• Basic Research •

Biocompatibility of light responsive materials prepared for accommodative intraocular lenses manufacturing

Chen-Zi Liu[1], Ming-Hao Sun[1], Wei Dai[1], Lan-Cao Hao[1], Si-Quan Zhu[1,2]

[1]Department of Ophthalmology, Beijing Anzhen Hospital, Capital Medical University, Beijing 100029, China
[2]Department of Ophthalmology, Xiamen Ophthalmology Center, Xiamen University, Xiamen 361004, Fujian Province, China

Correspondence to: Si-Quan Zhu. Department of Ophthalmology, Beijing Anzhen Hospital, Capital Medical University, No.2, Anzhen Road, Chaoyang District, Beijing 100029, China. siquanzhu@qq.com

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Abstract

● **AIM:** To investigate the biocompatibility and bacterial adhesion properties of light responsive materials (LRM) and analyze the feasibility and biosafety of employing LRM in the preparation of accommodative intraocular lenses (AIOLs).

● **METHODS:** Employing fundamental experimental research techniques, LRM with human lens epithelial cells (hLECs) and human retinal pigment epithelium cells (ARPE-19 cells) were co-cultured. Commercially available intraocular lenses (IOLs) were used as controls to perform cell counting kit-8 (CCK-8), cell staining under varying light intensities, cell adhesion and bacterial adhesion experiments.

● **RESULTS:** LRM exhibited a stronger inhibitory effect on the proliferation of ARPE19 cells than commercially available IOLs when co-cultured with the undiluted extract for 96h (P<0.05). Under other culturing conditions, the effects on the proliferation of hLECs and ARPE-19 cells were not significantly different between the two materials. Under the influence of light irradiation at intensities of 200 and 300 mW/cm^2, LRM demonstrated a markedly higher inhibitory effect on the survival of hLECs compared to commercially available IOLs (P<0.0001). They also showed a stronger suppressive effect on the survival rate of ARPE-19 cells, with significant differences observed at 200 mW/cm^2 (P<0.001) and extremely significant differences at 300 mW/cm^2 (P<0.0001). Additionally, compared to commercially available IOLs, LRM had a higher number of cells adhering to their surface (P<0.05), as well as a significantly greater number of adherent bacterium (P<0.0001).

● **CONCLUSION:** LRM, characterized by their excellent non-contact tunable deformability and low cytotoxicity to ocular tissues, show considerable potential for use in the fabrication of AIOLs. These materials demonstrate strong cell adhesion; however, during photothermal conversion processes involving shape deformation under various light intensities, the resultant temperature rise may harm surrounding cells. These factors suggest that while the material plays a positive role in reducing the incidence of posterior capsule opacification (PCO), it also poses potential risks for retinal damage. Additionally, the strong bacterial adhesion of these materials indicates an increased risk of endophthalmitis.

● **KEYWORDS:** light responsive materials; accommodative intraocular lens; biocompatibility; bacterial adhesion

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INTRODUCTION

Cataract, a leading cause of global visual impairment, remains a significant contributor to progressive and irreversible blindness in underdeveloped countries[1-3]. The primary therapeutic intervention for cataracts is the implantation of intraocular lenses (IOL)[4]. With the growing postoperative expectations of patients for satisfaction and optimal visual quality, our research focus on IOL technology has shifted from monofocal IOLs, which only achieve emmetropia, to premium IOLs. Premium IOLs encompass multifocal IOLs and accommodative IOLs (AIOL), aiming to provide unhindered vision across distances and reduce dependence on glasses[5-7]. While studies have indicated that multifocal IOLs face challenges in fully restoring accommodation, leading to issues such as glare and reduced contrast sensitivity, the emerging field of AIOLs, defined by their ability to dynamically adjust the eye's dioptric power with accommodative effort, holds promise in ophthalmology[8-11]. However, the accommodative power of currently used

AIOLs is constrained by the capsular bag. The effectiveness of AIOLs diminishes with the loss of capsular bag elasticity, a consequence of cataract extraction surgery and aging. Addressing this limitation by inventing adaptive AIOLs capable of modulating their accommodative power presents a potential solution to this challenge[11-12].

Consequently, we observed a study initiated by Song *et al*[13], in which they attempted to fabricate nano-liquid crystal composite materials by incorporating non-toxic nanoparticles with a pronounced photothermal effect into the liquid crystalline polymer (LCP) matrix, characterized by a low phase transition temperature. The nanocomposite material prepared with 0.05% (wt) PVP/CuS nanoparticles exhibits good transparency, with a spectral transmittance above 80% at the human eye's most sensitive wavelength of 550 nm and a refractive index of approximately 1.50, thus possessing suitable optical properties for lens fabrication. Moreover, this nano-liquid crystal material demonstrates exceptional non-contact zoom capabilities, with a focal length of 13.5 mm under 0 mW/cm^2 light intensity, reducing to 6.2 mm under 350 mW/cm^2. This deformability, achieved solely through changes in light intensity, lays the groundwork for the development of adaptive AIOLs. However, the biocompatibility of this novel light responsive material (LRM) and its potential impact on ocular tissue cells post-implantation require further experimental investigation.

