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Therapeutic Contact Lenses with A Nanomodified Surface for Corneal Rehabilitation After Donor Corneal Transplantation or other Eye Surgery Interventions on the Anterior Segment of the Eyeball

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Abstract

As the quality and complexity of surgical interventions on the eyes, such as operations on the anterior segment of the eye, increase, there is a need to improve the quality of not only surgical instruments, but also the use of various methods for successful postoperative rehabilitation. After the operation is completed, therapeutic contact lenses (TCL) are applied to the anterior segment of the eyeball, more precisely, to the cornea of the eye, to accelerate and properly heal the cornea. So far, soft contact lenses (SCLs) have been used instead of specially made TCLs. There is still no special production of TCL.

Ophthalmologists are well aware of eye diseases in patients using SCLs, sometimes very severe and dangerous, complications that occur more often due to violations of the mode and hygiene of wearing SCLs and due to allergic reactions to polymeric material.

Many assistive devices and products widely used in medicine and biology are made from inexpensive polymeric materials that must meet certain clinical and cost requirements. The main requirements for polymer products are to ensure aseptic properties, biocompatibility between the physiological environment and the surface of the polymer product, which can be achieved by processing the surface of the polymer, for example, by applying various carbon-containing films (CCF).

Surface Nano structuring (NSSP) of polymeric materials followed by surface nanomodification (NMSP) is carried out to achieve biocompatibility, to impart aseptic properties to the polymer surface, first of all. It is known that the surface of the polymer can also be used in microbiological laboratories as a medium for the growth of microorganisms, due to the natural formation of a biofilm on the surface of the polymer. That is, the use of a polymeric material is determined by the purpose of using this polymeric material, through certain properties of its polymeric surface. The aim of our work was to create real TCL for use in the period of postoperative rehabilitation of the cornea, after operations on the anterior segment of the eyeball. Until now, as is known, ordinary corrective SCLs are used as TCLs.

The same polymeric materials are used for the production of TCLs: polyethylene terephthalate (PET), polytetrafluoroethylene (PTFE) and polyvinylidene fluoride (PVDF) on the same production line as for the production of SCLs; with subsequent treatment of the polymer surface by deposition of carbon-containing films(CCF) at the final stage of the TCL obtaining.

Modification is carried out by applying nanocomposites from directed ion-plasma flows of vapors of gas mixtures or by magnetron sputtering.

The shape of the TCL is also changed in such a way that the inner surface of the empirically aspherical shape of the obtained TCL has a flat smooth surface, there are no dividing zones, such as: optical, peripheral, sliding, which makes the surface suitable for direct contact with the surface of the cornea after surgery. The nanostructured surface of the TCL excludes the growth of fibrous tissue on the cornea lying under the TCL. In the observed eyes, the desired positive postoperative result of healing and restoration of the cornea was achieved in 100% of cases.

One of the most positive aspects of the surface nanomodification technology is the possibility of simultaneous change in the relief of the inner surface of the TCL and ensuring its sterility.

The characteristic properties of the TCL surface, achieved through the use of NSS and NMS of the polymer surface, also provide: the absence of toxicity, the biocompatibility of the TCL surface, certain adhesive and repulsive properties for certain cells and cellular elements, as well as the specified properties of the nanocoating. That is, such a polymer surface treatment improves the quality and safety of polymer products, which can also be widely used in other fields of medicine and biology.

