

JUSTIFICATION OF THE GEL FORMERS SELECTION IN THE DEVELOPMENT OF OROMUCOSAL DRUG IN THE FORM OF TROCHES

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Introduction

Oromucosal medicines combine a large group of oral dosage forms. By type of action oromucosal drugs are divided into local (oropharyngeal, intended for use in a specific area of the oral cavity or throat), systemic action (sublingual, intended for absorption on the mucous membrane of the oral cavity) and mucoadhesive (intended for retention in the oral cavity by adherence to the mucous epithelium and may modify systemic absorption at the site of application) [3]. Particularly noteworthy is such dosage form as troches, which is gaining in special popularity in pediatric practice.

Troches are introduced on the pharmaceutical market in many countries of the world, for many years. The

combination of pleasant organoleptic characteristics and the ability to introduce a variety of active pharmaceutical ingredients (APIs) is an undeniable advantage in the development of medicines for children. The most commonly used type of this dosage form is "chewy type" troches [4].

Troches are aromatic and usually have a nice fruity taste. They are relatively easy to manufacture both in pharmacies and in industrial conditions. The hard part is preparing the basics. They are usually made from gelatine, but there are prescriptions based on pectin and agar-agar [4, 8].

In order to develop the optimal composition of troches for the further introduction into them of APIs, we conducted a study to select the most rational gel-forming agent and its concentration.

Materials & methods

Gel-forming agents gelatine (250 g/cm², according to Bloom), agar (800 g/cm², according to Bloom) and apple pectin were used as objects of the study.

The ratio of the ingredients of the samples is given in table 1.

Table 1. The composition of the samples of troches

Ingredient	Sample, concentration of ingredient, mass. %					
	1	2	3	4	5	6
Gelatine	-	-	-	18.11	8.65	21.64
Agar	-	21.65	8.65	-	-	-
Apple pectin	12.5	-	-	-	-	-
Purified water	35.35	21.65	34.63	11.89	34.63	21.64
Glycerol	35.34	43.27	43.29	56.57	43.29	43.29
Sugar	15.5	-	-	-	-	-
Glucose syrup	-	12.12	12.12	12.12	12.12	12.12
Citric acid	1.29	1.29	1.29	1.29	1.29	1.29
Fruit flavouring agent	0.01	0.01	0.01	0.01	0.01	0.01
Food colouring agent	0.01	0.01	0.01	0.01	0.01	0.01

The amount of gel-forming agent was calculated based on the well-known ratios of troches components, which are described in foreign and domestic literature [1, 2, 4-6, 8-9].

Samples with gelatine and agar were prepared in the following way: the calculated amount of gel-forming agent was poured with the calculated amount of purified water and left for swelling. Separately the concentrate of the other ingredients was prepared: citric acid was dissolved in the minimum amount of purified water and mixed with glucose syrup, glycerol, fruit flavouring agent and food colouring agent. When gelatine/agar swelled, it was melted on a water bath and mixed with the concentrate. The obtained mass was poured into silicone mold and placed in a refrigerator for hardening.

Samples with apple pectin were prepared the following way: the calculated amount of apple pectin was

mixed with half the sugar and heated to $(50.0 \pm 2.0)^\circ\text{C}$ with water purified with vigorous stirring. After swelling, it was mixed with the previously prepared concentrate, similar to the samples with gelatine and agar. The obtained mass was poured into silicone mold and placed in a refrigerator for hardening.

Results & discussion

The obtained troches were evaluated by the following quality indicators [7]: organoleptic control, uniformity of dosage units, dissolution time. The results are shown in table 2. Based on the above data, sample of troches No. 5 have the best consumer characteristics, which indicates the feasibility of further use of this ratio of components with gelatine as a gelling agent.

Table 2. Evaluation of the quality of troches samples on different gel-forming agents

Sample	Organoleptic characteristics	Uniformity of dosage units, g	Dissolution time, min.
1	Troches have not formed. The mass did not solidify to the desired consistency.	-	-
2	Troches with a pleasant fruity aroma, yellow in colour, sweet in taste, not transparent. They are easily torn, difficult to remove of the mold.	1.12 ± 0.053	10 min. 09 sec.
3	Troches with a pleasant fruity aroma, yellow in colour, sweet in taste, not transparent. They are easily torn, difficult to remove of the mold.	1.13 ± 0.055	8 min. 58 sec.
4	Troches with a pleasant fruity aroma, green in colour, sweet in taste, transparent. Contain undiluted gelatine particles.	1.13 ± 0.053	17 min. 18 sec.
5	Troches with a pleasant fruity aroma, green, sweet in taste, transparent.	1.12 ± 0.052	14 min. 11 sec.
6	Troches with a pleasant fruity aroma, green in colour, sweet in taste, transparent. Contains many particles of undiluted gelatine.	1.14 ± 0.053	18 min. 37 sec.