First of all, high histocompatibility is a fundamental and esteemed requirement for materials used in ophthalmic applications. Superior biocompatibility ensures the safety and stability of IOL implantation surgery[14]. Second, through prior research on the deformation ability of these LRM, it is noteworthy that changes in light intensity can simultaneously affect shape and temperature[13]. Therefore, it is imperative to investigate the impact of these changes on intraocular cells. Furthermore, the potential to reduce complications after IOL implantation surgery is currently a critical criterion for selecting IOL materials and underscores the research significance of modifying existing IOL materials[15]. Among these considerations, posterior capsule opacification (PCO) is the most common postoperative complication, resulting from the proliferation of remnants of lens epithelial cells (LECs)[16]. Numerous studies have indicated that IOL materials were one of the main factors influencing PCO. Therefore, evaluating the materials' ability to inhibit the adhesion, proliferation, and migration of LECs on their surfaces serves as a basis for determining their potential to reduce the incidence of PCO[17-19]. Meanwhile, endophthalmitis, the most severe postoperative complication, is complex in its pathogenesis. The varying adhesion of IOLs materials to bacteria can contribute to differences in the incidence of endophthalmitis[20-22].

In summary, to address the aforementioned issues, we conducted co-culture experiments with LRM and cells from eye tissues. Commercially available IOLs were used as controls, and we performed cell counting kit-8 (CCK-8) experiments, cell staining experiments under varying light intensities, cell adhesion experiments, and bacterial adhesion experiments. The results of these experiments will be analyzed to assess the feasibility of using the LRM for IOLs preparation. The analysis will focus on the compatibility between the material and eye tissue cells, the potential impact of material deformation on the stability of intraocular tissue, and whether it affects the occurrence of two major postoperative complications, PCO and endophthalmitis. This study marks the beginning of exploring a new material for the fabrication of AIOLs. The results are essential and provide significant guidance on whether this LRM can be used for AIOL fabrication. The expeditious application of this material in AIOL preparation is both necessary and crucial. Doing so can advance research and manufacturing in the realm of truly self-adaptive AIOL, offering promising prospects for patients undergoing cataract and refractive surgeries.

MATERIALS AND METHODS

Sample Preparation For the preparation of LRM, the method outlined in Song *et al*'s study[13] was followed. Initially, co-precipitation technique was used to create CuS nanoparticles[23]. The resulting precipitate was dried under vacuum at 60°C and stored at room temperature. Subsequently, the CuS nanoparticles with polyvinylpyrrolidone (PVP; Macklin Chemical Technology Co., Ltd., China) were modified, resulting in a mixture of CuS and PVP. This mixture was stirred with a magnetic stirrer for 24h at room temperature. Eventually, a mixture of 1,4-bis-[4-(6-acryloyloxyhexyloxy)-benzoyloxy]-2-methylbenzene (Jiangsu Hecheng Display Technology Co., Ltd., China), polyethylene glycol diacrylate 400 (Meryer Chemical Technology Co., Ltd., China), 6-dioxa-1,8-octane-diol (Konoscience Co., Ltd., China), 0.05% (wt) PVP/CuS modified nanoparticles, photo-initiator (TCI Co., Ltd., China), were prepared and cross-linking agent (Shanghai Dibo Chemical Technology Co., Ltd., China) in a certain ratio. The mixture was injected into a liquid crystal cell at 70°C, placed in an 80°C oven for 12h, and polymerized under the conditions of stretching the composite substrate with a 365 nm light source at 12 mW/cm² for 1h.

Photothermal Performance Testing The photothermal tests were performed using a hot stage (Shanghai Yiheng Scientific Instrument Co., Ltd., China), preset at an initial temperature of 37°C, in conjunction with a xenon lamp solar simulator (Beijing zhongjiao Jinyuan Technology Co., Ltd., China) for controlled light exposure temperature testing. The output power of the light source was adjusted, and the intensity of light was quantified using a light power meter (Beijing zhongjiao

Jinyuan Technology Co., Ltd., China). Furthermore, the surface temperature after 200s light exposure was characterized and recorded using an infrared thermal imager (Shanghai Spectrum Light Technology Co., Ltd., China).

Light-Driven Testing The light-driven tests were conducted on a hot stage, calibrated to an initial temperature of 37℃, utilizing a xenon lamp solar simulator for controlled light exposure. The changes in length of the LRM under different light intensities for 200s were accurately measured using a vernier caliper (Beijing Sanshi Maichuang Technology Co., Ltd., China).

Sample Handling The prepared LRM was cut into dimensions of 12.0 mm×12.0 mm×0.5 mm, cleaned with 75.0% ethanol, and sterilized in a high-pressure steam at 120℃ for 20.0min. Commercially available IOLs (LS-313MF15T, Oculentis, Netherlands) were used as a control group, following the same procedures for sample dimensions and sterilization. An additional blank control group was established.

Cell Culturing The human retinal pigment epithelium cell line (ARPE-19; ATCC, USA) and human LECs (hLECs, ATCC, USA) frozen in liquid nitrogen were resurrected overnight at 37℃. The next day, the cells were replaced in the prepared culture medium which was preheated to 37℃, and then were cultivated for 24h. When the clone growth of cells was reached 80%, the cells are digested and passaged by Tryple Express (Shanghai Baishuntai Biotechnology Co., Ltd., China), and then were passage into a new 96-well plate in a 1:4 ratio.

Cell Proliferation Samples were immersed in the medium containing hLECs and ARPE-19 cells for 24h in an incubator containing 5.0% carbon dioxide at a temperature of 37℃. The immersion solution was divided into stock solution and diluents at different ratios (1/2, 1/4, 1/8). Cells were cultured in different concentrations of the immersion solution for 24, 48, 72, and 96h, and cell viability was assessed using a CCK-8 (Dojindo Ltd., Japan) assay. Furthermore, blank control groups for independent cell culture of hLECs and ARPE-19 cells were set up. Absorbance at wavelengths of 450 nm was collected using a microplate reader (PerkinElmer Ltd., USA). Blank control groups for independent cell culture of hLECs and ARPE-19 cells were set up.

