http://pubs.acs.org/journal/acsodf



Article

Surface and Antifouling Properties of a Biomimetic Reusable Contact Lens Material

Shuang Liang, Ying Zheng, Vinay Sharma, Amanda Shows, Daniel Chuck Dunbar, Xinfeng Shi, and James Yuliang Wu*



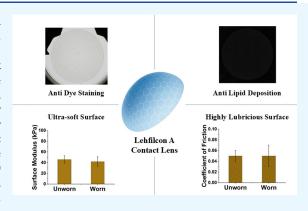
Cite This: ACS Omega 2025, 10, 19697-19704



ACCESS

III Metrics & More

ABSTRACT: A comprehensive in vitro and ex vivo study was conducted for a newly developed biomimetic silicone hydrogel contact lens material, lehfilcon A, with poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC) surface modification. In vitro studies, including Sudan Black staining and fluorescence imaging, were executed to assess the surface wettability and lipid deposition of contact lenses after simulated prolonged exposure. Additionally, the lens surface softness and lubricity were characterized by ex vivo studies, including atomic force microscopy and tribological testing. The PMPC-modified surface stayed hydrophilic and resisted lipid accumulation during the simulated wearing cycles. The coefficient of friction and surface modulus were maintained, even after 30 days of patient use. These findings demonstrate that the PMPC-modified material offers exceptional surface properties and antifouling performance, presenting an advancement in biomimetic contact lens technology.



Article Recommendations

INTRODUCTION

As a widely used medical device, silicone hydrogel (SiHy) contact lens (CL) material has gone through more than two decades of development and optimization. Compared to conventional hydrogel CLs, the SiHy CLs offer improved comfort and clinical performance, largely due to their high oxygen permeability, which is essential for maintaining ocular health. The incorporation of silicone-based monomers, such as 3-[tris(trimethylsiloxy)silyl]propyl methacrylate (TRIS), bis-(trimethylsiloxy) methylsilylpropyl glycerol methacrylate (SiMA), and polydimethylsiloxane (PDMS), enhances oxygen permeability, while hydrophilic components like 2-hydroxyethyl methacrylate (HEMA) and N-vinylpyrrolidone (NVP) improve hydration.² SiHy CLs also exhibit improved biocompatibility, which reduces irritation and inflammatory responses.³⁻⁶ Even though the silicon-oxygen bond provides efficient oxygen permeation, its hydrophobic nature can lead to the formation of hydrophobic domains on the lens surface, potentially increasing biomolecule surface deposition. These deposits may lead to reduced lens wettability, impaired visual acuity, and even discomfort or lens-related complications such as microbial keratitis. 6,10,11

Poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC) has been extensively studied and applied to many medical implantables due to its exceptional hydrophilicity, chemical stability, and biomimetic properties across a wide range of environmental and physiological conditions. ^{2,12–14} PMPC's

chemical structure is adopted from the phospholipid layer of cell membranes, making it a promising biomimetic material. The hydrophilic nature of the PMPC polymer ensures compatibility with biological systems and prevents unfavorable biological responses and reactions, such as inflammation, biomolecule fouling, and bacterial adhesion. By integrating PMPC onto the surface of the lehfilcon A contact lens, the PMPC's biomimetic advantages are combined with the oxygen permeability of a silicone hydrogel (SiHy) core, benefiting corneal health and wearing comfort. 2

Previous work demonstrated comparability between lehfilcon A and the corneal surface. Using atomic force microscopy (AFM) and scanning transmission electron microscopy (STEM), it was shown that the morphological features of the lehfilcon A PMPC-modified surface have a branched nanoscopic structure, which is similar to the natural corneal tissue and is drastically different from the SiHy base substrate. These studies also indicated the presence of a uniform 200–500 nm PMPC layer fully covering the surface. In addition, biomimetic branched PMPC structures enhance

Received: January 22, 2025 Revised: April 11, 2025 Accepted: April 17, 2025 Published: May 6, 2025





Table 1. Silicon Hydrogel (SiHy) CL Materials Used in This Study

USAN*	Lehfilcon A	Comfilcon A	Senofilcon C	Senofilcon A	Samfilcon A
Manufacturer	Alcon	CooperVision	Johnson & Johnson	Johnson & Johnson	Bausch + Lomb
Brand name	Total30	Biofinity	Acuvue Vita	Acuvue Oasys	Ultra
Water content (%)	55	48	41	38	46
D_{k} (Barrer)	123	128	103	103	114
Diameter (mm)	14.2	14.0	14.0	14.0	14.2
Base Curve (mm)	8.4	8.6	8.4	8.5	8.5
Recommended replacement frequencies	1-month	1-month	1-month	2-weeks	1-month

the lens surface wettability, softness, and lubricity through a fluid confinement mechanism. ^{16,18} Furthermore, its antifouling properties may be due to the hydrophilic nature of the biomimetic PMPC surface. A reduction of biomolecules and microorganisms on the PMPC-modified lens surface was confirmed by analyzing the adsorption of lipids and proteins and the adhesion of cells and bacteria. ¹⁹ Clinical evaluations of this new biomimetic lens material demonstrate its ability to maintain tear film stability, surface cleanliness, high wettability, and comfort over 30-day wear. ^{20–24}

In this study, further investigation was conducted on the unique properties of the PMPC-modified lens material lehfilcon A, and the focus was on lens performance with biomolecule interaction under physiological conditions. In vitro Sudan Black staining and fluorescence imaging studies were conducted to assess the surface wettability and lipid deposition of contact lenses after simulated prolonged exposure. Additionally, ex vivoAFM and tribological testing were performed to evaluate the lens surface softness and lubricity. The PMPC-modified surface stayed hydrophilic and resisted lipid accumulation during simulated wearing cycles. The coefficient of friction (CoF) and surface modulus were maintained even after 30 days of patient use. These findings demonstrate that the PMPC-modified material offers exceptional surface properties and antifouling performance, presenting an advancement in biomimetic contact lens technology.

