Prospects for the Use of Etafilcon A Soft Contact Lenses and Betaxolol Hydrochloride in the Ophthalmic Therapeutic System for Treatment of Glaucoma Combined with Myopia

Denis K.Naplekov[1], Elena T.Zhilyakova[1], Natalia V.Avtina[1], Alexandra V. Agarina[2*]

[1]*Belgorod State University, 308015, Russia, Belgorod, Pobedy St., 85*
[2]JS "Veropharm", 308017, Russia, Belgorod, Rabochaya st., 14
Email: 783767@bsu.edu.ru

Abstract
In this article the short description of soft contact lenses materials in terms of their use in the ophthalmic therapeutic systems and experimental results of their adsorptive properties in combination with the ophthalmic solution of Betaxolol hydrochloride are presented. Preliminarily it is determined that Russian pharmaceutical market of anti-glaucoma drug products and soft contact lenses can be characterized as a widely various. It is also known that currently the research of the alternative drug delivering systems is a relevant scientific field. In this research the soft contact lenses of brand 1-DAY ACUVUE® MOIST (Etafilcon A) and 0.5% ophthalmic solution of Betaxolol hydrochloride were chosen. The assay of betacolol hydrochloride in its ophthalmic solution before and after the process of adsorption was carried out by UV-spectrophotometry method. The evaluation of contact lenses adsorption potential was performed as a difference in concentrations between the native solution and the solution obtained after the adsorption. It's defined that within 10 hours the soft contact lenses adsorb 7.23 mg of Betaxolol hydrochloride from 3 ml of solution, which is sufficient for therapeutic effect. Preliminarily it's possible to conclude that that soft contact lenses 1-DAY ACUVUE® MOIST can be recommended for use in the ophthalmic therapeutic system in combination with the ophthalmic solution of Betaxolol hydrochloride.

Introduction

According to the data of World Health Organization, one of the most hazardous eye disease is glaucoma. Glaucoma is defined as a whole group of ophthalmic disorders, which is characterized by the constant or episodic increasing of the intraocular pressure (IOP) much higher than appropriate for people normal daily activity. If glaucoma is not cured on time, then it leads directly to irreversible destruction of retina [1]. Nowadays the relationship is investigated between pathogenesis of glaucoma and pathogenesis of the other eye disorders, especially those once that include the refractive system errors, in particular, myopia. With the probability of 85% glaucoma develops in the eyes that already have the myopic background. So, the patients with the eye refraction system errors are in the high-risk group of IOP increase and hence, glaucoma development [2].

Both for glaucoma treatment and the majority of other ophthalmic diseases it is justified to use the drug products that perform a local effect, in the majority of cases they are the eye drops. But it is known that only 5% of the active ingredient from one therapeutic dose is able to provide the therapeutic effect, but the other part goes to the system blood blood flow spreading all over the organism and causing the big number of negative side effects development. Moreover, it's determined that contact time of the ophthalmic solution with eye surface is rare to be more than 2 minutes while it's instilled [3].

In order to mitigate the disadvantages of the eye drops and to prevent the negative consequences of their use, the research and development of the new ways of extended and more safe ophthalmic eye delivery were launched, for instance, trying to increase the viscosity of the eye drops and various content recombination of the ophthalmic solutions, so the eye drops would pass through the cornea in more significant amounts [4, 6]. One of the most prospective and the relatively newest way vectors in the field of the controlled drug delivery is the development of the specialized ophthalmic therapeutic systems (OTS). In OTS the soft contact lenses (SCL) of various polymeric materials are supposed to be used as the drug carriers with the prolonged release [7, 8].

In the framework of the seeking of the new methods of drug therapy the development of this vector is justified by the high rate of glaucoma occurring in the background of myopia and by the tendency to the popularization of contact correction of the refractive system errors, which is getting more relevant these days among various groups of population.

That is why **the aim** of this research is the experimental study of etafilcon A soft contact lenses as a potential drug carrier using the 0.5% ophthalmic

solution of Betaxolol hydrochloride within the ophthalmic therapeutic system for treatment of glaucoma combined with myopia.

Materials and Methods of Research

In this research the soft contact lenses of brand 1-DAY ACUVUE® MOIST of etafilcon A and 0.5% ophthalmic solution of Betaxolol hydrochloride were used.

Method of assay for 0.5% ophthalmic solution of Betaxolol hydrochloride [10, 11, 12].

As the first step of this study, it was necessary to define the quantity of Betaxolol hydrochloride in its solution before the adsorption process is performed. The assay was carried out in Belgorod State National Research University, department of Pharmaceutical technology, using the method of UV-spectrophotometry with the help of the spectrophotometer SF-104. All calculations were done using the relative absorption coefficient for Betaxolol hydrochloride according to the formula 1:

$$C_x = \frac{W \times D}{E^{1\%}_{1см} \times l} \quad , \quad (1)$$

where W – determined dissolution rate for the assay of Betaxolol hydrochloride solution, which equals 50;

$E^{1\%}_{1см}$ – specific relative absorption coefficient of Betaxolol hydrochloride, which value is 38 in purified water [9];

D – optical density;

l – length of the spectrophotometric cells, which equals 10 mm.

The assay was carried out in the condition of the highest precision, which is why the in accordance with confidence level P = 99%, the value of Student's t-criterion t(P,f) was chosen as 3.71.

Method of soft contact lenses saturation with the soluton of Betaxolol hydrochloride.

To evaluate the adsorptive potential of the studied soft contact lenses, their tentative saturation was performed in the defined way: into 6 containers for soft contact lenses with 3 ml of 0.5% Betaxolol hydrochloride solution, 1 contact lens was put each. Every 2 hours from each container 1 contact lens was ejected, the concentration of the obtained solution was measured. The total time of the experiment was 10 hours.

