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The Study of the Processes of Saturation and Release of Bioactive Molecules by Various Polymers of Soft Contact Lenses for Prospective Transport Ophthalmic System

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Abstract: The study is devoted to the study of the processes of saturation and release of bioactive molecules from solutions of eye drops in soft contact lenses from a variety of polymeric materials. Creating an ophthalmic therapeutic system for the treatment of eye diseases of different etiology will increase the contact time of the dosage system with eye tissues thereby greatly enhancing the therapeutic effect.

Key words: Soft contact lenses, test molecule, spectrophotometry, taurine, timolol maleate, sodium sulfacetamide, chloramphenicol, standard sample

INTRODUCTION

Soft Contact Lenses (SCL) are used as a banding means during a postoperative period and as the method of drug introduction into an eye (Ambroziak *et al*., 2004; Ophthalmic lens; RF Patent, 2010; Novikov *et al*., 2012). Such an option of a drug agent therapeutic effect prolongation is a promising one from the standpoint of rational pharmacotherapy (Gulsen and Chauhan, 2004; Tighe, 2004).

Previously, some researchers conducted a series of calculations for the theoretical justification of SCL material choice and the experiments to study their surface and structure (Grobe *et al*., 1999; Jones and Dumbleton, 2005; Akopova *et al*., 2011; Zhilyakova *et al*., 2013). It was found that the methodology of molecule relation computer modeling concerning biologically active compounds and SCL structural elements allows at the early stages of this drug transportation means planning to the tissue of an eyeball to determine the materials that are especially suitable for the adsorption (retention) of a compound which significantly narrows the scope of a subsequent experiment (Zhilyakova *et al*., 2013; Nicolson and Vogt, 2001).

The aim of this research was to study the process of absorption-release of different polymers by lens material. These polymers consist of biologically active test molecules used in ophthalmology.

MATERIALS AND METHODS

Test preparation No. 1 (chloramphenicol): After the sorption of chloramphenicol for the lenses from etafilcon A 1 mL of solution was placed in a volumetric flask of 100 mL, the solution volume was adjusted with water to the mark and mixed.

The optical density was measured using SF-56 spectrophotometer at a wavelength of 278 nm in a cell dish with a layer thickness equal to 10 mm.

At the same time, the optical density of chloramphenicol reference solution was measured in the same conditions.

The preparation of chloramphenicol reference solution: 0.125 g of chloramphenicol (accurately weighed) was placed in a volumetric flask of 50 and 15 mL of warm distilled water (t = 40°C) was added and dissolved with stirring. After cooling it was adjusted to the mark by water and mixed.

The 1 mL of the solution was placed in a volumetric flask of 250 mL and the solution volume was adjusted to the mark by water.

The 1 mL of a Standard Sample (SS) contains 0.00001 g of chloramphenicol. Chloramphenicol content in grams per 2 mL of the solution was calculated according to the Eq. 1:

$$X = \frac{A_1 \times 0.00001 \times 250 \times 2}{A_0} \quad (1)$$

Where:

A_1 = The solution optical density of a test drug
A_0 = An optical density of chloramphenicol SS solution
0.00001 = The content of chloramphenicol in a standard sample solution (g)

Test preparation No. 2 (timolol maleate): The sorption of timolol maleate solution 0.5% was conducted on lenses

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made of etafilcon A. After sorption of 1 mL solution (<0.005) it was placed in a volumetric flask of 250 mL, the solution volume was adjusted to the mark with water.

Preparation of a standard sample solution: Approximately 0.05 g (accurately weighed) of timolol maleate standard was quantitatively transferred to a volumetric flask of 100 mL was dissolved in 50 mL of water and the solution volume was adjusted with water to the mark and mixed.

The 2 mL of the resulting solution was transferred into a volumetric flask with 50 mL volume of solution was adjusted with water to the mark and mixed.

The spectrophotometer SF-56 performed the determination of the test and the standard solution optical density at 294 nm in 1 cm dishes.

