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DEVELOPMENT OF THE COMPOSITION OF TABLETS FOR THE TREATMENT OF OTOLARYNGOLOGICAL DISEASES

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The prevalence of acute respiratory diseases, the particular severity of their course, as well as the frequent relapses and complications require constant search for new, more effective and safe medicines for their prevention and treatment and introduction of these drugs into clinical practice. Generally, most of the medications used in the treatment of acute respiratory viral infections have a number of side effects, and it is especially dangerous with their prolonged administration.

The aim of this study is to develop the composition and technology, as well as to perform the pharmaco-technological studies of the tablet solid dosage form obtained on the basis of a thick extract of clary sage with the antimicrobial effect. Bentonite clays of the Tajik deposit were also studied in the present work.

It should be noted that in the step of development of the solid dosage form an important element is the choice of excipients. In this work, we used the method of mathematical planning of the experiment, which allowed establishing the relationship between the composition of the tablet mass and the main pharmaco-technological parameters. In order to select the most appropriate excipients, the quality of tablets was studied according to the requirements of the European Pharmacopoeia (EP) and the State Pharmacopoeia Ukraine (SPhU) (appearance, uniformity of mass, resistance to crushing, tablet friability, disintegration, etc.) [1, 6].

To obtain the tablet mass with definite pharmaco-technological properties, dextrose monohydrate and finely dispersed bentonite clay were used as fillers. Bentonite clay upon wetting have the ability to adsorb a significant amount of liquid, swell and increase in volume, contributing to loosening. Due to this, the compressed particles are separated, opening up the possibility of penetration of the liquid into tablets [4, 5].

Studies by some authors [3, 5] concerning the tabletting technology issues indicate the advantage of the wet granulation process [2]. Most powdered substances are exposed to this processing method. In this regard, 5% bentonite solution was used as a granulating liquid.

Based on the analysis of literary sources the concentration of 25 mg was selected (taking into account humidity) in order to calculate the required amount of the active ingredient in a thick extract of clary sage leaves with the anti-inflammatory and antimicrobial effects. The tablets containing this thick extract were experimentally developed 7 model compositions of these tablets.

Wet granulation of the components of the tablet mass was performed in a

granulator of type YK-60 (China). Then wet masses granulated through a sieve (stainless steel mesh) with the hole diameter of 2 mm were dried in an oven at a temperature not exceeding 60°C, and then again rubbed through a sieve with the hole diameter of 2 mm.

During the experiment the modern research methods and laboratory equipment were used. Seven tablet compositions with various set of excipients were developed. The model samples of tablets included the following components: a thick extract of clary sage leaves, ascorbic acid (vitamin C), bentonite clay, dextrose monohydrate, lactose monohydrate, microcrystalline cellulose (MCC), talc, and magnesium stearate. These compositions were assessed for compliance with the requirements of the EP and SPhU monographs.

5% water-alcohol solution of bentonite was used as a moisturizing agent. The granules obtained were subjected to pharmaco-technological research methods, which determined the fractional composition, humidity and flowability (determination of the flow rate through a nozzle and the angle of repose).

The fractional composition or distribution of material particles by size, in a certain way, affects the flowability of powdered materials and, consequently, the smooth operation of tablet machines, the stability of the mass of the resulting tablets, the accuracy of the medicinal substance dosage, as well as the quality characteristics of tablets. The fractional-dispersed composition of the model compositions proposed was determined by the sieve method according to the SPU method.

The fractional composition of granulate is heterogeneous due to the different strength of granules. The highest content of particles larger than 2 mm was observed in model compositions 5 and 7 (up to 22%), while the lowest one (up to 9%) – in composition 2, which was also characterized by the highest content of the average fraction with the particle size of 1-2 mm (82%). It indicates a sufficient probability of obtaining tablets with a constant average mass.

The moisture-absorbing activity is an important indicator that affects the flowability of the tablet mass. We studied the dynamics of the tablet mass moisture absorption during the day.

As a result of the study established composition 2 (4.5%), which is the most acceptable, has the minimum moisture-absorbing activity.

Tablets with 12 mm in diameter were prepared with the preliminary wet granulation process using a TDP-5 tablet press (the weight of the tablet was 0.8 g). Tablets of various compositions were subjected to quality control procedures using the EP and SPhU methods by the following parameters: description, average mass and its deviation, disintegration, solubility, mechanical strength (resistance to crushing and tablet friability) and appearance.

According to the results of the studies of pharmaco-technological properties of the tablets prepared it has been found that the test samples are yellow tablets with a flat and smooth surface, and a cylindrical shape. The diameter of a tablet is 12.0 ± 0.2 mm. These compositions by disintegration and appearance meet the requirements of the SPhU [6].

The parameters of compositions 2, 3 and 5 also correspond to quality control standards (QCS) for tablets. By the indicator of the average mass and strength

compositions 1, 4, 6 and 7 do not meet the QCS requirements. Composition 2 containing 5% water-alcohol solution of bentonite as a humidifier significantly exceeds the quality characteristics of samples 3 and 5 by the indicators of disintegration, the average mass and strength. Its resistance to crushing is 68 N, tablet

The drug is yellow tablets with a flat and smooth surface, cylindrical shape with a breakline and a bevelled edge, the tablet diameter is 12.0 ± 0.2 mm. By their external parameters tablets meet the requirements of the SPhU [6].

Thus, by the results of the pharmaco-technological studies the technology for production of a thick extract of clary sage leaves and tablets based on it has been developed for the treatment of otolaryngological diseases. The present work is of interest for further studies of the drug developed and its introduction into the pharmaceutical production.

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