DEVELOPMENT OF ANTI-FOULING MATERIALS FOR BLOOD-CONTACTING DEVICES

An Undergraduate Research Scholars Thesis

by

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ABSTRACT

Development of Anti-fouling Materials for Blood-Contacting Devices

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The safety and efficacy of blood-contacting medical devices is hindered by thrombosis upon implantation in the body. Silicones and polyurethanes (PUs) are commonly used for hemodialysis catheters and other blood-contacting medical devices. However, due to their hydrophobic surfaces, they are susceptible to biological adhesion, including that of blood proteins and platelets that eventually result in thrombosis leading to device failure. Thus, this work explores the addition of a surface-modifying additive (SMA) into both silicones and PUs for their capacity to increase surface hydrophilicity. These SMAs are poly(ethylene oxide) (PEO)-silane amphiphiles comprised of an oligo(dimethyl siloxane) tether, a PEO segment, and a triethoxysilane crosslinking group. Several key parameters were investigated, including the concentration-dependent effects of these SMAs on water-driven restructuring and solvent selection for film fabrication. Using contact angle analysis, systematically prepared film compositions were evaluated for their ability to undergo water-driven surface restructuring to result in a hydrophilic, PEO-enriched surface. The SMA modified PU system was further analyzed in air- and water-equilibrated environments to evaluate its long-term efficacy in regard to water-driven restructuring, water-induced mass loss, and water uptake. The results demonstrated that silicones modified with PEO-silane amphiphiles were unaffected by solvent choice and able to restructure

at concentrations as low as 10 μmol SMA/g of silicone. Similarly, for PU modification, PEO-silane amphiphile concentrations at 10 μmol SMA/g of PU or greater resulted in substantial water-driven restructuring that was maintained after 2 weeks of air-equilibration. After 2 weeks of water-equilibration, both mass loss and water uptake were minimal; however, restructuring capacity diminished slightly, and only PU samples with 25 μmol SMA/g of PU or greater, maintained hydrophilic surfaces. Overall, these results show the potential for PEO-silane amphiphile SMAs to enhance the protein resistance and thromboresistance of both silicone- and PU-based blood-contacting medical devices.

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I am very grateful for my friends, colleagues, department faculty, and staff for enhancing my experience at Texas A&M University. They have made my college experience a unique and worthwhile one.

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CHAPTER I

INTRODUCTION

Silicones and polyurethanes (PUs) are extensively used in blood-contacting medical devices including hemodialysis catheters, vascular grafts, cardiac pacing leads, and catheter balloons [1]. Silicones exhibit properties such as high durability and flexibility, allowing for versatile use in the field of medical applications [2]. Likewise, PUs are durable, elastic, compliant, and resistant to fatigue, making them useful in various medical applications [3]. Additionally, PUs vary in hardness and are available in different grades that can be composed of aromatic polyether or polyester groups [4]. However, both silicone- and PU-based medical devices display poor protein resistance due to their hydrophobic nature, resulting in thrombus formation and ultimately medical device failure [5]. Formation of a thromboembolism can lead to obstruction of blood flow, resulting in poor patient outcomes [6]. For these reasons, silicones and PUs that can exhibit high resistance to protein adsorption will improve the safety and efficacy of blood-contacting medical devices, allowing for better patient outcomes.

The primary strategy to combat protein adsorption in both silicone- and PU-based medical devices is through the surface modification of the hydrophobic surface to a more hydrophilic surface. This can be achieved with the incorporation of poly(ethylene oxide) (PEO) in the silicone or PU material. PEO is a water-soluble polymer that has been known to be non-immunogenic and non-toxic, resulting in increased biocompatibility [7]. When in sufficient concentration at the biomaterial surface, hydrophilic PEO chains are thought to reduce protein adsorption primarily through steric repulsion and the blockage of adsorption sites [8-10]. These properties of PEO have been shown to reduce protein adsorption on biomaterial surfaces that are normally susceptible to adhesion [8, 11]. Traditionally, surface grafting has been the preferred method of incorporating

PEO onto a model substrate such as gold, silicon, and glass, resulting in enhanced hydrophilicity; however, these hydrophilic properties are not preserved when PEO is surface grafted onto silicone and exposed to air, resulting in hydrophobic recovery [12-15]. Thus, surface modifying additives (SMAs) have been adopted as a technique for incorporating PEO onto a silicone surface and reducing the inherent surface hydrophobicity found in silicones [16]. Previously, SMAs were used to bulk-modify a substrate via solvent-casting methods [12]. With solvent-based techniques, solvent choice has been shown to play a role in evaporation rate and surface roughness of polymer films fabricated via solvent-casting [17]. Using hexane and tetrahydrofuran (THF), respectively, PEO has been used as a SMA in silicones and PUs to manipulate their inherent surface properties for more favorable properties such as enhanced hydrophilicity and protein resistance [16, 18]. Thus, the lifetime and efficacy of blood-contacting medical devices may be prolonged with the addition of PEO.

