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Characterization and analysis of extended-wear silicone hydrogel contact lenses utilizing novel silicone macromers

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Abstract

Contact lenses are one of the most successful biomaterials in history with a global market estimated to be worth over \$17 billion in 2025. Silicone hydrogel contact lenses dominate the market and are complex biphasic biomaterials with several critical material properties needed for clinical use. Careful consideration of composition and chemistry is needed to identify formulations of lenses meeting all commercial standards with the potential for improved manufacturability, cost, and/or next generation use. Four silicone macromers were investigated in this work with varying symmetry of siloxane units and macromer structure, number of siloxane groups, branching, length, and concentration. Novel silicone hydrogel lenses were produced and evaluated for optical transmittance, elastic modulus, oxygen transmissibility, water content, and surface wettability. Several lenses met commercial standards and demonstrated an increase in oxygen permeability (Dk) and inverse relationship with elastic modulus and siloxane concentration, respectively. A hydrophobic/hydrophilic ratio below 1.4 was needed for a co-continuous water phase. Substitution of methoxypropyl groups for butyl groups increased hydrophobic microdomains leading to decreased optical quality and mechanical properties. Generally, fluorine-containing silicone macromers allowed for a wider range of successful compositions, and above a certain hydrophilic composition, the presence of trifluoropropyl groups resulted in improved solubility and optically clear lenses. Data also showed asymmetric siloxane macromers have potential to meet critical lens properties at lower overall siloxane content. New lens materials with wider composition ranges meeting all clinical lens properties is a significant challenge and may significantly expand the field.

KEYWORDS

contact lens biomaterials, monomethacryloxypropyl functional polydimethylsiloxane, ophthalmology, polymer network, polysiloxane

Liana Wuchte and Stephen DiPasquale contributed equally.

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1 | INTRODUCTION

Contact lenses are one of the most successful and safe biomaterials with over 200 million people wearing contact lenses worldwide.¹ The global market was worth over \$7 billion in 2015 and is estimated to be worth over \$17 billion in 2025.^{1,2} Silicone hydrogel contact lenses, first introduced in 1999, now dominate the market and make up 70% of lens fittings in the United States.³ Extended-wear silicone hydrogel contact lenses are complex biomaterials and designing lenses with advanced properties presents a significant engineering challenge. There are several well-defined bulk and surface material properties that must be met for a lens to be considered acceptable for use in the commercial market, such as optical transmittance, elastic modulus, oxygen transmissibility, water content, and surface wettability.⁴ Individually, these properties are not particularly difficult to achieve; however, the design of a novel silicone hydrogel polymer that fits multiple criteria simultaneously requires careful investigation. Properties that are deemed “commercially acceptable” can be determined by analyzing industry standards as well as investigating products and manufacturer information.

The latest focus of the field has been increasing lens comfort for users, which has been cited as the top reason patients stop using contact lenses.^{5–7} A number of potential causes for this discomfort relating to material properties have been of interest, including contact lens dehydration, poor surface wettability and lubricity leading to surface deposition during wear, poor continuous water phase/ion transport, high elastic modulus, and low oxygen permeability.⁸ Various iterations of modern contact lens materials have been developed to address these problems, and have included the following: increased contact lens water content at the expense of silicone content or by addition of internal wetting agents; increased continuous aqueous phase leading to better ion permeability; increased oxygen permeability by increased silicone content; decreased modulus by varying network architecture, siloxane groups, and chain length; advancements in surface treatments and covalent surface molecules; and water gradients within the lens with an increasing water content at the tear film interface and a higher silicone lower water content at the core.^{4,9,10} Aside from improving the properties of commercial contact lenses or the manufacturability of contact lenses, there is also a need for advanced contact lens properties that current contact lens materials cannot fully or adequately support. Some examples of the newest contact lens advancements are ocular drug delivery via contact lenses,¹¹ contact lenses acting as biosensors for disease, contact lenses with advanced embedded electronics, and specialty lenses that could help patients prevent the development of myopia.^{12–14} As new technologies are developed, the materials that serve as a platform for these advancements as well as knowledge of structure–property relationships must also advance. Thus, there is a significant need for the study and development of new silicone monomers and macromers and more robust silicone hydrogel formulations—mixtures that can handle the addition of new components or molecules without disrupting the often-delicate balance of hydrophilic and hydrophobic phases and associated polymer phase morphology that affects lens properties. Currently, there are significant composition limitations of silicone

hydrogel formulations due to maintaining all lens properties within commercial ranges. While new silicone macromers have been introduced in the last decade for improved contact lenses,¹⁵ more research is needed. The aim of this work was to identify new silicone hydrogel macromers and formulations that has potential to drive the discovery of the next generation of lens materials and systems. A wider range of lens compositions with suitable clinical properties will lead to more opportunities and better integration of future lens platforms for drug releasing lenses, electronic embedded lenses, and other new technologies that will significantly expand the applicability of lenses and the field.

In this study, we investigated the synthesis and properties of novel silicone hydrogel contact lenses produced using new symmetric and asymmetric silicone macromers. The state-of-the-art silicone macromer used in contact lenses today has a very simple architecture: an asymmetric structure with a methacrylate group on one end and a non-functional alkyl group on the other. It is expected that the silicone macromer structure, number of siloxane groups, branching, polymer polydispersity, concentration, and solubility have substantial effects on many polymer lens properties and the morphology of hydrophilic–hydrophobic domains. Careful consideration of composition and chemistry is needed to adequately identify the working ranges of formulations that can produce silicone hydrogel lenses that meet commercial lens standards of all design properties with the potential for improved manufacturability. New developments in the field of silane and silicone chemistry have given us tools to modify the silicone macromer structure to increase its miscibility with the hydrophilic component(s) of the lens formulation and improve the properties of the resulting contact lens. For example, it is challenging to improve oxygen transmissibility without negatively affecting optical and mechanical properties. To increase oxygen transmissibility and reach acceptable lens hydrophilicity and water content, monomers with a relatively small number of branched siloxane groups forming pendent structures have typically been used rather than linear or large block polysiloxanes that could not achieve the needed hydrophilicity. Recent advances in living anionic ring-opening polymerization of siloxanes have expanded both the range and precision of polysiloxanes as potential monomers for contact lenses.¹⁶

2 | MATERIALS AND METHODS

2.1 | Silicone hydrogel lens materials and synthesis

Methacryloxypropyltris (trimethylsiloxy) silane (TRIS), dimethylacrylamide (DMA), ethanol (EtOH), polyethylene glycol 200 dimethacrylate (PEG200DMA), polyethylene glycol 550 dimethacrylate (PEG550DMA), and 2-hydroxy-2-methylpropiophenone (photoinitiator) were purchased from VWR International (Radnor, PA). Ethylene glycol dimethacrylate (EGDMA) was purchased from Sigma Aldrich (St. Louis, MO). The following macromers were synthesized and provided by collaboration with Gelest, Inc. (Morrisville, PA) for incorporation into silicone hydrogel formulations: monomethacryloxypropyl functional polydimethylsiloxane, symmetric (MCS-M11, 800–1000 Da), monomethacryloxypropyl functional polydimethylsiloxane, methoxypropyl terminated, symmetric (MCS-

