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Hydrophobic modification of polymethyl methacrylate as intraocular lenses material to improve the cytocompatibility

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ABSTRACT

The development of posterior capsule opacification (PCO) after intraocular lenses (IOL) implantation for dealing with cataract is mainly due to the severe loss of the human lens epithelial cells (HLECs) during surgery contact. A novel poly (hedral oligomeric silsesquioxane-co-methyl methacrylate) copolymer (allyl POSS–PMMA) was synthesized by free radical polymerization method to promote the adhesion of HLECs. FT-IR and ^{1}H NMR measurements indicated the existence of POSS cage in the product, which demonstrated the successful synthesis of allyl POSS–PMMA copolymer. Effect of allyl POSS in the hybrids on crystal structure, surface wettability and morphology, optical transmission, thermodynamic properties and cytocompatibility was investigated in detail. X-ray diffraction peaks at 2θ~11° and 12° indicated that POSS molecules had aggregated and crystallized. Thermogravimetric analysis-differential scanning calorimeter and optical transmission measurements confirmed that the allyl POSS–PMMA copolymer had high glass transition temperatures (more than 100 °C) and good transparency. The hydrophilicity and morphology of PMMA and copolymers surfaces were characterized by static water contact angle and atomic force microscopy. The results revealed that the surface of the allyl POSS–PMMA copolymer displayed higher hydrophobicity and higher roughness than that of pure PMMA. The surface biocompatibility was evaluated by morphology and activity measurement with HLECs in vitro. The results verified that the surface of allyl POSS–PMMA copolymer films had more HLECs adhesion and better spreading morphology than that of PMMA film.

1. Introduction

Cataract surgery has increased rapidly in recent decades. Phacoemulsification combined with intraocular lenses (IOL) implantation is the first choice for cataract treatment on account of small incision, quick recovery and better postoperative vision [1–3]. However, posterior capsule opacification (PCO) is a common complication after cataract surgery caused by the immune response and residual human lens epithelial cells (HLECs) on the posterior capsule [4]. Wound healing promotes residual HLECs to proliferate, differentiate, and to deposit extracellular matrix, via autocrine and paracrine cell signaling. Although PCO has been extensively studied, there is no unified mechanism to explain the cause. Most current studies hypothesize that a multicellular secondary membrane results from migration and fibrosis of residual HLECs on the posterior capsule, forming elschnig pearls [5]. Others suggest that a single layer of residual anterior capsule epithelial cells migrate onto the posterior capsule and undergo metaplasia into myofibroblasts, pulling the posterior capsule into many tiny folds. Both mechanisms can contribute to the development of PCO [6].

In recent years, several reports have focused on how to prevent PCO. In addition to the position of the capsulorhexis, IOL material and optic design are important factors in the development of PCO [7–9]. The effect of IOL on PCO has been explained by various suppositions such as the separation of the posterior capsule from the anterior capsule, stretching of the capsule, compression, no space/no cells and adhesiveness of the IOL material. Out of all of the commercial IOLs, hydrophobic acrylic IOL especially poly (methyl methacrylate) (PMMA) has played an important role in cataract surgery soon after its introduction in the mid-1990s [10,11]. PMMA is the most common commercially available IOL material and is known for long-term stability. It is relatively inexpensive, inert and is well tolerated in the eye with minimal inflammatory reaction. PMMA IOL has good light transmission properties which can transmit a broad spectrum of light including near-ultraviolet

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light [12]. Unfortunately, the surgery contact can cause considerable HLECs loss between the comparatively hard PMMA IOL surface and the corneal endothelium. Based on the sandwich theory [13–15] of PCO, the rapid epithelialization of IOL that forms a cell monolayer between IOL and posterior capsule can fill up the space and finally reduce the occurrence of PCO.

The surface properties of a polymer can be modified in order to ensure that it will be better adapted to its final use. Basically, the surface energy of the polymer (hydrophilic vs. hydrophobic nature) can be modified according to two general methods: surface treatment and bulk modification. The surface treatment methods of PMMA mainly include plasma treatment [16], nanoparticles doping [17] and grafting of biological macromolecules [18–20]. The plasma treatment used as a surface modification method is simple, effective and without safety issues. Using plasma discharge, hydroxyl, carboxyl or other hydrophilic functional groups can be introduced onto the surface of intraocular lenses to improve its biocompatibility. Titanium dioxide nanoparticles have been used to modify IOL to enhance its biocompatibility [17]. Heparin surface modification (HSM) decreases adhesion of cells and inflammations after cataract surgery [18]. However, a recent study shows the ratio of PCO is high using HSM IOL. Recently, a 2-methacryloyloxyethyl phosphorylcholine (MPC) coating was produced, which decreased adhesion of platelet, macrophage, lens epithelial cells and bacteria [19]. Although plasma treatment method can alter the surface wetting properties of IOL, the hydrophilic performance may lose in a short time. Metal oxide nanoparticles and biomolecules modified intraocular lenses always have color and unstable defects. Comparatively, bulk modification is a stable, effective and controllable IOL modified method.