In the Grunlan research group, amphiphilic PEO-based SMAs have previously been developed for the bulk-modification of silicones. These PEO-silane amphiphiles are composed of a crosslinkable triethoxysilane (TEOS) group, an oligo(dimethyl siloxane) (ODMS) tether, and a PEO segment (Figure 1) [19]. PEO-silane amphiphile SMAs were incorporated into silicones using a hexane-based solvent-casting method [16, 20]. When exposed to an aqueous environment, PEO-silane amphiphiles in the SMA modified silicones restructured and presented the PEO segments at the surface, resulting in a hydrophilic, protein resistant surface [21, 22]. Given the successful bulk-modification and efficacy of the PEO-silane amphiphile SMA in silicone, we sought to understand the role of solvent choice in the film fabrication. PEO-silane amphiphile SMAs were incorporated into silicones via solvent-casting at increasing concentrations: 0, 10, 25, and 50 μmol PEO-silane amphiphile per 1 g of silicone. To assess the solvent-induced effects on film fabrication, several solvents including hexane, toluene, chloroform ($CHCl_3$), dichloromethane

(DCM), THF, and ethyl acetate (EtOAc) were investigated. Once fabricated, the effect of these solvents was characterized by evaluating SMA restructuring capacity using static contact angle analysis.

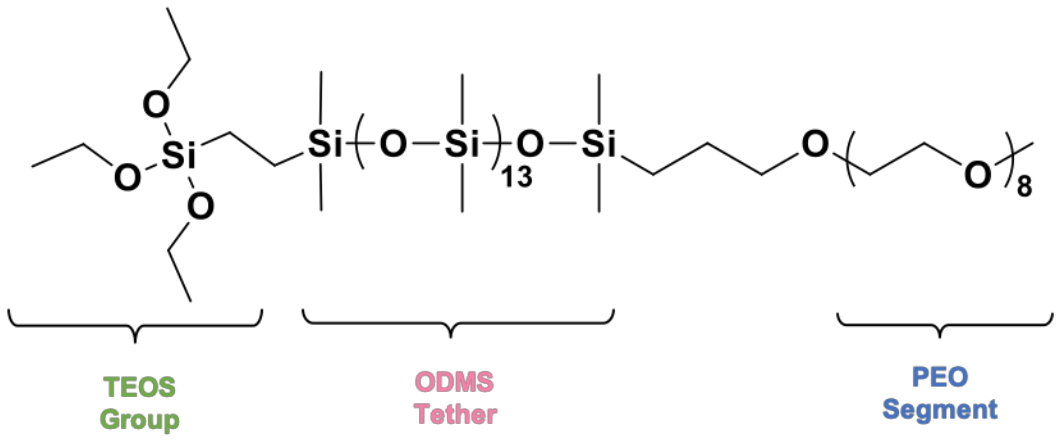

Figure 1. Chemical structure of the "XL diblock, m=13" PEO-silane amphiphile.

Additionally, PEO-silane amphiphile SMAs were incorporated in an aromatic polyether PU system via bulk-modification. These PU films were also fabricated via solvent-casting, specifically with THF. PU samples were modified with PEO-silane amphiphiles at 5, 10, 25, 50 and 100 μmol SMA per 1 g of PU to determine the minimum effective concentration for surface restructuring. These PU films were first evaluated for the capacity of the PEO-silane amphiphiles SMAs to undergo water-driven surface restructuring and produce a PEO-enriched, hydrophilic surface. To evaluate the long-term efficacy of the PEO-silane amphiphile SMAs in a PU system, air- and water-equilibrated studies were also performed. Lastly, water-induced mass loss (i.e. SMA leaching) and water uptake were measured to assess stability of the modified PU films following prolonged exposure to an aqueous environment.

CHAPTER II

MATERIALS AND METHODS

Materials

The following materials were used for the experiments described below. Allyl methyl poly(ethylene oxide) (Polyglykol AM 450, M_n = 292-644 g/mol per manufacture's specifications) was provided by Clariant. Vinyltriethoxysilane (VTEOS; M_n = 190 g/mol), α,ω-bis-(SiH)$ODMS_{13}$ ($ODMS_{13}$; M_n = 1096 g/mol), platinum (Pt)-divinyltetramethyldisiloxane complex (Karstedt's catalyst) was purchased by Gelest. Rhodium (I) tris(triphenylphosphine chloride) (Wilkinson's catalyst), and all solvents used in the study were purchased from Sigma-Aldrich. Glass microscope slides (75 mm x 25 mm x 1 mm) were purchased from Fischer Scientific. Medical-grade condensation-cure room-temperature-vulcanized (RTV) silicone elastomer (MED-1137) was purchased from NuSil Technology. Polyurethane pellets (Tecothane™ Thermoplastic PU; aromatic polyether TT-1074A) were provided by Lubrizol LifeSciences.

