

New drug delivery system in ophthalmology: results studying the surface structure of soft contact lenses from various polymer

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Abstract. The development of an ophthalmic therapeutic system includes research on the spatial structure of soft contact lens polymers and the study of the processes of saturation and release of medicinal substances from them. This allows you to determine the methods of saturation of contact lenses with medicinal agents and will open up new opportunities in the treatment of ophthalmological diseases. The purpose of this preliminary fragment of large-scale research was to study the surface structure of soft contact lenses made of various polymers. The following polymers were used in the work: Nelfilcon A, Hilafilcon B, Nezofilcon A, Etafilcon A, Lotrafilcon B. The following pharmaceutical substances were used: Brimonidine Tartrate, Betaxolol Hydrochloride, Pyridoxine Hydrochloride. The surface structure of soft contact lenses was studied using atomic force microscopy. Each material under study has a different surface character, which together with the differences in pore properties determines its individuality. Based on this, it should be assumed that the surface of soft contact lenses affects the possibility of their potential use as a means of delivering drug agent molecules to the eye tissues. In all cases of soft contact saturation, the highest absorption capacity was demonstrated by Hilafilcon B and Etafilcon A with a similar surface.

Keywords: *ophthalmic therapeutic system, soft contact lens, polymers, drug delivery system.*

1 Introduction

In order to fully deliver the drug substance to the tissues of the eye, as well as to increase the time of contact of the drug substance with the conjunctiva, alternative dosage forms for topical application, transport ophthalmic systems, have been developed and introduced into use [1-3]. Such systems include a wide range of eye inserts, differing in their physicochemical properties, the material from which they were made, and the ability to dissolve when placed

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directly on the surface of the eye. They are hard or soft products intended for placement on the cornea [4-7].

Compared with conservative ophthalmic dosage forms (eye drops), drug-saturated ophthalmic inserts have several advantages, namely: an increase in the contact time of the drug with the surface of the eye and, thus, an increase in bioavailability; the possibility of providing a sustained release of the drug and, thus, improving the effectiveness of drug therapy; a decrease in systemic side effects; reducing the number of components and, thus, reducing the risk of side effects during use; the introduction of the exact dose in the eye [8-10].

Soft contact lenses (SCL) is one of the classes of ophthalmic insertions. They are formed (coherent) structures. Their polymer network consists of repeating units of the same monomers forming long chains. These chains are connected together by internal cross-lines, which are responsible for the coherent system. Such systems do not dissolve, but can swell, absorbing water and aqueous solutions [11-12].

It is assumed that when using SCL as a means of drug delivery during the sorption and desorption process, the most significant role is given to the pores and surface character of polymeric materials.

New materials are being developed for soft contact lenses. Studies of modern ophthalmologists have also affected the sorption capabilities of SCL. However, the processes of saturation and release have been studied superficially in relation to drugs such as Atropine, Ofloxacin, Levofloxacin, and certain amino acids without quantitative analytical studies.

Thus, the development of an ophthalmic therapeutic system includes re-search on the spatial structure of SCL polymers, the study of the processes of drug saturation and release from SCL. This will make it possible to determine the methods for saturating contact lenses with medicinal agents, the choice of the desired material for SCL and, as a result, will open up new possibilities in the treatment of ophthalmic diseases.

The purpose of this preliminary fragment of large-scale studies was to study the surface structure of soft contact lenses from various polymers.

2 Experimental

The following SCL were used in the work:

- Alcon "Dailies Aqua Comfort Plus" (polymer - Nelfilcon A).
- Bausch & Lomb "SofLens Daily Disposable" (polymer - Hilafilcon B).
- Bausch & Lomb "Bio True One-day" (polymer - Nezofilcon A).
- Johnson & Johnson "Acuvue 1-Day Moist" (polymer - Ethafilcon A).
- Alcon "Air Optix Colors" (polymer - Lotrafilcon B).

The following pharmaceutical substances were used in the work: Brimonidine Tartrate (NDA 20613 / S-031), Betaxolol Hydrochloride (EP 8.0 07/2011: 1072), Pyridoxine Hydrochloride (EP 8.0 01/2010: 0245).

The surface structure of SCL from various materials was studied by atomic force microscopy (atomic force microscope with a Solver HV vacuum chamber).

Obtaining data on the amount of active substances transported by SCL on the surface was carried out using the gravimetric analysis method [13].