Timolol content in grams (X) in 2 mL of solution is calculated according to the Eq. 2:

$$X = \frac{A_1 \times a_0 \times 2 \times 250 \times 0.732 \times 2}{A_0 \times 100 \times 50 \times V_1} = \frac{A_1 \times a_0 \times 0.732 \times 2}{A_0 \times 10 \times V_1} \quad (2)$$

Where:

A_1 = The optical density of the test solution
A_0 = The optical density of timolol maleate Working Standard Sample (WSS)
a_0 = The weighed amount of timolol maleate WSS (g)
V = The volume of drug taken for quantification (mL)
0.732 = Conversion factor to timolol-base

Test preparation No. 3 (taurine): The study of the sorption was carried out for taurine lenses made of polymacon. The 1 mL (<0.04) was taken from the solutions after sorption and was placed in a volumetric flask of 200 mL. The solution volume was adjusted to the mark by water. The 5 mL of obtained solution were collected and placed in a volumetric flask of 200 and 1 mL of ninhydrin alcoholic solution was added, 5 mL of phosphate buffer solution with pH = 6.86, 2 mL of 0.05% ascorbic acid aqueous solution. The reaction mixture was heated in a boiling water bath at t = 90-95°C for 30 min then it was cooled and the solution volume was adjusted to the mark with water.

The absorption spectrum was taken from the resulting solution with the spectrophotometer SF-56. The values of optical density were noted at the maximum light absorption and a wavelength of 568 nm in a cell with the thickness of 10 mm relative to the reference solution.

Reference solution: A volumetric flask of 100 mL was filled with 1 mL of water, 1 mL of ninhydrin alcoholic solution, 5 mL of phosphate buffer solution with pH = 6.86 and 2 mL of ascorbic acid 0.05% aqueous solution were added. The reaction mixture was heated in a boiling water bath at t = 90-95°C for 30 min then it was cooled, the solution volume was adjusted with water to the mark and mixed. At the same time, the optical density of the colored solution was measured obtained at reaction with 1 mL of 0.1% taurine solution standard sample.

SS solution preparation: About 0.1 g (accurately weighed) of taurine standard was quantitatively transferred to a volumetric flask of 100 mL, the solution volume was dissolved in 50 mL of water to the mark and was mixed. The 1 mL of resulting solution was transferred into a volumetric flask of 200 mL, the solution volume was adjusted with water to the mark and mixed. The calculation of taurine amount in grams in 2 mL of solution was carried out according to the Eq. 3:

$$X = \frac{A_x \times a_0 \times 200 \times 200 \times 2}{A_0 \times V_x \times 5 \times 100 \times 200} \quad (3)$$

Where:

A1 = The optical density of the test solution
A_0 = The optical density of taurine WSS solution
a_0 = Weighed taurine WSS (g)
V = The volume of the drug taken for quantification (mL)

Test preparation No. 4 (emoksipin): Sorption was carried out on the lens made of polymacon. After the exposure, 1 mL (0.01) sampling was performed. The 1 mL of the solution was placed in a volumetric flask of 100 mL, the solution volume 1M was adjusted with hydrochloric acid solution to the mark and was mixed. The 10 mL of this solution were transferred into a volumetric flask of 100 mL, 50 mL of 1M hydrochloric acid solution were added, the resulting solution was purged with nitrogen for 3 min, the solution volume 1M was adjusted with hydrochloric acid to the mark and was mixed.

The optical density of the resulting solution was measured by SF-56 spectrophotometer at the maximum absorption at a wavelength of 297 nm in a cell with the thickness of 10 mm.

At the same time, the optical density of emoxipine SS solution was measured. The hydrochloric acid solution 1M was used as a comparison solution. The content of emoxipine in 2 mL of the preparation (in grams) was calculated according to the Eq. 4:

$$X = \frac{A_1 \times a_0 \times 2}{A_0 \times 10} \quad (4)$$

Where:

A_1 = The optical density of the test solution
A_0 = The optical density of emoxipine SS solution
a_0 = Emoxipine SS weighing

The preparation of emoxipine SS solution: About 0.1 g (accurately weighed) of emoxipine was placed in a volumetric flask of 100 mL, 40 mL of 1M hydrochloric acid solution were added, stirred until dissolved, the solution volume was adjusted with 1M of hydrochloric acid solution to the mark and mixed. The 1 mL of the resulting solution was transferred into a volumetric flask of 100 mL, the 1M solution volume was adjusted with hydrochloric acid solution to the mark and mixed.