Amphiphile Synthesis

PEO-silane amphiphiles with a siloxane tether and PEO segment length of 13 and 8, respectively, were prepared and characterized as shown previously with a two-step hydrosilylation procedure [19]. In brief, $ODMS_{13}$ was reacted with VTEOS through a regioselective hydrosilylation reaction using Wilkinson's catalyst. Next, Karstedt's catalyst was used to react the product with an allyl methyl PEO that had a repeat unit length of 8 to produce the "XL diblock, m=13" PEO-silane amphiphile.

Solvent Study Film Preparation

Glass microscope slides were rinsed with DCM and acetone; these slides were dried in a 120°C oven overnight. Silicone films were prepared via solvent-casting onto glass microscope

slides, as previously reported in Rufin et al. [20]. Each casting solution was composed of uncured MED-1137 dissolved in dry solvent to create a 25 wt% casting solution. Depending on solvent choice, 2 to 4 grams of uncured MED-1137 were used for each casting solution. The solvents used were hexane, toluene, $CHCl_3$, DCM, THF, and EtOAc. PEO-silane amphiphile was mixed into the casting solution with a vortexer at the following concentrations: 10, 25, and 50 μmol per 1 g of MED-1137. Solutions were solvent-casted onto clean glass microscope slides (2 mL per slide). These slides were contained in a polystyrene Petri dish to reduce the rate of solvent evaporation and prevent bubble formation. Films were allowed to cure for one week at room temperature (RT) prior to analysis. For each solvent, unmodified silicone films with no PEO-silane amphiphile were prepared in a similar fashion and served as controls.

Polyurethane Film Preparation

Glass microscopes slides were cleaned in the same manner as described above. PU pellets were washed with methanol to remove processing agents and low molecular weight components. These pellets were dried in a vacuum oven overnight at 120°C. PU pellets were dissolved in THF to form an 8 wt% casting solution. PEO-silane amphiphile was mixed into the casting solution with a vortexer at the following concentrations: 5, 10, 25, 50, and 100 μmol SMA per 1 g of PU. Solutions were solvent-casted onto clean glass microscope slides (2 mL per slide) and stored in a polystyrene Petri dish. Films were allowed to cure for one week at RT prior to analysis. Unmodified PU films with no PEO-silane amphiphile were prepared in a similar fashion and served as controls.

Water Contact Angle Analysis

Static contact angles (θ_{static}) of the prepared films were recorded at RT using a CAM-200 goniometer (KSV Instruments) equipped with an autodispenser, video camera, and drop-shape analysis software (Attension Theta). A 5 μL drop of deionized (DI) water was deposited on the

film, and the contact angle of the water droplet was recorded every 15 seconds over a 3-minute period. The reported values are the averages and standard deviations of the contact angle of three water droplets deposited on different regions of the same film. This evaluation was performed on both the silicone and PU films immediately following their respective 1 week cure times. PU films were subsequently subjected to air- or water-equilibration and re-tested as described below.

For the air-equilibrated study, after the initial θ_{static} measurements, the PU films were individually stored in a polystyrene Petri dish. Following conditioning times of 1 and 2 weeks, θ_{static} measurements were repeated as described above.

In regard to the water-equilibrated study, following the initial θ_{static} measurements, the PU films were submerged in 30 mL of DI water in polystyrene Petri dishes. After 1 and 2 weeks of submersion in DI water, the films were removed, briefly dried with a stream of air, and blotted with a paper towel. θ_{static} measurements were repeated on the films as described previously.

Water-induced Mass Loss

Clean glass slides were weighed, and SMA modified PU solutions were solvent-casted on the slides. After 1 week of curing, the coated slides were weighed again, and the difference from the initial slide measurement was recorded as the initial film mass (W_i). Each slide was placed in a polystyrene Petri dish and soaked in 30 mL of DI water at RT for 2 weeks. The coated slides were subsequently dried overnight at 50°C under reduced pressure and weighed. Again, the difference from the initial, uncoated slide measurement was noted as the final film mass (W_f). Measurements were performed on triplicate films, and water-induced mass loss was calculated using Equation 1.