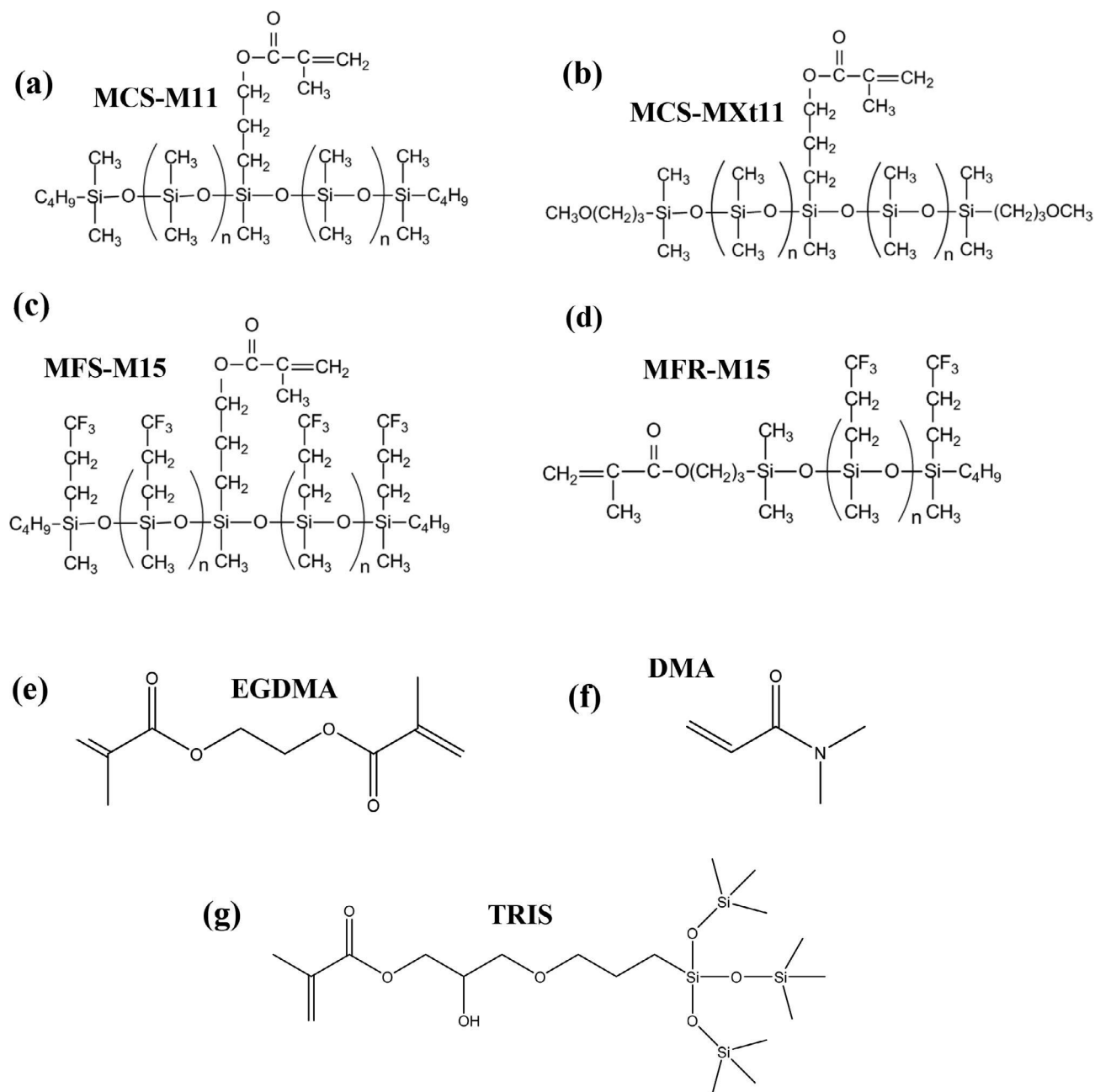


FIGURE 1 Molecular structures of silicone macromers incorporated into silicone hydrogel contact lenses. (A) monomethacryloxypropyl functional polydimethylsiloxane, symmetric (MCS-M11, 800–1000 Da), (B) monomethacryloxypropyl functional polydimethylsiloxane, methoxypropyl terminated, symmetric (MCS-MXt11, 1000 Da), (C) monomethacryloxypropyl functional polytrifluoro-propylmethylsiloxane, symmetric (MFS-M15, 800–1000 Da), (D) monomethacryloxypropyl terminated poly(3,3-trifluoropropyl)methylsiloxane, asymmetric (MFR-M15, 1200–1800 Da), (E) ethylene glycol dimethacrylate (EGDMA), (F) dimethylacrylamide (DMA), (G) methacryloxypropyltris(trimethylsiloxy)silane (TRIS)

MXt11, 1000 Da), monomethacryloxypropyl terminated poly(3,3-trifluoropropyl)methylsiloxane, asymmetric (MFR-M15, 1200–1800 Da), and monomethacryloxypropyl functional poly(trifluoropropyl) methylsiloxane, symmetric (MFS-M15, 800–1000 Da; Figure 1). All chemicals were used as received.

Selected silicone macromer, TRIS, and DMA made up over 90% of the formulation mass composition. Three different crosslinking molecules (EGDMA, PEG200DMA, and PEG550DMA) were used to study

the effects of crosslinker length and amount on the bulk material properties (from here on, referred to as “crosslinker”). Ethanol served as a mutual solvent or “bridge” for the hydrophilic and hydrophobic components in the formulation, as needed. Photoinitiator was added to all formulations at 1% by volume. Pre-polymerization solutions were combined in a centrifuge tube, thoroughly mixed with a fixed high-speed vortex mixer (VWR, Radnor, PA) for at least 2 min, and followed with 20 min of sonication in an ultrasonic bath (Branson, Danbury, CT).

The silicone macromers that were tested can be broadly referred to as “MCS-series” and “MF-series” macromers to distinguish the macromer structures. All macromers studied were methacrylate functionalized silicone macromers. The overall goal is to increase the polarity of the silicone macromer in order to reduce its hydrophobicity and reduce phase separation with the hydrophilic monomer (DMA). Three parts of the silicone macromer architecture are targets for modification: the non-methacrylate endgroup (e.g., MCS-MXt11), the size of the siloxane block (e.g., MCS-M11), and the polarity of the siloxane chain (e.g., MFR-M15). MCS-M11 and MCS-MXt11 (Figure 1A,B) are both symmetrical and both have dimethylsiloxane repeat units, differing only in end groups. MCS-M11 has butyl groups at both ends of its symmetric side chains, and MCS-MXt11 has methoxypropyl groups. The MF-series differs most significantly from the MCS-series macromers in this study with the inclusion of fluorine, replacing the dimethyl siloxane blocks with trifluoropropylmethylsiloxane blocks. MFS-M15 has symmetric side chains while MFR-M15 is asymmetric (Figure 1C,D).