■ EXPERIMENTAL SECTION

Contact Lenses. Five reusable SiHy CLs (lehfilcon A, comfilcon A, senofilcon C, senofilcon A, and samfilcon A) were evaluated. All lenses were obtained from the manufacturer in their original packaging. The properties of the CLs are shown in Table 1, and detailed information about the lens materials has been published previously.¹⁹

Subject-worn CLs from Alcon initiated clinical studies were obtained after one month (except 2 weeks for senofilcon A lenses) of daily wearing and cleaning for nanoindentation and tribological testing. The clinical studies were carried out in compliance with the Declaration of Helsinki. Informed consent was given and signed by all participants prior to enrollment in the studies.

In Vitro Sudan Black Staining. Sudan Black dye staining was used to screen the surface homogeneity and evaluate the surface coating coverage of the SiHy CLs qualitatively. The staining solution was prepared by mixing Sudan Black B dye (CAS No. 4197–25–5, Sigma-Aldrich, MO, USA), mineral oil (CAS No. 8042–47–5, Sigma-Aldrich, MO, USA), and vitamin E acetate oil (tocopherol acetate, CAS No. 7695–91–2, Sigma-Aldrich, MO, USA). The chemical structure of Sudan Black dye is shown in Figure 1. To prepare the solution, 70 g of mineral oil and 19.2 g of vitamin E acetate oil were combined in an amber glass bottle and heated to

Figure 1. Chemical structure of Sudan Black B dye.

approximately 70 $^{\circ}$ C for 30 min. After heating, 0.175 g of Sudan Black B dye was added, and the mixture was heated and stirred at 70 $^{\circ}$ C for an additional 30 min. The prepared solution was stored in a dark environment to maintain its stability.

Before staining, the solution was agitated for at least 30 min to ensure uniformity. CLs were removed from their packages and gently blotted to remove surface water. Each lens was submerged in 10 mL of the staining solution for 10 min with agitation.

After staining, the lenses were thoroughly rinsed with ultrapure water or deionized water to remove residual staining solution and gently blotted with a blotting cloth to remove excess liquid. The stained CLs were assessed for surface coating coverage using a bright-field microscope under black light conditions.

In Vitro Lipid Deposition. An in vitro lipid deposition experiment was designed to visualize the lipid deposition on CLs throughout the simulated wear and cleaning cycles. A lipid solution, including three nonpolar lipids and two fluorescently labeled nonpolar lipids, was prepared in chloroform. The three nonpolar lipids used were behenyl oleate (CAS# 127566-70-5, Nu-Chek Prep, MN, USA), cholesteryl oleate (CAS# 303-142-1, Sigma-Aldrich, MO, USA), and triheptadecenoin (CAS# 2438-40-6, Nu-Chek Prep, MN, USA). These three lipids were chosen as the representative lipids for wax ester (WE), cholesteryl ester (CE), and triglyceride (TAG), respectively. In addition, two fluorescently labeled nonpolar lipids – 1,2-dioleoyl-3-[16-N-(lissamine rhodamine B sulfonyl) amino]palmitoyl-sn-glycerol (Rh-TAG, CAS# 2260669-54-1, Avanti Polar Lipids, AL, USA) and 23-(dipyrrometheneboron difluoride)-24-norcholesteryl palmitate (TopFluor-CE, CAS# 2260795-57-9, Avanti Polar Lipids, AL, USA), were added to the solution at a 9:1 nonfluorescently labeled:fluorescently labeled mole ratio to facilitate confocal imaging. The overall ratio of CE, TAG, and WE was adopted from previous research results. 25 The concentrations of each lipid are given in Table 2.

The five types of CL were subjected to 7, 14, or 30 cycles of lipid deposition and cleaning. In each cycle, lenses were soaked in 5 mL of lipid solution for 1 s and then rinsed twice in 4 mL

Table 2. Nonpolar Lipid Concentration

lipid	concentration (mol/L)
Behenyl Oleate	3.52×10^{-4}
Cholesteryl Oleate	4.04×10^{-4}
Triheptadecenoin	2.95×10^{-5}
TopFluor-CE	4.49×10^{-5}
Rh-TAG	3.28×10^{-6}

of phosphate-buffered saline (PBS, Corning, NY, USA). Following rinsing, the lenses were soaked in a fresh aliquot of PBS for 30 min while shaking at 100 rpm. The lens cleaning process adhered to the manufacturer's instruction for use for Opti-FREE PureMoist Disinfecting Contact Solution (OFPM, Alcon, TX, USA). Specifically, lenses were rubbed in OFPM for 10 s on each side, rinsed under a steady stream of OFPM for 10 s on each side, and soaked in 4 mL of OFPM for at least 6 h. Lenses were collected for imaging after completing 7, 14, or 30 cycles.

