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Research on the Selection of a Certain Content of "Ambronat" Juice Syrup

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ABSTRACT

This article presents several experiments on the selection of a specific composition of Ambronat syrup. These selected several excipients in the selection of the sweetness and consistency and consistency of the syrup, based on which the ingredients were considered, and the result was the result of the selection of a moderate content.

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INTRODUCTION:

Currently, there are different approaches to the formation of drugs in the form of syrup. Syrups are transparent liquids containing one or more active substances, dissolved in concentrated aqueous solutions of sucrose or other sugars and having a specific taste and odor depending on their composition. If necessary, preservatives, antioxidants, stabilizers, corrigents, and other excipients are added to the syrups [2, 4].

The selection of the optimal combination of excipients, taking into account the specific properties of the composition of syrup, is one of the important stages in the development of technology of syrups, based on specific methods as a dosage form that improves their organoleptic properties.

Ambroxol hydrochloride is a powder with mucolytic and expectorant properties and belongs to the mucolytic agents in the therapeutic group. Its mucolytic and expectorant properties are due to the N-demethylated metabolite of bromhexine. It also has a secret motor and secretolytic effect. Ambroxol hydrochloride shows its effect after 30 minutes of oral administration and has an effect of 6-12 hours, depending on the dose [1, 5].

According to the literature, sucrose, glucose, fructose, sorbitol, mannitol, maltitol, xylitol are used as the basis of syrup in the preparation of the recommended syrup. Preservatives (alcohol, nipagin, nipazole, sorbic acid, etc.), stabilizers, corrigents are also added to the syrups as needed [3].

There is also the task of paying attention to the prevention of deficiency of this type of drug in the selection of excipients for syrups. The disadvantages of these types of drugs are instability, uniformity of dosage, storage, and so on.

RESULTS AND DISCUSSION:

When choosing a particular composition of syrup, it is especially important to choose a sweet-giving component that gives a sweet taste. To prepare Ambronat syrup, the first stage of research focused on the selection of a sweet-tasting component. For this, we used plain sugar juice, 70 % fructose, and sorbitol solutions.

It is known from the literature that the concentration of sugar syrup is 60-64 %. The concentration of syrup is 66-68 %, which leads to the formation of sugar during storage, i.e.

the formation of large crystals. If it drops below 60 %, the syrup will be able to ferment quickly. These cases were taken into account in the study.

The composition of these excipients is given in Table No. 1.

Table No. 1: The composition of the recommended simple syrups (the basis for syrup)

Components	**Syrups**			
	S-1	**S-2**	**S-3**	**S-3**
Sugar	64	-	-	-
Fructose	-	70	50	-
Sorbitol	-		20	70
Purified water	36	30	30	30

Preparation of syrups was carried out traditionally. For this purpose, concentrated solutions of sweeteners were prepared by heating to a temperature of 100 ^{0}C. The cooled ambroxol hydrochloride solution was then added. In this process, it was studied that the syrups prepared to correspond to 36 categories of purity in terms of microbiological purity.

Table No. 2 lists the ingredients selected with the above flavors, and the research was continued with these ingredients.

Table No. 2: Ingredients studied with flavors (basics)

Components	**Contents**			
	C-1	**C-2**	**C-3**	**C-3**
Ambronat hydrochloride	0,3г	0,3г	0,3г	0,3г
Sugar syrup	95	-	-	-
70% Fructose: sorbitol (2: 5) solution %	-	-	95	-
Sorbitol	-	95	-	-
70% Fructose Solution	-	-	-	95

Samples of syrups prepared for the study were placed in a tightly closed container and left to store naturally at 150 ° C to 25 ° C. From time to time we observed the growth of surface and internal microorganisms with the unaided eye for a month. In order not to make a mistake, the syrups were prepared and compared with continuous standard tests. We studied the quantitative analysis of microorganisms by the double-layer agar method in a Petri dish.

The results obtained are given in Table No. 3.

