MINI REVIEW

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Nanomaterials in the Management of Contact Lens-Associated Ocular Complication

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Abstract

Contact lens is the transparent hemisphere-shaped ophthalmic product worn by a large population all across the globe for improving vision. It is applied to the cornea of the eye not only for improving vision but also for the delivery of drugs. The contact lens has many benefits but it also causes several ophthalmic infections which include amoebic keratitis, fungal, bacterial, and viral keratitis. The development of bacterial biofilm in lens cases exacerbates the ocular infection after the application of contact lenses in the cornea. Contact lens often associated with discomfort and dry eye. Coating these contact lens with different nanomaterials and an antimicrobial agent is a very good approach to improve the quality and biological activity of lenses. Surface functionalization is the most commonly adopted, and versatile method to tailor the optical properties. This review highlights the new technology to achieve the sustained release of drugs from contact lens by controlling their chemical, mechanical, and optical properties..

Keywords: *bacteria, contact lens, nanomaterial coating, ocular drug, cornea*

Abbreviations: *AFM :atomic force microscopy; DLS :dynamic light scattering; EDS :energy dispersive x-ray spectroscopy; EPR :electron paramagnetic resonance; ESEM :environmental scanning electron microscope; FESEM :field emission scanning electron microscope; FTIR: fourier transform infrared spectroscopy; HPLC: high performance liquid chromatography; MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide]; NMR: nuclear magnetic resonance; SEM: scanning electron microscope; TEM: transmission electron microscope; XPS: X-ray photoelectron spectroscopy.*

Introduction

The contact lens is mainly used for improving vision. It is estimated that more than 150 million people wore contact lens globally [1]. But many contact lens wearers experience discomfort due to improper wetting, lubrication, and protein adsorption on the surface. This problem is further associated with the material used to design the contact lens since it reacts with the eye lacrimal fluid. Although the lens possesses a high water-bearing capacity, it causes eye dryness when used for prolonged periods [2]. The commercially available contact lens aims to correct the ocular visual error like myopia, astigmatism, and hyperopia. With the progress in material science, polymer-based material (Polymethyl methacrylates), silicone-based Polydimethylsiloxane[3], and poly (hydroxyethyl methacrylate) hydrogel are introduced in the production of contact lens [4]. An ideal contact lens material has high oxygen permeability and more diffusion constant [5]. Contact lenses are also used for drug delivery purposes. It acts as a drug carrier that facilitates the sustained release of the active pharmaceutical ingredient at the ocular site. To incorporate the drug into the contact lens matrix several methods are adopted.

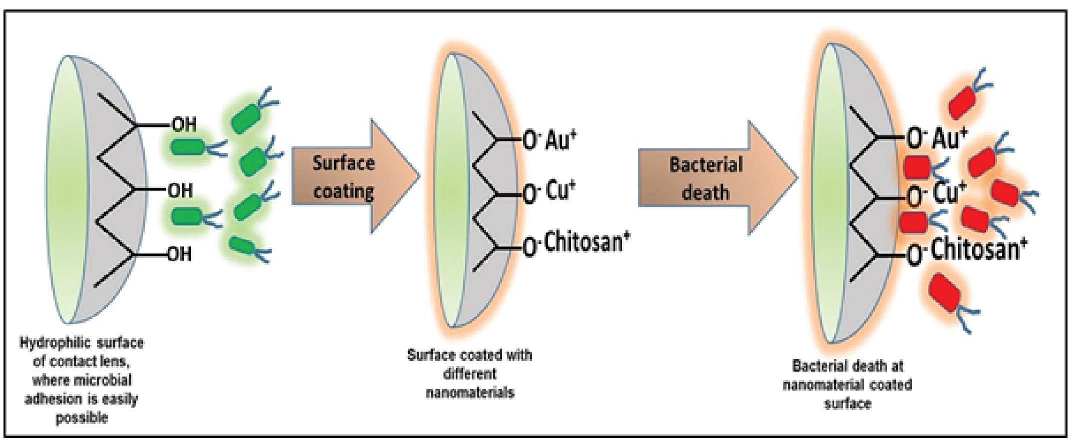

Figure 1. *Schematic representation of nanomaterial coating on the surface of contact lens.*

It includes (1) soaking the lens in a solution containing a drug, (2) molecular imprinting, (3) ionic interaction, and (4) emulsion-based loading of drugs [6].

Depending on the physical property the contact lens is classified into two types; soft contact lens and rigid contact lens. The soft gel in the contact lens is more prone to microbial adhesion and biofilm formation and sometimes it leads to microbial keratitis and corneal damage [7]. Gram-positive bacteria *Staphylococcus aureus, Streptococcus pneumonia* are the causative organism responsible for infiltrative keratitis, and acute red eye [8]. To overcome the microbe infection and the side effects associated with the contact lens, surface modification was done by different antimicrobial nanomaterials by impregnation or coating of different materials. For example, multifunctional zinc oxide nanoparticle-chitosan-gallic acid composite material coating on contact lens overcome the discomfort and eye dryness [2]. A combination of gallic acid and chitosan nanoparticles impart wettability and antioxidant properties in contact lenses.