$$\text{Water-induced mass loss (\%)} = [(W_i - W_f)/W_i] \times 100 \quad (1)$$

Water Uptake

For water uptake studies, PU films were prepared in triplicate on glass slides (3 per

composition). Each film was placed in a polystyrene Petri dish and subsequently submerged in 30 mL of DI water at RT. After 2 weeks, the films were removed from the Petri dishes, briefly dried with a stream of air, and blotted with a paper towel. The water content of the film was measured by thermal gravimetric analysis (TGA). A 11 ± 3 mg segment of film was excised from the glass slide with a razor blade and placed in a platinum TGA pan. Using a TA Instruments Q50 thermogravimetric analyzer, the weight loss of the film was measured as the sample was heated from RT to 150°C at a rate of 10°C/min. Water loss was recorded as a peak in the mass loss derivative curve between RT and approximately 140°C. Water content in weight percent of each film was determined by measuring the mass loss percent around the bounds of that peak. The reported water uptake values are the average water contents and standard deviation of three identically prepared films at the same submersion time.

CHAPTER III

RESULTS AND DISCUSSION

Silicone Modification

Water-driven Surface Restructuring in a Silicone System

The efficacy of amphiphiles as SMAs to increase the hydrophilic properties and enhance protein resistance in silicone systems is predicted to be governed by their ability to undergo water-driven surface restructuring to form a hydrophilic, PEO-enriched surface. Previously, this process was observed for silicones modified with "XL diblock, m=13" amphiphile [12, 16, 20]. The temporal measurement of the decrease in θ_{static} values was used to monitor the relative rate and extent of PEO migration to the surface-water interface of the silicone films. For the silicone films fabricated via solvent-casting with hexane, θ_{static} values were measured over a 3-minute period (Figure 2).

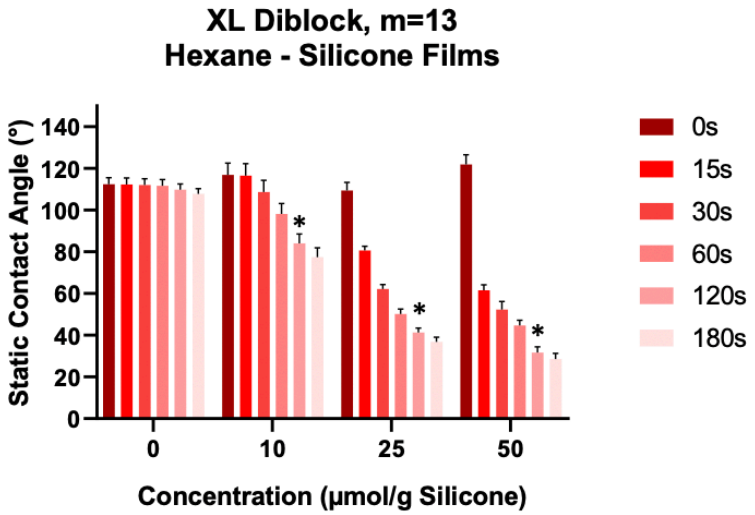

Figure 2. θ_{static} was measured for "XL diblock, m=13" modified silicones prepared via solvent-casting in hexane. Statistical analysis ($p < 0.05$): **120s, unmodified* v. *120s, sample*.

The unmodified silicone control and all SMA modified samples were hydrophobic when the water droplet was initially deposited on the surface of the films ($\theta_{static,\ 0s}$ = ~110°-120°), indicating that little to no PEO was present on the film surfaces. Even after 2 minutes post-deposition of the water droplet, the unmodified silicone remained very hydrophobic ($\theta_{static,\ 120s}$ = ~110°), as expected. In contrast, SMA modified silicones rapidly and substantially restructured to form hydrophilic surfaces with lower θ_{static} values. Sample at 10, 25, and 50 μmol PEO-silane amphiphile per 1 g of silicone displayed a $\theta_{static,\ 120s}$ of ~84°, ~42°, and ~32°, respectively. The degree to which each SMA modified film restructured varied in a concentration-dependent manner, with the higher SMA concentrations resulting in increasingly hydrophilic surfaces. Based on these results, it was observed that a SMA concentration of at least 10 μmol SMA/g of silicone in a silicone system via solvent-casting with hexane resulted in films that exhibited water-driven restructuring.

Silicone Solvent Study

The impact of solvents on the ability of SMA modified silicone samples to effectively restructure when exposed to an aqueous environment was also investigated. With hexane serving as the control solvent, other solvents of differing polarity, including toluene, $CHCl_3$, DCM, THF, and EtOAc were used in the process of solvent-casting SMA modified silicone films. The physical appearance of these films is shown in Figure A1 of the appendix. $\theta_{static,\ 120s}$ values for SMA modified samples at 0, 10, 25, and 50 μmol PEO-silane amphiphile per 1 g of silicone for each solvent were recorded and summarized in Table 1. Solvent-specific θ_{static} graphs are provided in Figures A2-A6 of the appendix. The unmodified silicone samples for each solvent resulted in hydrophobic surfaces ($\theta_{static,\ 120s}$ = ~105°-115°), as expected. For SMA modified samples, a concentration-dependent increase in hydrophilicity was observed $\theta_{static,\ 120s}$ values ranging from

~76°-88°, ~39°-46°, and ~22°-33° for 10, 25, and 50 µmol SMA/g of silicone, respectively. Thus, the different solvents explored in this study did not significantly affect the solvent casting process or the ability of SMA modified silicones to effectively restructure and create a hydrophilic surface when exposed to an aqueous environment.

