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Spectrophotometric determination of acyclovir in the suppository

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ABSTRACT

The research methods on the vacillator's development quantitative determination of in substance and suppositories by absorption spectrophotometer were conducted and there was chosen an optimal solvent and dilution stability and also was investigated an optical density over time, and concentration range ($2 \cdot 10^{-6}$– $2 \cdot 10^{-5}$ g / ml) was set, where the linear dependence of the optical density concentration was performed. The developed technique allows controlling composition and technology of suppositories with acyclovir and oils in an industrial environment.

Key words: acyclovir, suppositories, oils, absorption spectrophotometer method

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INTRODUCTION

According to WHO's data, in recent years around the world there has been a significant increase in the number of infectious diseases, sexually transmitted diseases (STD). Every day in the world are infected with STDs more than 300,000 people [1, 2]. Pharmacotherapy of the most common diseases includes a wide range of products. [3] The drug of choice for the treatment of primary episode of genital herpes is oral "acyclovir", which is the ancestor of acyclovir [4].

Acyclovir (9- [2-hydroxyethoxy methyl] guanine 9H) an acyclic analog of a natural nucleoside - 2'-desoxyguanosine. Today, there has been developing more than 400 products for the treatment of infections caused by the herpes simplex virus (HSV) types 1 and 2 on this basis. Getting into the affected cell HSV, acyclovir viral thymidine kinase under the influence transforms into acyclovir monophosphate, which, with the participation of cellular enzymes sequentially turns to acyclovir diphosphate and acyclovir triphosphate. Last assembly blocks viral DNA almost no effect on DNA replication almost no effect on DNA replication of human cells [5].

MATERIALS AND METHODS

There was used substance acyclovir (producer "Quimica Sintetica, SA", Spain, certificate of analysis № 2013-7 / 09-17 / 158 for the research, which meets the requirements of the ICC to the drug № UA / 9693 / 01/01), measuring utensils class A, reagent meets the requirements of HFCs, analytical balances AB 204 S / A METTLER TOLEDO, pH Meter PB-11 "Sartorius AG", spectrophotometer "SPECORD 200-222U2B".

RESULTS AND DISCUSSION

Quantification of acyclovir in the substance, drugs and in the samples of biological nature was carried out by various analytical techniques: spectral, immunological, and chromatographic [6, 7].

In the development of methodic of quantitative determination of acyclovir by spectrophotometry publications on research of spectral characteristics, depending on the nature of the solvent, and pH were learned. In the acidic and alkaline medium the absorption spectra of solutions of acyclovir ranging from 230-300 nm; and have maxima and

minima [7]. Acyclovir is slight soluble in the water, but soluble in dilute solutions of mineral acids and alkali metal hydroxides [6]. Literature data were confirmed experimentally in the following solvents: 0.1 M solution of hydrochloric acid and 0.1 M sodium hydroxide solution. The absorption spectrum of a solution of acyclovir in 0.1 M hydrochloric acid solution characterized by a single, fairly narrow absorption band with a maximum at the wavelength (256±2) nm, and the presence of "shoulder" in the field (280±2) nm (Fig. 1.1).

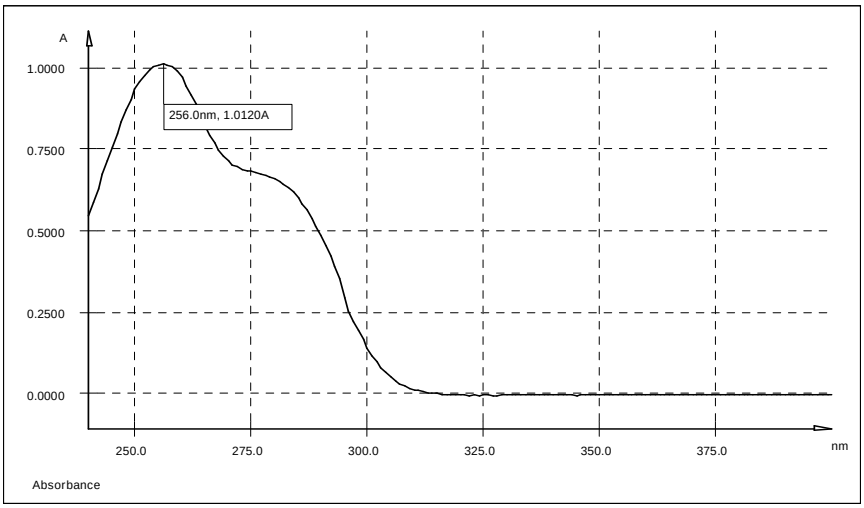

Fig.1. The absorption spectrum of acyclovir (2.0 10^{-5} g / ml) in 0.1 M hydrochloric acid solution

By increasing the pH of the solutions acyclovir observed bathochromic shift of the absorption maximum. At pH 12.0 the absorption spectrum of an acyclovir solution in 0.1 M sodium hydroxide solution is characterized by a maximum absorption wavelength (265 ± 2) nm, and there is a considerable broadening of the absorption band (Figure 2).