Introduction

There are many indications for the use of TCL in pathological conditions of the cornea. Indications fall into major broad categories: pain relief, accelerated corneal healing, corneal sealing, corneal protection. Thus, there is an obvious medical need to manufacture not only random SCLs, but special TCLs for rehabilitation purposes after microsurgical treatment on the anterior segment of the eyeball. The study of the possibility of using nanotechnologies to improve the quality of polymeric surfaces of various devices can ensure the widespread use of polymeric materials in medicine and biology, as one of the cheapest and most accessible materials, by imparting desired physical-chemical properties to polymeric surfaces using nanotechnologies, such as aseptic properties, biocompatibility. Perhaps the application of the effect of bio epitaxy could be very promising along the way. After a thorough study of the materials proposed after the discovery by Otto Wichterle in 1968 of the method for manufacturing SCLs, which is still considered fundamental, the new proposed methods for obtaining various SCLs are only modifications of the main Wichterle method. The level of modern development of eye surgery, especially microsurgery on the anterior segment of the eyeball, provides for the mandatory use of TCLs in the postoperative period of rehabilitation. However, there is no production of special TCLs; therefore, random SCLs are still used instead of the correct TCLs. In this case, TCL should have certain parameters and surface quality with a given surface relief, which can be obtained using the technology of appropriate surface treatment of the polymer intended for direct contact with the postoperative surface of the cornea of the eye. To do this, a smooth and uniform empirically aspherical shape of the TCL should be achieved, without irregularities, for example, transitions from the optical zone to the slip zone; a certain form of curvature and relief of the surface of the obtained TCL, which must have a surface radius of at least 164 degrees, because it is this surface contour that provides the physiological processes for of corneal cells migration, to restore physiological processes in the corneal tissue; NSMP of the TCL eliminates the formation of a biofilm on the treated polymer surface. Certain characteristics and geometry, when properly processed for the surface of the polymer, provide correct TCLs, in contrast to conventional SCLs, which are still used as pseudo-TCLs.

Materials and Metods

TCLs are produced on a conventional production line for SCLs. In shape, the obtained TCLs correspond to corneoscleral SCLs made using various polymers with high adhesion to their surface of carbon-containing nanofilms: polyethylene terephthalate (PET), polytetrafluoroethylene (PTFE), and polyvinylidene fluoride (PVDF). TCL should have the form of a spherical segment with the following dimensions: diameter 18 mm, thickness 0.3 mm, radius of curvature in the center 8.8 mm, height of the spherical segment 5.8-6.2 mm. The obtaining TCLs must also have an empirically aspherical shape with an external angle over the entire surface of at least 164 degrees; this form of curvature of the surface relief provides the processes of physiological migration of corneal cells. It is necessary to strictly observe the shape and topography of the TCL surface, which should ensure the preservation of the physiological processes of the corneal tissues when using these TCLs. At the final stage, to obtain the proper TCL, the surface of the obtained TCL is treated with NSSP, and then by means of NMSP using known nanotechnological methods for treating the surface of polymers by depositing a nanofilm on the surface of the TCL polymer in a special chamber.

Surface treatment of high molecular polymer materials is carried out on conventional equipment with planetary plates designed for surface treatment. The surface is preliminarily structured with ionic flows of reactive and/or inert gases to obtain a developed surface NSSP, which is then subjected to nanomodification - NMSP by the CCF sputtering method, which can be combined (single-layer, multilayer, monophasic). The homogeneity of the obtained films was 95%. By varying surface treatment methods (chemical, physical, electrochemical, surface nanomodification methods), it is possible to obtain combined carbon containing nanofilm (CCNF) with specified physico-chemical parameters determined by: chemical composition, atomic structure, surface charge on the surface, which set certain characteristics of the surface of the manufactured product. These properties of surface characteristics make it possible to obtain certain surface properties, such as aseptic, bactericidal properties, biocompatibility of the surface of the nanomodified polymer. Thus, the specified characteristics of the NMSP surface ensure the safety of the underlying living tissue in contact with the TCL treated by means of CCNF apply. Materials with NSS and subsequent NMS represent a separate class of synthetic nanomodified materials. Such coatings are in high demand for implant surface treatment, since artificial substitutes in contact with tissue liquid or living tissue require special surface treatment to improve biocompatibility. (1, 2, 3). Nano structuring of the surface of polymers was obtained by treating their surface with ions of reactive and noble gases and their mixtures (CF4, Ar, O2). Modification was carried out by two methods: deposition of CF4 from directed ion-plasma flows of hydrocarbon vapors 5–120 nm thick and magnetron sputtering of highly dispersed films.

