JUSTIFICATION OF THE METHOD FOR THE QUANTITATIVE DETERMINATION OF METRONIDAZOLE BENZOATE IN THE COMPOSITION OF OROMUCOSAL GEL

Orlenko D. S., Yakovenko V. K.*
National University of Pharmacy, Kharkiv, Ukraine

Introduction: Stomatitis and periodontitis are the conditions that dominate the structure of inflammatory diseases of the oral cavity. The treatment of gingivitis and periodontitis consists in regularly carried out hygienic treatment and the appointment of drugs that effectively inhibit the activity of microorganisms, slow down the formation of microbial accumulations and have an anti-inflammatory effect. Our gum gel contains a combination of 3 active pharmaceutical ingredients: metronidazole benzoate, miramistin and sodium hyaluronate and has antimicrobial, anti-inflammatory, reparative action. For the quantitative analysis of the substance metronidazole benzoate according to SPhU / EP, the method of titration in a non-aqueous medium is used.

The technique is selective with respect to compounds having an amino group in their molecular structure [EPh, 9th ed.]. However, the titration method that is used in the quantitative determination of the substance is not applicable for the determination of metronidazole benzoate in the finished dosage form due to the interfering effect of other components.

The method of absorption spectrophotometry in the UV region also does not allow a reliable quantitative assessment of the content of metronidazole benzoate due to the influence of other components of the drug [Panasenko, O. I., Donchenko, N. V., Hotsulya, A. S. Zaporizhzhya medical journal, 2013]. Monographs of finished dosage forms of metranidazole benzoate for oral administration, presented in the USP and BP, for the quantitative determination of APIs, the HPLC method is used, which has the highest selectivity with respect to the absorption spectrophotometry method. The aim of our work was to develop a method for the quantitative determination of metronidazole benzoate in the composition of a combined gel by HPLC.

Materials and methods: The object of the study was an oromucous gel containing metronidazole benzoate - 16 mg / g, miramistin - 5 mg / g, sodium hyaluronate - 2 mg / g. Quantitative determination was carried out by HPLC on a chromatograph with a diode array detector.

An Xterra RP18 chromatography column was used, Waters, 150 mm × 4.6 mm, sorbent particle size of 5 μm; mobile phase buffer solution pH 3.0: acetonitrile P in the ratio (35:65); wavelength 235 nm. Statistical processing of the research results was carried out according to the methods of SPhU 2.0, paragraph 5.3.

Results: Quantitative determination was carried out using a solution of a standard sample of metronidazole benzoate. The relative standard deviation (RSD) of the peak areas of the metronidazole benzoate chromatograms of the comparison solution corresponded to the requirements of SPhU and is 0.28 for 3 parallel injections.

The developed method was validated and its main validation characteristics were studied: specificity, linearity, correctness, convergence, etc. There are no peaks in the chromatograms of the placebo solution with retention times in the range $tR_i \pm w_i$ for the analytical solution; therefore, the placebo components do not affect the analysis results obtained using the studied method.

The technique is linear in the concentration range from 80% to 120%. The value of the systematic error is $\delta = 0.32$, which satisfies the condition $\delta \leq 0.51\%$. When determining the convergence of the method, the confidence interval of a single value is $\Delta z = 0.139$, which satisfies the condition $\Delta z \leq 1.6\%$.

Conclusions: The method for the quantitative determination of metronidazole benzoate in a combined gel by HPLC for all validation characteristics meets the requirements of SPhU and EP.