Table 1. $\theta_{static,\ 120s}$ values are shown for PEO-silane amphiphile modified silicones solvent-casted with different solvents.

		Static Contact Angle (°)			
		0 µmol/g	10 µmol/g	25 µmol/g	50 µmol/g
Solvent	Hexane	109.8°	84.1°	41.3°	31.7°
	Toluene	108.3°	85.3°	43.2°	32.6°
	$CHCl_3$	116.0°	87.6°	42.1°	22.4°
	DCM	111.6°	85.9°	46.1°	22.8°
	THF	106.6°	76.1°	44.5°	23.2°
	EtOAc	107.4°	80.2°	38.6°	28.2°

Polyurethane Modification

Water-driven Surface Restructuring in a Polyurethane System

The ability of the PEO-silane amphiphile to be incorporated in an aromatic polyether-based PU system was investigated in a similar manner. In particular, the efficacy of the SMA water-driven surface restructuring in a PU system to increase hydrophilicity was examined. Similar to silicone, it was predicted that the hydrophilicity of the SMA modified PU system was governed by its ability to form a PEO-enriched surface when exposed to an aqueous environment. Thus, temporal measurements of the θ_{static} values were used to monitor the rate and extent of PEO migration to the surface of the PU system. THF solvent-casted PU films were fabricated at various

concentrations (0, 5, 10, 25, 50, and 100 μmol PEO-silane amphiphile per 1 g of PU), and θ_{static} values were recorded over a 3-minute period (Figure 3).

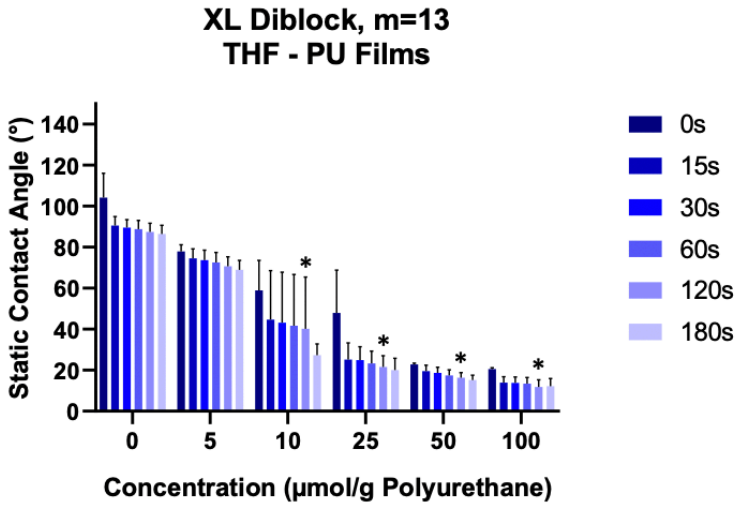

Figure 3. θ_{static} was measured for "XL deblock, m=13" modified PU films prepared via solvent-casting in THF. Statistical analysis ($p < 0.05$): **120s, unmodified* v. *120s, sample*.

After the water droplet was initially deposited on the film surface, the unmodified PU control was hydrophobic and had a $\theta_{static,\ 0s}$ value of ~105°. The SMA modified samples at 5, 10, 25, 50, and 100 μmol SMA/g of PU were more hydrophilic when the water droplet was initially deposited on the film surface ($\theta_{static,\ 0s}$ = ~78°, ~59°, ~48°, 23°, and 21°, respectively), indicating the potential presence of PEO on the surface of the film. The θ_{static} of the water droplet two minutes post-deposition was again recorded to determine the extent of the PEO migration to the surface of the films. While the unmodified PU expectedly exhibited very little change ($\theta_{static,\ 120s}$ = ~87°), all SMA modified PU films restructured to form hydrophilic surfaces. Concentration-dependent restructuring was observed as the SMA-modified silicone samples at 5, 10, 25, 50, and 100 μmol SMA/g of PU displayed a $\theta_{static,\ 120s}$ values of ~70°, ~40°, ~22°, ~16°, and ~12°, respectively. Thus,

the PEO-silane amphiphile was successfully incorporated into a PU system. In addition, it was observed that films with a SMA concentration of at least 10 μmol SMA/g of PU exhibited water-driven restructuring.