Figure 1. TCL

The surface charge characteristics of the treated, by means of CCF deposition, can promote adhesive properties or repel chemical composites, proteins, cells from the interface due to the generated active functional groups. Pretreatment of the polymer surface, for example, allows for covalent immobilization of cell-binding peptides derived from extracellular matrix proteins: fibrinogen, fibronectin, laminin and grafted peptides can provide an adequate matrix for subsequent cell migration. The properties provided by the spraying of CCF: the absence of toxicity, biocompatibility, obtaining a dispersed surface, make it possible to obtain effective TCLs, too. Mandatory properties provided by the use of surface nanomodification: lack of toxicity, biocompatibility, dispersed surface, make it possible to create artificial substitutes and apply them successfully.

Results

Study of antimicrobial activity. The surface structure was studied using a FemtoScan atomic force microscope with a maximum scanning area of 10x10 µm. For each surface of the sample, photographs were taken at different points. After obtaining the relevant results of toxicity studies of HC-treated PET, PTFE, PVDF (results of studies, antimicrobial activity is described in detail), polymers with deposition bands α-C:H (100 nm) were selected as starting materials. Experimental studies of polymers with CCF formed by ion-plasma methods have shown that the degree of surface dispersion and its microrelief, as well as methods for its modification, determine its surface properties and efficiency, in particular, antimicrobial activity (4). Gram-positive Staphylococcus aureus ATCC 29213 and Gram-negative Pseudomonas aeruginosa ATCC 27853 were used to study antimicrobial activity. To do this, 3-4 colonies of microorganisms cultured after 18-20 hours are suspended in 3 ml of saline. The suspension had a turbidity of 0.5 on the McFarland scale (1.5 x 108 cfu/ml). The base suspension was then diluted by diluting the serum with saline to a concentration of 15 cfu/ml. Samples of HSS polymers were cut into fragments with a size of 15x15 μm. A fragment of the substrate was placed in a test tube with a liquid nutrient medium to control the sterility of the coatings. Muller Hinton Bovril was used as the culture medium. From each test tube with different concentrations, 25 μl of the suspension was taken with a pipette and applied to individual fragments of the polymer substrate with GSS to control the growth of the culture. Such infected fragments were incubated in a humid environment with a thermostat at 37°C for 2 hours. After incubation, all fragments were placed in test tubes with 4 ml of nutrient medium and incubated again in a thermostat at 37°C for 48 hours. Antibacterial activity was assessed by the appearance of visible growth in test tubes with nutrient media after 48 hours. After obtaining the results of studies on the non-toxicity of PET, PTFE, PVDF samples treated with CCF, the treatment of the NSS polymer surface under the influence of UV radiation using ion plasma processes was developed to obtain the desired properties of the treated surface (4). This surface modification, which can be achieved in the process of plasma film deposition, is the result of the action of photons and active particles in the plasma, which react with surfaces at a certain depth without changing the bulk properties of the substrate material. Parameters such as gas types, processing power, processing time and operating pressure may vary. The process of ion-plasma deposition of CCF can change the surface energy. A certain film deposition can change almost any substrate geometry. The most important feature is the ability of CCF deposition applied to the surface of the polymer to be functioning, which cannot be provided by chemical surface treatment. In all experiments, as well as control samples for growing cultures, control of the sterility of the samples was also provided. Experimental results of the study of antimicrobial activity are presented in table (1). In test tubes with polymer samples without coatings of hydrocarbons, the growth of microorganisms was observed in all dilutions, which indicated a high turbidity of the media. The lack of antimicrobial activity of CCF against Pseudomonas aeruginosa in some samples can be explained by the fact that this microorganism is more resistant to various aggressive factors compared to Staphylococcus aureus. Of greater interest are the results showing the antimicrobial activity of CCF coatings against Pseudomonas aeruginosa in samples 11-16. Sample 15 inhibited growth even at a microbial concentration of 104 cfu/mL. Of greatest interest are samples 14 and 15, in which the growth of both types of microorganisms is suppressed. Analysis of the table. (1) showed that the maximum antibacterial activity of HC was observed in samples with the maximum relief (the ratio of the real surface to the geometric one was about ~100). Comparison of the results of the surface charge study and careful analysis of the data in Table (1) shows that the interaction between NSS and microorganisms may depend on two mechanisms. One of them is associated with electrostatic interaction, and a sample of this type is shown in Fig. 2, where the real surface is increased by a factor of 5-8, and the charge is 1-5 μC/m2. The second mechanism is associated with the dispersion parameters of the NSS, a sample of this type is shown in Fig. 3, where the value of the real surface is increased by about 100 times.