For example, lozenge samples on apple pectin (No. 1) were not formed, the texture remained semi-solid; samples of troches on agar (Nos. 2 and 3) were formed, but were opaque and easily destroyed when pressed; samples of gelatine troches (No. 4 and No. 6) contained too much

gelatine, some of which remained undissolved, resulting in deterioration of taste characteristics (less pleasant taste, “crunch”, sticking during chewing).

The critical parameters of the technological process of making troches are shown in table 3.

Table 3. Critical parameters of the technological process of troches preparation

Stage	Critical parameter	Critical parameter value
Gelatine swelling	Time of swelling	25-30 min.
Gelatine melting	36.0 – 37.0 °C	(36.0 ± 1.0) °C
Troches hardening	Temperature regime, hardening time	60 – 90 min. in the cold or cool place

Conclusions

1. A study on the selection of type of gel-forming agent and its quantity for the production of troches showed that samples of troches based on gelatine with its content of 8.65 mass. % have the best consumer characteristics. The obtained troches are with a pleasant fruity aroma, of green colour, sweet in taste, transparent.
2. Investigation of the quality of lozenge samples by organoleptic parameters, uniformity of content of dosage units and dissolution time showed that sample No. 5 fully meets the requirements of SPhU.
3. Critical parameters of the technological process (swelling of gelatine, melting of gelatine, hardening of troches) were established.

Justification of the gel formers selection in the development of oromucosal drug in the form of troches

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Introduction. Troches deserve special attention among the existing oromucosal dosage forms. They have good consumer characteristics and an adequate level of bioavailability, which makes it expedient to expand the range of medicines to be used in the form of troches, especially for pediatric use. The purpose of this work is to justify the optimal composition of troches by selecting the

DOI: 10.5281/zenodo.3572530

most rational gel-forming agent and its concentration.

Materials & methods. Gel formers gelatine (250 g/cm², according to Bloom), agar (800 g/cm², according to Bloom) and apple pectin were used as objects of the study. The ratio of the ingredients was investigated in 6 samples. Samples with gelatine and agar were prepared as follows: the calculated amount of gelatine or agar was poured with the calculated amount of purified water and left for swelling. When gelatine/agar swelled, it was melted in a water bath and mixed with concentrate of citric acid, glucose syrup, glycerol, fruit flavouring and food colouring. Samples with apple pectin were prepared as follows: the calculated amount of apple pectin was mixed with half the sugar and heated to (50.0 ± 2.0) °C with water purified with vigorous stirring. After swelling, it was mixed with concentrate of citric acid, glucose syrup, glycerol, fruit flavouring and food colouring. The resulting mass was poured into silicone form and placed in a refrigerator for hardening. **Results & discussion.** The obtained troches were evaluated by such quality indicators as organoleptic control, uniformity of dosage units, dissolution time. It was found that sample No. 5 shows the best consumer characteristics, while the other samples do not meet the requirements of the studied quality indicators. For example, sample No. 1 was not formed, the texture remained semi-solid; samples No. 2

and No. 3 were formed, but were opaque and easily destroyed when pressed; samples No. 4 and No. 6 contained too much gelatine, some of which remained undissolved, resulting in deterioration of taste characteristics (less pleasant taste, "crunch", sticking during chewing). The critical parameters of the technological process of troches preparation are time of gelatine swelling, temperature of gelatine melting, time of troches hardening. **Conclusion.** The findings showed that samples of gelatine-based troches with its content of 8.65 mass. % have the best consumer characteristics. The resulting troches are homogenous, with a pleasant fruity aroma and sweet taste. They meet the requirements of SPhU by the quality indicators organoleptic indicators, the uniformity of the dosage units and the dissolution time. The established critical parameters of the technological process and their values were established.

Keywords: gel; oromucosal; troches; gel formers

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