

Anti-microbial Contact Lenses and Lens Cases: a Developmental Review

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ABSTRACT: Contact lens users are susceptible to ocular complications due to the microbial contaminations related to Contact lenses, lens cases and solutions. Various antimicrobial technologies/ strategies have been incorporated in the development of the Contact lenses and cases in the past. Antimicrobial agents are being examined with the aim of analysing various passive technologies utilized in the manufacturing of antimicrobial contact lenses and contact lens cases. We hope that the consolidation of the various developments and ideas in this area will result in reduced contact lens-related microbial adverse events. In this review, we assessed various aspects particularly the passive chemical strategies employed in the available antimicrobial contact lens lenses, solutions and lens cases.

KEYWORDS: Antimicrobials—Contact lens—Lens case---CL solution---Passive Chemical strategy

I. INTRODUCTION

Contact lenses (CLs) are small, bowl-shaped plastic lenses which serve as a new anterior ocular surface of the eye and rest over the cornea or the sclera or both. Contact lenses are a convenient and popular method to correct refractive errors, with an estimated 140–145 million wearers globally [1].

Majority of users are using reusable contact lenses which are worn on daily wear basis and kept in multipurpose solution stored in contact lens cases. Ocular complications due to microbial contamination of contact lenses, lens cases and lens care solution one of the major concern of CL practitioners [2,3] may exacerbate by extended lens wear [4] and unsanitary lens care practices. Despite the improvement in contact lens materials, effectiveness of new lens care solutions, and improved contact lens wear practice still some patients' experience lens related unfavourable ocular reactions [2] mostly including contact lens induced acute red eye (CLARE) [5], contact lens-induced peripheral corneal ulcer (CLPU) [6], microbial keratitis (MK), etc

Poor surface quality of contact lens can cause Microbial adhesion on the lens surface [7], hypoxia and decreased resistance of corneal epithelium, poor lens hygiene and contact lens case contamination [8]. Even among the users adhering to good lens care practices, up to 92% of the contact lenses and lens cases were found to harbor disease caused by microbes [9].

II. MICROBIAL RESISTANCE STRATEGIES FOR CONTACT LENSES

The advancement of antimicrobial surface for contact lens and contact lens cases have expanded consideration in the previous decade to control the development of contact lens related complications. Various chemical strategies are taken on to design antimicrobial contact lenses which utilize chemical alteration to convert the surface properties to decrease the microbial adhesion and biofilm formation.

The passive and noncidal agents alter the properties of the material surface and prevent microbial adhesion onto the lenses & reduce the occurrence of infection. A potential drawback of lens case modification is that reduced adhesion onto the case may increase adhesion onto the contact lenses themselves. Following technologies are being tried for reducing contact lens induced infections.

A. PHOSPHORYLCHOLINE

MECHANISM OF ACTION: Hydrophilicity of silicone intraocular lenses was significantly increased after covalent attachment with 2-methacryloyloxyethyl phosphorylcholine (MPC) [10]. This significantly reduced platelet,

macrophage, and lens epithelial cell adhesion onto the surface, resulting enhanced surface biocompatibility and significantly decreased adhesion of *S. epidermidis* after 1 hour and reduced biofilm formation after 18 hours of incubation [11].

B. PHOSPHORYLINE-COATED PHEMA LENSES

In a study phosphorylcholine bound lenses reduced adhesion of a different strain of *P. aeruginosa* (6294) and strains of *S. pneumoniae* and *H. influenzae* [12]. In that study, phosphorylcholine seemed to reduce the adhesion of *H. influenzae* to lenses but did not affect adhesion of the strain *P. aeruginosa* and increased adhesion for 1 strain (out of tested) of *S. pneumoniae* (a bacterial type isolated from cases keratitis during lens wear)

Selan et al. in 2009 reported that Phosphoryline-coated PHEMA lenses possessed an increased wettability, reduced protein adsorption, and diminished bacterial adhesion of *P. aeruginosa* and *S. Epidermidis*[13]. The biofilms that did manage to form on phosphorylcholine-coated lenses were more susceptible to antibiotics such as Tazocin and gentamicin[13,14]. Similarly, alginic acid, a natural polysaccharide, was reported to improve the wettability and reduce the protein absorption on the contact lenses [15]

However, in vivo or in vitro efficacy of these passive non-cidal substances against virulent microorganisms such as *Pseudomonas* or *Acanthamoeba* is yet to be established, and there have been no reports of reduced bacterially driven adverse events (such as MK, CLARE, CLPU) in people wearing the phosphorylcholine containing lenses.