Lipid deposits on the CLs were visualized using a Zeiss LSM880 Confocal Microscope System (Carl Zeiss Microscopy, NY, USA). Three-dimensional (3D) images of the whole lens were acquired using a Fluar $2.5 \times / 0.12$ M27 objective with z-stack and tile scan modes. Each CL was imaged while being submerged in PBS to prevent lens dehydration. For high-magnification images, a Plan-Apochromat $20 \times / 0.8$ objective was used with a z-stack mode. Imaging was performed with a 561 nm diode-pumped solid-state laser, a 488 nm argon laser, and a 405 nm diode laser to visualize the lipids and the lens material.

Ex Vivo AFM Analysis. The Dimension FastScan Bio Icon Atomic Force Microscope (Bruker Nano, CA, USA) was used to measure the surface modulus of ex vivo CLs in lens packaging solution with a PFQNM-LC-A-CAL probe. This silicon tip on a silicon nitride cantilever has specific dimensions and properties: 345 nm thick, 54 μ m long, 4.5 μ m wide, a 45 kHz resonant frequency, and a 0.1 N/m spring constant. 16,18 Designed for quantitative nanomechanical measurements of soft biological materials, the AFM probe generated indentation force curves at 1.0 μ m/s velocities with a 300 (\pm 50) pN force set point using the "PeakForce QNM in Fluid" mode. The contact point was identified by the probe's background noise, and the indentation depth was measured from this point to the maximum displacement. The elastic modulus was calculated from the linear portion of the retract curve using the conesphere model. Average and standard deviation values were derived from five indentation force curves per sample. A comprehensive description of the indentation method used in the study, which includes probe dimensions, contact point determination, the mathematical model, and fitting for modulus calculation, has been previously published.1

Ex Vivo Tribological Testing. Surface lubricity of a material can be characterized using the CoF. In this study, CoF testing provided a reliable quantitative measure of the contact lens surface lubricity. A lower CoF means a more lubricious surface. Tribological testing of the ex vivo CLs was performed using an NTR2 Nano Tribometer (Anton Paar, Graz, Austria) with a high-resolution, piezo-controlled, linear-reciprocating stage. The counter surface was made by attaching a supercushioning, abrasion-resistant polyurethane rubber (0.040 in. thick; durometer 4000; McMaster-Carr, CA, USA) probe to the force sensor. A custom dome-shaped lens holder held the sample in place with small magnets and provided a packaging solution reservoir for hydration. 15,16 The stage reciprocated at 0.1 Hz with a stroke length of 0.5 mm. Normal load varied from 0.25 to 1 mN in 5 steps over 30 cycles per sample. The CoF data obtained from five samples of each lens type were utilized to compute the mean and standard deviation. The results from this testing will provide insights into how the extended interaction of the contact lens surface with biomolecules can impact its lubricity and may also highlight the role of antifouling properties of MPC in maintaining the surface lubricity of lehfilcon A lenses even after extended wear.

■ RESULTS AND DISCUSSION

The main purpose of this study is to conduct a comprehensive in vitro and ex vivo evaluation of this biomimetic lens material, lehfilcon A. Sudan Black dye staining was utilized to evaluate the MPC polymer coverage and integrity. Fluorescence imaging was used to analyze lipid deposition on the lens surfaces after simulated wearing cycles. Additionally, AFM and tribological testing were conducted on ex vivo lenses to assess the surface softness and lubricity after the recommended replacement frequency, providing insights into the mechanical and tribological properties of the lens surface under physiological conditions.

Sudan Black Staining. Five out-of-pack reusable CLs—lehfilcon A, comfilcon A, senofilcon C, senofilcon A, and samfilcon A—were imaged after Sudan Black dye staining using optical microscopy. Figure 2 presents the top-view images of the CLs after staining. The lehfilcon A lens showed no blue dye staining compared to the other reusable lenses, indicating complete hydrophilic surface coverage on the lehfilcon A lens.

Sudan Black B is a synthetic dye containing both diazo groups and aromatic rings, making it an effective lipophilic dye for detecting hydrophobic regions. When applied to CLs, the Sudan Black staining method serves as a specific screening tool to visualize the hydrophobic domains on the surface of the SiHy CLs. SiHy material consists of both hydrophilic and

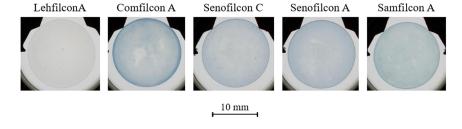


Figure 2. Top-view images of CLs stained by Sudan Black B dye for 10 min. The images were acquired by an optical microscope. Field of view (FOV): 17.2×17.2 mm.

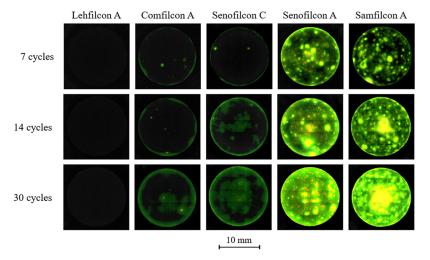


Figure 3. Top-view images of whole CLs after in vitro exposure to fluorescently labeled nonpolar lipids, TopFluor-CE (green) and Rh-TAG (red), after 7, 14, and 30 cycles of simulated wearing and cleaning. The lipid deposits were visualized by a confocal microscope. FOV: 15.6 × 15.6 mm. [The images of lehfilcon A, comfilcon A, senofilcon C, samfilcon A after 30 cycles, and senofilcon A after 14 cycles were reported in ref 2. Figure taken/reproduced with permission from American Chemical Society, copyright 2023.]

hydrophobic silicone components. Silicone tends to migrate to the lens surface due to its low free energy, resulting in a hydrophobic lens surface. This hydrophobicity may lead to biofouling, poor surface wettability, and reduced tear film stability. ^{7,9–11}

As shown by the Sudan Black staining, the lens surface was fully covered by the hydrophilic PMPC which acts as a good surface barrier, avoiding biomolecule deposition.

