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Hydrophilic surface modification of poly(methyl methacrylate)-based ocular prostheses using poly(ethylene glycol) grafting

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ABSTRACT

Ocular prostheses are custom-made polymeric inserts that can be placed in anophthalmic sockets for cosmetic rehabilitation. Prosthetic eye wearers have reduced tear amount, and they often experience dry eye symptoms including dryness, irritation, discomfort, and discharge. Most modern ocular prostheses are made of poly(methyl methacrylate) (PMMA), which is highly hydrophobic. Previous research has shown that improving the wettability of contact lens materials decreases its wearers discomfort by increasing lubrication. Therefore, hydrophilic modification of PMMA-based ocular prostheses might also improve patient discomfort by improving lubrication. We modified the surfaces of PMMA-based ocular prostheses using poly(ethylene glycol) (PEG), which is hydrophilic. To do this, we used two strategies. One was a "grafting from" method, whereby PEG was polymerized from the PMMA surface. The other was a "grafting to" method, which involved PEG being covalently bonded to an amine-functionalized PMMA surface. Assessments involving the water contact angle, ellipsometry, and X-ray photoelectron spectroscopy indicated that PEG was successfully introduced to the PMMA surfaces using both strategies. Scanning electron microscopy and atomic force microscopy images revealed that neither strategy caused clinically significant alterations in the PMMA surface morphology. In vitro bacterial adhesion assessments showed that the hydrophilic modifications effectively reduced bacterial adhesion without inducing cytotoxicity. These results imply that hydrophilic surface modifications of conventional ocular prostheses may decrease patient discomfort and ocular prosthesis-related infections.

1. Introduction

The removal of eyeballs has long been used for the treatment of ocular diseases, the leading indications being intraocular malignancy, severe trauma, and a painful blind eye [1]. Cosmetic rehabilitation using custom-made prosthetic devices, ocular prostheses, help these individuals to gain professional and social acceptance and alleviate other problems [2]. The prostheses are typically polymeric inserts that the patient places behind the eyelids and in front of the conjunctiva (Fig. 1A).

Patients wearing ocular prostheses often experience dry eye symptoms including dryness, irritation, discomfort, and discharge in the affected eye [3,4] (Fig. 1B). Tear insufficiency is found in up to 50% of patients with ocular prostheses, and dry eye symptoms are negatively correlated with the amount of tears [4,5]. The lack of lubrication in an anophthalmic socket can cause structural damage to the conjunctiva, which consequently results in inflammation, keratinization, and contracture of the socket [6,7].

The term "wettability" is traditionally used to describe the tendency for a liquid to spread over a solid surface [8]. The relationship between the wettability of contact lens materials and ocular discomfort has been widely studied, and the quality of the tear film over a lens is thought to play a key role in the lubrication of the lens/ocular surface, and it ultimately influences how much friction and ocular discomfort occurs [9,10]. Therefore, there has been much effort to make contact lens surfaces hydrophilic [9]. However, most modern ocular prostheses are made of poly(methyl methacrylate) (PMMA), which is highly hydrophobic, and, so far, the effort to make PMMA surfaces hydrophilic has been very limited [2].

Various synthetic and natural polymers have been used to make surfaces hydrophilic. Among them, poly(ethylene glycol) (PEG) has been widely employed as a surface coating material due to

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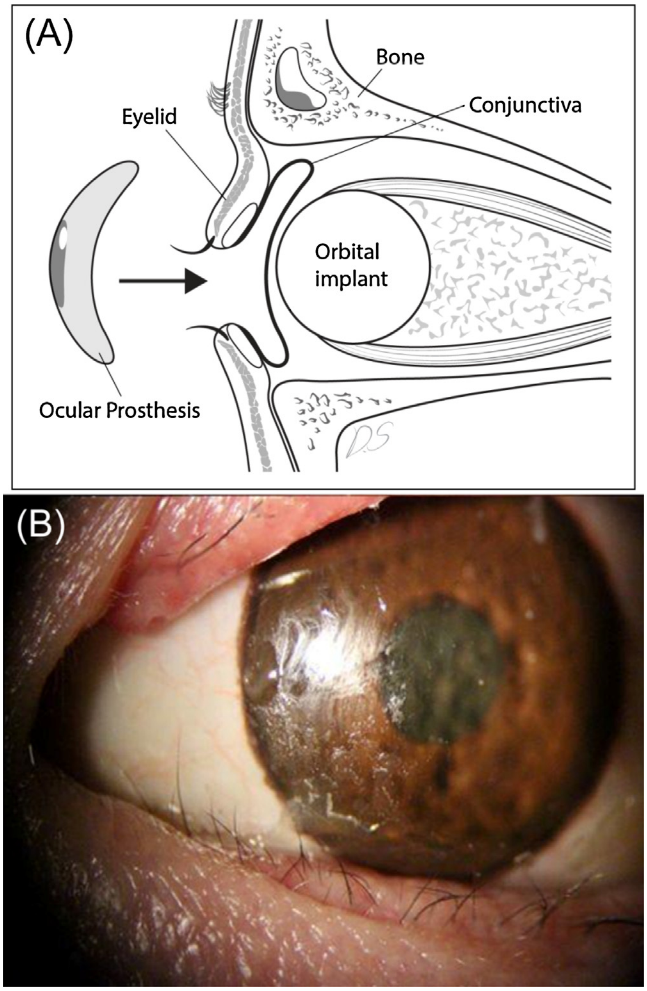