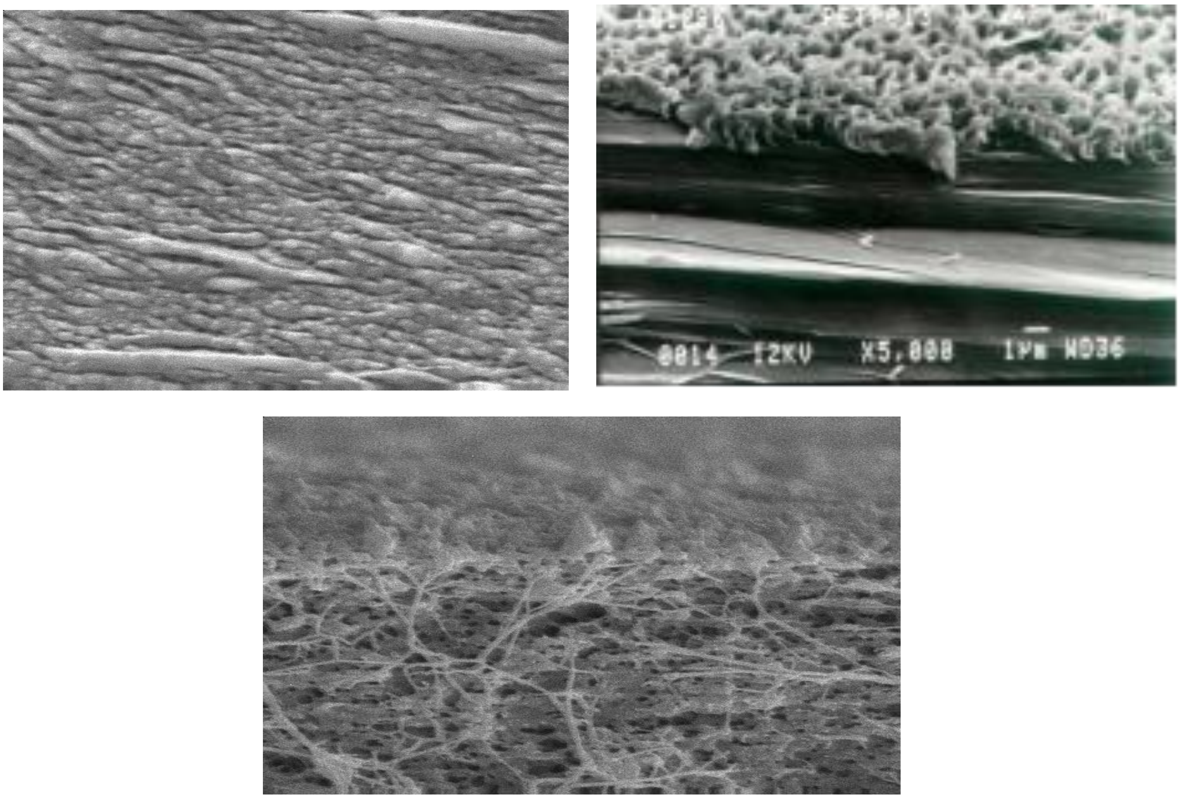

Figure 2. PTFE after treatment (etching).