Lipid Adsorption. The lipid deposition patterns on five types of reusable CLs—lehfilcon A, comfilcon A, senofilcon C, senofilcon A, and samfilcon A—were visualized by using 3D confocal imaging. Figure 3 presents top-view images of CLs after 7, 14, and 30 simulated wearing and cleaning cycles. The red color corresponds to the fluorescently labeled nonpolar lipid, Rh-TAG, excited by a 561 nm laser. The green color, corresponding to TopFluor-CE lipids, was excited by a 488 nm laser

The fluorescence intensities of Rh-TAG and TopFluor-CE were quantified for each lens type (n = 4) after 7, 14, and 30 cycles and are shown in Figure 4. One-way analysis of variance (ANOVA) with Tukey test was used to compare the amounts

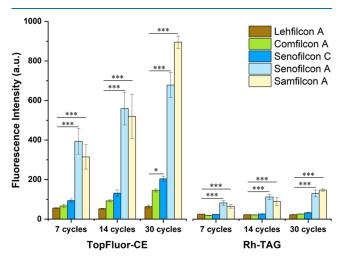


Figure 4. Fluorescence intensity of whole lens (n = 4) after 7, 14, and 30 cycles of lipid deposition. *p < 0.05; *** p < 0.01; *** p < 0.001.

of lipids deposited on the contact lenses. A p-value of <0.05 was considered significant and is highlighted with asterisks in Figure 4.

Lehfilcon A showed no visible Rh-TAG or TopFluor-CE lipid deposits at any time point. In contrast, comfilcon A, senofilcon C, senofilcon A, and samfilcon A exhibited Rh-TAG and TopFluor-CE lipid deposits as early as 7 cycles, with deposits increasing significantly after 14 and 30 cycles. Among these CLs, the highest levels of Rh-TAG and TopFluor-CE accumulation were observed after 30 cycles for all lens types. For both lipids, Lehfilcon A consistently showed the least lipid deposition among all CLs, with significantly lower levels than senofilcon A and samfilcon A at all time points, indicating its resistance to lipid accumulation and superior antifouling performance.

High-magnification 3D images of the five CLs after 14 or 30 cycles were captured. Figure 5 shows the cross-sectional view of the CL material (gray, excited by a 405 nm laser), Rh-TAG lipids (red), and TopFluor-CE lipids (green). The lehfilcon A lens had no visible Rh-TAG or TopFluor-CE deposition after 14 or 30 cycles, while comfilcon A, senofilcon C, senofilcon A, and samfilcon A CLs demonstrated visible lipid accumulation. The two nonpolar lipids showed distinct deposition patterns on the four reusable CLs: TopFluor-CE displayed a homogeneous distribution throughout the lens material, while Rh-TAG was predominantly near the lens surface.

The 3D confocal images of the lehfilcon A CL demonstrated minimal lipid accumulation even after 30 cycles of simulated wearing and cleaning. This antifouling performance is due to the PMPC zwitterionic surface coating, which draws in a water layer on the lens surface that creates a protective barrier.² This water-confined layer cannot be easily penetrated by hydrophobic tear lipids, thus preventing the adsorption of hydrophobic nonpolar lipids.¹⁶ Additionally, Sudan Black staining confirmed that the PMPC-modified surface has a complete surface coverage. Unlike conventional silicone hydrogel materials, which tend to develop hydrophobic domains due to their silicone content, the PMPC-coated surface maintains uniform surface hydration, which minimizes the exposure of hydrophobic silicone domains. Furthermore, the lehfilcon A showed minimal lipid deposition throughout 30 simulated

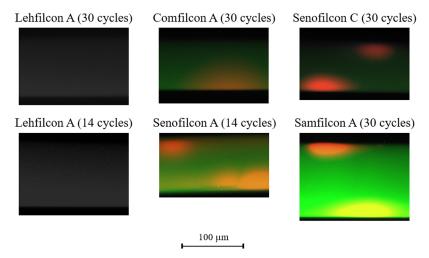


Figure 5. Cross-section view images of the CLs after in vitro exposure to fluorescently labeled nonpolar lipids, TopFluor-CE (green) and Rh-TAG (red), after 14 or 30 cycles of simulated wearing and cleaning. The lipid deposits on the lens surface and core were visualized with a confocal microscope. FOV: width: 236.2 μ m; height resolution: 0.34 μ m/pixel. [The lehfilcon A (30 cycles), comfilcon A (30 cycles), senofilcon C (30 cycles), senofilcon A (14 cycles), and samfilcon A (30 cycles) images were reported in ref 2. Figure taken/reproduced with permission from American Chemical Society, copyright 2023.].

wearing cycles, including repeated lens rubbing during the cleaning process, indicating that the PMPC preserved its integrity and may contribute to maintain lens wettability and long-term comfort. $^{20-24}$