Test preparation No. 5 (sodium sulfacetamide): Sorption was carried out on the lens made of polymacon. After sampling of 1 mL aliquot was placed in a volumetric flask of 200 mL, the solution volume was adjusted with water to the mark and mixed. The 1 mL of this solution was placed in a volumetric flask of 100 mL, the solution volume was adjusted to the mark with water and mixed.

The optical density of the resulting solution was measured at the wavelength of 256 nm in a cell with the thickness of 10 mm with respect to the reference solution. At the same time, the optical density of sodium sulfacetamide SS was measured.

The preparation of sodium sulfacetamide SS: About 0.2 g (accurately weighed) of sodium sulfacetamide were placed in a volumetric flask of 200 mL were dissolved in 50 mL of water, the solution volume was adjusted to the mark with water and mixed. The 1 mL of this solution was placed in a volumetric flask of 100 mL, thesolution volume was adjusted to the mark with water and mixed.

The calculation of sodium sulfacetamide (in grams) in 2 mL of the solution was performed according to the Eq. 5:

$$X = \frac{A_1 \times a_0 \times 2}{A_0} \quad (5)$$

Where:

A_1 = The optical density of the solution under study

A_0 = The optical density of sodium sulfacetamide solution

a_0 = The sodium sulfacetamide SS weighing

RESULTS AND DISCUSSION

The results of chloramphenicol determination are shown in Table 1. Thus, the maximum concentration of chloramphenicol in a lens makes 57% and is achieved after 2 h of incubation in the drug solution. With further keeping of the lens in the solution the concentration of chloramphenicol remains constant.

The results of chloramphenicol sorption studies on contact lenses of different polymers are presented on Fig. 1.

Figure 1 data shows that the sorption on the lenses from etafilcon A material is performed most completely (58%). At that the proportion of the drug in a lens made of balafilcon A makes 32% and in a lens made of polymacon this proportion makes 11%.

It is worth noting that a balafilcon A lens saturation with a drug substance occurs within 4 h. Thus, etafilcon A is the optimal material for contact lenses saturation with chloramphenicol.

The results of timolol maleate content in a contact lens are shown in Table 2. Thus, the maximum concentration of timolol in a lens makes 49% and it is achieved after 2 h of incubation in the drug solution.

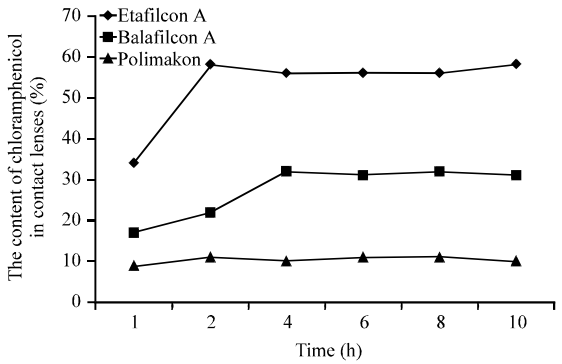

Fig. 1: Chloramphenicol sorption dynamics for various polymers of contact lenses

Table 1: Results of chloramphenicol determination in the contact lens made of etafilcon A

	Sorption period					
Chloramphenical	1 h	2 h	4 h	6 h	8 h	10 h
The optical density of solution (A_1)	0.197	0.128	0.131	0.130	0.134	0.126
Contents in 2 mL of chloramphenicol solution (g)	0.0033	0.0021	0.0022	0.0022	0.0022	0.0021
Contents of chloramphenicol in a lens (g)	0.0017	0.0029	0.0028	0.0028	0.0028	0.0029
Contents of chloramphenicol in a lens (%)	34	58	56	56	56	58

Table 2: Timolol content in a contact lens

	Sorption period					
Contents	1 h	2 h	4 h	6 h	8 h	10 h
The optical density of solution (A_1)	0.301	0.282	0.280	0.279	0.284	0.274
Contents in 2 mL of chloramphenicol solution	0.0056	0.0051	0.0051	0.0051	0.0051	0.0051
Contents of chloramphenicol in a lens (g)	0.0044	0.0049	0.0049	0.0049	0.0048	0.0049
Contents of chloramphenicol in a lens (%)	44	49	49	49	48	49

Table 3: The results of taurine optical density and content determination in a contact lens