Air-Equilibrated Study

After an initial θ_{static} measurement, the SMA modified PU samples were conditioned in air, and θ_{static} was measured after 1 and 2 weeks. To compare potential changes in restructuring capacity due to air-equilibration, $\theta_{static,\ 120s}$ values were recorded for the PU samples at t = 0, 1, and 2 weeks (Figure 4). Initially, the unmodified and 5 μmol SMA/g of PU samples had $\theta_{static,\ 120s}$ values of ~75° and ~76°, respectively. Conditioning in air for two weeks resulted in negligible changes in $\theta_{static,\ 120s}$ values for the unmodified and 5 μmol SMA/g of PU samples (~1° increase and ~1° decrease, respectively). For higher SMA concentrations (10-100 μmol SMA/g of PU), a more significant change in hydrophilicity was observed after conditioning in air. The initial measurement at t = 0 weeks for the 10, 25, 50, and 100 μmol SMA/g of PU samples exhibited $\theta_{static,\ 120s}$ values at ~50°, ~7°, ~5°, and ~5°, respectively. At t = 2 weeks, the 10, 25, 50, and 100 μmol SMA/g of PU samples had $\theta_{static,\ 120s}$ values of ~30° (~20° decrease), ~19° (~12° increase), ~15° (~10° increase), and ~6° (~1° increase), respectively. While the PU samples at higher SMA concentrations exhibited larger changes in $\theta_{static,\ 120s}$ values, they were still relatively hydrophilic, even at t = 2 weeks, indicating their ability to restructure when exposed to an aqueous environment. The results demonstrate that at concentrations of 10 μmol SMA/g of PU or more, SMA modified PUs retain their capacity to effectively undergo water-driven restructuring following air-equilibration.

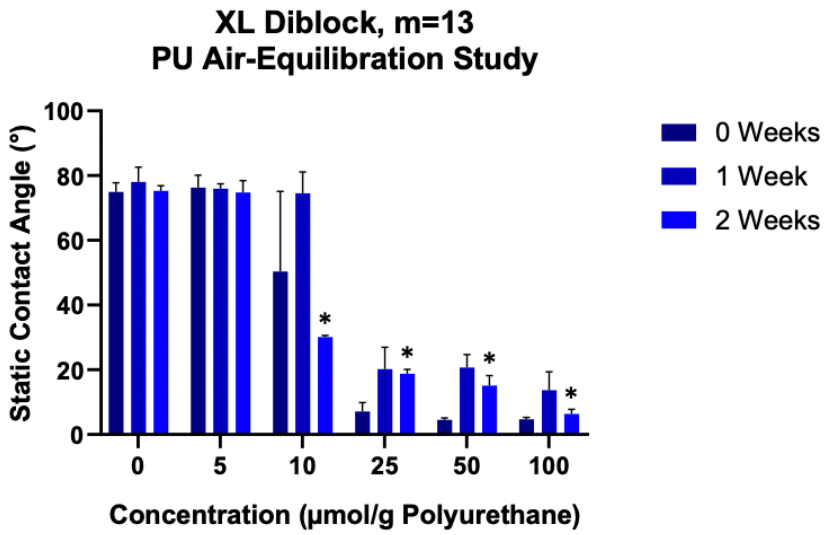

Figure 4. $\theta_{static,\ 120s}$ is shown for the "XL diblock, m=13" modified PU films following extended air-equilibration. Statistical analysis ($p < 0.05$): **2 wks, unmodified* v. *2 wks, sample*.

Water-Equilibrated Study

Water-driven restructuring was also examined for PU films that were conditioned in DI water over the course of 2 weeks. $\theta_{static,\ 120s}$ values were recorded at t = 0, 1, and 2 weeks for PU films throughout conditioning in water (Figure 5). Initially, at t = 0 weeks, the unmodified and 5 μmol PEO-silane amphiphile per 1 g of PU samples had $\theta_{static,\ 120s}$ = ~78° and ~67°, respectively. Following conditioning, there was minimal change in $\theta_{static,\ 120s}$ values observed for the unmodified PU samples (~1° increase). The 5 μmol SMA/g of PU samples exhibited a slightly higher $\theta_{static,\ 120s}$ values (~9° increase). A more significant change was observed in the 10, 25, 50, and 100 μmol SMA/g of PU samples after 2 weeks of conditioning in water. At t = 0 weeks, the 10, 25, 50, and 100 μmol SMA/g of PU samples had $\theta_{static,\ 120s}$ values of ~42°, ~12°, ~4°, and ~5°, respectively. At t = 2 weeks, these samples had $\theta_{static,\ 120s}$ values of ~53° (~11° increase), ~20° (~8° decrease), ~21° (~17° increase), and ~13° (~8° increase), respectively. While there were larger changes in $\theta_{static,\ 120s}$ values after 2 weeks of water-equilibration for these samples, they maintained low,

hydrophilic $\theta_{static,\ 120s}$ values in comparison to the unmodified PU sample, indicating their ability to restructure when exposed to an aqueous environment. The results demonstrate that at concentrations of 25 μmol SMA/g of PU or more, SMA modified PUs retain their capacity to effectively undergo water-driven restructuring following water-equilibration.