Calcein-AM/PI Cell Staining The samples were placed in cell culture wells, and hLECs and ARPE-19 cells were seeded separately at 37℃. Light intensity changes were tested using a xenon lamp solar simulator, with light power measured by a power meter. After irradiating the culture plates for 200s at 200 and 300 mW/cm^2 light intensities, a calcein-AM/PI cell staining (Solarbio Life Science Co. Ltd., China) assay was conducted. Red and green fluorescence photos were taken separately under the same field of view under a 10X microscope (Zeiss Co. Ltd., Germany). Image J (vision 1.8.0) was utilized to measure average fluorescence intensity.

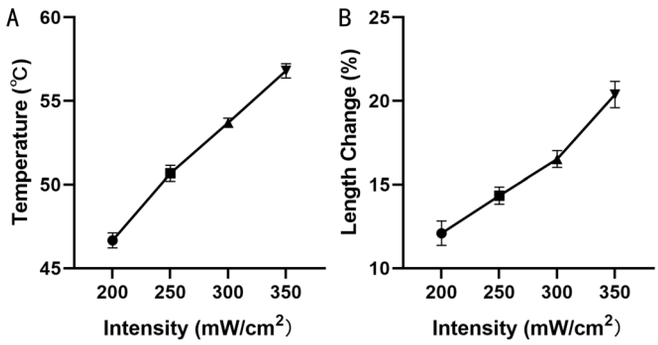

Figure 1 Characterization of light responsive materials properties
A: Temperature variation of light responsive materials after being irradiated with different light intensities for 200s; B: The length change rate of light responsive materials after being irradiated with different light intensities for 200s.

Cell Adhesion The samples were placed at the bottom of cell culture wells, and hLECs were subsequently seeded. After 24h of cell cultivation in an incubator containing 5.0% carbon dioxide at a temperature of 37℃, crystal violet staining (Solarbio Life Science Co. Ltd., China) was performed, followed by photography under a 10× microscope (Olympus Corporation, Japan). Image J was utilized to count the number of cells.

Bacterial Adhesion Staphylococcus aureus (Bena Culture Collection, China) was cultured overnight in G+ medium at room temperature. A phosphate buffer saline (PBS) suspension was prepared, and the bacterial concentration was adjusted to 10^8 cfu/mL using UV-visible spectrophotometry. The samples were incubated in 5 mL of bacterial suspension for 60min. After removal, the samples were fixed in electron microscope fluid, observed, and photo taken under an electron microscope (HITACHI Co., Ltd., Japan).

Statistical Analysis Analyses of the data were conducted using the GraphPad Prism (version 9.0). The differences between the two groups were assessed by using the independent *t*-test, and multiple groups were assessed by using one-way analysis of variance. Data were shown as the means±standard deviation (SD). Statistically significant results were determined to be *P* values below 0.05.

RESULTS

Characterization of Light Responsive Material Performance At a baseline temperature of 37℃, the nano-liquid crystal composite with 0.05% (wt) PVP/CuS exhibited incremental temperature elevations to 46.7℃, 51.2℃, 53.6℃, and 56.3℃ under light intensities of 200, 250, 300, and 350 mW/cm^2, respectively, after 200s of exposure (Figure 1A). Additionally, this material demonstrated length expansions of 12%, 14%, 16%, and 21% at light intensities of 200, 250, 300, and 350 mW/cm^2, respectively, following 200s of irradiation (Figure 1B).

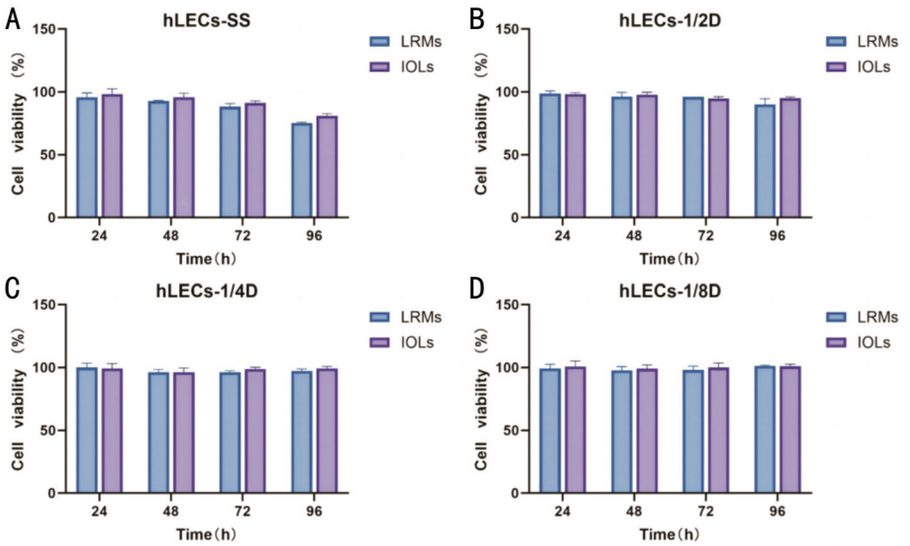

Figure 2 Co cultivation of immersion solution of LRMs and commercially available IOLs with hLECs A: Comparison of cell viability at different time points in co culture of hLECs with the stock solution; B: Comparison of cell viability at different time points in co culture of hLECs with the 1/2 diluents; C: Comparison of cell viability at different time points in co culture of hLECs with the 1/4 diluents; D: Comparison of cell viability at different time points in co culture of hLECs with the 1/8 diluents. LRMs: Light responsive materials; IOLs: Intraocular lens; hLECs: Human lens epithelial cells; SS: Stock solution; 1/2D: 1/2 diluents; 1/4D: 1/4 diluents; 1/8D: 1/8 diluents.