Polymers were synthesized via free-radical photopolymerization as either contact lenses or polymer sheets. Contact lenses were made by transferring 27 μL of silicone hydrogel pre-polymer solution into polypropylene contact lens molds (plano) to produce lenses with 14.8 mm diameter, 8.4 base curve, and 100 μm center thickness. Polymer sheets were synthesized between two glass panels, separated by 0.5 mm thick Teflon spacers, and clamped together with metal clips. Free-radical polymerization was performed with an ultraviolet spot cure (OmniCure S2000, Excelitas, Waltham, MA) equipped with a bandpass filter to limit the wavelengths of emitted light to 250–450 nm and set to an intensity of 35 mW/cm^2 for 2–5 min. The intensity of light was measured with a radiometer (ILT1400, International Light Technologies, Peabody, MA) through the mold materials being used. Polymers were carefully removed from molds with tweezers before further analysis or testing. Each silicone hydrogel was synthesized at a specific ratio of (macromer + TRIS)/DMA, referred to as the hydrophobic/hydrophilic ratio, and 1:1 PEG200DMA/EGDMA and ethanol at a concentration of 5 mass % and 10 mass %, respectively. Hydrophobic/hydrophilic ratios were selected for various physical property testing based on qualitative analysis of synthesized lenses. If hydrogels synthesized at a specific hydrophobic/hydrophilic ratio demonstrated qualitative postsynthesis phase separation, samples were not tested for physical properties. Visible phase separation renders hydrogels unusable as contact lens materials due to low optical transmittance as well as structural properties that result in the hydrogels unable to be manipulated for various physical property analysis methods. As such, formulations that demonstrated qualitative phase separation after synthesis or structural properties that rendered hydrogels unable to be manipulated were excluded from analysis.

2.2 | Water content and equilibrium weight swelling ratio

Silicone hydrogel contact lenses were removed from molds and placed in a vacuum oven (Sheldon Manufacturing, Cornelius, OR) at 25°C

and 28 in. Hg until the weight change of the dried polymers was less than 0.1%. Dry polymer mass was recorded, and lenses were then submerged in DI water until equilibrium was reached. Fully hydrated lenses were weighed once again, after carefully dabbing excess water from the surface of the lens using Kimwipes (Kimberly-Clark, Roswell, GA). Equilibrium weight swelling ratio was calculated by dividing the difference between the mass of the swollen lens and dry lens by the mass of the dry lens.

2.3 | Elastic modulus

A benchtop mechanical tester (EZ-X Electromechanical Tester, Shimadzu, Columbia, MD) equipped with a 100 N sensor and 500 N capacity screw flat grips were prepared according to Shimadzu protocol, with proper calibration and equilibration sequences completed prior to experiments. The thickness (T), width (W), and gauge length [G (L)] of each sample tested was measured with a digital caliper and all measurements were recorded for later calculations. Samples were tightly secured in the grips and a tensile test was performed until the sample reaches the ultimate breaking point. When each test was complete, force versus stroke data over time was converted to stress versus strain figures to calculate elastic modulus (the slope of the curve). Metal punches were used to cut hydrated polymer sheets into a standard dumbbell shape, using a printed template to ensure consistency.

2.4 | Oxygen permeability

Oxygen permeability (Dk) analysis was conducted by the polarographic method, utilizing an oxygen permeometer (201T Oxygen Permeometer, Createch/Rehder-dev Co, Chesterfield Township, MI) and polarographic cell (Createch/Rehder-dev Co, Chesterfield Township, MI). Edge-corrected Dk values were calculated according to ISO 18369.4. Silicone hydrogel contact lenses were hydrated in a saline solution and lens thickness measured with an electronic micrometer. Lenses were placed on the polarographic oxygen sensor (Createch/Rehder-dev Co, Chesterfield Township, MI) with an 8.7 mm base curve. Measurements were recorded at 100% humidity and 35°C.

2.5 | Optical transmittance

Contact lenses were fully hydrated in deionized (DI) water or phosphate buffered saline (PBS). Small discs were cut from prepared contact lenses and placed in individual wells of a transparent, flat-bottom, 96-well plate. Each well with a polymer sample was filled with 200 μL of DI water or PBS. Optical transmittance was measured with a plate reader (Infinite M200 Pro, Tecan, Mannedorf, Switzerland), taking absorbance scans at wavelengths of light across the visible light spectrum (between 400 and 750 nm at 10 nm increments). Optical density values from absorbance readings were used to calculate transmittance values. Commercial values were acquired by studying four of the largest contact lens companies (Johnson & Johnson, Alcon, CooperVision,

and Bausch + Lomb) and their contact lens products currently available to patients. For example, for a contact lens to be considered optically clear by industry standards, the minimum commercially accepted transmittance value of modern silicone hydrogel contact lenses is 85%.^{17–20}

2.6 | Contact angle

Silicone hydrogel contact lenses were synthesized and plasma coated in a Plasma Prep III plasma cleaner (SPI Supplies, West Chester, PA) using oxygen as the feed gas. Treated lenses were cut with a cork borer to form small circular polymer discs. Contact angle with water was measured by placing a 1 μ l droplet of DI water on the surface of the plasma coated silicone hydrogel discs, and the angle of the water droplet on the surface of the polymer was analyzed with a surface contact angle imaging goniometer (Ramé-hart, Succasunna, NJ).

2.7 | Statistical analysis

Statistical difference was analyzed via two-tail t-test with $p > .05$ considered not significant. Results are presented as mean \pm SD with $n \geq 3$.

3 | RESULTS

3.1 | Water content

Water content of contact lenses synthesized with four different macromers using various hydrogel formulations is shown in Figure 2. Published water content values for commercial silicone hydrogel contact lenses currently on the market range from 24% to 56%.^{17,18,20,21} Although silicone hydrogel lenses may provide acceptable oxygen transport regardless of water content due to silicone content alone, adequate water content is critical for the development of a co-continuous ion/water permeable hydrogel phase needed for ocular homeostasis, compatibility, and tear exchange.^{22–26} For all formulations studied, lens water content exponentially decreased as hydrophobic/hydrophilic ratio increased (Figure 2A). For all four silicone macromers, formulations synthesized at 0.7 and 1.0 hydrophobic/hydrophilic ratio exhibited water content greater than 24%, within the middle of the commercial range. Lens produced with MCS-M11 and MFR-M15 at 1.4 hydrophobic/hydrophilic ratios demonstrated water contents above 24%, but at the lower end of the commercial range. However, lenses produced with any of the macromers at hydrophobic/hydrophilic ratios of 3.3 and higher exhibited very low water content, much lower than 24%. For the silicone macromers tested, results suggest that a hydrophobic/hydrophilic ratio of below 1.4 is necessary for enough water content that assures a continuous aqueous phase throughout the lens.