Fig. 1. (A) Schematic diagram of a human orbit with an ocular prosthesis. The ocular prosthesis is designed to fit in between the eyelids and the conjunctiva. The orbital implants replace the volume deficit created by eye removal surgery. (B) Slit-lamp photograph of a man wearing an ocular prosthesis. Note that there is dried mucus debris on the surface of the ocular prosthesis.

its remarkable hydrophilicity and biocompatibility. Typically, PEG has been incorporated onto biomaterial surfaces via surface grafting, plasma polymerization, surface interpenetrating networks, or simple adsorption of PEG-containing block copolymers [11–15]. Although PEG has also been used to modify the surface of PMMA, most applications have been limited to PMMA-based intraocular lenses and microchips [16–19]. To the best of our knowledge, the use of PEG for coating ocular prostheses has not previously been studied.

In this study, we modified PMMA-based ocular prostheses with PEG using two different strategies. One was a “grafting from” method, whereby PEG was polymerized from the PMMA surface. The other was a “grafting to” method, which involved PEG being covalently bonded to an amine-functionalized PMMA surface. After surface modification was confirmed using various characterization techniques, the cytotoxicity and bacterial adhesion associated with the surface-modified PMMA samples were evaluated.

2. Materials and methods

2.1. Materials

Poly(ethylene glycol) methacrylate (PEG-MA) (molecular weight [MW] 360), benzophenone, benzyl alcohol, sodium periodate, methoxypolyethylene glycol amine (PEG-amine) (MW 500), 3-aminopropyltriethoxysilane (APTES), and glutaraldehyde (25% in solution) were purchased from Sigma-Aldrich Corp. (St. Louis, MO, USA). PMMA was purchased from VIPI Corp. (VIPI Flash, São Paulo, Brazil). The phosphate-buffered saline (PBS, 0.1 M, pH 7.4) used during the grafting procedures included 1.1 mM potassium phosphate monobasic, 3 mM sodium phosphate dibasic heptahydrate, and 0.15 M NaCl in deionized water. All the ocular prostheses and PMMA matrixes used for the experiment were fabricated by one of the authors (S.W.B), who is an experienced ocularist according to the standard procedures [2].

2.2. Surface modifications of PMMA-based ocular prostheses

2.2.1. Surface modification via photoinduced grafting involving the polymerization of PEG-MA

The surface of a PMMA matrix was modified using a two-step process based on photoinduced grafting involving the polymerization of PEG-MA, which is similar to a process used in previous studies [20,21]. In the first step, 100 μL benzophenone solution (10 wt%) in ethanol was dropped on the PMMA surface and uniformly covered the surface. The benzophenone solution was then allowed to evaporate in a fume hood to ensure deposition of the benzophenone on the surface. In the second step, a monomer solution consisting of PEG-MA, benzyl alcohol (0.5 wt%), and 0.5 mM sodium periodate was coated onto the benzophenone-immobilized PMMA surface and exposed to 365-nm ultraviolet (UV) light at 300 mW/cm^2 (Ultracure 100ss Plus, EFOS Inc., Mississauga, Canada). After UV exposure for 30 min, the PMMA matrixes were rinsed thoroughly with deionized water and immersed in ethanol to remove the monomers that were not covalently bonded to the PMMA surfaces.

2.2.2. Surface modification via grafting of PEG-amine

The second method of surface modification involved grafting PEG-amine onto APTES-modified PMMA surfaces. First, PMMA matrixes were treated with oxygen plasma for 30 min to generate hydroxyl groups on the surface. The hydroxylated PMMA surfaces were then silanized by incubating them in 5% v/v APTES and 95% v/v ethanol for 1 h at room temperature. After thoroughly washing the PMMA matrixes with ethanol to remove the APTES that was not covalently bonded to the PMMA surfaces, they were cured at 80 °C for 1 h. The APTES-modified PMMA matrixes were then immersed in a solution of 2.5% v/v glutaraldehyde in PBS for 3 h at room temperature to functionalize the aldehyde groups, and they were subsequently left to react with PEG-amine (11 wt% in PBS) for 12 h.

2.3. Characterization of surface modifications

The surface-modified PMMA matrixes were chemically analyzed using X-ray photoelectron spectroscopy (XPS; K-Alpha XPS System, Thermo Fisher Scientific Inc., Waltham, MA, USA). In addition, the change in wettability caused by each surface modification was confirmed by measuring the contact angle using a contact angle goniometer (Phoenix 300, S.E.O. Co., Ltd, Ansung, Korea). Spectroscopic ellipsometry (SE MG-1000, Nano-View Co., Ltd., Seoul, Korea) was used to obtain refractive index and the thickness of PEG layer. The ellipsometric parameters psi(Ψ), del(Δ) were acquired over wavelength range from 380 to 890 nm with incidence angle of 70° in air at room temperature. Thickness was measured at three different points of three different substrates to obtain average thickness values and standard deviation. Cauchy model was utilized and data were fitted using implemented software. The PMMA surface morphology was also observed using scanning electron microscopy (SEM; JSM-7001F, JEOL Ltd., Tokyo, Japan), and 3D topo-