DEVELOPMENT OF THE QUALITY CONTROL METHODS FOR ANALYSIS OF COMBINED EXTEMPORANEOUS OINTMENT

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Introduction. Pharmacies are responsible for delivery of large numbers various products and services, increasing patient safety and ensuring efficient and effective pharmacy practices. Because of increasing demands for better services, pharmacy policy should take a focus on constant improvement of quality control methods for drugs.

The general purpose of quality assurance in the pharmaceutical industry is to help for each patient get safe, effective and of acceptable quality medicines.

Recently there has been a trend towards the return and expansion of the extemporaneous manufacturing in Ukraine. It can be explained by the presence some advantages of extemporaneous recipe front of manufacture drugs. Such as, individual prescriptions for preparing medicines, where you can take into account patient status or character his disease. Also pharmacist can change some compound of prescription, if patient has some allergic reaction on it. These are very useful for preparing children's medicines. Besides, drugs prepared at a pharmacy are cheaper than drugs prepared at a factory.

Quality control of medicinal products for today is a basic requirement to ensure the effective and safe treatment. For proper control of dosage forms that are manufactured in pharmacies, it is necessary to improve the available methods of monitoring their quality, as well as to develop new ones.

Ointments are homogeneous and semi-solid dosage forms, that is intended for external application to the skin or mucous membranes. They composed of a base and medical substances equally distributed in them, as you see these dosage forms are simple in using, but in the same time they are quite effective.

The recipes of ointments are varied, and often include several components, so the development of control methods of active pharmaceutical ingredients in extemporaneous dosage forms for today is very important.

The **aim** of our work is developing the methods for identification and quantitative determination of active pharmaceutical ingredients in extemporaneous ointment:

Rp.: Streptocidi 1,0
Novocaini 0,5
Sulfuris 0,5
Ung. Tetracyclini 3% - 15,0
M. D. S.

Materials and methods. Analytical studies were performed at spectrophotometer Evolution 60S. For operation were used measuring glassware of class A and excipients met the requirements of the State Pharmacopoeia of Ukraine.

Results and discussion. Since studied ointment is a multicomponent, we propose to carry out separation of the components during the sample preparation for their identification.

A weighed sample of the ointment was dissolved in hexane R and then were extracted the water soluble components. The aqueous layer was separated and carried out the identification of procaine hydrochloride by the reactions: bleaching of potassium permanganate (1 g/l) solution, the formation of Schiff’s bases and formation of azo dye. Also in aqueous layer the tetracycline hydrochloride was identified by the reactions: formation of anhydrotetracycline (violet color) and with ferric III chloride solution. The reactions of identification the chlorides for both substances are also made.

A suspension of sulfur and sulfanilamide in hexane is treated with hydrochloric acid and the sulfanilamide is determined by reaction to a primary aromatic amino group. The hexane suspension is passed through a paper filter, dried and set fire to the dry filter. The blue color of the flame and the characteristic smell of sulfur dioxide indicate the presence of sulfur in the composition of the ointment.

This multicomponent ointment is very difficult from the point of view of the analyst. Using the most appropriate titration methods for the pharmacy is impossible because each of the components will interfere with the definition of the other. To this aim we developed the following methods of analysis of each component.

Tetracycline hydrochloride is proposed to determine in the ointment by direct spectrophotometric method. Procaine hydrochloride and sulfanilamide do not interfere with this analysis, because they do not absorb light in the visible region of the spectrum.

One of the main requirements, which allow to use spectrophotometric methods for assay of substance, is the subordination to Bouger-Lambert-Beer law.

After series of study we have been able to establish that the solution of tetracycline hydrochloride obeys this law within concentrations from 0,5 to $3,15*10^{-3}$ mg/ml, specific absorption rate is 342,5±8,5.

The sample of the ointment is dissolved in hexane R and tetracycline hydrochloride is extracted with a phosphate buffer solution with pH 4.5. During study stability solutions of tetracycline hydrochloride in the different solvents and completeness extraction, phosphate buffer solution (pH 4,5) showed the highest result, that's why we chose it .Absorbance is measured at 357 nm wavelength. The quantitative content is calculated according to the standard method, using as a standard SPS of tetracycline hydrochloride.

Linearity was studied in the range of 80-120% of the nominal concentration. The obtained experimental data confirm the correctness of this criterion (b = 0.9917; Sb = 0.0142; a = 0.0170; Sa = 1.4360; S0 = 0.5516). The technique is characterized by correctness and convergence (ΔZ = 0,9421%, δ,% = 0,81%). In the inter-laboratory study, the systematic error was δ = 0.78%. The proposed quantification technique will give correct results in other laboratories, since the predicted total uncertainty of the analytical technique does not exceed the critical value of the maximum permissible total uncertainty.

Procaine hydrochloride is proposed to be determined by the method of extraction photometry, which is based on the reaction of formation of the ion associate with methyl orange and subsequent extraction of the associate formed with chloroform. To avoid the influence of tetracycline hydrochloride on the absorption of this associate, it is proposed to convert the indicator into an acid form by changing the pH of the resulting solution. Absorbance is measured at 522 nm wavelength. The quantitative content is calculated according to the standard method, using as a standard SPS of procaine hydrochloride.

After series of experimental studies we established that the procaine hydrocloride solution obeys Bouger-Lambert-Beer law within concentrations from 0,02 to 0,5 mg/ml.

Sulfanilamide in the composition of this ointment is proposed to be determined by titration in sum with procaine hydrochloride using nitritometry, with further recalculation after determining the quantitative content of procaine hydrochloride photometrically.

The quantitative determination of sulfur does not regulate by SPhU.

Conclusions. The developed methods for identification and quantitative determination of compounds in combine extemporaneous ointment will be used in the further development of technological instructions for this dosage form and in the stability studies.