Table No. 3: Results of the study of microbiological purity of "Ambronat" syrup (without preservatives)

Number of samples	**1g live microorganisms**				***Staphylococcus aureus*. Bacteria belonging to the family *Entero-bacteriacae*, *Pseudomonas aeruginosa***	
	bacteria		**fungi**			
1	**One hour after preparation**	**at a temperature of 300 C for 5 days**	**1 hour after**	**5 days after**	**1 hour after**	**5 days**
2	50	370	Less than 10	Less than 10	no	no
3	80	560	Less than 10	Less than 10	no	no
4	70	310	Less than 10	Less than 10	no	no
5	40	740	Less than 10	Less than 10	no	no

From the data presented in Table No. 3, it can be seen that the prepared syrups are not sterile and contain a complex of bacteria. After one hour of prepared syrups, microbiological purity is normal. Those stored at 300S provide a good environment for microorganisms to multiply. This foundation has no bacteriostatic effect. By the tenth day of the storage state, dizziness was observed in the syrup samples. It has been speculated that this may be due to bacteria.

This in turn indicates the need to add preservatives. The issue of stabilizers should also be considered.

The next stage of research was devoted to the selection of preservatives and samples of syrup with the following preservatives, which are widely used in practice and approved for use in oral formulations: potassium sorbate, nipagin, and sodium benzoate.

Studies continued with testing the microbiological purity of freshly prepared syrups. In using these preservatives, we used the concentrations recommended in the literature and studied the microbiological purity of the solution by adding the above ingredients to a simple syrup.

The results obtained are given in Table No. 4.

The studies planned and investigated the presence of bacteria, fungi, enterobacteria, and other gram-negative bacteria belonging to the family *Staphylococcus aureus, Entero-bacteriacae, Pseudomonas aeruginosa*. These studies are the main factors influencing the microbiological purity of the prepared syrup. The substances we selected for the above studies not only perform a preservative function, but some also have bacteriostatic and bioactive properties (sodium benzoate).

From the indicators given in Table No. 4, it can be seen that the microbiological purity indicators improved in syrups with the addition of preservatives. 0.5 % sodium benzoate added as a preservative is well soluble in water. This feature is of great importance in the technology of jam. Based on the data provided in the literature, sodium benzoate (0.5 g) was obtained as a preservative to ensure the microbiological purity of the syrup.

Table No. 4: Results of testing the microbiological purity of "Ambronat" syrups prepared with preservatives

Conservant	**Live microorganisms in 1 g of syrup**			**Presence of live microorganisms *Salmonella, Staphylococcus aureus*, bacteria belonging to the family *Pseudomonasaeruginosa Enterobacteriaceae* and other gram-negative bacteria**
	Bacteria	**Fungi**	***Enterobacteriaceae* and other gram-negative bacteria**	
Sodium benzoate 0,2%	30	less than 10	10	No
Sodium benzoate 0,5%	20	less than 10	8	No
Nipagin 0,1%	40	less than 10	13	No
Nipagin 0,2%	30	less than 10	11	No
Potassium sorbate 0,1%	35	less than 10	16	No

In the selection of the composition of "Ambronat" syrup, sodium benzoate was obtained not only as a preservative but also as the second main bioactive substance with expectorant properties. This, in turn, further increases the expectorant properties of Ambronat hydrochloride at the recommended value.

Therefore, we selected 0.5 % sodium benzoate for further studies.

To increase the solubility of drugs, to prevent redox reactions during storage and use, as well as to improve the bitter taste of ambroxol hydrochloride in the syrup are added correctors and stabilizers - citric, ascorbic acid, sodium citrate, sodium hydroxide. Therefore, in addition to sugar, we also obtained 0.067 g of citric acid. This in turn determines the position of citric acid and 0.172 g of sodium citrate as a stabilizer and citric acid as a corrigent.

