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DEVELOPMENT OF THE COMPOSITION, TECHNOLOGY AND METHODS OF STANDARDIZATION CHEWABLE TABLETS WITH OATS EXTRACT AND QUERCETIN

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ABSTRACT

The composition masticatory tablets with oat extract and quercetin during the development stages was investigated and substantiated, also the technology of getting them was developed. Also, these substances of the high performance liquid chromatography (HPLC) method in accordance with the requirements of the SPhU were identified and qualitatively defined. By results of researches the number of active substances in the developed in the pharmaceutical form was determined.

Key words: Chewable tablets, Oats extract, Quercetin.

INTRODUCTION

Despite the economic crisis, the pharmaceutical market continues to evolve intensively by generating double-digit growth rates. An important role in this development plays a pharmaceutical science. Occurs shifting emphasis in scientific activity with research institutions to pharmaceutical manufacturers, that is accompanied positive changes: in the last 6 years scientists have received 800 new molecules [1]. But the difficult path of the chemical laboratory where invented the active pharmaceutical ingredient to the final consumer, who has to get a ready drug quality assured, very lengthy and costly through almost an unmanaged and the uncontrolled neither by terms nor by expenditures development and implementation processes new drug (drugs). The pharmaceutical science has a particular of development. All elaborations in pharmaceutical industry are carried out for their of further of the successful implementation and operation for a long time. Resulting in increased requirements as the process of developing and introduction of new drugs, so and to the result of development, manufacturing and making available to the end user qualitative, safe and affordable medicines [2]. Nowadays an urgent task for of the pharmaceutical science and practice is not only reaction completely new drugs, but also the improvement of existing ones the purposes of expansion their of Pharmacological action and indications for use, particularly when it comes to developing drugs with the use of natural components [3]. In this aspect of our scientific researches directed at the improvement of composition and technology and of the known drug Quercetin production of PJSC SIC "Borshchahivskiy CPP" through the use of the dry oats seed extract as an additional of active substance [4].

Purpose

The purpose of our work was study of the composition, technology and standardization of techniques of chewable tablets with the dry oats extract and quercetin with of general tonic and of adaptogenic effects.

MATERIALS AND METHODS

Substances of the dry oats seed extract and quercetin, granules and ready tablets are prepared as objects of study were selected. For the study used the following methods: microscopical, organoleptic, pharmaco-technological.

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In order to identify and of quantitative determination of the active ingredients in the developed of dosage form have used HPLC method according with the requirements of the SPhU [5].

RESULTS AND DISCUSSION

In the development process the following composition of chewable tablets was investigated and substantiated: of the dry oats seed extract, quercetin, the pectin citrusy, of glucose monohydrate, sugar, the flavoring powdered (orange), talc, magnesium stearate. On the basis of technological researches was developed the technological scheme of chewable tablets comprising the following stages: preparation of the dosage form components, obtaining mass by granulation tabletting mixture of active and supplementary substances, tableting and dust elimination, packaging, labeling.

Experimentally substantiated the technological parameters of preparation of chewable tablets of the oats extract and quercetin (conditions of preparation semiproduct, the sequence of stages, pressing conditions etc.) on which developed production schedules.

Test for identification and of quantitative determination of the dry oats seed extract is carried out by HPLC in accordance with the requirements of the SPhU 2.2.29, 2.2.46. Contents of the dry oats seed extract is measured of the peak of ferulic acid.

On the chromatogram with the test solution obtained carrying out of technique "Quantitative determination of the dry oats seed extract" the retention time of the main peak of the ferulic acid must meet the retention time of the main peak of the ferulic acid of standard solution on the chromatogram with an accuracy of ± 2%.

The absorption spectrum of the principal peak on the chromatogram of the ferulic acid of the test solution obtained at carrying out of technique "Quantitative determination of the dry oats seed extract" must meet the absorption spectrum of the main peak of the ferulic acid of standard solution on the chromatogram.