The lipids used in this method, CE, WE, and TAG, were selected to mimic the natural lipid composition of the tear film. The tear film lipid layer plays a critical role in preventing tear evaporation and maintaining ocular surface stability, and its dysfunction is closely related to dry eye symptoms. ^{28–34} With advances in high-performance liquid chromatography (HPLC) and mass spectrometry (MS), researchers were able to identify and quantify the lipid composition of the tear film. Unlike cell membrane lipids, which are predominantly phospholipids and cholesterol, the tear lipid film consists mostly of nonpolar lipids (approximately 95% in meibum), including WE (30–50 mol %), CE (30–45 mol %), and a small percentage of TAG (~2 mol %). ^{35,36}

Previous research on lipid deposition on CL can be categorized into in vitro and ex vivo approaches.³⁷⁻³⁹ While ex vivo analyses enable comprehensive lipidomic profiling of lenses worn by patients, they do not provide spatial information about the lipids. Surface lipids are particularly significant as they can form hydrophobic microdomains, leading to additional biomolecules or microorganisms' accumulation, which can result in decreased lens wettability and wearer comfort. In vitro studies, on the other hand, allow for the use of fluorescently labeled lipids to visualize the deposition patterns and distributions on the CL surface. An important consideration is whether the fluorescent dye changes the size and polarity of the lipid molecules. Previous research demonstrated the same deposition patterns of labeled and unlabeled cholesteryl ester on different CLs. 40 Another critical factor is the choice of the lipids. Most prior studies utilized fluorescently labeled cholesterol, phospholipids, or cholesteryl ester for evaluating lipid deposition. 40-42 Cholesteryl and phospholipids are minor components of tear lipids and do not accurately represent the tear film's composition. In this study, we employed two fluorescently labeled nonpolar lipids-TopFluor-CE (cholesteryl ester) and Rh-TAG (triglyceride) to replicate the key components of tear film lipids. The

confocal images shown in Figure 3 demonstrated TopFluor-CE and Rh-TAG deposited on comfilcon A, senofilcon C, senofilcon A, and samfilcon A as early as 7 cycles, and increased to the highest levels of accumulation after 30 cycles, and similar findings were reported in previous publications. As shown in Figure 5, distinct deposition patterns were observed: TopFluor-CE displayed a homogeneous distribution throughout the lens material, consistent with prior findings, 40,42 while Rh-TAG, for the first time, spatial visualization was found predominantly near the lens surface on reusable CLs without surface treatment.

AFM Indentation and CoF Testing. To confirm that these biomolecule-repellent capabilities are maintained even after 30 days of on-eye wearing during patient use, AFM nanoindentation and tribological testing were performed on ex vivo lenses.

Figure 6 shows the average surface modulus values for the five reusable ex vivo CLs that were subjected to AFM surface

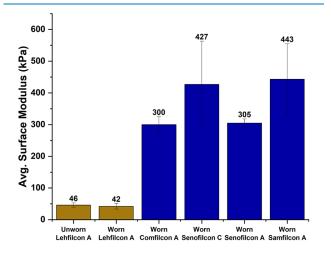


Figure 6. Average surface modulus (n = 5 force curves from 1 sample) by AFM indentation of PMPC-modified CL before and after 30 days of wearing and four reusable CLs after 30 days (except senofilcon A: 14 days).

indentation testing at 300 (± 50) pN force. The unworn lehfilcon A (46 kPa) and worn lehfilcon A (42 kPa) showed comparable average surface modulus values, both lower than the average surface modulus values for worn comfilcon A, senofilcon C, senofilcon A, and samfilcon A, which were 300, 427, 305, and 443 kPa, respectively. This difference shows the exceptional softness of the PMPC-modified lehfilcon A lens, and it remains consistent even after 30-day wearing.

The average CoF values for the five reusable ex vivo CLs are shown in Figure 7. The CLs were tested in fully hydrated

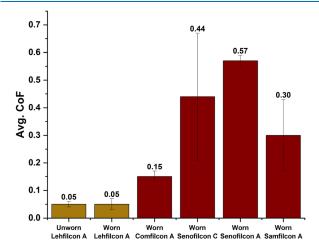


Figure 7. Average coefficient of friction (CoF) (n = 5) by tribological testing of PMPC-modified CL before and after 30 days of wearing and four reusable CLs after 30 days (except senofilcon A: 14 days).

conditions under low contact pressure, simulating the ocular environment. Consistent with the surface modulus results, the average CoF for unworn and worn lehfilcon A remained the same, i.e., 0.05. The average CoF values for worn comfilcon A, senofilcon C, senofilcon A, and samfilcon A were 0.15, 0.44, 0.57, and 0.30, respectively, all higher than those of lehfilcon A before and after wearing. The difference indicates the superior lubricity of the PMPC-modified surface. The CoF data for other unworn lenses has been previously published. 44

AFM indentation and lubricity testing methods, specially developed for very soft surfaces, were used to compare the properties of the unworn and worn lehfilcon A CL. 16,18 As predicted, the biomimetic and antifouling nature of PMPC preserved the lens surface characteristics even after prolonged interaction with ocular biomolecules. The surface modulus and CoF values for unworn and worn Lehfilcon A CLs are comparable. Surface modulus and CoF are both very sensitive to the water-holding capacity of any material. Higher water content at the surface reduces the modulus and creates a softer exterior. Similarly, the abundance of water at the surface acts as an excellent lubricant to reduce the CoF during interaction with counter surfaces. 14 The superhydrophilic nature of PMPC is to be credited for providing such desirable surface properties. Even after 30 days of wearing, which includes lens handling, soaking in lens care solution, and finger rubbing for cleaning, the durability and robustness of the branched PMPC structures on the lehfilcon A CL surface maintained its antifouling properties, surface softness, and lubricity.