Evaluation of the adsorption potential of soft contact lenses containing Betaxolol hydrochloride.

The preparation of the sample remained the same for the obtained solution after the sorption process as for assay of the native 0.5% ophthalmic solution of Betaxolol hydrochloride.

To evaluate the amount of the adsorbed Betaxolol hydrochloride the volume of the container must be taken into account and calculated using the formula 2:

$$m_{srp} = (C_0 - C_i) \times 3 \ , \quad (2)$$

where m_{srp} – amount of Betaxolol hydrochloride in soft contact lenses, mg;

C_0 – initial concentration of the Betaxolol hydrochloride solution before the sorption process, mg/ml;

C_x – concentration of the Betaxolol hydrochloride solution after i-hours of sorption, mg/ml;

3 – volume of the container filled, ml.

Results and Discussion

The results of the six-fold assay for 0.5% Betaxolol hydrochloride ophthalmic solution and their statistical processing is presented in table 1.

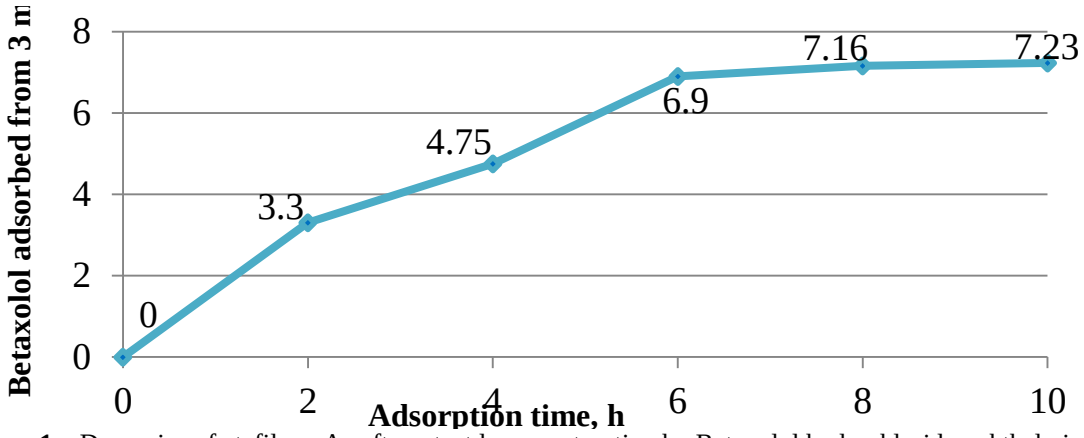
Таблица 1 – The results of assay for Betaxolol hydrochloride in the ophthalmic solution and evaluation of the test method correctness

n	C_i	$\overline{C}$	S	$\varepsilon_{\overline{C}}$	Δ%
1	0.563	0.551	8.23×10^{-3}	0.015	2.69
2	0.552				
3	0.551				
4	0.538				
5	0.554				
6	0.547				

From table 1 it's seen that the method of the assay for Betaxolol hydrochloride in ophthalmic solution is correct and precise. The relative error of the method equals 2.69%.

The next step was the saturation of the studied soft contact lenses in the way described above in this article.

The dynamics of the adsorption of Betaxolol hydrochloride by soft contact lenses from the solution is shown in picture 1 and table 2.



Picture 1 – Dynamics of etafilcon A soft contact lenses saturation by Betaxolol hydrochloride ophthalmic solution within the defined time

As it's seen from the picture 1, the adsorption process appeared to be more intensive within 6 hours, after that the adsorption speed of Betaxolol hydrochloride became slower.

Таблица 2 – Results of evaluation for Betaxolol hydrochloride content in soft contact lenses of etafilcon A

	Adsorption process time, h					
	0	**2**	**4**	**6**	**8**	**10**
D_i of obtained solution	0.428	0.344	0.303	0.253	0.242	0.239
C_i of obtained solution, mg/ml	5.63	4.53	3.98	3.33	3.18	3.15
Betaxolol h/cl in lenses (m_{srp}), mg	0	3.30	4.75	6.90	7.16	7.23

According to the data from table 2, 7.23 mg of Betaxolol hydrochloride are adsorbed by etafilcon A soft contact lenses from 3 ml solution within 10 hours of the experiment. The daily exposure of Betaxolol hydrochloride was calculated and appeared to be 1.12 mg if it's used twice a day 2 drops into each eye as it's recommended in the instruction for the drug product. Hence, the therapeutic concentration of Betaxolol hydrochloride in soft contact lenses is reached after 2 hours of their saturation.

Conclusion

In the framework of the performed complex of experiments the UV-spectrophotometric method of assay for 0.5% ophthalmic solution of Betaxolol hydrochloride was optimized and further justified and carried out for assay of Betaxolol hydrochloride in the solution after 10 hours of soft contact lenses saturation. Statistically it was determined that the assay method of Betaxolol hydrochloride meets the acceptance criteria requirements for precision and repetitiveness if 99% of confidence level is taken into account. The relative error appeared to be 2.69%, which is appropriate value that allows the method to be used in further research using various materials of soft contact lenses.

During the evaluation of adsorptive potential of etafilcon A soft contact lenses it was determined, that the therapeutic concentration of Betaxolol hydrochloride in them is reached within 2 hoursand equals 3.30 mg. Overall amount of Betaxolol hydrochloride taken from the solution within 10 hours of the experiment equals 7.23 mg. Hence, etafilcon A soft contact lenses of brand 1-DAY ACUVUE® MOIST are preliminarily recommended for use in therapeutic ophthalmic system as a drug carrier of Betaxolol hydrochloride for treatment of glaucoma combined with myopia.

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