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APPLICATION OF FT-IR SPECTROSCOPY FOR DETERMINATION OF CLARITHROMYCIN IN PHARMACEUTICALS

Method for the qualitative and quantitative assessment of clarithromycin – macrolide antibiotic – in pharmaceutical formulations was developed by using Fourier-transform infrared (FT-IR) transmission spectroscopy for quality control. The calibration model was developed based on simple Beer's law using the FT-IR carbonyl region (C=O) from 1,750 to 1,675 cm^{-1}. Statistical analysis of the results was developed by using TQ Analyst program and based on the least square method. The good coefficient of determination was achieved $R^2 = 0.9973$. Recovery was achieved from 98 to 106%. The method based on the FT-IR spectroscopy for the quantitative analysis of clarithromycin in pharmaceutical formulations is a fast and promising technique.

Introduction. Clarithromycin is antibiotic, semisynthetic macrolide consisting of 14-membered lactone ring (Fig.1). Clarithromycin has antibiotic spectrum, it participates against respiratory pathogens and it is one of the main means of prevention and treatment (in combination with other chemotherapeutic agents) of mycobacteriosis in HIV infection [1].

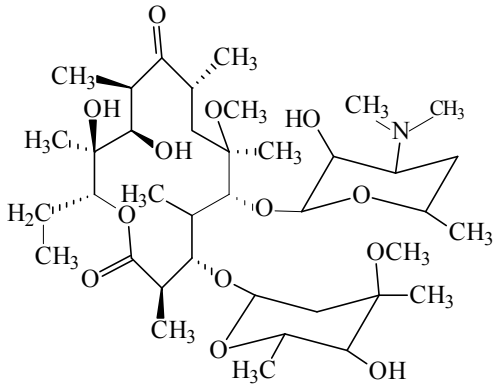

Fig. 1 Chemical structure of clarithromycin

For qualitative and quantitative control of clarithromycin medicines IR spectroscopy and HPLC are used, respectively [2]. Various electrochemical and other methods are also developed. Analysis with these methods requires the use of expensive solvents, complex sample preparation and time consuming. FT-IR spectroscopy is the primary method of identifying a drug substance included in all pharmacopoeia. IR spectra may be obtained not only for pure substances, but also for medicaments. At the same time excipients included in the drug should not suppress the spectrum of the active substance [2]. In the modern pharmaceutical analysis of drugs it is important to develop reliable express methods in order to identify, to carry out quantification of the active substance and its uniform distribution. Therefore, the development of fast methods of qualitative and quantitative analysis on the basis of FT-IR spectroscopy is an urgent task [3].

Main part. The aim of the work is to explore the possibility of using FTIR spectroscopy not only for quality but also for quantitative analysis in pharmaceutical formulations. The objects of study were commercial preparations “Clarithromycin” produced by JV limited company Farmland Belarus. According to the Core Data Sheet each tablet contains 250 mg of clarithromycin and the following excipients: corn starch, microcrystalline cellulose, sodium glycolate, talc purified, povidone K-30, magnesium stearate.

Identification of clarithromycin in medicine was carried out by the characteristic absorption bands. A spectrum of substances of clarithromycin was used as comparison spectrum.

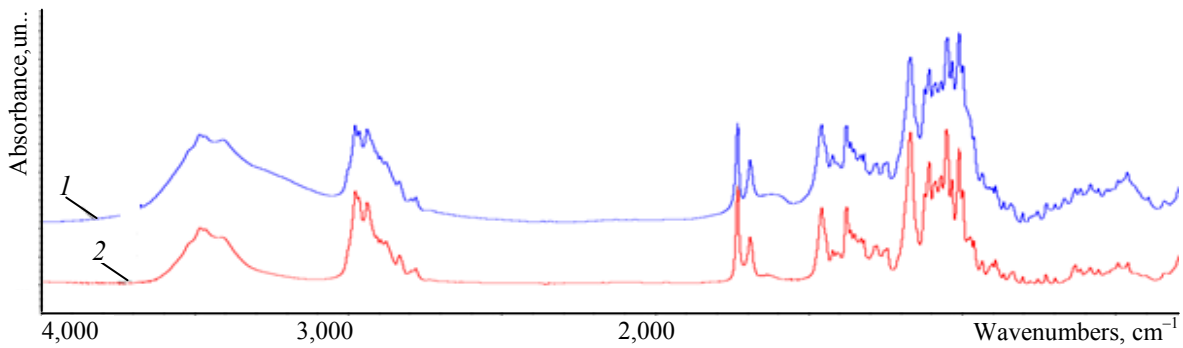

Fig. 2. IR spectra of clarithromycin tablet (*1*) and a standard sample of clarithromycin (*2*)