For this, 4 ml of a known mixture density model mixture were measured in 6 containers, placed in them for 5, 10, 20, 30, 45, and 60 minutes SCL with known masses. Upon reaching each time point of the saturation process, the mass of the contact lens was measured.

Taking into account the correlation of the quantitative content of the pharmaceutical substance per unit volume of the model mixture with its density, the mathematical processing of the results was carried out according to formula 1.

$$U_{px} = \frac{(M_{fscl} - M_{escl}) \times T_0 \times 1000}{\rho_0} \quad (1)$$

Where:

U_{px} - the amount of active pharmaceutical substance found on the surface of the MCL at the time point "X", mg;

M_{fscl} - mass of saturated SCL, g;

M_{escl} - mass SCL to saturation, g;

T_0 - medicinal substance content in a unit volume of the model mixture, g/ml;

ρ_0 - density of the model mixture, mg/ml.

The following model solutions were used in the work, selected from the line of those studied by technological priorities (the working numbering of the samples was preserved): model solution No. 1, containing 0.2 g of Brimonidine Tartrate and 0.3 g of Pyridoxine Hydrochloride in 100 ml; model solution No. 2, containing 0.56 g of Brimonidine Tartrate and 0.3 g of Pyridoxine Hydrochloride in 100 ml.

3 Experimental

In order to understand the processes of saturation of SCL with drug solutions, we studied the surfaces of polymers studied by SCL on the basis of their 3D projections obtained by atomic force microscopy. SCL surfaces were evaluated from the point of view of the type of their relief, the number of pores in general and in areas of the indicated area, as well as the depth and diameter of pores. The results are presented in table 1.

From the data of table 1 it can be seen that pores, depending on the type of polymer, may or may not be present on the surface of the SCL. Moreover, it was found that the pores have different lengths, widths and depths.

Figures 1-5 and Table 2 show 3D projections and surface characteristics of polymers studied by SCL.

As can be seen from Figures 1-5 and Table 2, each material studied has a different surface character, which, combined with differences in the properties of pores, determines its individuality. Based on this, it should be assumed that the surface of SCL affects the possibility of their potential use as a means of delivering molecules of drug agents to eye tissues.