C. POLY(ETHYLENE GLYCOL) (PEG)

Poly(ethylene glycol) (PEG) of varying chain lengths has also been studied to modify surface properties of contact lenses and contact lens cases. Surface-modified silica nanoparticles, chemically grafted with UV crosslinkable acrylates and PEG groups, were coated onto polypropylene cases. Similar to quorum sensing inhibitors, incorporation of molecules such as PEG or phosphorylcholine may reduce the build-up of dead or living microbes.

The adhesion forces of 9 bacterial strains including *Pseudomonas*, *Staphylococci*, and *Serratia* were reduced by about 10 fold on coated cases. As such, mild rinsing removed 10–100 times more bacteria, and surface modification increased bacterial susceptibility to anti-microbial lens care solutions by 2–3 fold. Furthermore, the coating was non-cytotoxic, suggesting that surface modifications using PEG have great potential for medical devices [16].

D. SUPERHYDROPHILIC ZWITTERIONIC

Super-hydrophilic zwitterionic interfaces are bioinert, non-cytotoxic, and resistant to nonspecific adsorption of bacteria, proteins, and lipids [17]. Such a coating was applied to silicone hydrogel contact lenses, and prevented *P. aeruginosa* and *S. epidermidis* adhesion.

E. COMBINATIONS OF POLYCATIONIC BACTERICIDAL BACKGROUND LAYER AND A ZWITTERIONIC OUTER LAYER

A recent study created a dual layered surface, with a polycationic bactericidal background layer and a zwitterionic outer layer [18]. Polycationic surfaces exhibit efficient antimicrobial activity, but elicited high cytotoxicity and experience severe surface accumulation of dead bacteria, which would not work well in a contact lens application. The newly designed surface overcame this problem. The zwitterionic outer layer prevented bacterial accumulation by forming a hydration layer, while the polycationic inner layer killed the bacteria that did manage to attach to the surface. Further, reported that the zwitterionic layer is toxic to mammalian cells. Such a technology is well suited for contact lens applications.

Cheng et al. in a recent study developed broad-spectrum antimicrobial and antifouling coatings by conjugating adhesive catechol, antifouling PEG, and hydrophobic urea/ethyl groups to branched poly(ethylenimine) (bPEI) [19]. The coating applied to contact lenses was resistant to autoclaving and did not change light transmission. Coated lenses inhibited bovine serum albumin adsorption over 24 hours, and exhibited antifouling effects against *S. aureus*, *P. aeruginosa*, *C. albicans*, and *F. solani* over seven days. It also showed high biocompatibility. Such a combination of material showed promising future direction to modify the surface property in contact lens research [19].

F. PVA FILMS REINFORCED WITH OXIDIZED/POLYMERIZED PRODUCTS OF HYDROQUINONE (HQ), PYROGALLOL (PG) AND EPINEPHRINE (EP)

C Dhand et al. (2016) showed potent antimicrobial activity against pathogenic Gram-positive bacterial strains. HQ and PG films retain their antimicrobial efficacy even after steam sterilization, highlighting the first example of antimicrobial coating agents for contact lenses [20].

G. NATURAL COMPOUNDS

El-Dash et al. reported, adding four natural compounds honey, jasmine oil, Calendula ocinalis petal extract and Buddlejasalviifolia leaf extract into the contact lens care solution. Addition of these compounds prevents biofilm formation and removed preformed biofilm on soft contact lenses. Interestingly, Calendula ocinalis and Buddlejasalviifolia extracts showed an excellent effect on inhibition and removal of biofilms. [21]