Investigations were carried out using FT-IR of Nexus 670 Thermo Nicolet in the transmission mode in the range of 4,000–400 cm^{-1} averaging 32 scans at a resolution of 4 cm^{-1}. Samples were prepared as KBr tablets of 13 mm in diameter weighing 250 mg. Background spectrum was registered before recording the spectrum of each sample which is then subtracted. From a comparison of the tablet spectra and the sample of clarithromycin spectra it can be concluded that the absorption spectrum of clarithromycin in tablet is not suppressed by auxiliaries. Therefore, this method is suitable for the identification of clarithromycin in medicines.

Calibration curve was obtained with nine standard with clarithromycin content from 0.2 to 1 mg. Quantitation was carried out by peak area in the region of carbonyl absorption bands: 1.750–1.675 cm^{-1} (Fig. 3).

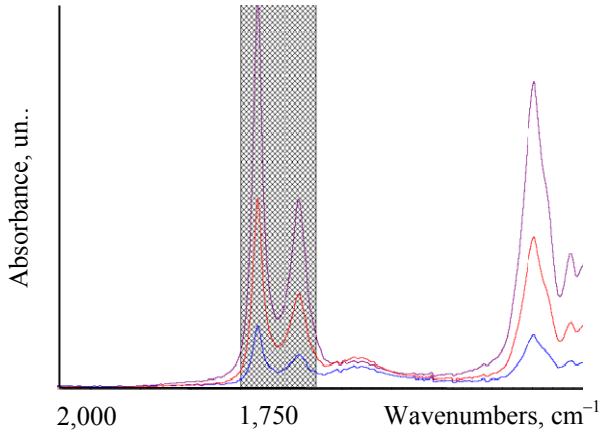

Fig. 3. Region of absorbance carbonyl groups of clarithromycin standards

The studies have shown a good dependence of the peak area of the concentration of clarithromycin. In this area there is not a superposition of peaks of test components and excipients (Fig.4). Data processing was performed with TQ Analyst, using Beer's law, technique of least squares. The equation of the calibration curve is $y = 15.0 \cdot x$, the coefficient of linear regression, $R^2 = 0.9973$ (Fig. 5).

The applicability of the developed technique of quantitative analysis of clarithromycin was determined on the commercial product containing clarithromycin, 250 mg (tablet weights approximately 500 mg). According to the research, the content of clarithromycin in the drug was (244.51 ± ± 6.92) mg. Admissible deviation of weight of acting substances in the tablet with a dosage of 10 to 1,000 mg must not exceed ± 7.5%, or in this case, ± 18.25 mg. This example confirms the possibility of using FT-IR spectroscopy for the quantitative determination of clarithromycin in medicines.

To eliminate the interference of absorption of carbonyl groups of clarithromycin and some groups of additives as well as water at 1,630 cm^{-1}, which could affect the quantitation method "entered:found" was applied. 5, 10 and 15 mg of the standard sample of clarithromycin was added to finely ground tablet (50 mg) (28.94 mg clarithromycin). Measurements were performed three times at each of the points and determine the coefficient of the extraction.

Calculation of the recovery efficiency was carried out by the formula (1) [4, 5].

$$Z = \frac{C - A}{B} \cdot 100, \quad (1)$$

where Z – the recovery efficiency, %; C – found content of clarithromycin in 50 mg tablet, after the addition of the standard, mg; A – content of clarithromycin in 50 mg tablet before the addition of the standard, mg; B – amount of injected standard sample of clarithromycin, mg.