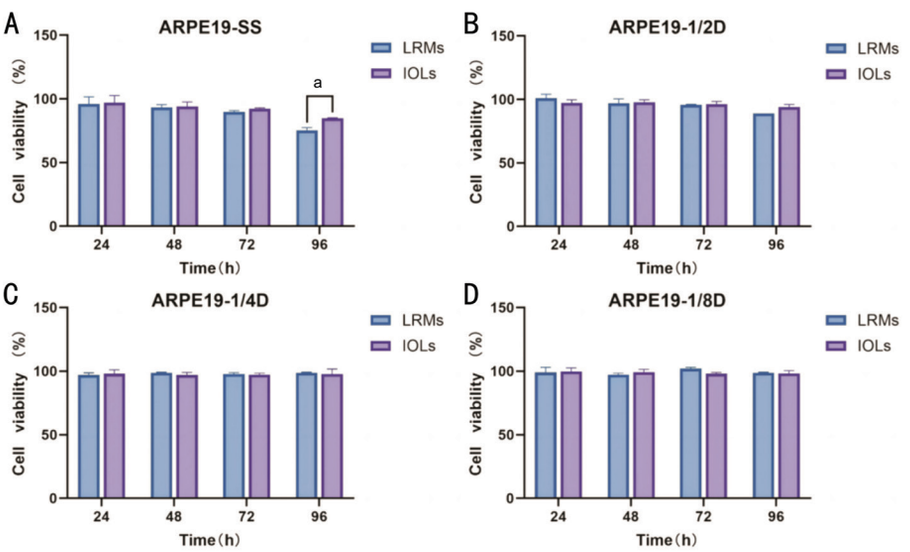

Figure 3 Co cultivation of immersion solution of LRMs and commercially available IOLs with ARPE-19 cells A: Comparison of cell viability at different time points in co culture of ARPE-19 cells with the stock solution; B: Comparison of cell viability at different time points in co culture of ARPE-19 cells with the 1/2 diluents; C: Comparison of cell viability at different time points in co culture of ARPE-19 cells with the 1/4 diluents; D: Comparison of cell viability at different time points in co culture of ARPE-19 cells with the 1/8 diluents. LRMs: Light responsive materials; IOLs: Intraocular lens; ARPE-19: Human retinal pigment epithelium cell line; SS: Stock solution; 1/2D: 1/2 diluents; 1/4D: 1/4 diluents; 1/8D: 1/8 diluents. [a]P<0.05.

Cell Proliferation Set the cell viability rates of the blank control groups to 100%, and compared the measured absorbance values to obtain the cell viability rates of different dilution ratios of LRM and commercially available IOLs immersion solution after co culturing with cells for 24, 48, 72, and 96h. The impact of the LRM extract on hLEC proliferation was not significantly different from that observed with commercially available IOLs (Figure 2). However, a notable statistical difference was observed in the effect on ARPE-19 cell proliferation after 96h of co-culture with the stock solution of LRM (P<0.05; Figure 3).

Calcein-AM/PI Cell Staining At a light intensity of 200 mW/cm^2 for 200s, hLECs co-cultured with LRM exhibited a survival rate of 86.57%±1.24%, which was significantly lower compared to 97.69%±0.74% for hLECs co-cultured with commercially available IOLs, indicating a highly significant difference (P<0.0001). At a higher light intensity of 300 mW/cm^2 for 200s, the survival rates were recorded as 74.2%±1.76%