3.2 | Mechanical properties

Figure 3 shows the average elastic modulus values of various silicone hydrogel lenses, varying the silicone macromer and hydrophobic/hydrophilic ratio. For the systems studied, there is an inverse relationship between the hydrophobic/hydrophilic content and the elastic modulus. As the hydrophobic/hydrophilic content in the lens increases, the lens modulus decreases. For the MCS-series macromers and MFS-M15, which are all symmetric silicone macromers with average molecular weights ranging between 800 and 1000 Da, a clear decrease in the elastic modulus can be seen with increased hydrophobic content. However, polymers produced with MFR-M15, the only silicone macromer tested that has an asymmetric structure and a slightly higher molecular weight (1200–1800 Da), showed that elastic modulus was not as sensitive to changes in hydrophobic content in this system. Recent studies of multicomponent silicone hydrogels have shown that discontinuity in the silicone phase of the polymer can influence mechanical properties, including elastic modulus.²⁷ The hydrogel hydrophilic component has been identified as the “hard segment” and the silicone phase (hydrophobic) as the “soft segment” within silicone hydrogel systems, which is why a decreasing concentration of “soft segments” or even a discontinuous silicone phase often results in a less elastic polymer, with higher elastic modulus values.^{28,29} For silicone hydrogel contact lenses currently on the market, elastic modulus values are between 0.5 and 2.0 MPa^{17,18,21,30} with values less than 1 MPa being superior in terms of comfort and decreased adverse events. Lenses prepared with MCS-M11 and MFS-M15 macromers exhibited modulus values below 1 MPa, but only at values of hydrophobic/hydrophilic ratios above 2.6 and 7.5, and 7.5, respectively.

Variation of the crosslinker and concentration can also alter modulus. Thus, lenses that had the highest elastic moduli shown in Figure 3 (lenses made with MCS-MXt11 and MFR-M15) were produced at lower hydrophobic/hydrophilic ratios with crosslinker variation to ascertain if modulus values below 1 MPa could be achieved. Several trends can be observed by varying the crosslinker concentration and length which are shown in Figure 4 at a fixed hydrophobic/hydrophilic ratio of 0.7. First, by only decreasing crosslinking monomer concentration, lenses prepared with these monomers at relatively low hydrophobic/hydrophilic ratios (and hence high moduli) were able to reach moduli values in the commercially relevant range and at values below 1 MPa (black circle data points, PEG200DMA and EGDMA). Thus, for all lens systems studied and presented in Figure 3, which had ratios of 1.4, 2.6, and 7.5, modulus values less than 1 MPa can be achieved. A common trend therefore in Figure 4 is a decrease in the concentration of crosslinker resulted in an decrease in elastic modulus, which is seen in the literature for other hydrogel systems.^{31,32} Another common trend is that compositions with longer crosslinking monomers at a fixed crosslinker concentration resulted in polymers with decreased modulus. The crosslinking monomers EGDMA, PEG200DMA, and PEG550DMA have approximately 1, 4.5, and 12 ethylene glycol groups respectively. Lenses produced with

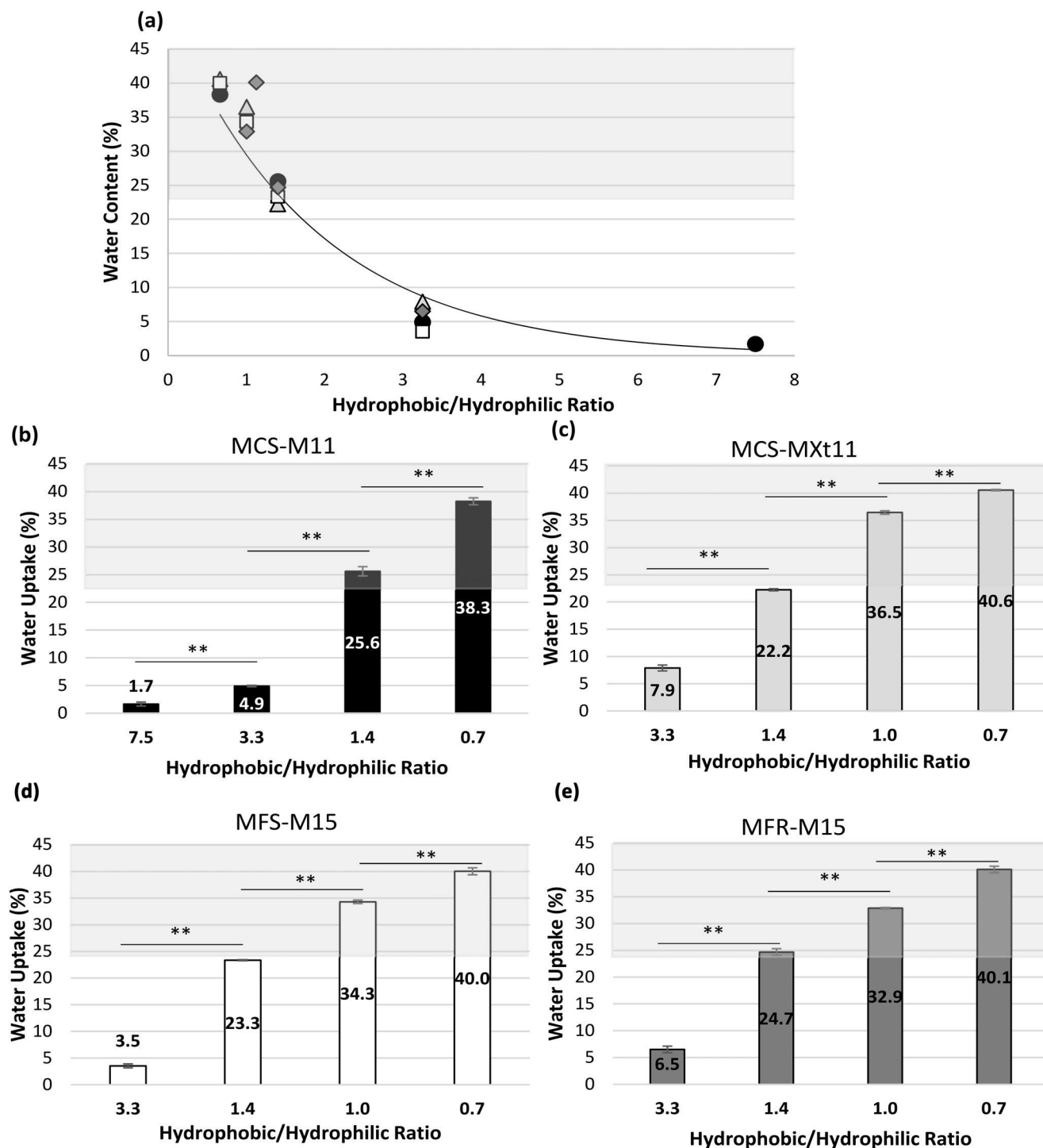


FIGURE 2 Water content of silicone hydrogel lenses synthesized with different silicone macromers. Shaded region represents silicone hydrogel contact lens commercial range for water content. (A) Water content increasing hydrophobic/hydrophilic ratio (●) MCS-M11, (△) MCS-MXt11, (□) MFS-M15, (◊) MFR-M15. (B) MCS-M11, (C) MCS-MXt11, (D) MFS-M15, (E) MFR-M15 (t-test, not significant [NS] $p > .05$, $*p < .05$, $**p < .01$, error bars represent \pm SD, $n = 3$)