Based on the study of the absorption acyclovir solutions spectra of in acidic and alkaline medium is selected as solvent 0.1 M sodium hydroxide solution.

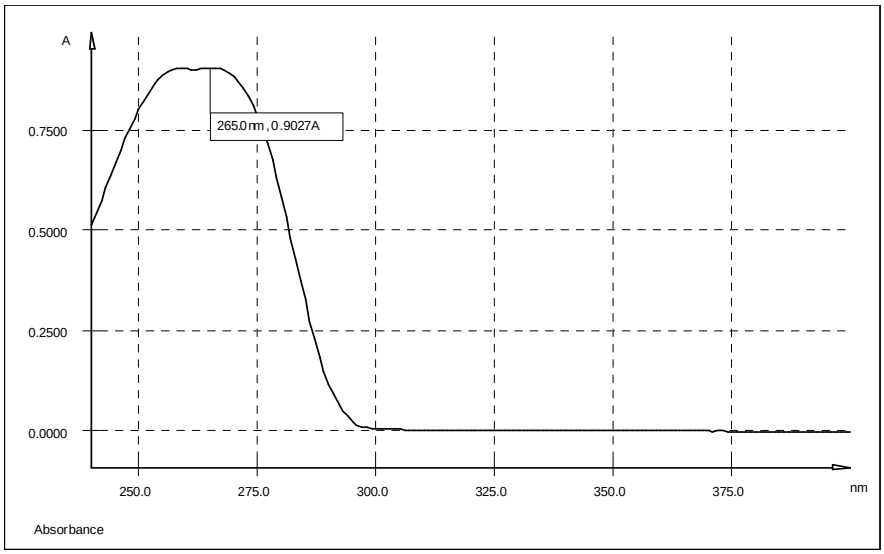

Fig. 2. The absorption spectrum of acyclovir (1,96 · 10^{-5} g / ml) in 0.1 M sodium hydroxide solution

During the research there was selected breeding acyclovir so that the absorption coefficient of the solution was in the range 0.2-0.7, set the concentration range of the substance, which has been observed a linear relationship (Figure 3).

To confirm the stability of the solvent has been studied absorbance solution of acyclovir in time. Preparing solutions of the substance of acyclovir in 0.1 M sodium hydroxide solution and absorbance was measured at 265 nm. The results are shown in Table 1.

According to studies the optical density of the solutions with a pH of 12.00 is stable for 60 minutes.

We have investigated the metrological characteristics of the standard method of spectrophotometric method on the model solutions substance acyclovir (Table 2).

Table 1 Studying of the optical density of the solution of acyclovir in time

pH	Acep.					RSDt, %	δ, %
	0 min	15 min	30 min	45 min	60 min		
12.0	0.4590	0.4592	0.4588	0.4588	0.4594	0.097	0.12

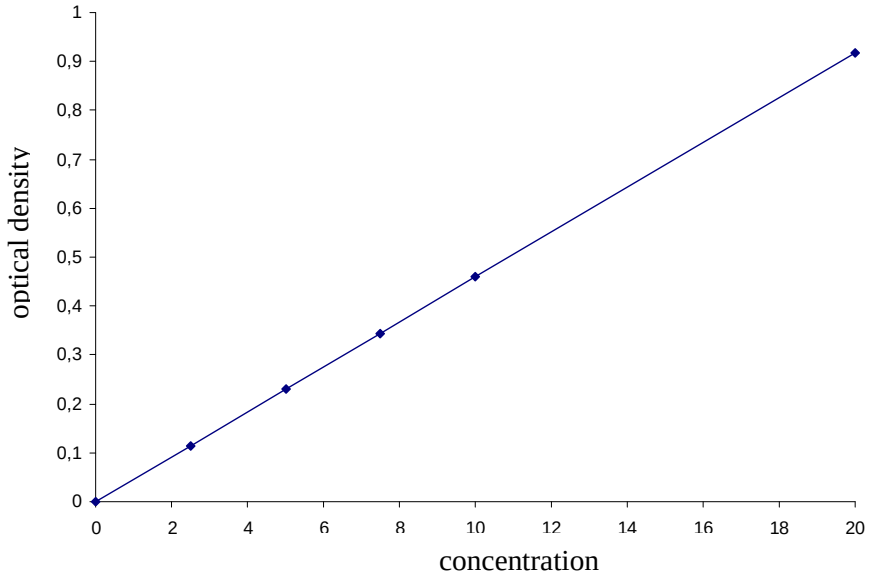

Fig. 3. A plot of optical density (A) of the concentration of acyclovir

Based on the studies it has been developed acyclovir quantitative determination technique by absorption spectrophotometry in the UV spectrum area 0.1 M sodium hydroxide solution is used as a solvent. The relative error in the determination is ± 0.07 %.