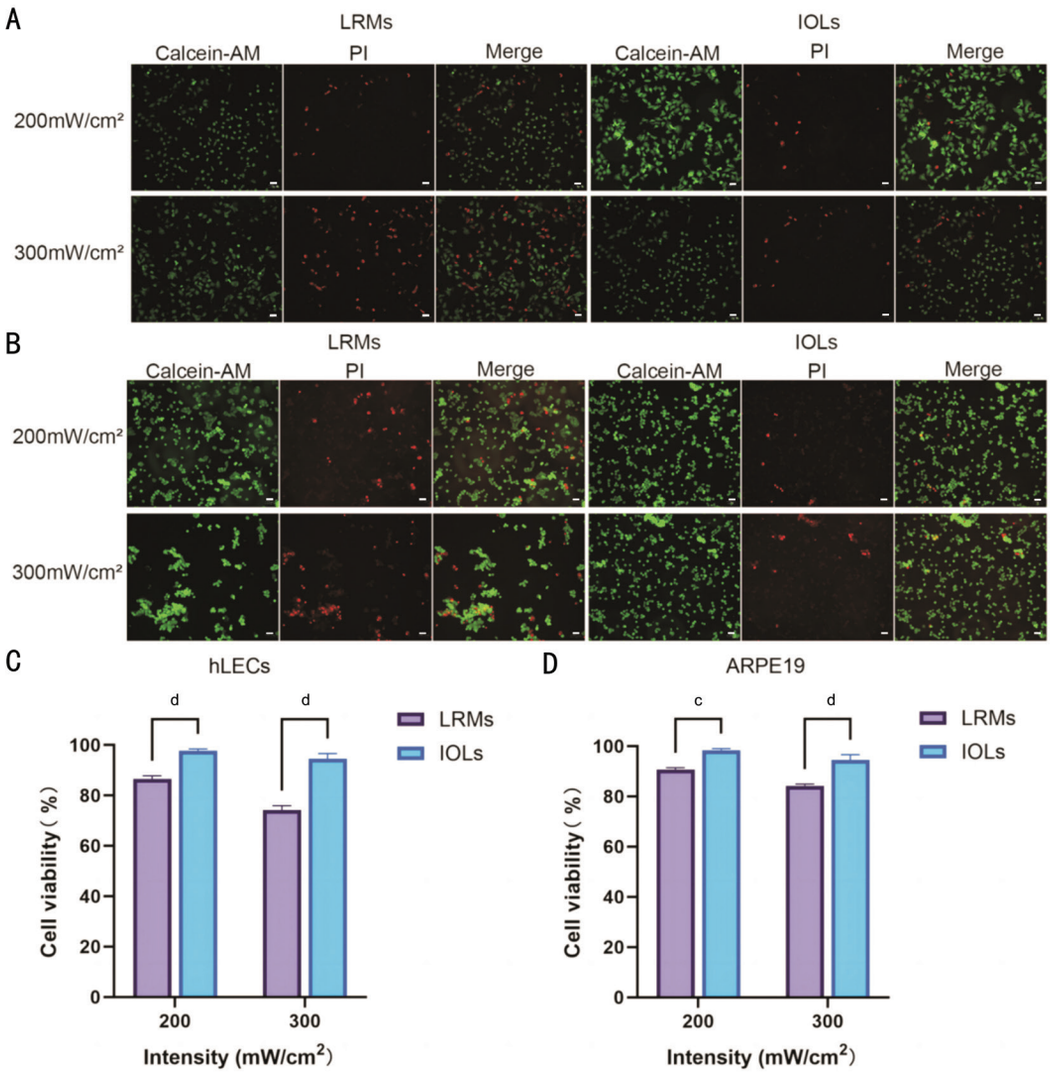

Figure 4 Effects of LRM and commercially available IOLs on cell viability under different light intensities irradiation A: Observation of Calcein-AM/PI cell staining of hLECs under 200 and 300 mW/cm^2 light intensities irradiation under light microscope (scale bar: 100 μm); B: Observation of Calcein-AM/PI cell staining of ARPE-19 cells under 200 and 300 mW/cm^2 light intensities irradiation under light microscope (scale bar: 100 μm); C: Comparison of the effects of LRMs and commercially available IOLs on the viability of hLECs under 200 and 300 mW/cm^2 light intensities irradiation; D: Comparison of the effects of LRMs and commercially available IOLs on the viability of ARPE-19 cells under 200 and 300 mW/cm^2 light intensities irradiation. LRMs: Light responsive materials; IOLs: Intraocular lens; hLECs: Human lens epithelial cells; ARPE-19: Human retinal pigment epithelium cell line. $^c P<0.001$, $^d P<0.0001$.

for the LRM group and 94.58%±2.01% for the commercially available IOLs group, again showing a highly significant difference ($P<0.0001$; Figure 4A, 4C). In the case of ARPE-19 cells, notable differences in survival rates were observed at 200 mW/cm^2 (90.63%±0.85% for LRM *vs* 98.41%±0.67% for commercial available IOLs, $P<0.001$) and at 300 mW/cm^2 (84.22%±0.76% *vs* 94.53%±2.07%, $P<0.0001$; Figure 4B, 4D).

Cell Adhesion The data revealed that the count of hLECs adhered to the surface of LRM was quantified as 112±25.94. In contrast, for commercially available IOLs, this count was significantly lower at 58±1 ($P<0.05$; Figure 5).

Bacterial Adhesion Employing Image-Pro Plus 6.0 software (Media Cybernetics, Inc., Rockville, MD, USA) with a set standard scale of 1.0 k 50.0 μm. For each image, bacterial width (in micrometers) and count were quantitatively measured. The experiment revealed that the number of bacteria adhered to the surface of the LRM was significantly higher at 69.33±1, compared to a substantially lower count of 7.4±1 on commercially available IOLs ($P<0.0001$; Figure 6).

DISCUSSION

In an ideal scenario, AIOLs should be able to fully emulate the natural accommodative mechanism intrinsic to the human eye. This would enable IOLs to sustain exceptional accommodative ability across various focal points, free from limitation by factors such as distance and intraocular structures, including the capsule. Presently, the AIOLs commercially available primarily achieve adjustment by modifying the structure or design of the IOLs, thereby inducing a positional shift within