In addition, the exceptional lubrication properties observed for PMPC-modified surfaces can be attributed to the strong hydration capability of polyzwitterionic brushes, as previously demonstrated by Chen et al., where surfaces coated with polyzwitterionic brushes exhibited extremely low friction coefficients even at physiological pressures due to robust hydration layers. ¹⁴ This is consistent with recent findings by Ishihara et al., who highlighted that the phosphorylcholine groups in PMPC strongly bind water molecules, creating a hydration shell that significantly enhances surface lubricity and reduces biomolecule adhesion. ² Thus, the superior lubrication performance of the PMPC-modified lehfilcon A lenses observed in this study aligns well with the mechanisms described in the literature.

CONCLUSIONS

This study provides both in vitro and ex vivo evidence demonstrating the superior antifouling properties of lehfilcon A with the PMPC-modified surface. Using Sudan Black staining, fluorescence lipid deposition imaging, AFM nano-indentation, and tribological testing, the results showed that this biomimetic contact lens was fully covered by PMPC with minimal lipid deposition after 30 simulated wearing cycles. Additionally, the lens maintained ultrasoft and lubricious surface properties even after 30 days of patient use. These findings indicate that PMPC surface modification effectively preserves its initial properties, including antifouling capabilities and mechanical performance, ensuring a consistent wearing experience from day 1 to day 30. In addition, the results suggest that the PMPC modification may contribute to improved tear film stability, ocular health, and wearer comfort.

The biomimetic design of PMPC is inspired by the structure of corneal epithelial cells and can be an example for future material design. Beyond contact lenses, this advanced surface modification technology could be applied to other medical devices as a surface treatment to reduce biofouling and enhance biocompatibility. Also, the methodologies used in this study, such as AFM and lubricity testing, can serve as a framework for assessing different materials, connecting laboratory testing, and real-world performance.

AUTHOR INFORMATION

Corresponding Author

James Yuliang Wu — Alcon Research, LLC, Fort Worth, Texas 76134, United States; orcid.org/0000-0002-9540-7182; Email: james.wu@Alcon.com

Authors

Shuang Liang — Alcon Research, LLC, Fort Worth, Texas 76134, United States

Ying Zheng — Alcon Research, LLC, Duluth, Georgia 30097, United States

Vinay Sharma – Alcon Research, LLC, Fort Worth, Texas 76134, United States

Amanda Shows — Alcon Research, LLC, Fort Worth, Texas 76134, United States

Daniel Chuck Dunbar – Alcon Research, LLC, Fort Worth, Texas 76134, United States

Xinfeng Shi — Alcon Research, LLC, Fort Worth, Texas 76134, United States

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.5c00682

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Funding

This research received no external funding.

Notes

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Sterling Institutional Review Board

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We extend our gratitude towards Siv Chov and Miti Naik for conducting Sudan Black staining work. In addition, we thank Dr. Vidhya Subramanian for providing some of the lenses used in this study.

REFERENCES

- (1) Nicolson, P. C.; Vogt, J. Soft Contact Lens Polymers: An Evolution. *Biomaterials* **2001**, 22 (24), 3273–3283.
- (2) Ishihara, K.; Shi, X.; Fukazawa, K.; Yamaoka, T.; Yao, G.; Wu, J. Y. Biomimetic-Engineered Silicone Hydrogel Contact Lens Materials. *ACS Appl. Bio Mater.* **2023**, *6* (9), 3600–3616.
- (3) Jacob, J. T. Biocompatibility in the Development of Silicone-Hydrogel Lenses. *Eye Contact Lens* **2013**, *39* (1), 13–19.
- (4) Pozuelo, J.; Compañ, V.; González-Méijome, J. M.; González, M.; Mollá, S. Oxygen and Ionic Transport in Hydrogel and Silicone-Hydrogel Contact Lens Materials: An Experimental and Theoretical Study. J. Membr. Sci. 2014, 452, 62–72.
- (5) Papas, E. B. The Significance of Oxygen during Contact Lens Wear. Contact Lens Anterior Eye 2014, 37 (6), 394-404.
- (6) Tighe, B. J. A Decade of Silicone Hydrogel Development: Surface Properties, Mechanical Properties, and Ocular Compatibility. *Eye Contact Lens* **2013**, 39 (1), 4–12.
- (7) Jacob, J. T.; Levet, J.; Edwards, T. A.; Dassanayake, N.; Ketelson, H. Visualizing Hydrophobic Domains in Silicone Hydrogel Lenses with Sudan IV. *Investig. Ophthalmol. Vis. Sci.* **2012**, *53* (7), 3473–3480.
- (8) Jones, L.; Senchyna, M.; Glasier, M. A.; Schickler, J.; Forbes, I.; Louie, D.; May, C. Lysozyme and Lipid Deposition on Silicone Hydrogel Contact Lens Materials. *Eye Contact Lens* **2003**, *29* (IS), S75–S79.
- (9) Nichols, J. J. Deposition on Silicone Hydrogel Lenses. *Eye Contact Lens* **2013**, 39 (1), 20–23.
- (10) Luensmann, D.; Jones, L. Protein Deposition on Contact Lenses: The Past, the Present, and the Future. *Contact Lens Anterior Eye* **2012**, 35 (2), 53–64.
- (11) Panaser, A.; Tighe, B. J. Function of Lipids Their Fate in Contact Lens Wear: An Interpretive Review. *Contact Lens Anterior Eye* **2012**, 35 (3), 100–111.
- (12) Ishihara, K. Revolutionary Advances in 2-Methacryloyloxyethyl Phosphorylcholine Polymers as Biomaterials. *J. Biomed. Mater. Res. Part A* **2019**, *107* (5), 933–943.
- (13) Nowak, T.; Nishida, K.; Shimoda, S.; Konno, Y.; Ichinose, K.; Sakakida, M.; Shichiri, M.; Nakabayashi, N.; Ishihara, K. Biocompatibility of MPC: In Vivo Evaluation for Clinical Application. *J. Artif. Organs* **2000**, *3*, 39–46.
- (14) Chen, M.; Briscoe, W. H.; Armes, S. P.; Klein, J. Lubrication at Physiological Pressures by Polyzwitterionic Brushes. *Science* **2009**, 323 (5922), 1698–1701.
- (15) Shi, X.; Cantu-Crouch, D.; Sharma, V.; Pruitt, J.; Yao, G.; Fukazawa, K.; Wu, J. Y.; Ishihara, K. Surface Characterization of a Silicone Hydrogel Contact Lens Having Bioinspired 2-Methacryloy-loxyethyl Phosphorylcholine Polymer Layer in Hydrated State. *Colloids Surfaces B Biointerfaces* **2021**, 199, No. 111539.
- (16) Sharma, V.; Shi, X. C.; Yao, G.; Zheng, Y.; Spencer, N. D.; Wu, J. Y. Fluid Confinement within a Branched Polymer Structure Enhances Tribological Performance of a Poly(2-Methacryloyloxyethyl Phosphorylcholine)-Surface-Modified Contact Lens. *R. Soc. Open Sci.* **2024**, *11* (10), 10.