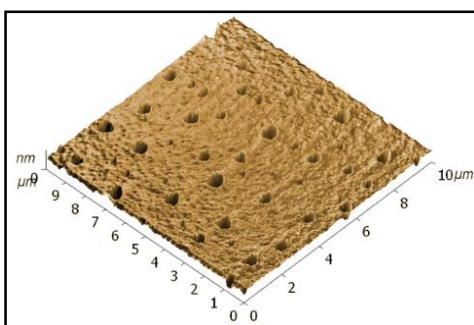


Fig. 1. 3D projection of SCL from Nelfilkona A

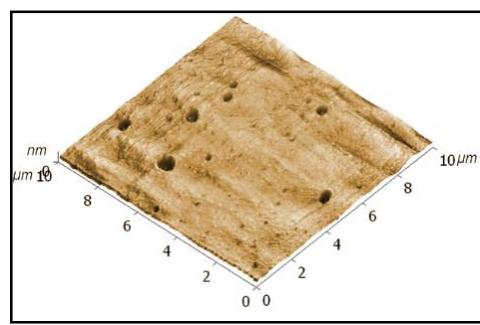


Fig. 2. 3D projection of SCL from Hilafilkon B

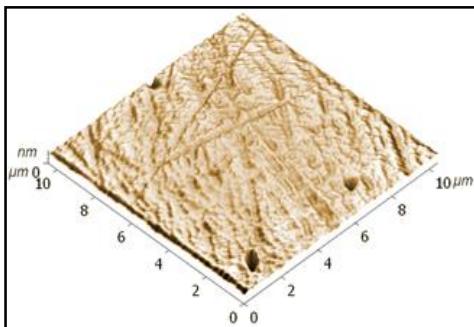


Fig. 3. 3D projection of SCL from Nezofilcona A

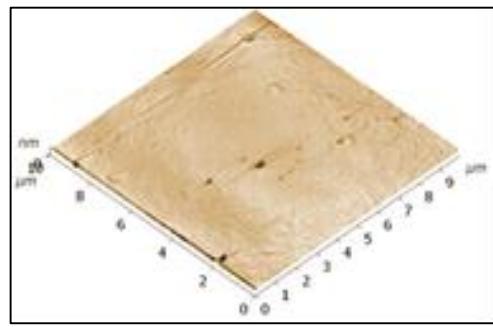


Fig. 4. 3D projection of SCL from Etafilcona A

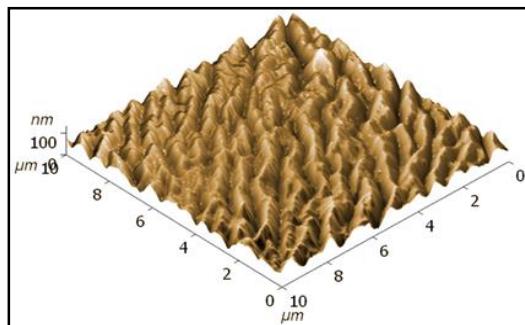


Fig. 5. 3D projection of SCL from Lotrafilcon B

Table 1. Characterization of the pores of the studied polymers SCL

SCL material	The number of pores in the specified area				Pore density, pcs./cm ²	Pore Depth, nm	Pore Width, μm
	25 μm ²	100 μm ²	400 μm ²	900 μm ²			
Nelfilcon A	10	52	190	278	0,426	20,0-22,5	0,1-0,5
Hilafilcon B	4	22	84	176	0,178	13,0-16,7	0,08-0,7
Nezofilcon A	0	3	20	72	0,040	34,5-54,5	0,3-0,8
Ethafilcon A	5	15	53	74	0,140	9,8-23,9	0,1-0,3
Lotrafilcon B	0	0	0	0	0,000	0	0

Table 2. Characteristics of the surfaces of the studied polymers

SCL material	Surface character
Nelfilcon A	Rough fine-grained
Hilafilcon B	Fine-grained with low elongated tubercles
Nezofilcon A	Small tuberous, dissected by hollows
Ethafilcon A	Smooth, excised with rare thin tubercles
Lotrafilcon B	Pronounced tuberous, no pores

The results of studying the saturation of SCL from various Brimonidine Tartrate are presented in Figure 6.

As can be seen in Figure 6, the largest amount of tartar Brimonidine on the surface of the SCL was found starting from the 20th minute of the experiment. By the end of the experiment, 0.154 mg of Brimonidine Tartrate was found on the surface of the SCL lenses from Nelfilcon A; Chilafilcon B - 0.166 mg; Nezofilkona A - 0.150 mg; Ethafilcon A - 0.160 mg; Lotrafilcon B - 0.152 mg. Differences in the degree of saturation of SCL can be explained by the difference in the structure of their surfaces.

The results of studying the saturation of SCL from various materials of Pyridoxine Hydrochloride (model solution No. 1) are presented in Figure 7.

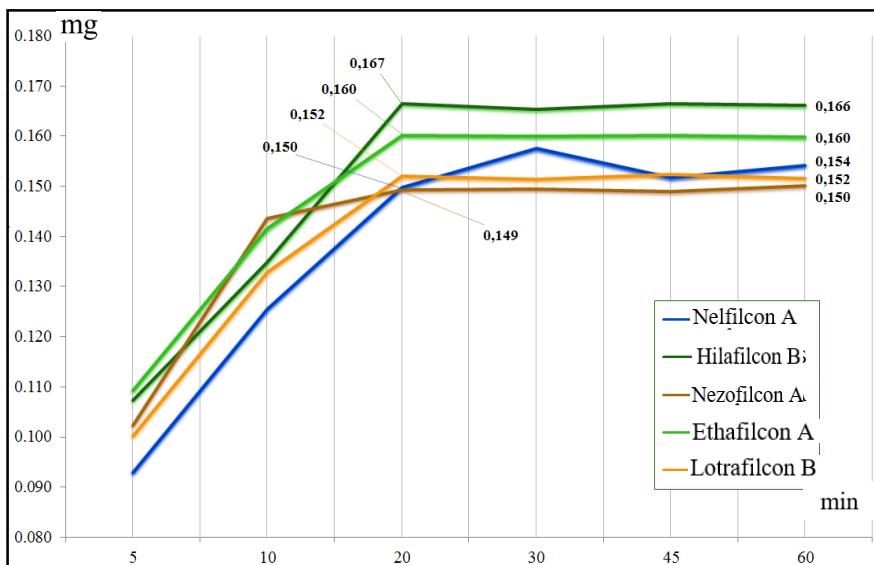


Fig. 6. Dynamics of saturation of SCL from various Brimonidine Tartrate (the ordinate axis - the amount of Brimonidine Tartrate model solution No. 1 on the lens, mg; the abscissa axis - the duration of saturation, min)

As can be seen from the data presented in Figure 7, the largest amount of Pyridoxine Hydrochloride was found on the surface of the SCL from the 20th minute of the experiment, after which there were no significant variations in its amount. By the end of the saturation process, 0.231 mg of Pyridoxine Hydrochloride was found on the surface of the SCL lenses from Nelfilcon A; Chilafilcon B - 0.249 mg; Nezofilkona A - 0.225 mg; Etafilcon A - 0.240 mg; Lotrafilcon B - 0.227 mg.