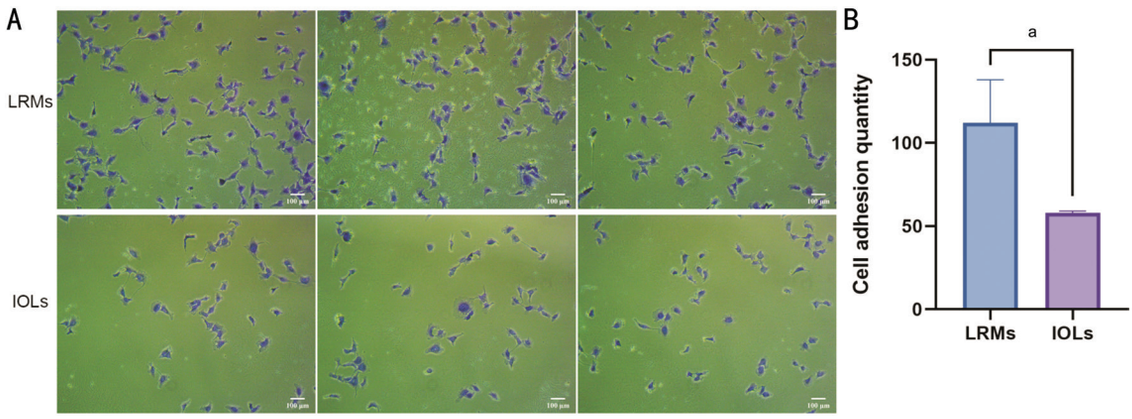

Figure 5 Cell adhesion assays A: Observation of cells adhering on the surfaces of LRM and commercially available IOLs under light microscope (scale bar: 100 μm); B: Comparison of the number of cells adhesion on the surface of LRM and commercially available IOLs. LRMs: Light responsive materials; IOLs: Intraocular lens. [a]*P*<0.05.

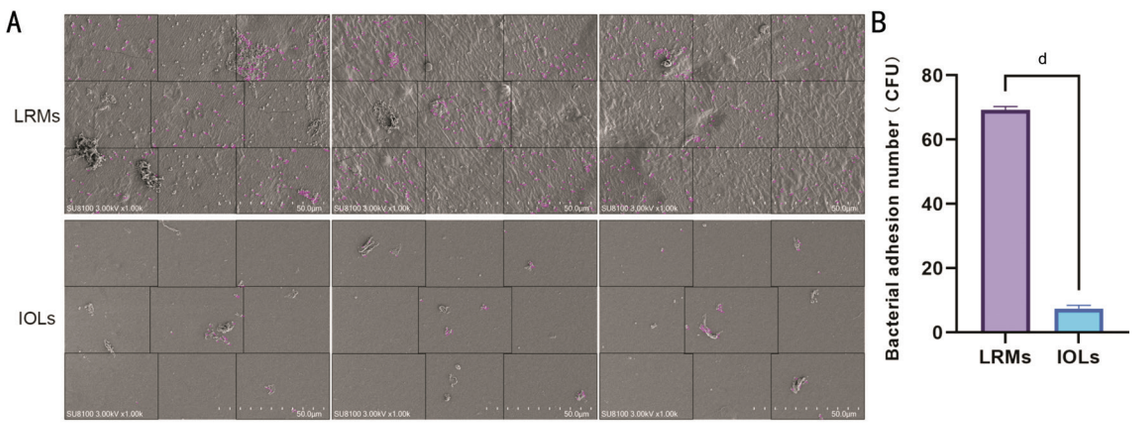

Figure 6 Bacterial adhesion assays A: Observation of bacteria adhering on the surfaces of LRM and commercially available IOLs under electron microscopy (scale bar: 50 μm); B: Comparison of the number of bacteria adhesion on the surface of LRM and commercially available IOLs. LRMs: Light responsive materials; IOLs: Intraocular lens. [d]*P*<0.0001.

the eye under the influence of the capsule. However, this adjustment mechanism is significantly constrained by capsule hardening or fibrosis and has a limited scope[11,24]. In response to this predicament, an increasing number of researchers are investigating novel materials for the fabrication of IOLs, aiming to achieve remote, non-contact control of the IOLs. Ward *et al*[25] endeavored to incorporate a two-dimensional titanium carbide coating onto the surface of hydrophobic acrylic IOLs, leveraging its excellent electrical conductivity and optical properties to effect changes in refractive index and light transmittance under the application of an external electric field. Carpi *et al*[26] attempted to design and manufacture electrically-driven optical lenses using dielectric elastomers, where voltage application led to a reduction in lens diameter and an increase in thickness, thereby modifying the focal length. These aforementioned studies have offered valuable insights for the fabrication of adaptive AIOL materials. However, they all necessitate the support of other energy sources such as electricity, which poses practical challenges and potential safety risks to the human body. Song *et al*[13] integrated PVP/CuS particles with photothermal conversion effects into an LCP, enabling the composite material to deform under light control, leading to an alteration in focal length. This process does not require the assistance of other media or methods and can achieve the aim of focal length adjustment solely through the modulation of the light intensity received by the human eye. It currently represents a more ideal and clinically applicable material for the preparation of adjustable IOLs. This study successfully synthesized a light responsive composite liquid crystal material containing 0.05% (wt) CuS/PVP nanoparticles. Through photothermal performance and optical drive experiments, the prepared LRM exhibited robust photothermal performance and deformability, fully demonstrating the repeatability and operability of this LRM preparation method.

The materials predominantly utilized in the fabrication of IOLs encompass polymethyl methacrylate (PMMA), silicone, and acrylate materials[27]. Intrinsically, these materials lack adjustability, rendering them unsuitable for the production of adaptive AIOLs. Nonetheless, their extensive

clinical application has verified their stability in terms of biocompatibility and safety. In this study, we selected the hydrophilic acrylate IOL produced by Oculentis, Netherlands, model LS-313MF15T, which was unopened and within its expiry date prior to use. This IOL is currently widely used in clinical practice, has a substantial clinical foundation, and there have been no reports of adverse effects. Therefore, choosing this lens as a standard control in clinical applications is both justified and reliable. The potential for the synthesized LRM to be further exploited for the production of AIOLs, and its integration into practical clinical application, represents a critical area of focus that necessitates immediate research attention. The biocompatibility of IOLs typically considers the interaction between the lens capsule and the uvea, yet the biocompatibility of the uvea itself is not the central focus of clinical research[28-29]. More specifically, the interaction between IOLs and the cells within the lens capsule mirrors the capsule biocompatibility of IOLs. This factor bears significant clinical importance, as it determines the short-term and long-term effects of IOL implantation[29].