PEG200DMA and PEG550DMA had lower modulus values than lenses prepared with equal amounts of EGDMA and PEG200DMA. The modulus of lenses produced with PEG200DMA and PEG550DMA were within error of each other and is potentially due to decreased reaction of the longer crosslinker due to diffusion

limitations of growing polymer chains and/or an increased discontinuous silicone phase. Overall, an important point to note to reiterate is that with relatively small changes in crosslinker concentration, there are a wide range of lenses with modulus values within the commercial range.

FIGURE 3 Elastic modulus of silicone hydrogel lenses synthesized with different silicone macromers at different hydrophobic/hydrophilic ratios. Shaded region represents silicone hydrogel contact lens commercial range for elastic modulus. (●) MCS-M11, (○) MCS-MXt11, (○) MFS-M15, (●) MFR-M15. Data labels/numbers above each dataset indicate the hydrophobic/hydrophilic ratio of the formulation (t-test, not significant [NS] $p > .05$, * $p < .05$, ** $p < .01$, error bars represent \pm SD, $n = 5$)

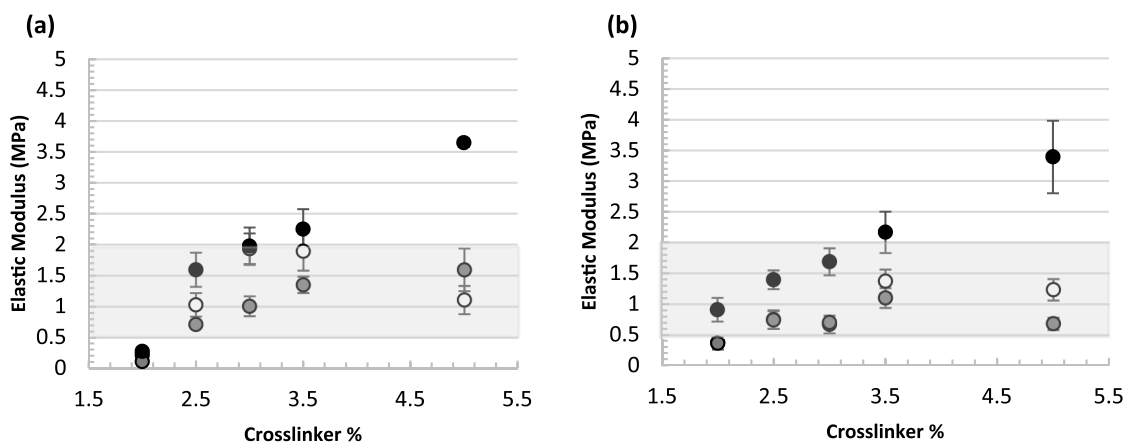
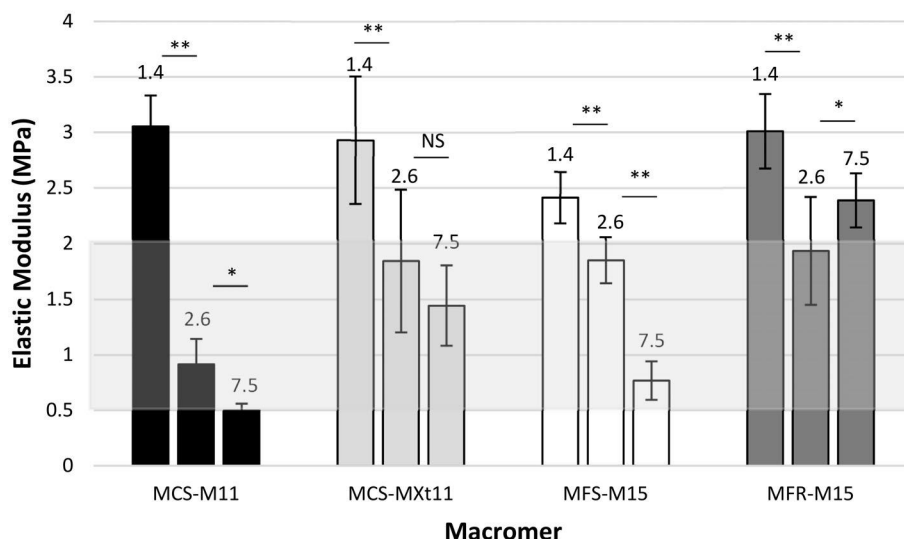


FIGURE 4 Crosslinker length and mass % effects on elastic modulus of silicone hydrogel lenses synthesized with different silicone macromers. Shaded region represents silicone hydrogel contact lens commercial range for elastic modulus. (A) MCS-MXt11 0.7 hydrophobic/hydrophilic ratio, (B) MFR-M15 0.7 hydrophobic/hydrophilic ratio. (○) PEG550DMA, (●) (PEG200DMA), (●) PEG200DMA, and EGDMA (1:1). Error bars represent \pm SD, $n = 5$

3.3 | Oxygen permeability

In the literature, oxygen permeability values (Dk) are reported for commercial silicone hydrogel products ranging from 60 to 140×10^{-11} ($\text{cm}^2/\text{sec} \cdot (\text{mL O}_2)/(\text{mL-mmHg})$) which can be simply written as 60–140 barrer.^{17–20} Figure 5 highlights oxygen permeability of five different silicone hydrogel lenses for each silicone macromer formulated lens. Every tested formulation fell within the commercial range for Dk except for a single formulation (MCS-M11, 2.6 hydrophobic/hydrophilic ratio), which demonstrated a Dk of 41 ± 8 barrer. An increase in silicone content correlating with increased oxygen permeability is observed in Figure 5A and matches the expected trend.^{33–36} However, the highest Dk values produced from the lenses produced with MCS-M11 and MCS-MXt11 do not contain adequate hydrophilic content (7.5 hydrophobic/hydrophilic ratio) and exhibited low water content. An important concept in the design of contact lenses is how the various

properties must be met simultaneously by a single material. With water content specifically considered, the formulations with less than 24% water content are not considered feasible options for silicone hydrogel lenses despite the high oxygen permeability due to the potential for poor ion transport due to the probability of non-continuous aqueous phase from water content being too low. When considering the compositions within acceptable water content bounds, lenses with 1.1 hydrophobic/hydrophilic ratio resulted in the highest Dk value across all four silicone macromers, among which the lens made with MFR-M15 silicone macromer produced the highest average Dk of 112 ± 2 barrer.