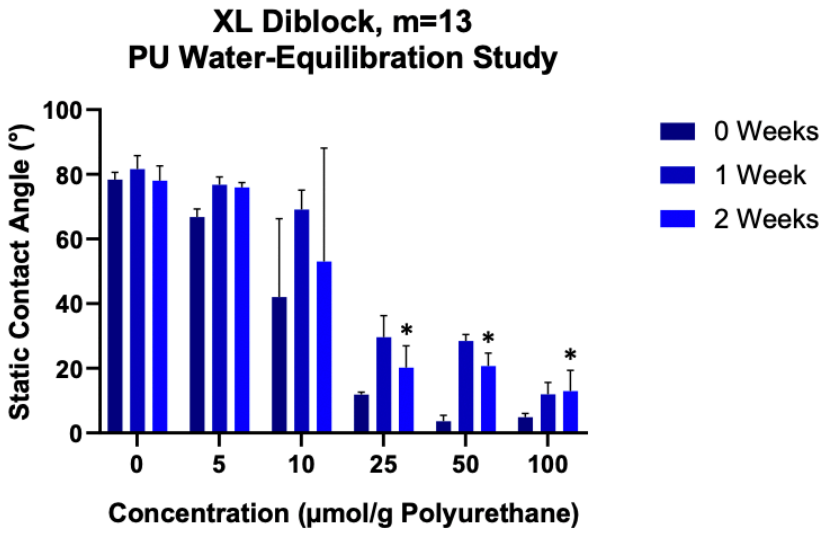

Figure 5. $\theta_{static,\ 120s}$ is shown for the "XL diblock, m=13" modified PU films following extended water-equilibration. Statistical analysis ($p < 0.05$): **2 wks, unmodified* v. *2 wks, sample*.

Water-Induced Mass Loss Study

Water-induced leaching of SMAs from the PU samples was monitored over 2 weeks of water-equilibration. The change in mass of each sample was measured before and after 2 weeks of conditioning to assess potential for leaching (Figure 6). Unmodified PU samples exhibited a mass loss of about 1.6%. PU samples with 5, 10, 25, 50, and 100 μmol PEO-silane amphiphile per 1 g of PU displayed an average mass loss of about 0.28%, 2.3%, 0.40%, 2.1%, and 2.0%, respectively. No concentration-dependent trends were observed and the overall mass loss, following 2 weeks of conditioning, was minimal for these PU samples. Thus, for PEO-silane amphiphile modified PUs, SMA leaching did not occur at a significant level following water-equilibration.

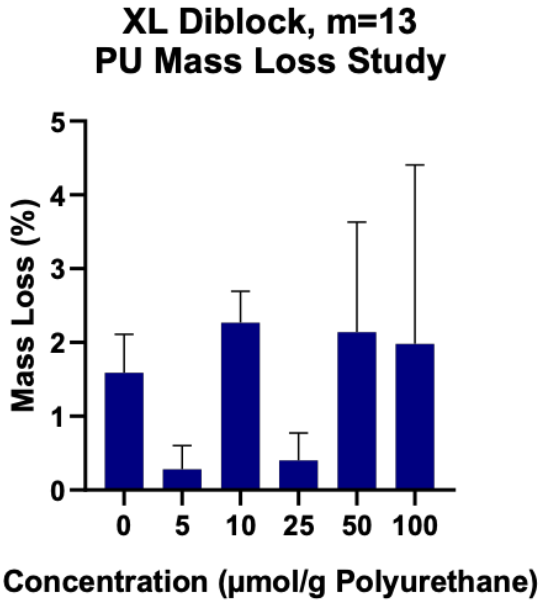

Figure 6. Film mass loss is shown for each PU film after 2 weeks of water-equilibration. Statistical analysis ($p < 0.05$): **unmodified* v. *sample*.