We used the following reactive and materials, such as acetonitrile and methanol for chromatography; the high-purity water MiliQ, trifluoroacetic acid. The proposed such conditions chromatography: the chromatographic column SunFireTM (Waters), 100x4.6 mm, a particle size of 3.5 microns or similar; the flow rate 1 ml/min.; the wavelength of detection 320 nm; the volume of injection 100 ml; the temperature of the column thermostat 25 ^{0}C. The gradient program is presented in the table 1:

The mobile phase A. 0.05% (v/v) the solution of trifluoroacetic acid in acetonitrile.

The mobile phase B. 0.05% (v/v) the solution of trifluoroacetic acid.

The solvent

The methanol and the water in a ratio of 50:50 (volume/volume) are mixed and degassed.

The reference solution

1,500 g (the exact weight) working a standard sample (WSS) of the dry oats seed extract placed in the flask Erlenmeyera capacity of 100 ml, is added 50.0 ml of solvent and stoppered. The resulting solution was stirred on a shaker to the full dispergation, and then treated for 30 minutes in the ultrasonic bath, stirring occasionally. Is cooled the solution to the room temperature and is centrifuged for 10 minutes at a speed of 8000 rev/min. The supernatant is filtered through nylon filter (0.45 micron).

The test solution

Rubbing 20 tablets of the drug and is transferred of powder a sample of equivalent to 1500 mg of the dry oats seed extract placed in the flask Erlenmeyera capacity of 100 ml, is added 50.0 ml of solvent and sealed. The resulting solution is stirred on a shaker to the full dispergation and then treated for 30 minutes in the ultrasonic bath, stirring occasionally. The solution is made cool up to the room temperature and is centrifuged for 10 minutes at a speed of 8000 rev/min. The supernatant is filtered through nylon filter (0.45 micron).

Methods

100 ml of a reference solution is chromatographed on the liquid chromatograph, reaching suitability of the chromatographic system. Parameters of the chromatographic system suitability calculated by peak of ferulic acid:

- an approximate retention time peak of ferulic acid is 13 minutes;
- the efficiency of the chromatographic system designed for the peak of a ferulic acid chromatographic reference solution must be at least 2000 of theoretical plates;
- the symmetry coefficient the peak of ferulic acid must be not more than 1.5;
- the relative standard deviation according to the requirements the SPhU, 2.2.46.

The content of the dry oats seed extract (X) in a single tablet, in mg, calculated by the formula:

$$X = \frac{S_1 \times m_0 \times 50 \times b}{S_0 \times m_1 \times 50} = \frac{S_1 \times m_0 \times b}{S_0 \times m_1}$$, where:

S_1 – the average value of the peak area of ferulic acid, calculated with the chromatograph of the test solution;

S_0 – the average value of the peak area of ferulic acid, calculated with the chromatograph of the reference solution;

m_0 – the mass of sample of the dry oats seed extract, in mg, taken for preparation of the reference solution;

m_1 – the mass of the sample drug, in grams;

b – the average weight of a tablet, in grams.

The chromatogram with the reference solution and the test solution are presented according on Figures 1, 2.

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The test by of identification and quantitative determination of quercetin is carried out by HPLC according to the conditions the SPhU 2.2.29, 2.2.46.

On the chromatogram with the test solution obtained carrying out of technique "Quantitative determination of the quercetin" the retention time of the main peak of the quercetin must meet the retention time of the main peak of the quercetin of standard solution on the chromatogram with an accuracy of ± 2%. The absorbtion spectrum of the principal peak on the chromatogram of the quercetin of the test solution obtained at carrying out of technique "Quantitative determination of the quercetin" must meet the absorption spectrum of the main peak of the quercetin of standard solution on the chromatogram.

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The mobile phase A. 0.05% (v/v) the solution of trifluoroacetic acid in acetonitrile.