At the Pharmaceutical University Drug Technology Department a new dosage form has been developed. They are suppositories with acyclovir and oils [5]. Suppositories meet all solid dosage forms requirements. [9] The quantitative determination technique of acyclovir in suppositories is based on technique aforementioned [10].

Table 2 The metrological characteristics of methods of quantitative determination of acyclovir by spectrophotometry

Xi was found, %	$\bar{X}$	S^2	S	P	t (P,v)	Sx,r	RSDx,%
99,56 100,15 99,80 99,75 100,27 99,63	99,86	0,0821	0,286	0,95	2,78	0,00286	0,28

The specificity for the method of absorption spectrophotometry confirming is based on the need to prove that the relative systematic error, caused by additive substances, is not significant in comparison with maximum permissible analysis uncertainty. The assessment of excipients influence was being conducted by measuring the optical density of the solution prepared as described for the samples suppositories without acyclovir (A_{blank}) and acyclovir substance solution in 0.1 M sodium hydroxide solution at a dilution of 1.07 × 10-5 g / m (A_{subst}), the quantity of acyclovir is needed for 3.0 g of medication.

Optical density three average measurements are: A_{blank} = 0.0042; A_{subst} = 0.4590. The systematic error is about 0.92%. It is significantly less than technique systematic error.

$$\delta_{exc} = \frac{100 \cdot 0.0042}{0.4590} = 0.92\%$$

Based on studies quantitative determination method of acyclovir in suppositories was developed.

Method: accurate mass of triturated suppositories mass is put into a flask with ground joint; 100 ml 0.1 M of sodium hydroxide solution are added and heated on water bath at 40 °C until complete bases dissolution.

The solution is cooled and filtered through a thick paper filter into a volumetric flask 250.0 ml. Extraction is repeated twice with respectively 100 ml and 50 ml of 0.1 M of sodium hydroxide solution. The solutions are cooled and then filtered in the same flask, and adjusted with the same solvent up to the mark.

1.50 ml of the resulting solution are added to a volumetric flask and adjusted to 100.0 ml to the mark 0, M with sodium hydroxide solution.

The standard solution sample (SSS) 0.0200 g of acyclovir substance put into 100.0 ml volumetric flask, 70 ml of 0.1 M sodium hydroxide are added and stirred until dissolved substance is adjusted to the mark with the same solvent. 2.50 ml of the resulting solution was added to a volumetric flask and adjusted to 50.0 ml to the mark with 0.1 M sodium hydroxide.

The absorbance of the test solution and SSS was measured at a wavelength (265 ± 2) nm in a 1 cm cell, as the reference solution using 0.1 M sodium hydroxide solution.

Acyclovir content in a suppository, in grams, based on the average weight of the suppository, is calculated by the formula:

$$X_{,г} = \frac{A_i \cdot m_{cm} \cdot 250 \cdot 2.5 \cdot 100 \cdot m_{cep.20}}{A_{cm} \cdot 100 \cdot 1 \cdot 50.1.50 \cdot m_{д/а}} = \frac{A_i \cdot m_{cm} \cdot 2.5 \cdot m_{cep.20}}{A_{cm} \cdot 0.3.m_{д/а}}$$

- Optical density of the test solution;
- Optical density of the working standard solution;
- The average weight of twenty suppositories (g);
- Sample weight of acyclovir for solution working standard, (g);
- Sample weight of suppositories taken for analysis (g).

The content of acyclovir in the suppositories is from 0.135 g to 0.165 g metrological characteristics quantifying acyclovir suppositories are presented in Table 3.

Table 3 Analysis results suppositories acyclovir and essential oils

X_i	$\bar{X}$	S^2	S_{av}	P	t(P,v)	E, %	$S_{x,r}$	RSD_x,%
0.146 0.149 0.152 0.149 0.153 0.157	0.151	1.48×10^{-5}	0.0016	0.95	2.78	2.89	0.01059	1.059

The method was tested on laboratory samples of suppositories with oils. The relative error in the determination of not more than 1.1 %. The technique is simple and fast, convenient for in-process control of drug production in an industrial environment.

To study the stability during storage of suppositories 5 series of laboratory samples contour packaging film PVC brand EP-73 GOST 252-88 at 8-15 ºC and “scarf” were laid down in a dry, dark place. Today, the shelf life is 6 months suppositories. Observations of the shelf-life of the drug continue.

CONCLUSION

1. The methods of quantitative spectrophotometric determination of acyclovir in substance and in suppositories with acyclovir and oils were developed.

2. The method can be used in an industrial environment when in process analyzing of suppositories.

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