This study selected two cell types, hLECs and ARPE-19 cells, for biocompatibility assessments[30]. The outcomes of the CCK-8 assay indicated that the LRM demonstrated no cytotoxic effects on hLECs when contrasted with commercial IOLs. Notably, even after a co-cultivation period of 96h, there was no inhibition of cell proliferation, suggesting the promising stability of this material. LRM exhibited a relatively strong inhibitory effect on cell proliferation only after being co-cultured with ARPE-19 cells in the undiluted extract for 96h, suggesting that prolonged co-culture in this undiluted state enhances the material's inhibitory effect on cell proliferation. However, this difference was not observed when the extract was diluted to half its concentration. Furthermore, when the extract was diluted to quarter and eighth concentrations, the LRM showed stable and improved low cytotoxicity compared to commercially available IOLs. These results indicated that reducing the concentration of the LRM's extract effectively mitigates its mild inhibitory effect on cell proliferation during prolonged contact with ARPE-19 cells. This is of significant clinical importance as IOLs are typically implanted in the capsular bag, where complex components like water and proteins can effectively reduce the concentration of the lens extract in contact with ARPE-19 cells, thereby exhibiting low cytotoxicity. The integration of nanoparticles into LCP to engineer more functional structures represents a highly promising direction in materials science research[31]. In recent years, LCP has witnessed escalating applications in biomedical domains. Its inherent attributes, including orderliness, fluidity, rigidity, chemical inertness, low water absorption, and the potential to foster tissue regeneration, render it suitable for human implant research[32]. In the realm of ophthalmology, Jeong *et al*[33] have successfully designed and conducted animal experiments with an implantable artificial retina fabricated from LCP. This study carried out preliminary evaluations of the low cytotoxicity of this nanocomposite liquid crystal material, making it a viable candidate for intraocular implantation materials in terms of biological safety.

An additional critical measure of capsule biocompatibility is characterized by the decrease in postoperative complications, which include PCO and endophthalmitis. In the previous section on photothermal-driven experiments, we observed that as light intensity escalated, the surface temperature of the LRM also increased. To assess the effects of changes in photothermal intensity on ocular tissue cells, we employed the same method of light intensity control and utilized calcein-AM/PI cell staining to evaluate the effects of the LRM and commercially available IOLs on the survival rates of ocular tissue cells. The experimental results indicated that, compared to commercially available IOLs, the survival rates of hLECs and ARPE-19 cells co-cultured with the LRM were markedly lower under light intensities of 200 and 300 mW/cm^2, highlighting significant differences. This suggested that the unique photothermal properties of the LRM negatively affected cell survival rates. During the calcein-AM/PI cell staining evaluation, an amplification in light intensity due to photothermal driving was noted to lead to an augmented count of dead cells in the vicinity of the material. This observation could be ascribed to the photothermal consequences of the integrated copper nanoparticles. When the initial temperature is 37℃, the surface temperature of the LRM can reach 46℃ and 53℃ under the irradiation of 200 and 300 mW/cm^2 light intensity, which will inevitably affect the activity of the surrounding cells of the materials. Further analysis revealed that, under the same light intensities, the survival rates of cells co-cultured with the LRM were noticeably lower for hLECs compared to ARPE-19 cells. This indicated that the LRM had a stronger inhibitory effect on the survival of hLECs than on ARPE-19 cells, implying that hLECs were more sensitive to increased temperatures and the thermal energy converted from light absorption was more lethal to hLECs.

During the cell adhesion assays involving hLECs, the LRM was identified to manifest enhanced cell adhesion in contrast to commercially available IOLs. Commercially available IOLs are manufactured from hydrophilic acrylic substances, which, when juxtaposed with the routinely used hydrophobic acrylic substances in clinical practice, exhibit a higher propensity for epithelial cell adhesion[34]. This implies that the findings of the cell adhesion assay contradict the deductions made by Song *et al*[13], where the LRM displayed a water contact angle analogous to that of hydrophobic acrylic IOLs,

suggesting diminished cell adhesion. A plausible explanation for this anomaly could be that the LRM in this study was not exposed to the standard polishing and finishing procedures that commercially available IOLs typically undergo, resulting in a surface structure with increased roughness. The genesis of PCO is multifaceted and encapsulates elements such as the individual characteristics of the patient, surgical factors, and the properties of the IOL materials. These elements can catalyze excessive postoperative proliferation, migration, and differentiation of hLECs, culminating in the manifestation of PCO[34]. The main clinical manifestations of PCO include decreased visual acuity, reduced contrast sensitivity, refractive changes, and altered color perception, which severely impair the physical and mental health of patients' post-cataract surgery and significantly reduce postoperative satisfaction. Currently, there are no effective pharmacological prevention strategies for PCO; posterior capsular laser surgery remains the primary treatment. However, this technique also entails risks of secondary complications such as IOL damage, cystoid macular edema, and retinal detachment. The design of existing commercially available AIOLs is predicated on changes in relative intraocular positions, increasing the likelihood of contact with the posterior capsule post-implantation and thereby elevating the risk of PCO. In contrast, our LRM are independent of the capsular bag effect and alter shape solely in response to light intensity changes, thereby adjusting refractive power. According to calcein-AM/PI cell staining experiments, when light intensity increases and the material undergoes shape changes, the survival rate of hLECs cells surrounding the LRM is significantly lower than that around commercially available IOLs. This suggests that the thermal energy converted by LRM after exposure to light has a lethal effect on surrounding cells, effectively preventing the adhesion, migration, and proliferation of nearby hLECs cells, inhibiting their migration and proliferation, thus playing a positive role in reducing the incidence of PCO. Although studies have shown that the selection of artificial lenses in clinical application is not only guided by evidence-based guidelines[35]. we believe that the emergence of higher-quality, more functional artificial lenses will more comprehensively meet clinical needs and provide better options for the relevant population. Therefore, the discovery and exploration of the advantageous properties of this LRM have significant clinical benefits.