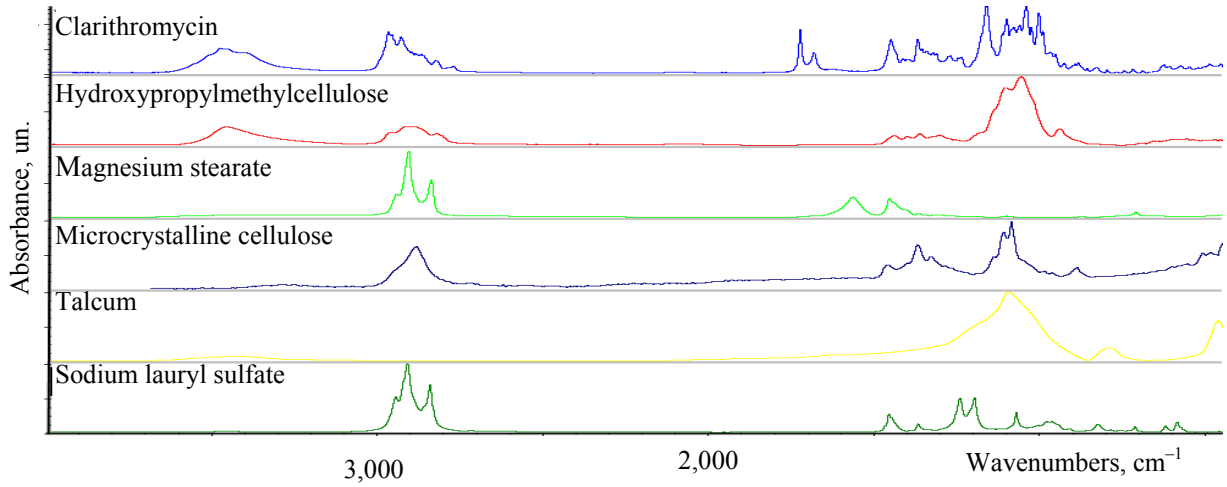

Fig. 4. Infrared spectra of clarithromycin and excipients

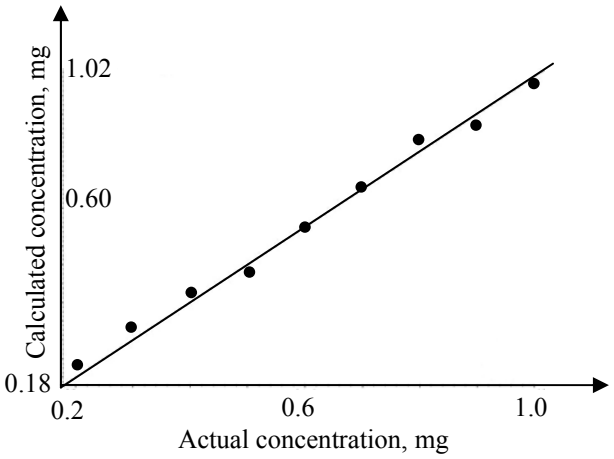

Fig. 5. Calibration of clarithromycin standarts

The results of this study are given in the table.

The results of content analysis of clarithromycin by analysis of spiked samples

Initial content, mg	entered, mg	found, mg	Recovery efficiency, %
28.9	5	34.2	106.0
28.9	10	38.7	98.0
28.9	15	44.0	100.6

Acceptable recovery efficiency is 90–108% [3]. The obtained results satisfy these requirements, which means that there is no overlay of the absorption bands of clarithromycin and excipients and they have no effect on the signal intensity, which confirm the possibility to control the amount of clarithromycin in medicine with given additive substances. The equation of the calibration curve by the method of least squares had the form $y = 0.93 \cdot x + 0.59$. Coefficient of linear regression was $R^2 = 0.9954$.

Conclusion. Research conducted have shown that the method of Fourier-transform infrared spectroscopy can be used not only for qualitative but also for the quantitative analysis of clarithromycin in pharmaceutical formulations for the evaluation of the quality index as “uniformity of content”. This will reduce the cost and time of analysis compared with traditionally used method HPLC. Moreover, the application of FTIR spectroscopy method does not require dissolution of the drug and the extraction of the active substance, and it can also be used for the simultaneous determination of additives, including the insoluble components contained in pharmaceuticals.

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