3.4 | Optical transmittance

Figure 6 highlights the optical transmittance data of various silicone hydrogel lenses, made from four different formulations (0.44, 1.0, 1.4,

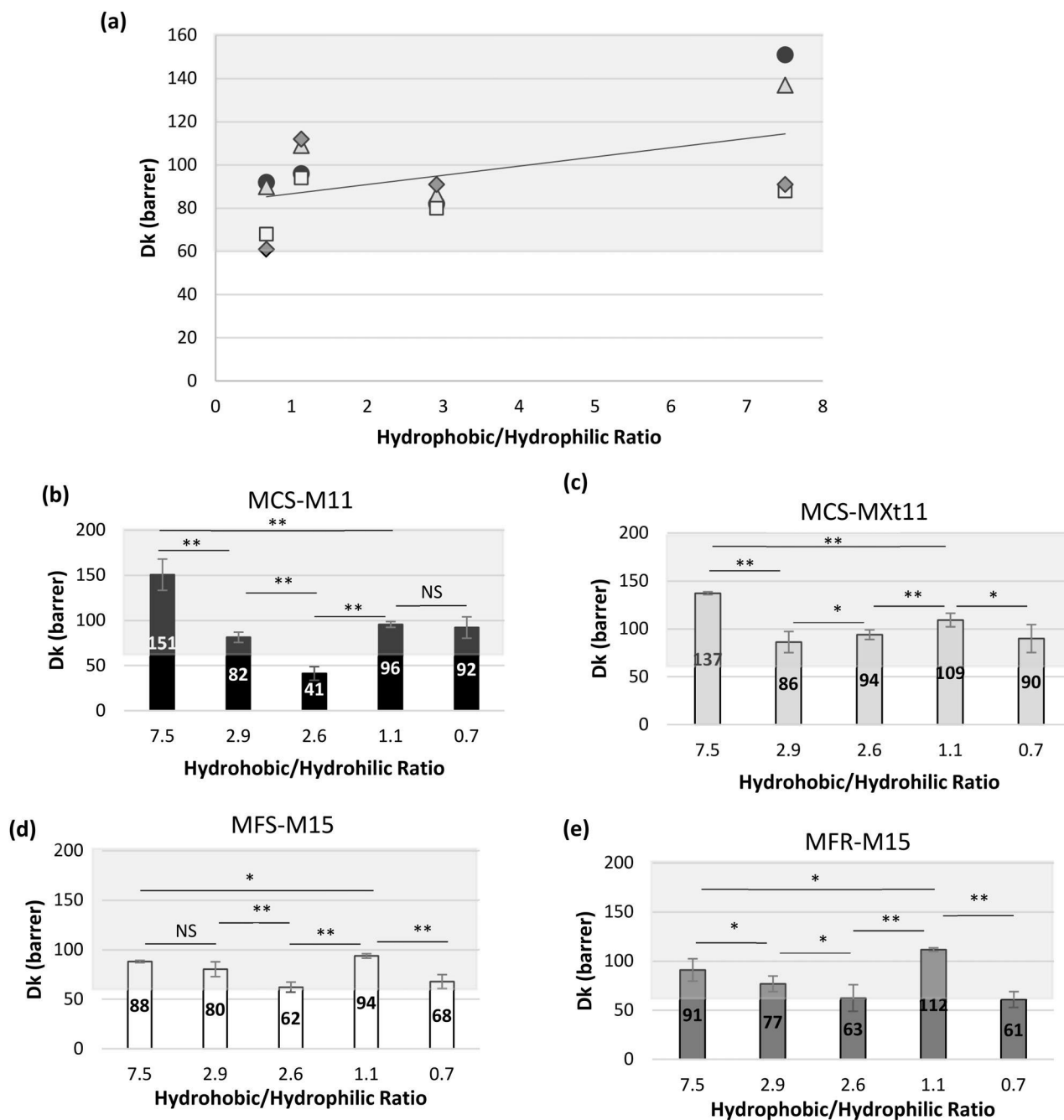


FIGURE 5 Oxygen permeability of silicone hydrogel contact lenses synthesized with different silicone macromers. Shaded region represents silicone hydrogel contact lens commercial range for Dk. (A) Dk values increasing hydrophobic/hydrophilic ratio (●) MCS-M11, (△) MCS-MXt11, (□) MFS-M15, (◆) MFR-M15. (B) MCS-M11 (C) MCS-MXt11 (D) MFS-M15 (E) MFR-M15 (t-test, not significant [NS] $p > .05$, * $p < .05$, ** $p < .01$, error bars represent \pm SD, $n = 5$)

and 3.3 hydrophobic/hydrophilic ratio) designed to highlight changes to the ratios of components and choice of silicone macromer. Formulations demonstrating an optical transmittance of above 85% are considered optically clear and suitable for use as a contact lens material.^{17–20} At the hydrophobic/hydrophilic ratios tested, lens optical transmittance remained relatively constant (Figure 2A).

Lenses produced with MCS-M11 (0.44 and 1.4), MCS-MXt11 (3.3), MFS-M15 (0.44, 1.0, 1.4, and 3.3) and MFR-M15 (0.44 and 1.0)

all demonstrated >85% optical transmittance from 400 to 700 nm, falling within the commercial range for contact lens materials.

Lenses produced with MCS-MXt11 (0.44 and 1.4) and MFR-M15 (1.4) all demonstrated <85% optical transmittance from 400 to 700 nm.

Lenses produced with MCS-M11 (1.0 and 3.3), MCS-MXt11 (1.0), and MFR-M15 (3.3) all had visible phase separation in the formulation and produced lens and were not included in the analysis. For