The mobile phase B. 0.05% (v/v) the solution of trifluoroacetic acid.

The solvent. The methanol and the water in a ratio of 50:50 (volume/volume) are mixed and degassed.

The reference solution

40 mg (the exact weight) working a standard sample (WSS) of the quercetin placed in the flask capacity of 50 ml, is dissolved in 10 ml of methanol followed by addition of solvent (methanol) to the mark. A sample of the resulting solution of 5.0 ml is placed in the volumetric flask of 50 ml, lead up volume to the mark solvent (methanol) and mix.

The test solution

Rubbing 20 tablets of the drug and is transferred of powder a sample of equivalent to 80 mg of the quercetin placed in the flask capacity of 100 ml, is added 50.0 ml of solvent, then treated for 30 minutes in the ultrasonic bath, stirring occasionally. The resulting solution is stirred on a shaker to the full dispergation, and then treated for 15 minutes in the ultrasonic bath, stirring occasionally. The solution is made cool up the solution to the room temperature, is dissolved followed by addition of solvent (methanol) to the mark. The resulting solution is centrifuged for 10 minutes at a speed of 4000 rev/min. The supernatant 5,0 ml is transferred in the volumetric flask of 50 ml, lead up volume to the mark solvent (methanol) and mix. Then filtered through nylon filter (0.45 micron), discarding the first two milliliters of filtrate.

Methods

100 ml of a reference solution is chromatographed on the liquid chromatograph, reaching suitability of the chromatographic system. Parameters of the chromatographic system suitability calculated by peak of ferulic acid:

- an approximate retention time peak of ferulic acid is 13 minutes;
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- the relative standard deviation according to the requirements the SPhU, 2.2.46.

The content of the dry oats seed extract (X) in a single tablet, in mg, calculated by the formula:

$$X = \frac{S_1 \times m_0 \times 50 \times b}{S_0 \times m_1 \times 50} = \frac{S_1 \times m_0 \times b}{S_0 \times m_1}$$, where:

S_1 – the average value of the peak area of ferulic acid, calculated with the chromatograph of the test solution;

S_0 – the average value of the peak area of ferulic acid, calculated with the chromatograph of the reference solution;

m_0 – the mass of sample of the dry oats seed extract, in mg, taken for preparation of the reference solution;

m_1 – the mass of the sample drug, in grams;

b – the average weight of a tablet, in grams.

In the one tablet should be from 90,0 to 110,0 mg of the dry oats seed extract. The chromatogram with the solvent, the reference solution and the test solution are presented according on Figures 3, 4, 5.

In one tablet should be from 36.0 to 44.0 mg of quercetin.

Therefore, we worked the composition, technology and standardization of medicinal product in the form of chewable tablets with quercetin and of oats seed extract. This drug can be used as a general adaptogenic and tonic.

Table 1. The gradient program

The time (min.)	The mobile phase A (% rpm)	The mobile phase B (% rpm)	The elution mode
0-1	8	92	Isocratic mode
1-20	8 → 25	92 → 75	Linear gradient
20-30	25 → 100	75 → 0	Linear gradient
30-33	100	0	Isocratic mode
33-33,5	100 → 8	0 → 92	Linear gradient
42	8	92	Isocratic mode

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Table 2. The gradient program

The time (min.)	The mobile phase A (% rpm)	The mobile phase B (% rpm)	The elution mode
0-1	8	92	Isocratic mode
1-20	8 → 25	92 → 75	Linear gradient
20-30	25 → 100	75 → 0	Linear gradient
30-33	100	0	Isocratic mode
33-33,5	100 → 8	0 → 92	Linear gradient
42	8	92	Isocratic mode

