozenges (lollipops), chewable tablets, chewable troches, chewing gums [3, 4].

Troches and lozenges became particularly popular with the pediatric population due to their high compliance, pleasing organoleptic characteristics and easiness of administration [5, 6, 7].

In the group of anthelmintic drugs, as of February 5, 2020, no drugs are presented in the form of troches, which indicates the feasibility of developing such a drug for further use in pediatric practice.

We offered a drug with the active pharmaceutical ingredient albendazole in the form of chewable troches [8, 9] and studies were conducted to select the optimal gel-forming agent [10] and flavorings as correctors of taste characteristics [11].

The purpose of this work is to develop the technology of chewable troches under the conditional name "Albenpast" and to establish the critical points of the production process. Troches exhibit broad-spectrum anthelmintic activity at low toxicity. Indications for use are helminthiasis of the digestive system in children caused by nematodes, cetodes, microsporiodioscodes, giardiasis, mixed helminthiasis.

Materials and methods

Pure substances (albendazole, gelatin, glycerol, purified water, glucose syrup, fructose, citric acid, fruit flavoring, food coloring) and samples of troches on their basis were used as the study subjects.

The research methods used are reflected in the State pharmacopoeia of Ukraine (SPhU).

Results and discussion

The ratio of components of troches "Albenpast" are given in table 1.

Table 1. Composition of the troches "Albenpast" samples

Ingredient	Sample, g per 10 troches	
	1	***2***
Albendazole	1.0	1.0
Gelatin	7.15	7.15
Purified water	21.5	21.50
Glycerol	35.70	35.70
Glucose syrup	10.0	-
Fructose	-	10.0
Citric acid	1.05	1.05
Fruit flavoring	0.01	0.01
Food coloring agent (green / yellow)	0.01	0.01

The proposed compositions of troches "Albenpast" 1 and 2 differ in the type of sweetness flavoring: 1 contains glucose syrup, 2 contains fructose. The replacement of glucose syrup with fructose is advantageous in the production of an anthelmintic agent for children in need of glucose control. Based on our previous research, we proposed the following technology for the preparation of chewable troches "Albenpast": a weighed amount of gelatin (7.15 g) is placed in a porcelain cup, poured with 20 ml of purified water and left to swell for 30 min.

In a separate porcelain cup a concentrate of flavorings is formed: 1.05 g of citric acid is dissolved in 1.5 ml of purified water, 10.0 g of glucose syrup (or fructose) and 35.70 g of glycerol are added and mixed thoroughly until homogeneity. To the resulting mixture 0.01 g of flavoring fruit and food coloring (green / yellow) is added and mixed thoroughly until homogeneity.

After the gelatin swells, it is heated in a water bath until dissolution and mixed with the concentrate, avoiding the formation of bubbles. To the finished gelatin mass 1.0 g of pre-sifted albendazole is added and mixed thoroughly until homogeneity, avoiding the formation of bubbles. The resulting mass is poured into silicone form and placed in a refrigerator for freezing. The finished product is chewable troches with a pleasant fruity aroma, of green / yellow color, sweet in taste. Technological scheme of preparation of chewable troches "Albenpast" is shown in Fig. 1. The forecasted types of production control at each stage of the production process are additionally given.

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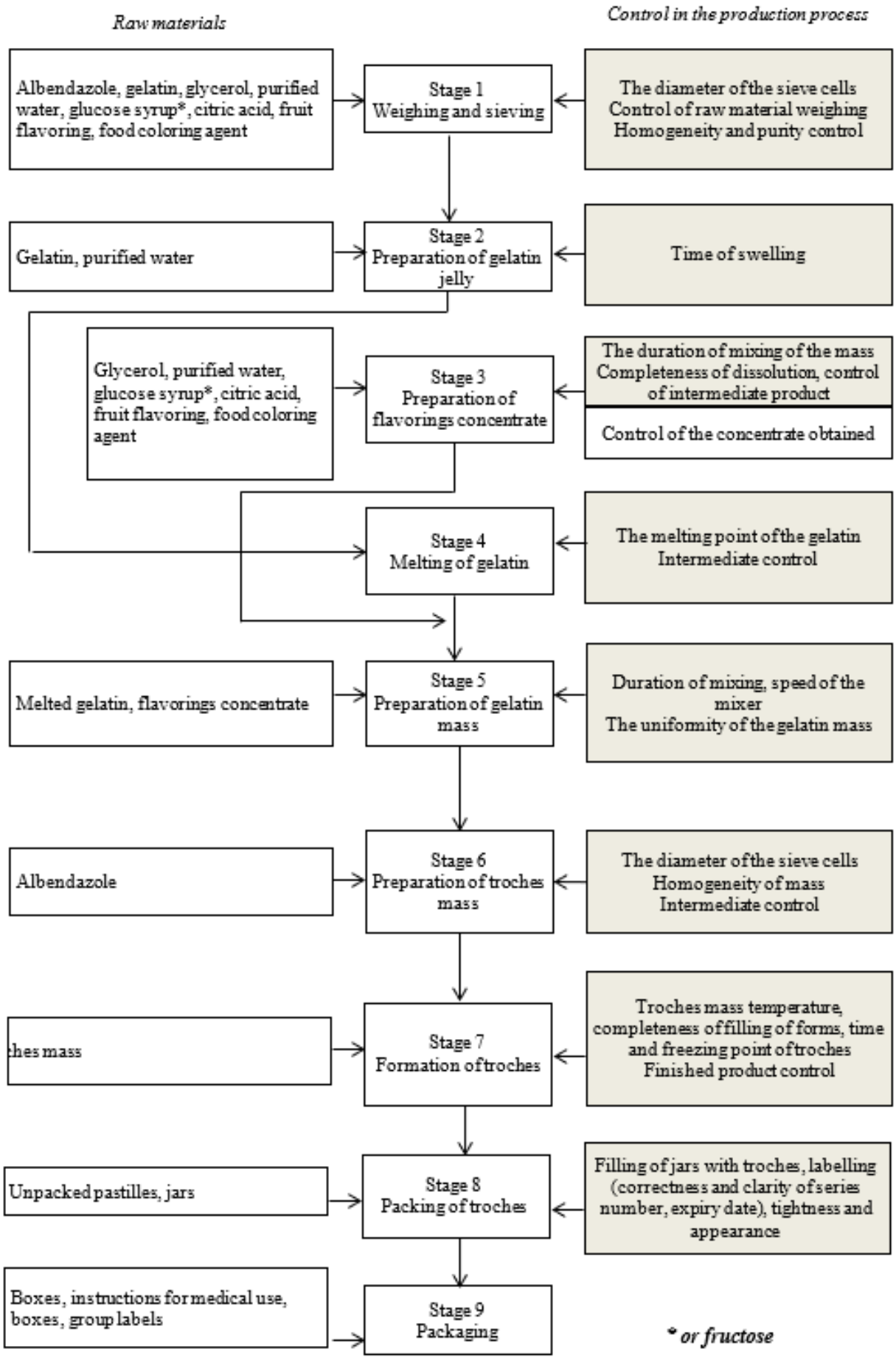