The results of studying the saturation of SCL of various Betaxolol Hydrochloride are presented in Figure 8.

The largest number of drugs on the surface of the SCL was detected at the 20th minute of the saturation process. For the remaining time of the experiment, no significant fluctuations in the amount of Betaxolol Hydrochloride were found on the surface of the SCL of various materials. By the end of the saturation process, 0.255 mg of Betaxolol Hydrochloride was found on the surface of SCL lenses from Nelfilcon A; Chilafilcon B - 0.297 mg; Nezofilkona A - 0.261 mg; Ethafilcon A - 0.295 mg; Lotrafilcon B - 0.233 mg.

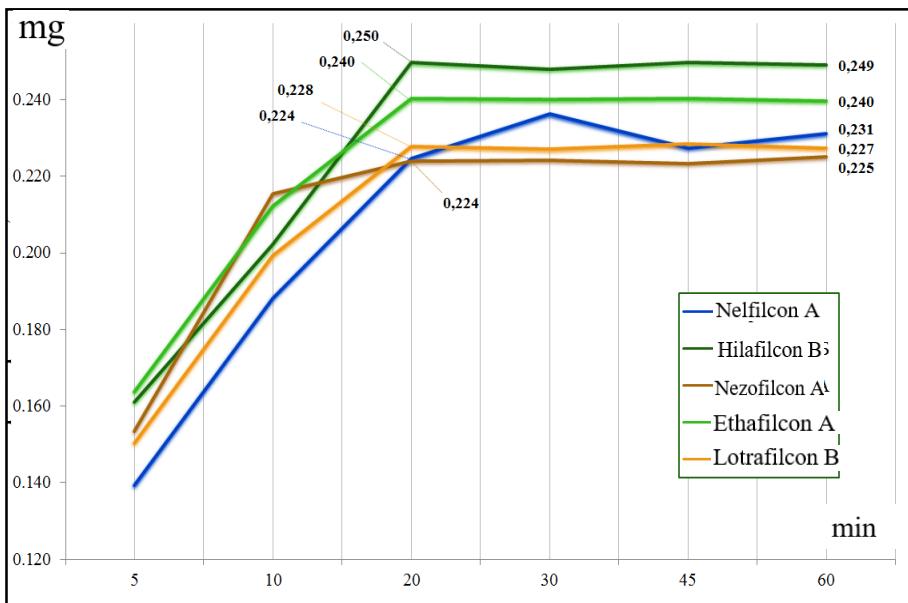


Fig. 7. Dynamics of saturation of SCL from various Pyridoxine Hydrochloride material (the ordinate axis - the amount of Pyridoxine Hydrochloride model solution No. 1 on the lens, mg; the abscissa axis - the duration of saturation, min)

