DEVELOPMENT OF THE METHODS OF ANALYSIS OF N-(4-TRIFLUOROMETHYLPHENYL)-4-HYDROXY-2,2-DIOXO-1H-2Λ^6,1-BENZOTHIAZINE-3-CARBOXAMIDE

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Introduction. The problem of creating of new highly effective medicines with minimal side effects is one of the main tasks of modern pharmaceutical industry. Interesting objects of study in this regard is benzothiazine derivatives, especially oxicams – derivatives of 1,2-benzothiazine-1,1- dioxide that show high analgesic action and use for pain treatment of various origin. Taking oxicams for a long time often accompanied by a large number of side effects. For the solving of this problem a group of R-4-hydroxy-2,2-dioxo-1H-2λ^6,1-benzothiazine-3-carboxamides that are the structural isomers of oxicams were synthesized. One of them is N-(4-trifluoromethylphenyl)-4-hydroxy-2,2-dioxo-1H-2λ^6,1-benzothiazine-3-carboxamide – substance with the highest analgesic effect and low level of toxicity.

N-(4-trifluoromethylphenyl)-4-hydroxy-2,2-dioxo-1H-2λ^6,1-benzothiazine-3-carboxamide was obtained by the reaction between methyl ester of 4-hydroxy-2,2-dioxo-1H-2λ^6,1-benzothiazine-3-carboxilic acid and 4-trifluoromethylaniline in the presence of xylol.

Aim. To develop the methods of identification and assay of N-(4-trifluoromethylphenyl)-4-hydroxy-2,2-dioxo-1H-2λ^6,1-benzothiazine-3-carboxamide and procedures required.

Materials and methods. The object of researching is the substance of N-(4-trifluoromethylphenyl)-4-hydroxy-2,2-dioxo-1H-2λ^6,1-benzothiazine-3-carboxamide. The object was checked for possibility to form colored complex with the solution of the salt of heavy metals (copper (II) sulphate, ferric (III) chloride), to give reaction for fluorides and sulphates after mineralization.

For assay method of alkalimetry was chosen. The mass for analysis was measured by analytical balance Axis ANG-200. The results of alkalimetrical determination of the object were subjected to the statistical processing.

Results and discussion. The identification of analyzed substance was successfully proven. The results of statistical processing of assay showed that the relative uncertainty did not exceed the average value of 0,81 %.

Conclusion. Methods of identification and assay of N-(4-trifluoromethylphenyl)-4-hydroxy-2,2-dioxo-1H-2λ^6,1-benzothiazine-3-carboxamide method of UV-spectrophotometry were developed.

DEVELOPMENT OF QUALIFICATION AND QUANTIFICATION METHODS OF 4-METHYLPYRIDINE-2-AMIDE 1-PENTYL-2-OXO-4-HYDROXYQUINOLINE-3-CARBOXILIC ACID

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Introduction. Tuberculosis is the second major cause of death in adults as a result of infectious disease with nine million new cases and close to 1.8 million deaths every year. The treatment of TB is difficult due to the unusual structure and the chemical composition of the cell wall of the mycobacterium; this makes many antibiotics ineffective and prevents drugs entry. This problem has lead to the development of new structural classes of antitubercular agents.

A great deal of interest in this regard are quinolone derivatives. One of them is 4-methylpyridine-2-amide 1-pentyl-2-oxo-4-hydroxyquinoline-3-carboxilic acid. It shows a high level of antimycobacterial activity.

Aim. This work aims to develop new analytical methods of identification and assay for antimycobacterial agent - 4-methylpyridine-2-amide 1-pentyl-2-oxo-4-hydroxyquinoline-3-carboxilic acid which is based on their structure and chemical properties.

Materials and methods. The object of our investigation is the substance of 4-methylpyridine-2-amide 1-pentyl-2-oxo-4-hydroxyquinoline-3-carboxilic acid.

Due to the presence in the structure of the object enolic hydroxyl group it can form colored complex with heavy metals such as copper (II) sulphate, ferric (III) chloride or cobalt (II) chloride in alkaline medium.

Method of UV-spectrophotometry also can be used for identification and assay. Absorbance was measured by the spectrophotometer Evolution 60 S Thermo Scientific in the wavelength range from 200 to 400 nm. For measuring mass for analysis analytical balance Axis ANG-200 was used. The results of spectrophotometric quantitative determination of the 4-methylpyridine-2-amide 1-pentyl-2-oxo-4-hydroxyquinoline-3-carboxilic acid were subjected to the statistical processing.

Results and discussion. The identification of the object was successfully confirmed. The results of statistical processing of quantification displays the relative uncertainty did not exceed the average value of 1,43 %.

Conclusion. Analytical methods of identification and assay of 4-methylpyridine-2-amide 1-pentyl-2-oxo-4-hydroxyquinoline-3-carboxilic acid were developed successfully.

THE PROGNOSIS OF TOTAL UNCERTAINTY OF THE SPECTROPHOTOMETRIC METHOD BY SPECIFIC ABSORBANCE

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Introduction. Uncertainty is the parameter associated with the measurement result for the defined study. Uncertainty characterizes the spread of values that can be reasonably attributed to the measured. The prognosis of uncertainty of the analysis is an important stage of the analytical cycle and is necessary for improving the validation characteristics of the analysis technique: increasing the accuracy, reliability, correctness and reproducibility of the determination, expanding the range of values studied, accelerating the test, reducing the error of the analysis results.

Aim. The aim of our work is to assess total uncertainty of the spectrophotometric determination of riboflavin, prednisolone sodium phosphate, prednisolone and chloramphenicol in the substances by specific absorbance.

Materials and methods. The pharmacopoeial spectrophotometric assay methods (State Pharmacopoeia of Ukraine) for quantitative determination of riboflavin, prednisolone sodium phosphate, prednisolone and chloramphenicol in the substances by specific absorbance were used. SPhU requirements for maximum permissible errors for volumetric glassware, balances and devices were used.

Results and discussion. There are pharmacopoeial requirements for the total uncertainty of the analysis results (Δ_{As},%), expressed as a one-way confidence interval with a probability of 95%, based on the tolerances of the substance content: $\Delta_{As}(\%) \le \max \Delta_{As} = B$. The total relative uncertainty of the analysis (Δ_{As},%) in the case of the specific absorbance method has the following form: $\Delta_{As}^2 = \delta_{noise}^2 + \Delta_{FAO}^2 + \Delta_{SP}^2 + \delta_{cal}^2 \le \max \Delta_{As}^2$, where: δ_{noise} – uncertainty caused by impurities and auxiliary substances, Δ_{FAO} – uncertainty of the final analytical operation, Δ_{SP} – uncertainty of sample preparation, δ_{cal} – calibration uncertainty.

The uncertainty estimate associated with the background absorption (δ_{noise}%) at the analytical wavelength shows the insignificance of the sum of the information coefficients of the impurities (decomposition products and auxiliary substances) in comparison with the maximum permissible uncertainty of the analysis maxΔ_{As}. The significance of the uncertainty of the final analytical operation is obtained within the framework of a large interlaboratory experiment and is 0.49%. The value of Δ_{FAO} is insignificant in comparison with the uncertainty of the calibration and with the maximum permissible total uncertainty of the maxΔ_{As} analysis for all drugs. Uncertainty of sample preparation was predicted taking into account the requirements of the SPhU to measuring glassware and balances (Fig. 1). The calibration