Additionally, in the calcein-AM/PI cell staining experiments, attention must be given to the stronger inhibitory effect on the survival of ARPE-19 cells by LRM under different light intensities. The suppressive effect on ARPE-19 cell viability was notably enhanced when the light intensity was increased from 200 to 300 mW/cm^2, compared to commercial available IOLs. This inhibitory effect increases with light intensity, *i.e.*, as the surface temperature of the material rises, indicating potential retinal damage during light-induced deformation. However, the essence of this damage is due to the thermal lethal effect on the surrounding cells caused by the increased surface temperature of the material. In our experiments, one possible reason for this outcome is that ARPE-19 cells were directly placed on the material's surface. After IOL implantation, typically within the capsular bag, the extent and range of the thermal effect produced during the deformation process, as well as its potential to cause direct damage to the retina, still need further verification through *in vivo* animal experiments.

IOLs implanted post-cataract surgery constitute a significant origin of intraocular microorganisms, and are strongly implicated in the onset of endophthalmitis[21]. The process of bacterial adhesion to IOLs is multifaceted and can be streamlined as non-specific interactions. The range of bacterial adhesion forces noted are intimately linked to the surface structure, hydrophilicity/hydrophobicity, and surface tension attributes of IOL materials. IOLs with amplified hydrophobicity frequently demonstrate robust bacterial adhesion[36]. This may elucidate the findings from the bacterial adhesion analysis, where our LRM displayed markedly potent bacterial adhesion compared to commercially available IOLs. The principal cause of this stark difference likely pertains to the intrinsic hydrophobicity and surface structure of the material. The significant differences observed in the results are conjectured to be due to the rough surface structure of the materials: During the preparation of the materials, no surface treatment was applied, whereas commercially available IOLs typically exhibit a surface roughness of approximately 2 nm, achieved through meticulous roller polishing. To address the issue of increased bacterial adhesion—attributable to the intrinsic structural characteristics of the material, which could potentially impact the incidence of postoperative endophthalmitis—it is essential to reduce the surface roughness in subsequent IOL preparations and enhance post-treatment processes such as grinding and polishing. This is crucial for improving the antimicrobial properties of the material. Additionally, incorporating anti-adhesive heparin molecules on the surface of LRM or adding antimicrobial drugs to the composite during preparation could be considered. Heparin-modified IOLs have demonstrated effectiveness in anti-adhesion and anti-inflammatory actions in clinical trials and are currently employed successfully in clinical applications[37]. The integration of antimicrobial drugs with IOLs is also a focus of current research for many scholars, exploring surface modification methods, immersion methods, or monomer combination techniques[38]. This requires more targeted research for different materials and preparation methods. The high bacterial adhesion noted in

this study does not negate the feasibility of this material as an intraocular implant. The aforementioned methods are effective in reducing the incidence of postoperative endophthalmitis by compensating for the inherent deficiencies of IOLs. If combined with the preparation of LRM, these approaches could effectively leverage the advantages of LRM while mitigating their shortcomings, thereby making them an optimal choice for creating new, adaptive IOLs that truly meet clinical needs and effectively address clinical challenges.

In summation, the photo responsiveness of the nano-composite material imbued with 0.05% (wt) PVP/CuS is unequivocally manifested. Its outstanding non-contact variable focusing capability, characterized by its simplicity, has the potential to become a raw material for preparing adaptive AIOLs. This study was primarily oriented towards investigating the potential applicability and viability of this material for intraocular implants, with a specific focus on IOLs, from a biocompatibility standpoint. The objective was to discern disparities between this material and established commercial IOLs and to identify domains where design optimization is feasible. The results of this study indicate that the LRM has low cytotoxicity and is feasible for the preparation of IOLs. The LRM demonstrates strong cell adhesion; however, during photothermal conversion processes involving shape deformation under various light intensities, the resultant temperature rise may harm surrounding cells. These factors suggest that while the material plays a positive role in reducing the incidence of PCO, it also poses potential risks for retinal damage. Additionally, the strong bacterial adhesion of these materials indicates an increased risk of endophthalmitis. These findings suggest that before further clinical application, the material should undergo *in vivo* animal experiments. It should be implanted into the eye after being fabricated to the specifications and size of commercial artificial lenses to investigate potential retinal functional damage and observe post-implantation inflammatory responses. Efforts should also be made to reduce the material's bacterial adhesion through surface modification or molecular alteration techniques, thereby enhancing its antimicrobial properties. It is anticipated that a suite of studies centered on this LRM will catalyze the evolution of genuinely adaptive adjustable IOLs, effectuating significant advancements in the domain of refractive cataract surgery and opening new avenues for interdisciplinary interactions between materials science and ophthalmology.

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