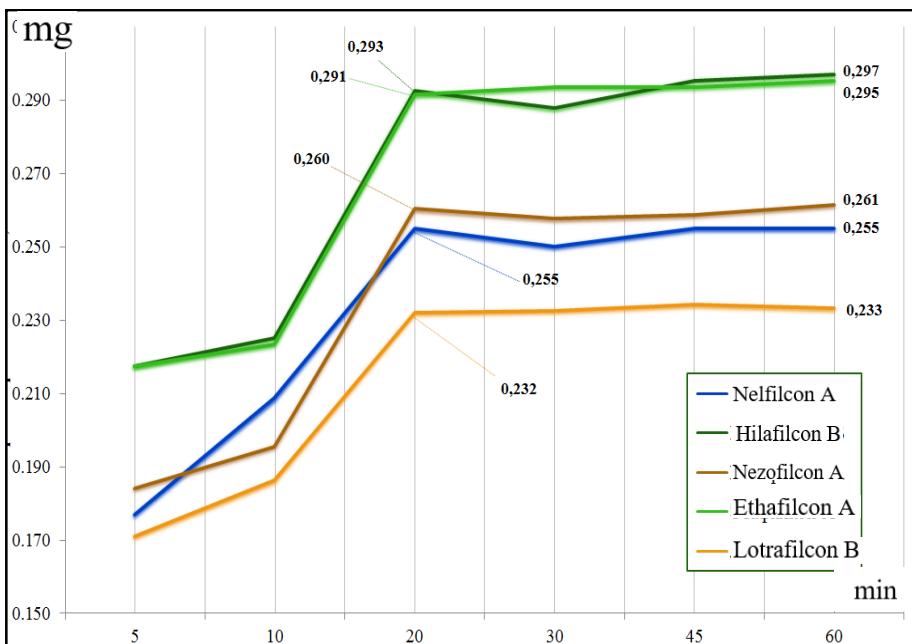


Fig. 8. Dynamics of saturation of SCL from various Betaxolol Hydrochloride material (the ordinate axis - the amount of Betaxolol Hydrochloride model solution No. 2 on the lens, mg; the abscissa axis - the duration of saturation, min)

As follows from the data shown in Figure 9, the SCL of all the materials studied is able to saturate with Pyridoxine Hydrochloride from model solution No. 2. Similar to model solution No. 1, the largest amount of the drug substance on the surface of the SCL was found at the 20th minute of the saturation process.

The results of studying the saturation of SCL from various materials of Pyridoxine Hydrochloride (model solution No. 2) are presented in Figure 9.

During the remaining time of the experiment, there were no significant fluctuations in the amount of Pyridoxine Hydrochloride on the surface of the SCL of various materials. At the end of the saturation process, 0.137 mg of Pyridoxine Hydrochloride was found on the surface of SCL from Nelfilcon A; Hilafilcon B - 0.159 mg; Nezofilkona A - 0.140 mg; Ethafilcon A - 0.158 mg; Lotrafilcon B - 0.128 mg.

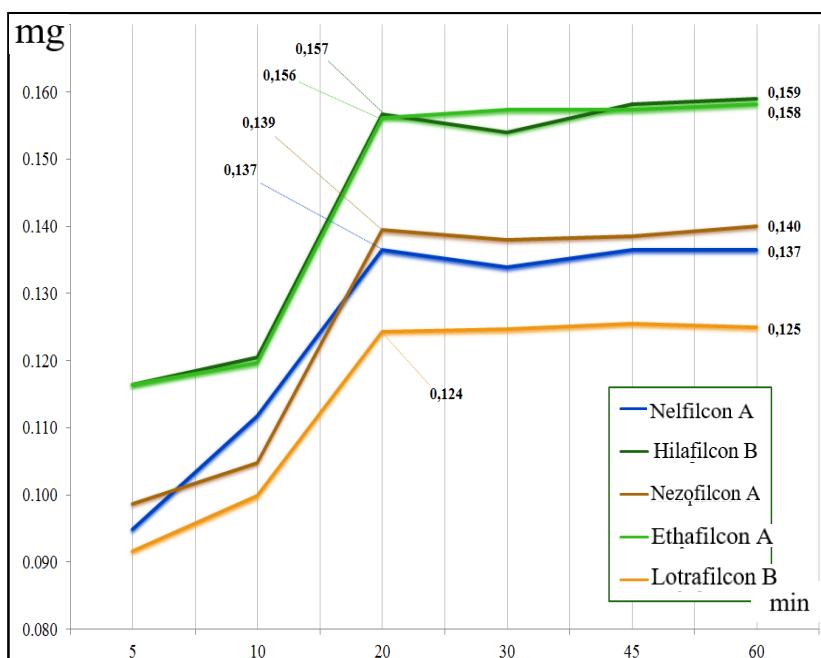


Fig. 9. Dynamics of saturation of SCL from various Pyridoxine Hydrochloride material (the ordinate axis - the amount of Pyridoxine Hydrochloride model solution No. 2 on the lens, mg; the abscissa axis - the duration of saturation, min)

4 Conclusion

So, as a result of a series of experiments, it was found that:

1. the surface of SCL from different polymers is predictably different, which gives an occasion to study the dependence of the processes of saturation of SCL with drug solutions on the morphological features of these surfaces;
2. in all cases of SCL saturation, the highest absorption capacity was demonstrated by Hilafilcon B and Etafilcon A with a similar surface.

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