Polyhedral oligomeric silsesquioxane (POSS) is a novel cage-like structure of the organic–inorganic hybrid molecules [21–23]. The main structure of POSS consists of two parts: a cage-like inorganic core based on Si—O—Si bonds and the shell composed of eight surrounded organic groups, which may be designed according to needs. The inner diameter of POSS is about 0.53 nm and the outer diameter is generally between 1 nm and 3 nm due to different organic functional groups. POSS has regular structure, good biocompatibility, small scale and large surface area, which make POSS as one of the most potential next generation biomaterials. POSS macromers with different shells have been doped into polystyrene [24], PMMA [25,26], polyurethane [27], polyethylene [28], ethylene–propylene [29], etc. by the way of copolymerization with other polymer monomers to change its mechanic, thermodynamic, surface or biological properties. Previous study [25] found that POSS and polymer hybrid is capable of forming a colorless transparent material, which does not affect the light transmittance. The cytotoxicity of POSS was also investigated and it was found that the toxicity of POSS is very low, almost non-toxic. Therefore, POSS nanomaterial is more suitable than other materials for ophthalmology biological repair alternatives. However, there is almost no reference about the studies on POSS used for IOL modification.

In order to improve the biocompatibility of PMMA used as IOL material and achieve the rapid epithelialization, surface characteristics of PMMA can be changed through bulk modification. In this work, polymer of allyl POSS–PMMA was prepared using radical random copolymerization method. A schematic of the synthesis procedure is presented in Scheme 1. The number-average molecular weight (Mn) and weight-average molecular weight (Mw) of allyl POSS–PMMA copolymer and PMMA were measured by gel permeation chromatography (GPC). The effect of POSS on the crystallization, thermodynamic properties, optical performance and surface properties of allyl POSS–PMMA were studied in detail with various techniques. Furthermore, cell viability assay was performed to determine biocompatibility of the allyl POSS–PMMA copolymer with HLECs by fluorescein diacetate (FDA) and Cell Counting Kit-8 (CCK-8) methods.

2. Materials and methods

2.1. Materials and reagents

Isobutyl (allyl)-POSS(R), [(allyl)(isobutyl)$_7$Si$_8$O$_{12}$] (allyl POSS) from Hybrid Plastics Co. and methyl methacrylate (MMA), azobisisobutyronitrile (AIBN), ethyl acetate, ethanol and tetrahydrofuran (THF) from Aldrich were used as received.

2.2. Material surface preparation and characterization

2.2.1. Synthesis of allyl POSS–PMMA copolymers

Allyl POSS–PMMA copolymers containing 0.01 or 0.02 weight of the allyl POSS monomers have been synthesized by free-radical polymerisation. The typical synthesis process (0.02 allyl POSS–PMMA) is described as follows: in a 50 mL round bottom flask, allyl POSS (0.34 g, 0.40 mmol), MMA (2.0 g, 20.0 mmol) and AIBN (0.025 g, 0.15 mmol) were dissolved in ethyl acetate (16 mL) and THF (4 mL) under a nitrogen atmosphere. The mixture was heated to 60 °C under constant magnetic stirring to initiate the polymerisation reaction, and the polymerisation was then carried out at the elevated temperature for 24 h. After the reaction, the solution was dropped into excess ethanol to precipitate the polymer. The polymer was then purified via three dissolving/precipitating cycles, and finally dried at 30 °C in vacuum for 24 h.

2.2.2. Preparation of material surfaces

The material surfaces of PMMA and allyl POSS–PMMA were spin-coated onto many kinds of substrates including glass slide, silicon wafer, PET sheet and quartz plate (1×2 cm^2) from ethyl acetate (0.5% (*w*/*w*) at 1500 rpm for 60 s). The coatings were dried at 25 °C for 24 h and for 12 h under vacuum at 30 °C. Glass slide, silicon wafer and quartz plate used for coating preparation were cleaned in "piranha" (7:3 (v/v) H_2SO_4/H_2O_2) for 1 min and water for 10 min respectively, and then dried with N_2.

2.2.3. Characterization of the polymers and material surfaces

2.2.3.1. Characterization of the polymers. Molecular weights and distributions of all polymer samples were characterized by GPC performed in THF (1.0 mL/min). Calibration was carried out using a series of near-monodisperse polystyrene standards. ^{1}H NMR was measured with a Bruker 400 NMR spectrometer at 25 °C, using deuterio-chloroform ($CDCl_3$) as solvent and tetramethylsilane (TMS) as the internal standard. Fourier transform infrared spectra (FT-IR) were measured on a FT-IR spectrometry (Bruker Optics). X-ray diffraction (XRD) was performed on a powder diffractometer (Philips 1140/90) using Cu radiation 1.54 Å. The samples were analyzed at room temperature over a 2θ range of 5–50° with sampling intervals of 0.04°.

2.2.3.2. Characterization of material surfaces.

2.2.3.2.1. Surface morphology. Surface morphology was measured by atomic force microscope (AFM, SPA 400, Seiko instrument Inc.). AFM images were performed in the tapping mode under ambient conditions using a commercial scanning probe microscope, equipped with a silicon cantilever, nanosensors, typical spring constant 40 N m^{-1}.

2.2.3.2.2. Surface wettability. Surface wettability of the films was measured by Drop Shape Analysis (KRŰSS, DSA10-MK2). The sessile dropping method was used to detect surface of the film with different times after the ultrapure water droplet contacted the film. The contact angle formed between the sample surface and droplet was measured using built-in microscope and software provided by manufacturer. All the measurements were performed at least in triplicate and the data were presented as mean ± standard deviation.