Nanomaterials can be administered in the ocular system in the form of a dispersible solution [9], immobilization of material on a surface, material integrated with the hydrogel system, or direct coating of effective nanomaterials on the surface. Silicone hydrogel is the widely used material for contact lens production but it also has a few drawbacks like less hydration tendency, microbe adherence, and protein adsorption [10]. Impregnation of an antimicrobial compound on a contact lens is the conventional approach to fight against bacteria or other microbes. This issue addresses the coating of different nanomaterials on the surface of the contact lens to enhance its efficacy (Figure1).

Contact lens associated infection in the eye

When the contact lens comes in connection with the cornea of the eye, the tear film is separated into two parts. The first layer covers the posterior part of the lens and the second layer covers the anterior part of the lens. Because of this distribution of tear film in the anterior part of the contact lens, the wettability of the contact lens is less as compared to the cornea, and this imbalance causes dry eye condition. It is also observed that the high friction between the contact lens and the conjunctiva surface causes the inflammation of the ocular surface due to the release of inflammatory cytokines and matrix metalloprotease [11]. Major symptoms of contact lens infection include dry eye, irritation and itching in the eye, blurred vision, foreign body sensation, and eye strain. A study carried out in UK based hospital has reported that the contact lens wearer is more likely to develop corneal infection (microbial keratitis) as compared to those who don't wear the contact lens [12]. Major risk factors responsible for infection include overnight wear, ocular disease history, frequent touch with non-sanitized hands, failing to wash, and poor storage of contact lenses. The most common source of infection is the poor sanitization of contact lens storage cases. Infection associated with contact lens lead to ocular disease like microbial keratitis, contact lens-induced acute red eye, and peripheral ulcer. Microbial keratitis is identified by the corneal epithelial cells damage accompanied by continuous severe pain subsequently lead to loss of vision or surgical intervention [13]. Biofilm formation on a contact lens is a very serious threat and it is very challenging to control the biofilm formation due to the rapid development of resistance to lens care solution. The table given below has listed the name of microbes responsible for infecting contact lenses (Table1).

Nanomaterial coating on contact lens

The current strategy for designing the contact lens mainly focused on a coating of multifunctional material on the lens to improve the hydration and bactericidal action. In the last few decades, the nanomaterial coating approach in the fabrication of contact lenses has been explored. Incorporation of a drug in contact lens follows the multiple strategy (1) Drug loading in nanoparticle system by dispersing them in varying concentration and then mixed with monomer or polymer system [32] (2) adding suitable surfactants in monomer and then polymerized along with drug or nanoparticle [33] (3) soaking contact lens directly in the dispersion of nanoparticles containing drug [34] (4) chemical bonding between drug and contact lens [35]. The silver nanoparticle has gone under several investigations and silver deposited lens cases are commercially available in the market [36,37]. But silver nanoparticle is not used directly in contact lens because it prohibits the proliferation of corneal cells. On the other side copper [38], zinc nanoparticles [39], copper doped zinc oxide [40], zinc doped copper oxide [41] nanomaterial could be coated on contact lenses. Selenium-based nanocoating [42] on contact lenses and lens cases have the same role. Zwitterionic polymeric nanomaterials coating on contact lens electrostatically bind with the aqueous contents of the eye region, to promote stable hydration [43]. Earlier carried out work employed the use of hydrophilic polymers for the functionalization of the surface of contact lenses to improve the wettability [44]..

Chitosan-based nano-coating on contact lenses

Chitosan is a well-known material due to its biocompatibility, biodegradability, and unique property to reduce protein deposition on biomaterials [45]. Contact lenses have direct exposure to the different bacteria, viruses, and fungus, in the adverse condition it causes a serious threat to the ocular region of the eye. To overcome this problem chitosan-based nanocomposite materials have wide application in the fabrication of the surface of contact lenses. Engineers have developed the electrohydrodynamic atomization process for the nano-coating of materials on the surface of contact lenses [46]. This approach was adopted to control the release of the drug (for example-timolol maleate) using chitosan as a carrier. Polymers polyvinyl pyrrolidone and poly (N-isopropyl

Table 1. *Microbes responsible for contact lens infection*

Bacteria	Corynebacterium xerosis [14], Delftia acidovorans[15], Acinetobacter radioresistans[12], Staphylococcus aureus [16], Staphylococcus hemolyticus[12] Pseudomonas aeruginosa [17,18], Staphylococcus epidermidis [19], Achromobacter xylosoxidans [15], Escherichia coli [16], Micrococcus luteus [12], Serratia marcescens [20], Klebsiella pneumoniae [14], Stenotrophomonas maltophilia [15], Streptococcus haemolyticus [14], Serratia liquefaciens [21]
Virus	Herpes simplex virus-1 [22-24],
fungus	Candida albicans [25], Aspergillus nidulans [26], Fumigati species [27] Bipolaris species [28], Aspergillus spp conidiophores [27], Aspergillus udagawae [27], Fusarium solani [29],
Other organisms	Acanthamoeba trophozoites [13,30], Acanthamoeba castellanii [31],