- (17) Shi, X.; Sharma, V.; Cantu-Crouch, D.; Yao, G.; Fukazawa, K.; Ishihara, K.; Wu, J. Y. Nanoscaled Morphology and Mechanical Properties of a Biomimetic Polymer Surface on a Silicone Hydrogel Contact Lens. *Langmuir* **2021**, *37* (47), 13961–13967.
- (18) Sharma, V.; Shi, X.; Yao, G.; Pharr, G. M.; Wu, J. Y. Surface Characterization of an Ultra-Soft Contact Lens Material Using an Atomic Force Microscopy Nanoindentation Method. *Sci. Rep.* **2022**, 12 (1), 1–13.
- (19) Ishihara, K.; Fukazawa, K.; Sharma, V.; Liang, S.; Shows, A.; Dunbar, D. C.; Zheng, Y.; Ge, J.; Zhang, S.; Hong, Y.; Shi, X.; Wu, J. Y. Antifouling Silicone Hydrogel Contact Lenses with a Bioinspired 2-Methacryloyloxyethyl Phosphorylcholine Polymer Surface. *ACS Omega* **2021**, *6* (10), 7058–7067.
- (20) Capote-Puente, R.; Bautista-Llamas, M. J.; Manzoni, C.; Sánchez-González, J. M. Pre-Lens Tear Meniscus Height, Lipid Layer Pattern and Non-Invasive Break-Up Time Short-Term Changes with a Water Gradient Silicone Hydrogel Contact Lens. *Life* **2022**, *12* (11), 1710.
- (21) Capote-Puente, R.; Sánchez-González, J. M.; Sánchez-González, M. C.; Bautista-Llamas, M. J. Evaluation of Celligent® Biomimetic Water Gradient Contact Lens Effects on Ocular Surface and Subjective Symptoms. *Diagnostics* **2023**, *13* (7), 1258.
- (22) Capote-Puente, R.; Bautista-Llamas, M. J.; Sánchez-González, J. M. Tear Film Dynamics between Low and High Contact Lens Dry Eye Disease Questionnaire (CLDEQ-8) Score with a Lehfilcon A Silicone Hydrogel Water Gradient Contact Lens: A Non-Invasive Methodology Approach. *Diagnostics* **2023**, *13* (5), 939.
- (23) Call, T.; Pucker, A. D.; McGwin, G.; Franklin, Q. X.; Logan, A. Real-Time Ocular Comfort Reporting in Monthly Replacement Contact Lens Wearers. *Clin. Optom.* **2023**, *15*, 97–103.
- (24) Wesley, G.; Giedd, B.; Hines, B.; Bickle, K.; Pearson, C.; Lorentz, H. Safety and Efficacy of a New Water Gradient Biomimetic Monthly Replacement Spherical Contact Lens Material (Lehfilcon A). Clin. Ophthalmol. 2022, 16, 2873–2884.
- (25) Lam, S. M.; Tong, L.; Duan, X.; Petznick, A.; Wenk, M. R.; Shui, G. Extensive Characterization of Human Tear Fl Uid Collected Using Different Techniques Unravels the Presence of Novel Lipid Amphiphiles. *J. Lipid Res.* **2014**, *55* (2), 289–298.
- (26) Pfüller, U.; Franz, H.; Preiß, A. Sudan Black B: Chemical Structure and Histochemistry of the Blue Main Components. *Histochemistry* 1977, 54 (3), 237–250.
- (27) Tighe, B. J.; Contact Lens Materials. In *Contact Lenses*; Philips, A. J.; Speedwell, L., Ed.; Butterworth- Heinemann: Oxford, UK, 2007; 59–78.
- (28) Cwiklik, L. Tear Film Lipid Layer: A Molecular Level View. Biochim. Biophys. Acta Biomembr. 2016, 1858 (10), 2421–2430.
- (29) Georgiev, G. A.; Eftimov, P.; Yokoi, N. Structure-Function Relationship of Tear Film Lipid Layer: A Contemporary Perspective. *Exp. Eye Res.* **2017**, *163*, 17–28.
- (30) Lam, S. M.; Tong, L.; Yong, S. S.; Li, B.; Chaurasia, S. S.; Shui, G.; Wenk, M. R. Meibum Lipid Composition in Asians with Dry Eye Disease. *PLoS One* **2011**, *6* (10), No. e24339.
- (31) Lam, S. M.; Tong, L.; Duan, X.; Acharya, U. R.; Tan, J. H.; Petznick, A.; Wenk, M. R.; Shui, G. Longitudinal Changes in Tear Fluid Lipidome Brought about by Eyelid-Warming Treatment in a Cohort of Meibomian Gland Dysfunction. *J. Lipid Res.* **2014**, *55* (9), 1959–1969.
- (32) Lam, S. M.; Tong, L.; Reux, B.; Duan, X.; Petznick, A.; Yong, S. S.; Khee, C. B. S.; Lear, M. J.; Wenk, M. R.; Shui, G. Lipidomic Analysis of Human Tear Fl Uid Reveals Structure-Specific Lipid Alterations in Dry Eye Syndrome. *J. Lipid Res.* **2014**, *55* (2), 299–306
- (33) Rohit, A.; Stapleton, F.; Brown, S. H. J.; Mitchell, T. W.; Willcox, M. D. P. Comparison of Tear Lipid Profile Among. *Optom. Vis. Sci.* **2014**. 91 (12), 1391–1395.
- (34) Millar, T. J.; Schuett, B. S. The Real Reason for Having a Meibomian Lipid Layer Covering the Outer Surface of the Tear Film A Review. *Exp. Eye Res.* **2015**, *137*, 125–138.

