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IMPROVEMENT OF THE METHOD OF QUANTITATIVE DETERMINATION OF AZITHROMYCIN WITH CETIRIZINE IN A MODEL MIXTURE

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ANNOTATION

The improvement of the methodology for the quantitative determination of azithromycin with cetirizine in a model mixture using the HPLC method is described. The developed technique is selective for the determination of azithromycin and cetirizine in a combined drug model mixture. The developed technique can be used as a cross-cutting technique in the analysis of the determination of active substances in dosage forms.

Relevance

The discovery and introduction into clinical practice of macrolide antibiotics has become one of the greatest achievements in the history of antimicrobial therapy. Recently, much attention has been paid to the synthesis of new forms of antibiotics. The spectrum of antimicrobial activity of macrolides covers almost all respiratory bacterial pathogens, including atypical microorganisms naturally resistant to beta-lactam antibiotics. Due to the unique pharmacokinetic and pharmacodynamics properties of azithromycin, it occupies a dominant position in the treatment of respiratory bacterial infections, an adequate antimicrobial spectrum, the presence of immunomodulatory and anti-inflammatory activity, safety and economic benefits when used.[1,2]

Currently, there is a relatively small number of works on the determination and detection of azithromycin in dosage forms.[3]

Determination of macro quantities of azithromycin is important for evaluating the pharmacological action and effectiveness of antibacterial therapy, identification of active substances in dosage forms, as well as its metabolites in biological matrices. This, in turn, places increased demands on the quality control of medicines and the improvement of methods for the quantitative determination of antibiotics. An important problem remains the development of new, more sensitive and selective methods of their analysis. There is also a problem of the presence of falsified samples on the pharmaceutical market, which makes it urgent to develop, improve, unified and sufficiently expressive methods of quality control of medicines containing this group of antibiotics, and in particular azithromycin. The solution of this issue should go in parallel with the validation of developed or improved analytical methods of analysis. According to the recommendations of ICH Q2 B, the requirements for the validation of analytical techniques should be taken into account, which consist in determining: accuracy, reproducibility, sensitivity, stability (interlaboratory reproducibility), linearity and other metrological characteristics. Thus, the specificity and selectivity of the analytical method are determined by its ability to reliably determine the medicinal substance in the presence of impurity compounds, degradation products and excipients.

The purpose of the research. Improvement of the methodology for the quantitative determination of azithromycin and cetirizine in a model mixture, as well as validation of the developed methodology for the indicator "Specificity".

Research methods. Chromatography was performed on a gas-liquid chromatograph (HPLC) of the Shimadzu LC-20 (DAD), Japan. Validation of analytical methods were carried out in accordance with the recommendations of the ICH (International Council for Harmonization) Topic Q 2 (R1) «Validation of Analytical Procedures Text and Methodology»

RESULTS

The development of an improved technique for the quantitative determination of azithromycin in a model mixture and validation parameters were carried out by HPLC method. The following chromatography conditions selected experimentally:

Chromatographic column: 150 mm long column with an internal diameter of 4.6 mm, Waters X-Terra RP18,

5mkm, or a similar column can be used after appropriate validation.

Mobile phase: Buffer solution based on ammonium phosphate, pH 9.8: acetonitrile (35: 65).

Flow rate: 1.0 ml/min. Detector: UV at a wavelength of 210 nm.

Temperature: 40 ^{o}C. Injection volume: 10 µl.

Analysis time: 10 min.

Working. Concentration: azithromycin - 500 mcg/ml, cetirizine – 50 mcg/ml.

Then the suitability of the chromatographic system was determined, where: RSD: ≤ 2.0%; resolution between the peaks of azithromycin and cetirizine: 1.0; asymmetry coefficient: 1.5.

Preparation of a buffer solution based on ammonium phosphate, pH 9.8: dissolve 0.264 g of ammonium phosphate bi-substituted in 1000 ml of water (0.002M) and adjust its pH to 9.8 by adding an ammonia solution using a pH meter to control the pH. Then filtered and degassed in vacuum through a 0.45 microns membrane filter.

Solvent preparation: The mobile phase is a buffer solution pH 9.8.

Preparation of a standard solution of azithromycin: about 50 mg (exact weight) of a standard sample (RS) of azithromycin is placed in a measuring flask with a capacity of 100 ml, dissolved in a solvent, the volume of the solution is made up with solvent to the mark and mixed. (500 mcg / ml).

Preparation of a standard solution of cetirizine: about 50 mg (exact weight) of RS cetirizine is placed in a measuring flask with a capacity of 100 ml, dissolved in a solvent, the volume of the solution is made up with solvent to the mark and mixed. 10 ml of the resulting solution is placed in a measuring flask with a capacity of 100 ml, the volume of the solution is made up with solvent to the mark and mixed (50 micrograms / ml).

Preparation of the test solution: about 2.5 g (exact weight) of the model mixture is placed in a measuring flask with a capacity of 100 ml, dissolved in a solvent, the volume of the solution is made up with solvent to the mark and mixed. Filtered through a 0.45 microns membrane filter.

10 ml of the test solution and standard solutions are alternately chromatographed on a liquid chromatograph, obtaining at least 5 chromatograms for each of the solutions.