Table 2. *Nanomaterial coating on contact lenses*

Material and synthesis	Chemical and biological properties	Effective against/ application	Characterization and validation	Ref.
Coordination of copper ions(Cu2+) and poly (carboxylbetaine-co-dopamine methacrylamide) coating on contact lens.	Improved surface wettability, broad-spectrum antimicrobial activity, reduce protein adsorption, biofilm inhibition	E.coli, P.aeruginosa, S. aureus, C. albicans	SEM, XPS, EPR, NMR	[49]
Zinc oxide- chitosan-gallic acid nanocomposite coating by the sonochemical approach	Antioxidant properties, enhanced wettability, antimicrobial properties, biocompatible with human cell line	S. aureus	Water contact angle, FESEM, EDS, AFM	[2]
Nanosilver-based Sol-gel nanocomposite (Silica zirconia sol impregnated with silver NP) coating on contact lens cases	Biofilm inhibition in contact lens cases	S. aureus, P.aeruginosa	SEM, MTT assay	[50]
Contact lens solution conjugated with silver and gold nanoparticles	Anti-amoebic activity in a dose-dependent manner, low cytotoxicity against a fibroblast cell line	Acanthamoeba castellani strain	Cytotoxicity assay, DLS, SEM, TEM	[51, 52]
Contact lens loaded with gold nanoparticles and soaked in varying concentration of timolol	Glaucoma treatment without compromising the contact lens optical property,	Glaucoma and visionary defect	Optical transparency study, In vitro drug release study, In vivo study in rabbit tear, TEM, DLS	[53]
Metal coated nanofiber on hydrogel-based contact lens composed of poly(3,4-ethylene dioxythiophene) and polystyrene sulfonate	Irritation free, permeable to gases, optical transparency, better integration with corneal cells	-	In vivo study on rabbit eye, Electroretinogram recording, SEM, ESEM, electrochemical impedance spectra	[54]
Graphene-based nanomaterial impregnated on contact lens by direct laser interference patterning graphene film using Nd: YAG laser(neodymium-doped yttrium aluminum garnet).	Grating size 0.93 to 3.03 µm in contact lens surface, Two-dimensional (2D) patterns obtained through double-time laser interference, monitoring the optical properties of eye, flexible and conductive material.	-	Contact angle measurement, ocean optic spectrometer for characterization of optical properties	[55]
Silica nanoparticle coated on contact lens cases by chemical mediated grafting using UV cross-linkable acrylates and polyethylene glycol	Resist the protein and nucleic acid adsorption to prevent bacterial adhesion, biofilm inhibition	Pseudomonas, Staphylococci, Serratia strain	AFM, water contact angle measurement, biofilm assay	[21]
Phomopsidione nanoparticle coated contact lens using solvent antisolvent precipitation method for synthesizing nanoparticles and polyvinyl alcohol employed as a coating agent.	Sustained release of drug for 48 hours from the contact lens, Polyvinyl alcohol reduces the immunogenicity, negative zeta potential allow its incorporation in silicone hydrogel	S. marcescens, P. aeruginosa	HPLC, TEM, SEM, Zeta potential, In vitro drug release study, Agar diffusion assay.	[56]
Diamond gel-based nanoparticulate loaded contact lens	Lysozyme activated release of timolol could be done from the gel-based carrier	Glaucoma treatment	FTIR, Zeta potential, TEM, tensile strength test, drug release study	[57]
Nanostructured UV blocking contact lens by polymerization of a bicontinuous nanoemulsion	The photochromic property, better oxygen permeability, good hydration, and stiffness	UV blocking contact lens	oxygen permeameter, SEM, tensile tester, UV spectrophotometer, In vitro study in cell culture, and In vivo study in a rabbit eye	[58]

acrylamide) can be used to encapsulate the drug which can be electrically atomized into the contact lens surface to produce a nano-coating [46]. This strategy has proven to be useful in the management of glaucoma [46]. Chitosan-based materials modulate the drug release as well as enhance the permeation of the drug due to its mucoadhesiveness [47]. Chitosan doesn't cause any harm to corneal epithelial cells. The cationic nature of chitosan facilitates its interaction with the cell membranes followed by the penetration into tight junction protein which helps in the paracellular transport of drugs [48]. The table given below has briefly described the different nanomaterials and their significance (Table2).

Summary

Dry eye and microbial keratitis is the most common condition observed in those people who wore the contact lens on regular basis. Apart from the treatment of visionary defect, contact lens has been also exploited for slow and sustained release of drugs in the ocular cavity. Hydrogel-based material is used in contact lens production but it possesses many drawbacks, to overcome this issue different nanomaterials are coated on the surface but many of them are not available commercially. More work is required to be done to commercialize these products after a successful clinical trial. We attempted to describe the biochemical property of different nanomaterials which can alter the functionality of contact lenses. For example, protein adsorption, wettability, and microbial adhesion, three are important parameters that need to be regulated and controlled while designing the contact lens and contact lens cases.

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