	Sorption period					
Contents	1 h	2 h	4 h	6 h	8 h	10 h
The optical density of solution (A_1)	0.151	0.145	0.149	0.153	0.150	0.148
Contents in 2 mL of taurine solution (g)	0.022	0.021	0.022	0.023	0.022	0.022
Contents of taurine in a lens (g)	0.058	0.059	0.058	0.057	0.058	0.058
Contents of taurine in a lens (%)	58.000	59.000	58.000	57.000	58.000	58.000

Table 4: Results of optical density measurement and emoxipine content in a contact lens made of polymacon

	Sorption period					
Contents	1 h	2 h	4 h	6 h	8 h	10 h
The optical density of solution (A_1)	0.315	0.237	0.241	0.235	0.244	0.231
Contents in 2 mL of emoxipine solution (g)	0.012	0.009	0.009	0.009	0.009	0.009
Contents of emoxipine in a lens (g)	0.008	0.011	0.011	0.011	0.011	0.011
Contents of emoxipine in a lens (%)	40.000	55.000	55.000	55.000	55.000	55.000

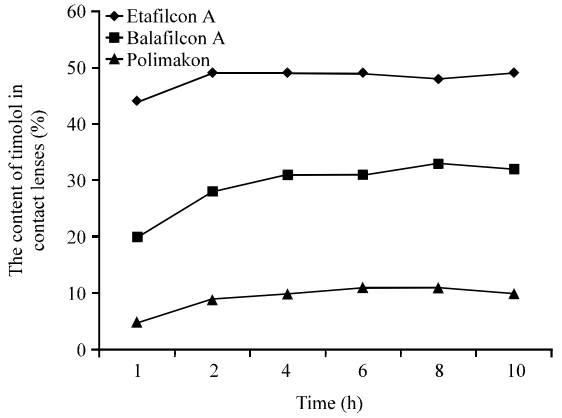

Fig. 2: Timolol sorption dynamics on various contact lens polymers

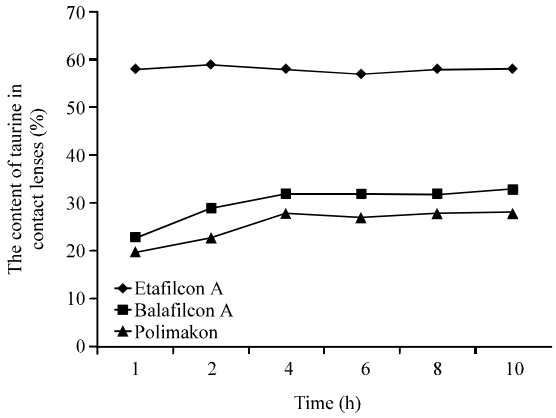

Fig. 3: Taurine sorption dynamics on various polymers of contact lenses

The results of timolol sorption research on the contact lenses of different polymers are reflected by Fig. 2.

According to Fig. 2 data, the sorption on lenses from etafilcon A material occurs most completely (49%). At that the proportion of the drug substance in the lens of balafilcon A makes 33% and in the lens made of polymacon, it makes 11%. It is worth noting that the saturation of balafilcon A and polymacon lenses with a drug substance occurs within 4 h while the maximum concentration of timolol in the etafilcon lens is observed even after 2 h.

Thus, the optimum material for contact lens saturation with timolol is etafilcon A. The results of taurine content determination in the lens are shown in Table 3.

Thus, the maximum concentration of taurine in a lens makes 58% and is achieved in a 1 h of its keeping in the drug solution.

The results of taurine sorption research on contact lenses of different polymers are presented in Fig. 3. The analysis of the Fig. 3 data confirms that the sorption on polymacon lenses occurs most completely (58%). At that the proportion of the drug substance in balafilcon A lens makes 33% and in etafilcon A lens it makes 28%. It is worth noting that the saturation of balafilcon A and etafilcon A lenses with the drug substance occurs within 4 h while the maximum concentration of taurine in a polymacon lens is observed after 1 h.

Thus, polymacon is the optimum material for contact lens saturation with taurine. The results of optical density measurement and emoxipine quantification in a contact lens are shown in Table 4.

Thus, the maximum concentration of emoxipine in a lens makes 55% and it is achieved within 2 h of keeping the drug in the solution.