The content of azithromycin, in grams, in 100 g of the model mixture, is calculated by the formula:

$$X = \frac{S_1 \cdot a_0 \cdot 100 \cdot P \cdot 100}{S_0 \cdot a_1 \cdot 100 \cdot 100} = \frac{S_1 \cdot a_0 \cdot P}{S_0 \cdot a_1}$$

where,

S_1 - is the average value of azithromycin peak areas calculated from chromatograms of the test solution;

S_0 - is the average value of azithromycin peak areas calculated from chromatograms of azithromycin RS solution;

a_0- is the weight of the RS azithromycin, in grams;

a_1- is the weight of the gel attachment, in grams;

P - is the content of azithromycin in RS azithromycin, as a percentage.

The content of cetirizine, in grams, in 100 g of the model mixture, is calculated by the formula:

$$X = \frac{S_1 \cdot a_0 \cdot 100 \cdot 10 \cdot P \cdot 100}{S_0 \cdot a_1 \cdot 100 \cdot 100 \cdot 100} = \frac{S_1 \cdot a_0 \cdot P \cdot 0{,}1}{S_0 \cdot a_1}$$

where,

S_1- is the average value of the peak areas of cetirizine, calculated from chromatograms of the test solution;

S_0- is the average value of cetirizine peak areas calculated from chromatograms of RS cetirizine solution;

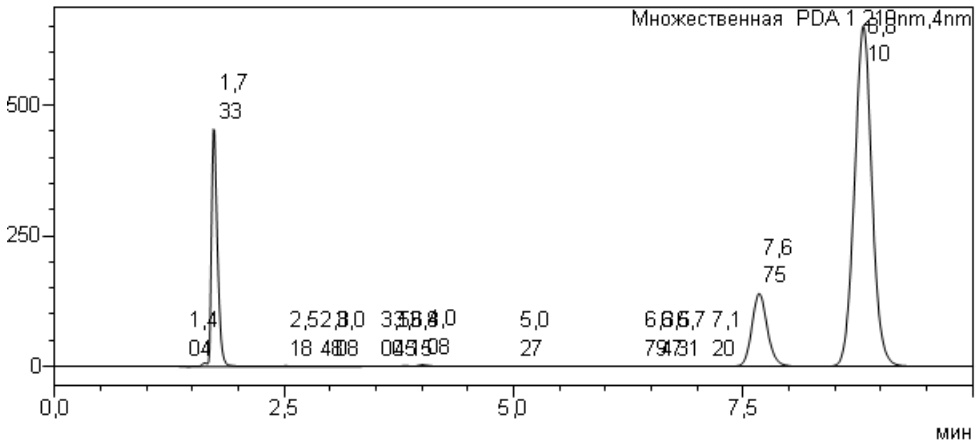
a_0- is the weight of the RS cetirizine, in grams;

a_1- is the weight of the gel attachment, in grams;

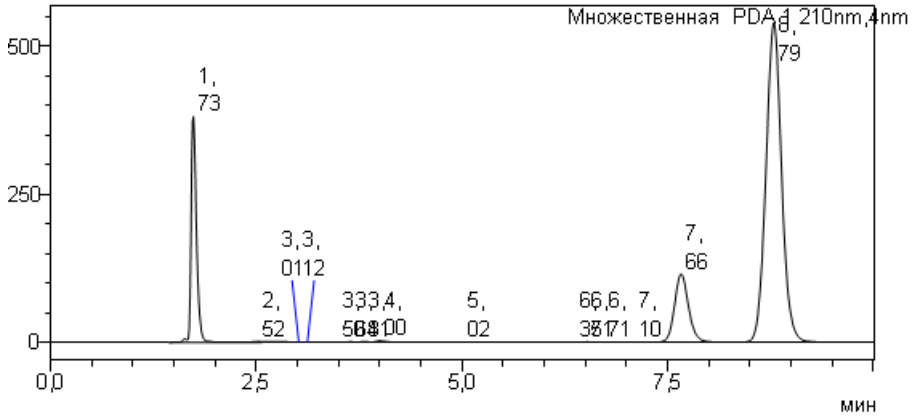
P - is the content of cetirizine in RS cetirizine, in percent.

Determination of method specificity

The specificity of this analytical procedure was proved by comparing the analyzed substance and the standard sample. Graphs 1 and 2 show chromatograms of standard and test solutions of the model mixture.



Graph 1: Chromatogram of the standard solution.



Graph 2: Chromatogram of the test solution of the model mixture (Azithromycin 500 mcg/ml, cetirizine, 50 mcg/ml).

The retention time of the main peak of azithromycin and cetirizine is observed on the obtained chromatograms. Accordingly, the chromatogram of the test solution corresponds to the retention time of the peaks of azithromycin and cetirizine with the chromatograms of the standard solution.

The acceptance criterion was determined by the retention time of azithromycin and cetirizine on the chromatogram of the sample, which should correspond to the retention time of azithromycin and cetirizine on the chromatogram of the standard solution.

CONCLUSION

The method of quantitative determination of azithromycin and cetirizine in a model mixture using the HPLC method has been improved. The developed technique is selective for the determination of azithromycin and cetirizine in a combined drug model mixture. The developed technique can be used as a cross-cutting technique in the analysis of the determination of active substances in the dosage form.

LIST OF USED LITERATURE

1. State Register of Medicines, Medical Devices and Medical Equipment, Tashkent, 2020; 2021.
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