Figure 1. The chromatogram with the reference solution

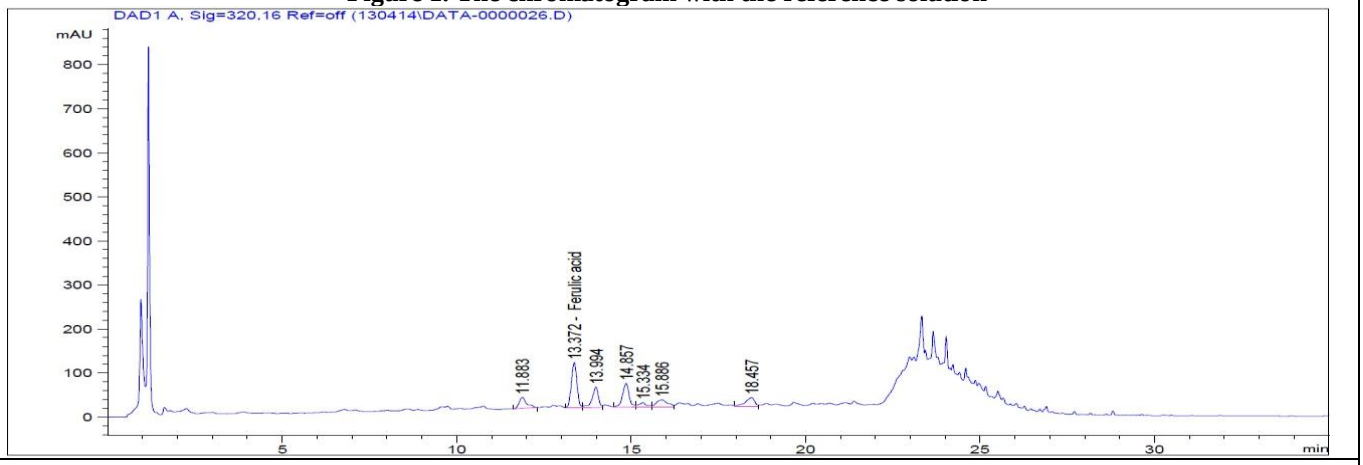