Fig. 1. Technological scheme of production of chewing troches “Albenpast”

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The critical parameters of the production process were established experimentally (Table 2).

Table 2. Critical parameters of the production process of chewable troches "Albenpast"

Stage	Critical parameter	The value of the critical parameter
2. Preparation of gelatin jelly	Time of swelling	25-30 min.
3. Preparation of flavorings concentrate	Duration of mixing of the mass	20-25 min.
4. Melting of gelatin	The melting point of the gelatin	(36.0 ± 1.0) °C
5. Preparation of gelatin mass	Mass mixing duration, temperature mode, agitator speed	15-20 min. (34.0 ± 1.0) °C 0.9 s^{-1}
7. Formation of troches	Temperature mode, freezing time	60 – 90 min in the cold or cool place (8.0-12.0 °C)

The obtained troches samples were evaluated according to the following quality indicators [2]: organoleptic control, uniformity of dosage units, uniformity of mass, dissolution time. The results of the studies are given in Table 3.

Table 3. Results of the quality control of chewable troches "Albenpast"

Indicator, unit of measure	Value	Compliance with the requirements of SPhU
Organoleptic control	Chewing troche with pleasant fruity aroma, of green / yellow color, sweet in taste	Responds
Uniformity of dosage units, g	6.9±0.29	Responds
Uniformity of mass,%	4.3	Responds
Dissolution time	15 min 27 sec	Responds

As can be seen from the results in table 3, chewable troches under the conditional name "Albenpas" made according to the proposed technology, meet the requirements of the State Pharmacopoeia of Ukraine in all quality indicators, which indicates the feasibility of adapting the proposed technology in the production process.

Conclusions

1) The technological process of preparation of chewable troches under the conditional name "Albenpast" is described and the technological scheme of production is given.
2) Critical parameters of the production process and their values are given.
3) The results of the quality control of the obtained chewable troches according to the main quality indicators in accordance with the requirements of the State Standard are given.

Critical parameters of the production process of oromucosal drug for the treatment of helminthiases in children

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Introduction. Troches are very popular in children due to their high compliance, pleasing organoleptic characteristics and easiness of administration. Nevertheless, the expanding range of drugs in this dosage form still lack anthelmintic products. In order to introduce the new anthelminthic drug in the form of chewable troches under the conditional name "Albenpast", there were conducted the studies over selection the optimal gel-forming agent and flavorings as correctors of taste characteristics. The purpose of this work is to develop the technology of chewable troches under the conditional name "Albenpast" and to establish the critical points of the production process. **Materials & methods.** As the objects of research the pure substances (albendazole, gelatin, glycerol, purified water, glucose syrup, fructose, citric acid, fruit flavoring, food coloring) and samples of troches on their basis were used. The research methods used are reflected in the State pharmacopoeia of Ukraine. **Results & discussion.** Research was conducted against the chewable troches "Albenpast" to the composition of the components of which the patent is claimed. Compositions of troches 1 and 2 differ in the type of sweetness flavoring: 1 contains glucose syrup, 2 contains fructose. Composition 2 is offered for the use in children who need to control the level of glucose. The production process offered includes 9 stages with critical points in 2, 3, 4, 5 and 7. Additionally, for each stage the possible types of quality control are described. The further quality control of the obtained by the offered technology samples of chewable troches showed their full correspondence with the requirements of SPhU. **Conclusion.** The technological process of production of chewable troches is offered and the technological scheme of their production is given. Critical parameters of the production process and their values are identified and described. The results of the quality evaluation of obtained chewable troches according

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to the main quality indicators in accordance with the requirements of SPhU are presented.

Keywords: oromucosal drug, production, helminthiases, children

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