H. PHOMOPSIDIONE NANO PARTICLE

Phomopsidione ($C_7H_{10}O$) is a novel ketone derivative isolated from *Diaporthe flaxinii* ED2. Studies has demonstrated that phomopsidione has low toxicity in animal models, worthwhile of further investigations [22]. Searching a natural alternative to replace silver ions, the antimicrobial efficiency of the contact lens model was tested on bacterial keratitis clinical strains. In a very recent Study, Yusoff Bin Sahadan et al. showed the phomopsidione nano-particle were coated onto silicone hydrogel contact lens by soaking the lenses (ACUVUE TrueEye™ 14.2 mm diameter) into 2% nanoparticle solution for 24 h at 4 °C. Phomopsidione nanoparticles coated contact lens showed sustainable release pattern of drug for 48 h. The contact lens models exhibited inhibition of keratitis causing microorganisms, particularly on Gram negative bacteria. And showed a significant growth reduction (up to 99%) on the tested microorganisms, [23].

III. PHYSICAL FACTORS AFFECTING THE EFFICACY OF ANTIMICROBIAL TECHNOLOGIES FOR CONTACT LENSES

1. Biocompatibility – Surface modifications designed for antimicrobial activity may unintentionally also be cytotoxic to corneal epithelial cells, such as NSAIDs and free radical-producing agents. Biocompatibility is the most crucial factor to consider while designing antimicrobial contact lenses. The standard in vitro characterization should use human corneal epithelial cell lines, as the contacts would be in physical contact with the cornea. in vivo experiments are necessary to establish the safety of modified lenses. [24]
2. Water content and wettability - Water content of a lens is an important factor for user comfort and safety. Lower water content hydrogels have been reported to show greater lens hydration, which contributes to higher comfort for the user. [25] Furthermore, water content has been reported to be a significant factor affecting in vitro adhesion of *A. castellanii* onto soft contact lenses [26]. Groups developing antimicrobial contact lenses should take care to measure the water content of their modified lenses. Similarly, wettability of the hydrogel surface is a critical variable for evaluating physiological compatibility, as the lenses will be in contact with the tear fluid. Most groups evaluate wettability through contact angle measurements.
3. Oxygen permeability - Oxygen is a critical factor for corneal health, and hypoxia decreases the cornea's ability to protect itself from microbes. Silicon hydrogel contact lenses have higher oxygen transmissibility than conventional hydrogel lenses, and have been more widely adopted in recent years. [27] Thus surface modifications should not alter the oxygen transmissibility significantly to avert hypoxia-related complications.
4. Light transmittance and refractive index- Antimicrobial lenses must have adequate light transmittance and refractive index that do not inhibit normal vision. One report of translucent lenses shows very poor light transmittance, 45%. Surprisingly, most studies of antimicrobial contact lenses have not quantitatively characterized the light transmittance of the lenses. This could be because the developed lenses appeared optically clear by visual inspection, so this factor must be considered in further investigations.
5. Stability – It is important to recognize that the physical properties of the modified contact lens reported for unautoclaved lenses may be significantly different than those after autoclaving. Clear lenses often turned opaque after autoclaving, indicating a phase separation, which maybe due to increased water content, which increased flexibility of the material [28]. Thus it is important to inspect the stability of the modified contact lens, as these chemical modifications may not be steady enough to go through the sterilization techniques and product life cycle of commercial contact lenses.

IV. CONCLUSION

Antimicrobial Peptides along with Passive surface modifications are also attractive technology for their biocompatible nature, robustness, and obstructive microbial adhesion characteristics, respectively.

Surface coated or copolymerized antimicrobial materials are more appealing compared with leach and release technique. With the successive development and availability of different types of silicone hydrogel lenses in the market, implementation of antimicrobial techniques needs careful research. Each technique needs to be tested with all the possible contact lens care products available in the market to rule out any side effect. Extensive human trials are required to rule out the efficacy of each antimicrobial technologies.

Overcoming the perceived issues of toxicity to mammalian cells, resistance development by the microbes, physiological changes in the eye, changes that may occur to the normal microbiota of the eye that in itself may provide some protection against infection of the ocular surface, and even issues of the environment during manufacture of the lenses (i.e., release of metals in waister products) requires further extensive research and carefully designed clinical and manufacturing testing. There is need for developing an ideal antimicrobial technology for reducing contact lens related complications.

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