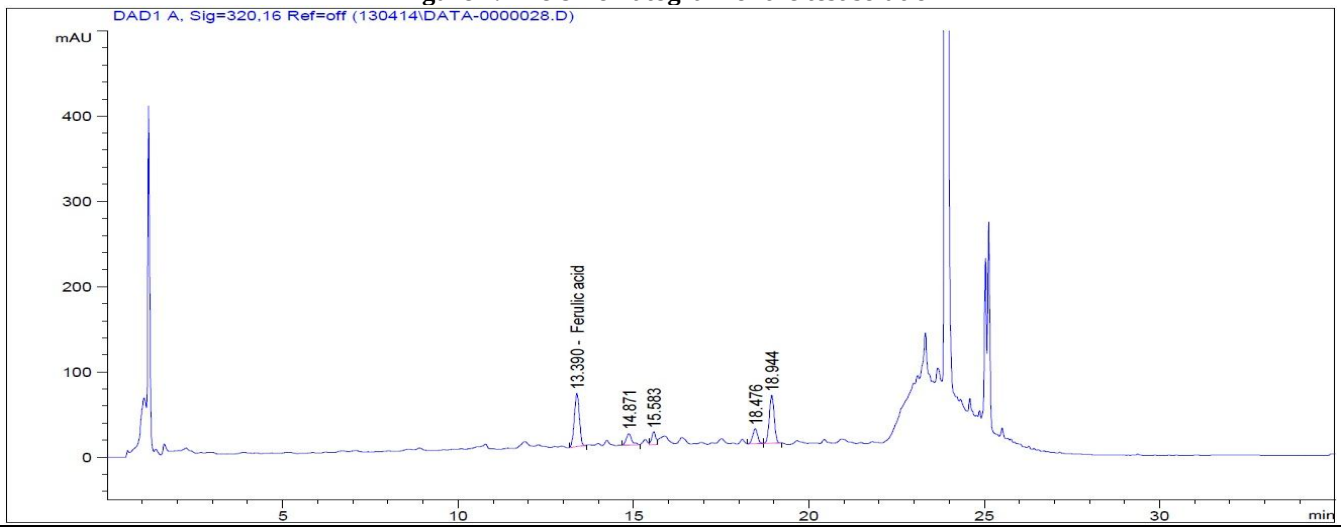
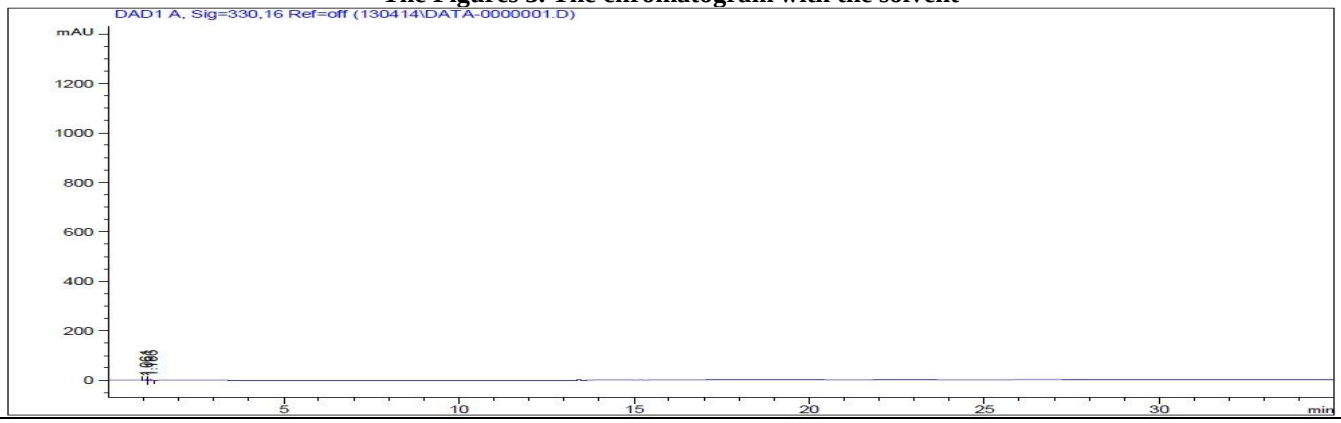