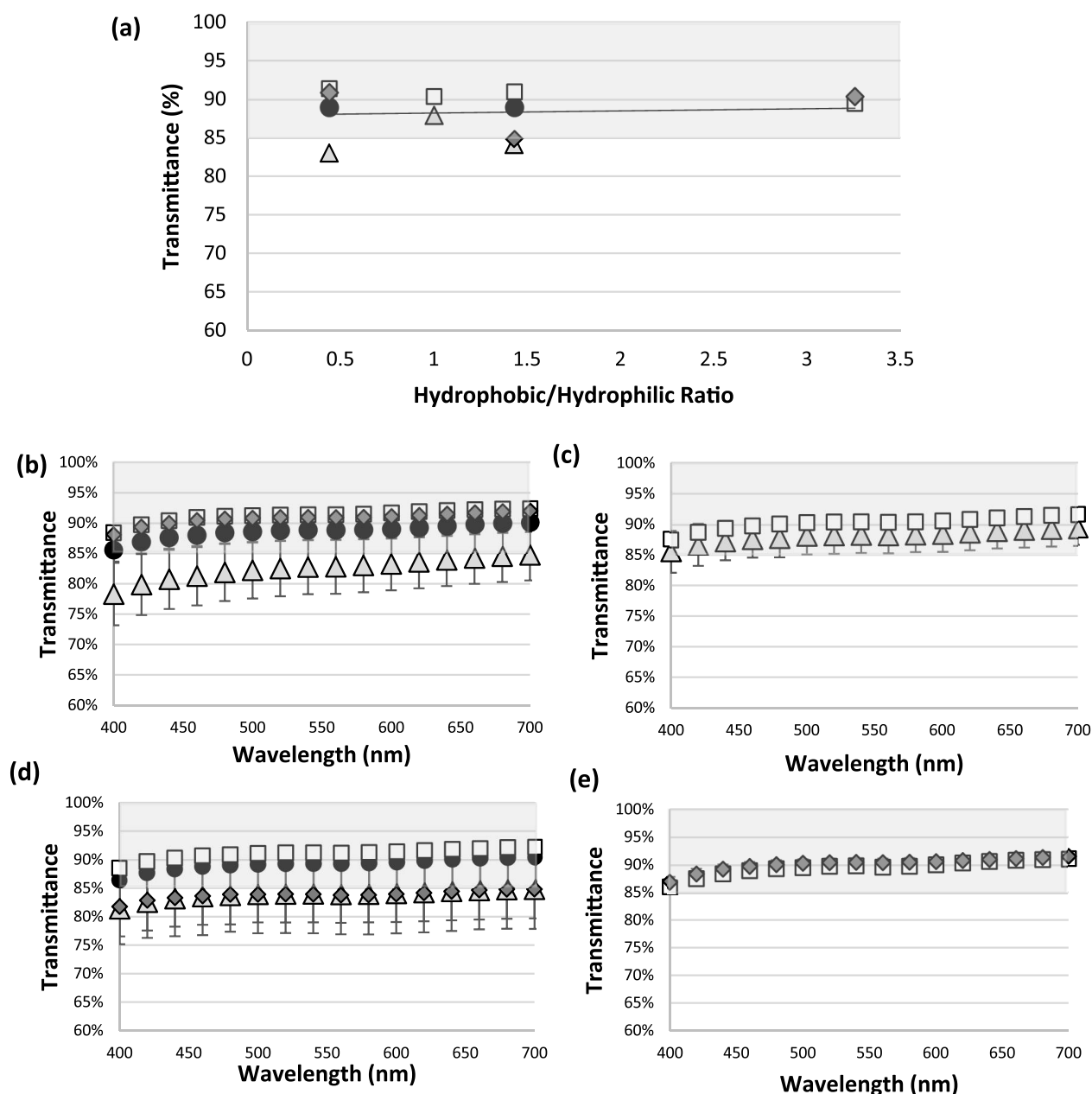


FIGURE 6 Optical transmittance of silicone hydrogel contact lenses synthesized using different silicone macromers with increasing hydrophobic/hydrophilic ratio. Shaded region represents silicone hydrogel contact lens commercial range for optical transmittance. (●) MCS-M11 (△) MCS-MXt11 (□) MFS-M15 (◆) MFR-M15. (A) Transmittance at 560 nm increasing hydrophobic/hydrophilic ratio. Full visible spectrum optical transmittance at hydrophobic/hydrophilic ratio: (B) 0.44 (C) 3.3 (D) 1.4 (E) 1.0. Error bars represent \pm SD, $n = 3$

MCS-MXt11, these results, especially at higher concentrations are likely due to the substitution of methoxypropyl groups for butyl groups, which could increase hydrophobicity and disrupt the hydrophobic/hydrophilic balance and increase hydrophobic microdomains within the formulation/lens.

A significant variable to consider among these four macromers in this study is the presence of fluorine: MFS-M15 and MFR-M15 contain fluorine and MCS-M11 and MCS-MXt11 do not. It has been reported that the incorporation of fluorinated functionality dramatically increases the solubility of silicone macromers with hydrophilic

components, like DMA.³⁷ Lenses produced with both MF-series macromers had higher average transmittance values than lenses containing the MCS-series macromers in the silicone hydrogel system at a hydrophobic/hydrophilic ratio of 0.44. Lenses produced with MFS-M15 and MFR-M15 were both also optically clear with 1.0 hydrophobic/hydrophilic ratio while MCS-M11 and MCS-MXt11 produced hydrogels with visible phase separation at the same hydrophobic/hydrophilic ratio due to poor solubility with DMA and increased hydrophobic domains. With DMA content greater than 35% mass of the formulation (a hydrophobic/hydrophilic ratio lower than 1.4), the

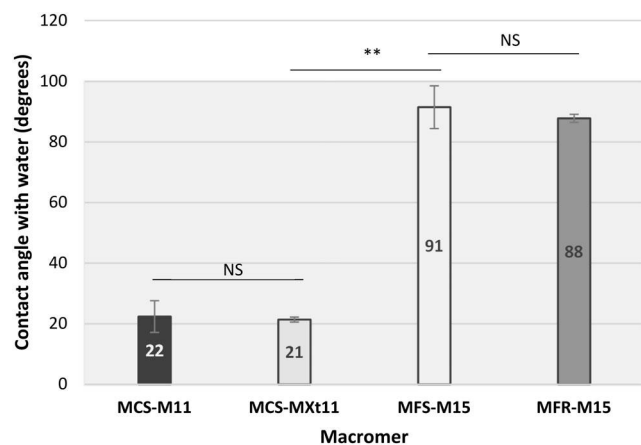


FIGURE 7 Surface wettability of silicone hydrogel contact lenses synthesized with different macromers. Shaded region represents silicone hydrogel contact lens commercial range for contact angle. (●) MCS-M11, (○) MCS-MXt11, (○) MFS-M15, (●) MFR-M15. Formulation was synthesized with 2.9 hydrophobic/hydrophilic ratio. (t-test, not significant [NS] $p > .05$, $*p < .05$, $**p < .01$, error bars represent $\pm SD$, $n = 6$)

presence of trifluoropropyl groups resulted in improved solubility and optically clear lenses when compared to the lenses produced with macromers not containing fluorine. The MFR-M15 and MFS-M15 macromers were also the only macromers to produce optically clear lenses without any TRIS included and with suitable silicone content (data not shown).