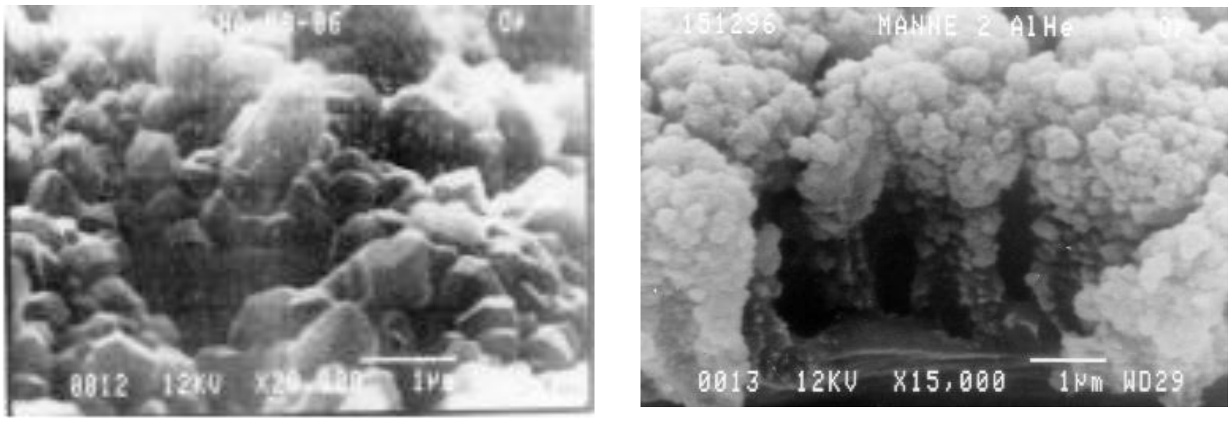

Figure 3 Microphotograph of super porous NSS.

№	Polymer/ deposition Conditions	Indicator m/o	Innoculation dose (cfu/ml)				
			10^5	10^4	10^3	10^2	10
1	PTFE: 1. treated CF_4 2. α-C:H (50 nm)	Ps. aerug.	+	+	+	+	±
		S. aureus	+	+	±	–	–
2	PTFE, smooth 1. α-C:H (50 nm)	Ps. aerug.	+	+	+	+	+
		S. aureus	+	+	+	+	+
3	PTFE: 1. treated CF_4 2. α-C:H (100 nm)	Ps. aerug.	+	+	+	±	±
		S. aureus	+	+	–	–	–
4	PTFE, smooth 1.α-C:H (100 nm)	Ps. aerug.	+	+	+	+	+
		S. aureus	+	+	+	–	–
5	PET: 1. treated CF_4 2. α-C:H (50 nm)	Ps. aerug.	+	+	+	+	+
		S. aureus	+	+	+	+	+
6	PET, smooth 1. α-C:H (50 nm)	Ps. aerug.	+	+	+	+	+
		S. aureus	+	+	+	+	+
7	PET: 1.treated CF_4 2. α-C:H (100 nm)	Ps. aerug.	+	+	+	+	+
		S. aureus	+	+	+	–	–
8	PET, smooth 1.α-C:H (100 nm)	Ps. aerug.	+	+	+	+	+
		S. aureus	+	+	+	+	–
9	PVDF: 1. treated CF_4 2. α-C:H (50 nm)	Ps. aerug.	+	+	+	+	±
		S. aureus	+	–	–	–	–
10	PVDF, smooth 1. α-C:H (50 nm)	Ps. aerug.	+	+	+	+	+
		S. aureus	+	–	–	–	–
11	PVDF: 1.treated CF_4 2. α-C:H (100 nm)	Ps. aerug.	+	+	+	–	–
		S. aureus	+	–	–	–	–
12	PVDF, smooth 1. α-C:H (100 nm)	Ps. aerug.	+	+	±	–	–
		S. aureus	+	–	–	–	–
13	PTFE(relief): 1. treated CF_4 2. α-C:H (100 nm)	Ps. aerug.	+	+	±	–	–
14	PTFE(relief), 1. α-C:H (100 nm)	Ps. aerug	+	+	–	–	–
15	PVDF(relief): 1. treated CF_4 2. α-C:H (100 nm)	Ps. aerug.	+	–	–	–	–
16	PVDF(relief), 1. α-C:H (100 nm)	Ps. aerug.	+	±	–	–	–