- (35) Butovich, I. A. The Meibomian Puzzle: Combining Pieces Together. *Prog. Retin. Eye Res.* **2009**, 28 (6), 483–498.
- (36) Willcox, M. D. P.; Argüeso, P.; Georgiev, G. A.; Holopainen, J. M.; Laurie, G. W.; Millar, T. J.; Papas, E. B.; Rolland, J. P.; Schmidt, T. A.; Stahl, U.; Suarez, T.; Subbaraman, L. N.; Uçakhan, O.; Jones, L. TFOS DEWS II Tear Film Report. *Ocul. Surf.* 2017, 15 (3), 366–403.
- (37) Saville, J. T.; Zhao, Z.; Willcox, M. D. P.; Blanksby, S. J.; Mitchell, T. W. Detection and Quantification of Tear Phospholipids and Cholesterol in Contact Lens Deposits: The Effect of Contact Lens Material and Lens Care Solution. *Investig. Ophthalmol. Vis. Sci.* **2010**, *51* (6), 2843–2851.
- (38) Omali, N. B.; Subbaraman, L. N.; Heynen, M.; Lada, M.; Canavan, K.; Fadli, Z.; Ngo, W.; Jones, L. Lipid Deposition on Contact Lenses in Symptomatic and Asymptomatic Contact Lens Wearers. *Contact Lens Anterior Eye* **2021**, *44* (1), 56–61.
- (39) Pucker, A. D.; Thangavelu, M.; Nichols, J. J. In Vitro Lipid Deposition on Hydrogel and Silicone Hydrogel Contact Lenses. *Investig. Ophthalmol. Vis. Sci.* **2010**, *51* (12), 6334–6340.
- (40) Masoudi, S.; Willcox, M. A Method for Studying Lipid Adsorption to Silicone Hydrogel Contact Lenses. *Biofouling* **2021**, *37* (8), 862–878.
- (41) Walther, H.; Phan, C. M.; Subbaraman, L. N.; Jones, L. Differential Deposition of Fluorescently Tagged Cholesterol on Commercial Contact Lenses Using a Novel in Vitro Eye Model. *Transl. Vis. Sci. Technol.* **2018**, 7 (2), 18.
- (42) Qiao, H.; Luensmann, D.; Heynen, M.; Drolle, E.; Subbaraman, L. N.; Scales, C.; Riederer, D.; Fadli, Z.; Jones, L. In Vitro Evaluation of the Location of Cholesteryl Ester Deposits on Monthly Replacement Silicone Hydrogel Contact Lens Materials. *Clin. Ophthalmol.* **2020**, *14*, 2821–2828.
- (43) Luensmann, D.; Omali, N. B.; Suko, A.; Drolle, E.; Heynen, M.; Subbaraman, L. N.; Scales, C.; Fadli, Z.; Jones, L. Kinetic Deposition of Polar and Non-Polar Lipids on Silicone Hydrogel Contact Lenses. *Curr. Eye Res.* **2020**, *45* (12), 1477–1483.
- (44) Phan, C. M.; WY Chan, V.; Drolle, E.; Hui, A.; Ngo, W.; Bose, S.; Shows, A.; Liang, S.; Sharma, V.; Subbaraman, L.; Zheng, Y.; Shi, X.; Wu, J.; Jones, L. Evaluating the in Vitro Wettability and Coefficient of Friction of a Novel and Contemporary Reusable Silicone Hydrogel Contact Lens Materials Using an in Vitro Blink Model. Contact Lens Anterior Eye 2024, 47 (2), No. 102129.