When directly comparing MFS-M15 and MFR-M15, MFS-M15 containing lenses resulted in higher optical transmittance across all four formulations. MFR-M15 has a larger average molecular weight (between 1200 and 1800 Da) than MFS-M15 (between 800 and 1000 Da), and MFS-M15 has a symmetric structure, while MFR-M15 is asymmetric. Polymer chain length and structural symmetry are two of the most prevalent factors demonstrated in the literature in relating to polymer solubility. In a 2017 study, increasing polymer chain length/molecular weight of silicone macromers was shown to have a negative effect on optical transmittance, resulting in decreased light transmittance when compared to shorter macromers with the same functionality and silicone content.²⁷ The higher molecular weight of MFR-M15 likely had a negative effect on the optical transmittance. The symmetry of the macromer structure is also another important variable to consider. There are some studies that suggest symmetrical molecules are generally less soluble by relating solubility with the melting point of their crystalline structures, but with these macromers that is not the case.^{38,39} Linear polysiloxanes and polysiloxane block polymers have been problematic in producing silicone hydrogel polymers, with insufficient solubility for copolymerization with components like DMA. Through a series of solubility studies, it was found that symmetric macromers had a reduced tendency to phase separate and create microdomains when compared to asymmetric macromers of similar molecular weight.⁴⁰ This is attributed to the “bisecting” of the long polydimethylsiloxane chain, which results in two shorter dimethylsiloxane blocks and a central polar functionality of the macromer.

3.5 | Surface wettability

Contact angle of water on plasma-coated silicone hydrogel contact lenses synthesized with different silicone macromers at a hydrophobic/hydrophilic ratio of 2.9 is shown in Figure 7. This ratio was chosen to represent a primarily hydrophobic formulation to demonstrate effectiveness of plasma coating. The MFR-M15 and MFS-M15 containing lenses exhibited contact angles of $88^\circ \pm 1^\circ$ and $91^\circ \pm 7^\circ$ respectively, while MCS-M11 and MCS-MXt11 containing lenses exhibited contact angles of $22^\circ \pm 5^\circ$ and $21^\circ \pm 1^\circ$ respectively. Although $>90^\circ$ is considered the typical contact angle value that determine a hydrophobic versus hydrophilic surface, commercial contact angle of silicone hydrogel lenses have ranged anywhere from 31 to 102° in published experimental data.^{41–44} Thus, results in Figure 7 suggest that surface-passivated lenses synthesized using all four macromers would be suitable for use as contact lens materials.

The increase in contact angle in MFR-M15 and MFS-M15 containing lenses can be attributed to the fluorine content. Fluorinated chemical groups are often used in coating surfaces to make them hydrophobic and are known for water-repellant properties.⁴⁵ Materials that are coated with fluorocarbons (perfluorinated) exhibit very low surface energy, which results in water or oil remaining as droplets on the surface.⁴⁶ Fluorine, as the most electronegative element, significantly affects the chemical reactivity of an organic molecule and makes them less prone to bonding, contributing to high chemical stability.⁴⁶ Although these fluorine-containing contact lenses may have a less wettable surface, they are also highly resistant to surface deposits and lipid uptake which significantly affect comfort and extended wear capabilities.^{37,47–49}

4 | DISCUSSION

Optical transmittance was affected by varying the silicone macromers, particularly by the differences in structure (symmetric or asymmetric), molecular weight, and the presence of fluorine and methoxypropyl groups. For example, lenses synthesized using MF-series macromers (MFS-M15 and MFR-M15) demonstrated greater optical transmittance values when compared to the lenses produced with MCS-series macromers. Optical transmittance, which is directly related to the polymer microstructure and polymer phase morphology, can also serve as a metric for solubility, so the improved clarity of the lenses prepared with MF-series macromers was attributed to better silicone macromer solubility with TRIS and DMA. The MFR-M15 and MFS-M15 macromers were also the only macromers to produce optically clear lenses without any TRIS included. These results suggest that the MF-series' improved solubility and clarity and could contribute toward a more robust formulation for next generation lenses. These improved properties were likely due to the presence of the trifluoropropyl groups in the silicone macromers. Conversely, the fluorine content also had a significant effect on the contact angle of the silicone hydrogels as well: MFR-M15 and MFS-M15 containing lenses exhibited increased water contact angles when compared to lenses containing

the MCS-series macromers. However, when surface-passivated, the MF-series macromers produced a suitable contact angle for use as contact lenses.

The hydrophilic content is a critical component in contact lens materials, and the hydrophilic-hydrophobic balance in these formulations significantly affected the lens properties. Water content studies confirmed that the hydrophilic content within these systems is an influential variable, as expected, regardless of which silicone macromer was used. As previously mentioned, adequate water content is needed in silicone hydrogel lenses for a co-continuous water phase to form within the hydrogel, which is critical for ion transport and lens biocompatibility, movement on the eye, post-lens tear turnover, and metabolic waste removal.^{4,49} This means that a minimum amount of hydrophilic content relating to water content is needed for a lens to have high potential for a co-continuous water phase and be considered suitable for use, and the water content data suggested that a hydrophobic/hydrophilic ratio of below 1.4 was necessary for appropriate water content in the materials tested. This was a significant factor when considering the oxygen permeability data, as the silicone content of the contact lenses correlated with the oxygen permeability properties in these materials. Although the MCS-M11 and MCS-MXt11 based silicone hydrogels synthesized with 7.5 hydrophilic/hydrophobic ratio produced oxygen permeability values as high as 151 and 137 barrer, respectively, they did not meet the minimum water content value required. The next highest oxygen permeability value was found with the MFR-M15 (1.1 hydrophobic/hydrophilic ratio), with 112 barrer. In nearly every formulation tested, the Dk was within the commercially acceptable range. It should be noted that the differences in distribution of polar functionality between the lens bulk and surface undoubtedly occur but were not examined in these studies.

Mechanical testing verified that the elastic modulus of the novel silicone hydrogel lenses could be tailored to fit into the acceptable range by altering the formulation. In particular, the elastic modulus could be adjusted by altering the crosslinker content, crosslinker length, the silicone macromer used, and the hydrophilic-hydrophobic composition of the polymer. The data suggested that changes to the crosslinker content alone could likely produce a tailorable elastic modulus value less than 1 MPa, regardless of which silicone macromer or initial formulation was selected.

5 | CONCLUSIONS

In this study, several novel silicone hydrogel materials were examined and characterized for potential use as silicone hydrogel contact lenses by analyzing five key lens bulk and surface material properties: optical clarity, water content, elastic modulus, oxygen permeability, and surface wettability. Changing variables within the silicone hydrogel formulations and effects on the corresponding lens properties were highlighted, and variables studied included silicone macromer structure and functionality, crosslinker length and concentration, and the hydrophobic-hydrophilic composition.

Ultimately, this work shows that novel silicone macromers were incorporated into silicone hydrogel lenses with resulting material properties suitable for clinical use. Lenses produced with the new silicone macromers, particularly those of the MF-series, which contained fluorine, could meet commercial standards in a wider range of compositions. These macromers have asymmetric (MFR-M15) and symmetric (MFS-M15) siloxane groups with molecular weights ranging from 800 to 1800 Da with the asymmetric containing lenses meeting clinical design properties, especially modulus and oxygen transport, with lower overall siloxane content which could increase manufacturability and decrease cost. Also, a wider range of lens compositions meeting clinical properties will lead to more opportunities in the field and better potential integration of future lens platforms such as drug releasing lenses, electronic embedded lenses, and other new technologies.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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