Figure 2. The chromatogram of the test solution



The Figures 3. The chromatogram with the solvent



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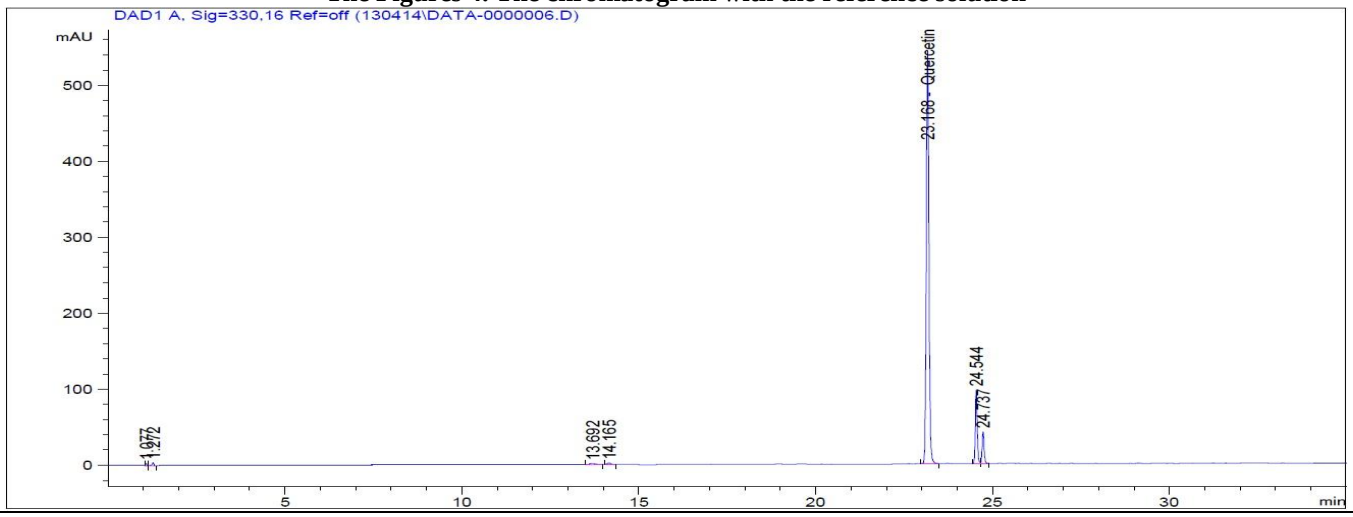
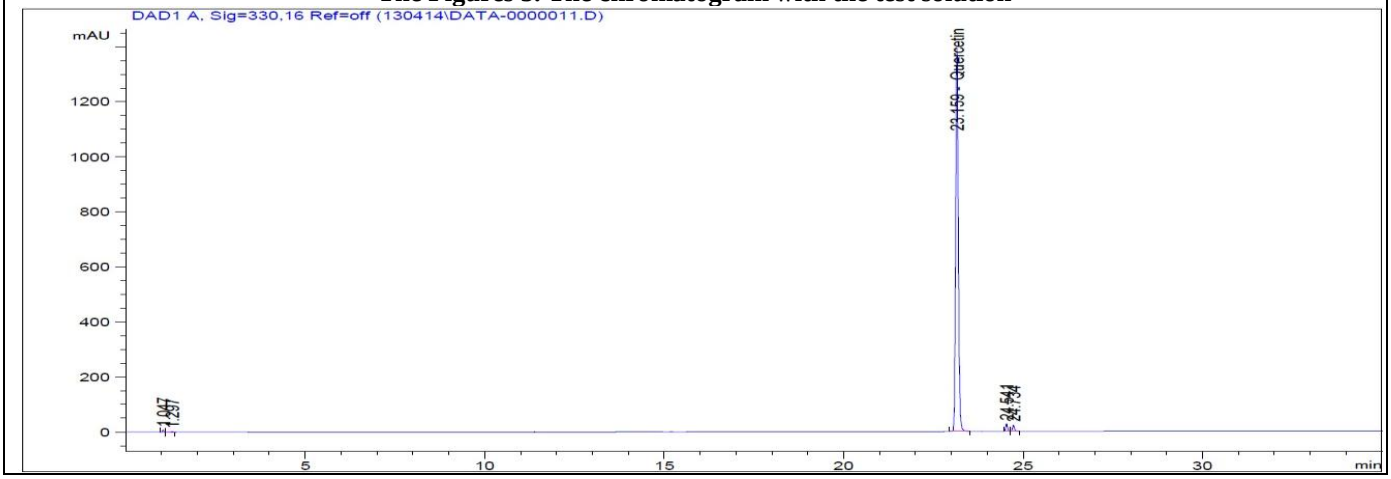
The Figures 4. The chromatogram with the reference solution



The Figures 5. The chromatogram with the test solution



CONCLUSION

1 Based on results of physicochemical and pharmaco-technological researches obrruntovaly composition and developed technology for chewable tablets with the dry of oats extract and quercetin.

2 Conducted the study on the selection of quality indicators designed tablets and methods for their control.

3 By results of researches identified a number of active substances in the developed dosage form.

Prospects of scientific researches

Scientific researches concerning of the dry oats extract combined with quercetin has allowed give "second wind" of the known drug "Quertyn." The perspective in the this study, in our opinion, is the creation of new dosage forms of this composition, such as hard gelatin capsules. This is significant considering that reducing the number of auxiliary substances in the dosage form without compromising on quality and efficiency of the product are a top priority of pharmaceutical technology.

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