The results of emoxipine sorption studies on the contact lenses of different polymers are reflected in Fig. 4. The data analysis of the Fig. 4 confirms that the sorption on polymacon lenses is performed most completely (55%). At that the proportion of the drug substance in balafilcon A lens makes 24% and the corresponding proportion in

Table 5: Results of sodium sulfacetamide quantitative determination in a contact lens

	Sorption period					
Contents	1 h	2 h	4 h	6 h	8 h	10 h
The optical density of solution (A_1)	0.295	0.254	0.260	0.257	0.251	0.255
Contents in 2 mL of sodium sulfacetamide solution (g)	0.252	0.208	0.208	0.204	0.208	0.208
Contents of sodium sulfacetamide in a lens (g)	0.148	0.192	0.192	0.196	0.192	0.192
Contents of sodium sulfacetamide in a lens (%)	37.000	48.000	48.000	49.000	48.000	48.000

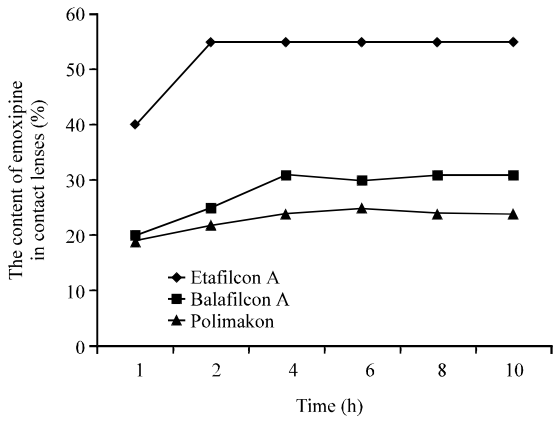

Fig. 4: The dynamics of emoxipine sorption on various polymers of contact lenses

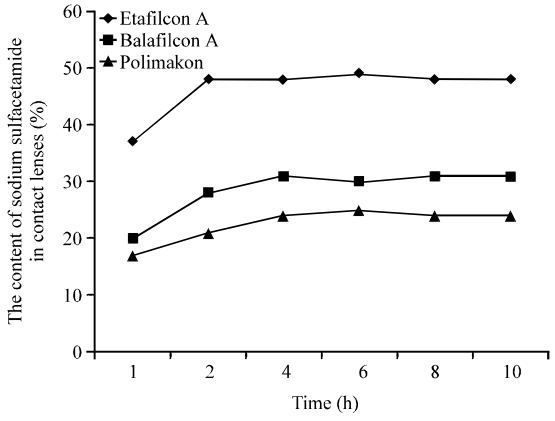

Fig. 5: The dynamics of sodium sulfacetamide sorption on various polymers of contact lenses

etafilcon A lens makes 31%. It is worth noting, that the saturation of balafilcon A and etafilcon A lenses with the drug substance occurs within 6 and 4 h, respectively while the maximum concentration of emoxipine in a polymacon lens is observed after 2 h.

The data confirm that polymacon is the optimal material for contact lens saturation with emoxipine. The optical density and the sodium sulfacetamide content in a contact lens results are shown in Table 5.

Thus, the maximum concentration of sodium sulfacetamide in a lens makes 48% and is achieved after 2 h of incubation in the drug solution. With further keeping of a lens in the solution the concentration of sodium sulfacetamide remains constant.

The results of sodium sulfacetamide sorption studies on contact lenses of different polymers are reflected in Fig. 5.

The result reflected in Fig. 5 confirms that the sorption on polymacon lenses occurs more completely (48%). At that the drug content in balafilcon A lens makes 31% and the drug content in etafilcon A lens makes 24%. It is worth noting that the saturation of balafilcon A and etafilcon A lenses with the drug substance occurs within 4 h and the maximum concentration of sodium sulfacetamide in a polymacon lens is observed after 2 h.

The data confirm that polymacon is an optimal material for contact lens saturation with sodium sulfacetamide.

CONCLUSION

The method of spectophotometery studied the saturation and release process of five drugs on the lenses made of different materials.

It was determined that etafilcon a is an optimum material for contact lenses saturation with chloramphenicol and timolol maleate. The saturation of balafilcon A lenses with timolol maleate occurs within 2 h and the saturation with chloramphenicol occurs within 4 h.

It was found that polymacon is the best material for contact lens saturation with taurine, emoxipine and sodium sulfacetamide the maximum concentration of taurine in a lens made of polymacon is observed after 1 h and the maximum concentration of emoxipine and sodium sulfacetamide is occurred within 2 h. The obtained experimental data will form the basis for further research and development.

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