Propylene glycol was also obtained as a bactericidal agent. To increase the solubility of the bioactive substance, we used polysorbate 80, polyethylene glycol, propylene glycol, ethyl alcohol. It has been noted that propylene glycol simultaneously acts as a thickener in solution in syrups. This means that increase the viscosity of the solution facilitates their dosing. It is known from the literature that propylene glycol is used in liquid oral dosage forms at a concentration of 10-25%. We determined using the microbiological analysis to check the preservative properties of propylene glycol. In this case, we determined the amount of diffusion of microorganisms in agar in the strains of *S. aureus* and *E. coli*. In our studies, we used *Staphylococcus aureus* (ATSS 25923) and *Escherichia coli* (ATSS 25922) tests. To do this, the microbial mass is prepared in a sterile 0.9 % isotonic solution to prepare a microbial mixture, then the solution is diluted to a concentration of 1 ml - 10 TB with an optical standard solution indicating the turbidity of the solution. The resulting mixture is dropped into the medium in a pipette with three drops and flattened in the same way as with a spatula. Microbial culture pots are dried at room temperature for 15-20 minutes and cut into agar with a diameter of 9 mm using a sterile cartridge case and placed in a thermostat. The incubation period at a temperature of 37 ° C in a thermostat lasts 18–20 hours. The growing areas of the microorganisms are then identified using a micrometer. The results showed that propylene glycol at all concentrations has antimicrobial properties against *Staphylococcus aureus* and *Escherichia coli* bacteria. However, an increase in antimicrobial properties was observed in propylene glycol solution at a concentration of 10% to 15%. It was observed that the antimicrobial effect in propylene glycol did not change with increasing concentration (15% to 25%). Therefore, 15% propylene glycol solution was selected as a preservative for further studies. We also obtained 96% ethyl alcohol to ensure the solubility of ambroxol hydrochloride.

Several ingredients have been studied for the individual and complex use of the above excipients. Of these, the composition of 9 compositions, which showed similar indicators, is given in Table No. 5.

Table No. 5: Recommended "Ambronat" syrup composition of the contents

Ingredients Name	Ingredients								
	1	2	3	4	5	6	7	8	9
Sorbit	-	-	20,0	40,0	-	45,0	-	25,0	20,0
Fructose	-	65,0	20,0	25,0	-	-	-	40,0	20,0
Sugar	65,0	–	25,0	–	65,0	20,0	65,0	–	25,0
Methylcellulose	1,67	1,0	–	–	–	–	0,56	–	–
Hydroxyethylcellulose	–	–	0,9	0,3	0,5	0,5	0,5	0,5	0,5
Citric acid	0,1	–	0,167	–	0,067	0,2	0,067	0,2	0,2
Sodium citrate	1,0	–	–	–	0,172	0,1	0,1	0,1	0,1
Aromatizer	0,072				0,28			0,37	
Sodium benzoate	–	–	0,3	–	0,5	–	–	0,1	0,1
Propylene glycol (ml)	10,28	–	–	10,0	10,32	10,0	10,32	10,0	10,0
Ethyl alcohol 96%		7,5			9,0			10,0	
Purified water	**Up to 100 ml**								

The next stage of research was continued by determining the quality of the syrups obtained in the 9 compositions mentioned above. The following qualitative indicators of syrup were studied: organoleptic properties, pH, viscosity, density, amount of foreign substances.

According to the studied indicators, all the compositions except the T-5 composition are not at the required level with some of the studied quality indicators. For example, syrups obtained in the compositions T2, T3, and T9 do not meet the demand with pH values. T3, T4 compositions have the highest viscosity index. With the index of the density of syrups, all compositions except T5 show a high index. As for foreign substances, only syrups obtained in T5 and T6 compositions were found to be in demand. However, it was observed that the content density in composition 6 was high and not at the level of demand.

CONCLUSIONS:

Thus, based on the results of studies with the above compositions, the composition of the 5th composition was selected for the "Ambronat" syrup, and this composition became the basis for further research.

Conflict of interest statement. The authors declared no conflict of interest.

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