Table 1. Antimicrobial properties of samples

Discussion and Conclusions

Nanotechnology is a relatively new area of science, also associated with the creation of new materials with new surface characteristics of polymer products and devices to expand the horizon of their practical application. For example, these new technological possibilities open the prospect of a new approach to solving some medical problems by programming certain physico-chemical characteristics of the nanomodified polymer surface to obtain certain desired surface properties, such as, for example, imparting aseptic properties to the polymer surface to prevent the risk of biofilm formation, as well as to achieve biocompatibility, bio epitaxy effect.

In the early 1990s, there was such a boom with the idea of modifying the surfaces of many products and devices made of widely available and cheap polymeric material for medical and biological purposes by using nanocomposite films deposition for the treatment of polymeric surfaces, for example, surgical accessories, polymer surfaces: joints (damaged and artificial), on various silicone prostheses (mammary gland, for example).

It's well known that silicone can degrade under carbon film (CCF) releasing toxic silicone oil.

Subsequently, in particular, in statistical studies, cases of malignant neoplasms were identified in such patients with covered silicone prostheses. Thus, then it became clear that at the current level of using the technological capabilities of nanomodification of polymer surfaces, only more thoroughly and in detail studied technologies for the use of nanomodification of polymer surfaces and the positive results of their application can be considered for further development of this direction, with the possibility of surface treatment of polymeric materials. Thus, the use of various containers made of polymeric material for guaranteed aseptic storage and transportation, for example, donor implants in special polymer packaging, for guaranteed storage and safe transportation, storage and transportation of the donor cornea, in particular, the manufacture and use of TCLs used for several days in the postoperative rehabilitation period after ophthalmic operations on the anterior segment of the eyeball. All these proposals are supported by patents for inventions.

The chemical and physical properties of NMSP can promote adhesion, repulsion or transfer of chemical compounds, proteins, cells from the surface of the medium through the active functional groups of NMSP. The chemical and physical properties of NMSPs after preliminary nanostructuring of the polymer surface (NSSP) using various surface treatment modes are determined by the chemical composition, atomic structure, and surface charge on the treated surface and can affect corneal tissues lying under TCL. TCLs can succour maintain cell membrane polarization and may influence the behavioral responses of corneal cells. This phenomenon can be successfully used both to restore the structure of the cornea and to ensure proper regeneration of the cornea.

The quality and properties of the polymer surface treated in this way also affect the underlying corneal tissue when using TCL. Thus, the TCL surface is able to maintain cell membrane polarization and influence the behavioral responses of living corneal cells. This phenomenon can be successfully used both to restore the structure of the operated cornea and to control the process of corneal regeneration. Epithelial and stromal cells of the cornea, having a different nature, are able to change their shape and functional activity depending on the characteristics of the extracellular matrix, as well as on the biochemical properties and geometric configurations of the CCNF. This may provide certain opportunities for the regulation and acceleration of the restoration of underlying living tissues, in this case, in the process of restoration and healing of the cornea after operations on the anterior segment of the eyeball.

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6th Euro BioMat 2021 Presentations:

6. The relief of surface migration determines the structure and behavior for each moving living cell

7. THE EYE DIAPHRAGM LOSS COMPENSATION BY MEANS OF ARTIFICIAL IRIS USE

8. The allogeneic transplants preservation.