Water Uptake

Modified PU films were subjected to aqueous conditioning, and water uptake was gravimetrically evaluated after 2 weeks (Figure 7). The unmodified PU control sample exhibited minimal water uptake (~0.45%). Likewise, the SMA modified PU samples at concentrations less than or equal to 50 µmol PEO-silane amphiphile per g of PU had minimal water uptake. These values were ~0.32%, ~0.45%, ~0.53%, and ~1.7% for the 5, 10, 25, and 50 µmol SMA/g of PU, respectively. Water uptake was slightly higher at 2.3% for SMA modified PU samples at 100 µmol SMA/g of PU. While differences in water uptake were observed at higher concentrations, overall water uptake for SMA modified PU films was deemed to be minimal as this level of water uptake did not substantially affect the water-driven surface hydrophilicity observed in the previous water-equilibration study. Thus, this amount of water uptake did not seem to contribute to any decrease in surface hydrophilicity after conditioning in water.

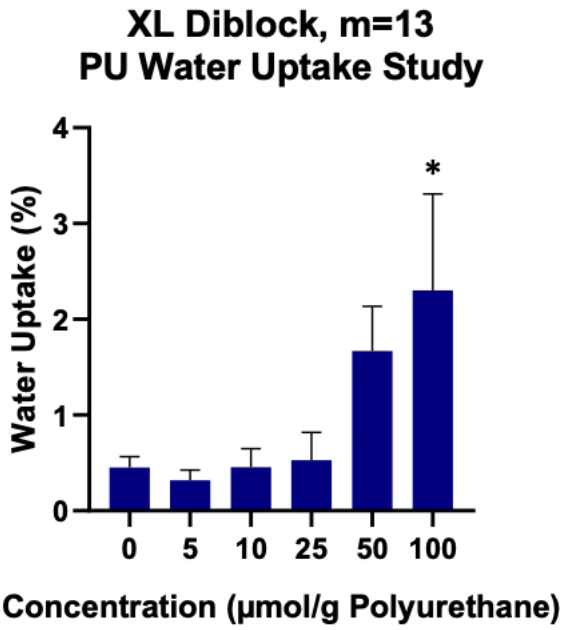

Figure 7. Film water uptake is shown for each PU film after 2 weeks of water-equilibration.

Statistical analysis ($p < 0.05$): **unmodified* v. *sample*.

CHAPTER IV

CONCLUSION

The hydrophobicity of silicones and PUs results in poor resistance to protein adsorption, resulting in platelet adhesion and thrombus formation. Bulk-modification of silicones and PUs with hydrophilic, protein resistant PEO can be employed to circumvent the inherent, hydrophobic challenges of these materials. The efficacy of PEO to resist protein adsorptions depends on its ability to restructure when exposed to an aqueous environment to form a PEO-rich layer at the surface.

In this study, both silicones and aromatic polyether-based PUs were bulk-modified with a PEO-silane amphiphile containing a siloxane tether and a PEO segment. For the silicone testing, we first confirmed that the PEO-silane amphiphile could be effectively incorporated into silicone via solvent-casting with hexane. These were tested at various concentrations (0, 10, 25, and 50 μmol SMA/g of silicone) and evaluated for their ability to undergo water-driven surface restructuring to form a hydrophilic surface. Similar to previous studies, we saw the minimum effective concentration to be 10 μmol SMA/g of silicone [20]. Additionally, various solvents were explored for the film fabrication to determine their effect on SMA restructuring capacity. Films were prepared at 0, 10, 25, and 50 μmol SMA/g of silicone with the following solvents: toluene, $CHCl_3$, DCM, THF, and EtOAc. Irrespective of concentration, it appeared that solvent choice did not significantly affect the ability for SMA modified silicones to restructure in an aqueous environment.

PEO-silane amphiphiles were successfully incorporated in a PU system at 5, 10, 25, 50 and 100 μmol SMA/g of PU via solvent-casting with THF. Similar to the silicone films, the SMA modified PU films exhibited water-driven restructuring to form a hydrophilic, PEO-rich surface.

Rapid and substantial water-driven restructuring of PEO-silane amphiphile was observed at concentrations as low as 10 μmol SMA/g of PU. The long-term efficacy of PEO-silane amphiphiles in the PU films was also investigated with air- and water-equilibrated studies. After 2 weeks of conditioning in air, SMA modified PU films with at least 10 μmol SMA/g of PU were able to maintain their restructuring capacity and form hydrophilic surfaces. For water conditioned samples, SMA modified PU films maintained restructuring at concentrations of at least 25 μmol SMA/g of PU. Furthermore, SMA modified PU samples conditioned in an aqueous environment over the course of 2 weeks were found to have minimal water-induced mass loss and water uptake.

In conclusion, PEO-silane amphiphiles were successfully incorporated in both a silicone and PU system. In silicones, bulk-modification of these SMAs with various solvents using a solvent-cast method did not appear to adversely affect restructuring capacity. In a PU system, the PEO-silane amphiphiles showed efficacy and stability even after 2 weeks of conditioning in air or water. Therefore, these SMAs show potential for enhancing protein resistance in both silicone- and PU-based blood-contacting medical devices.

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Appendix

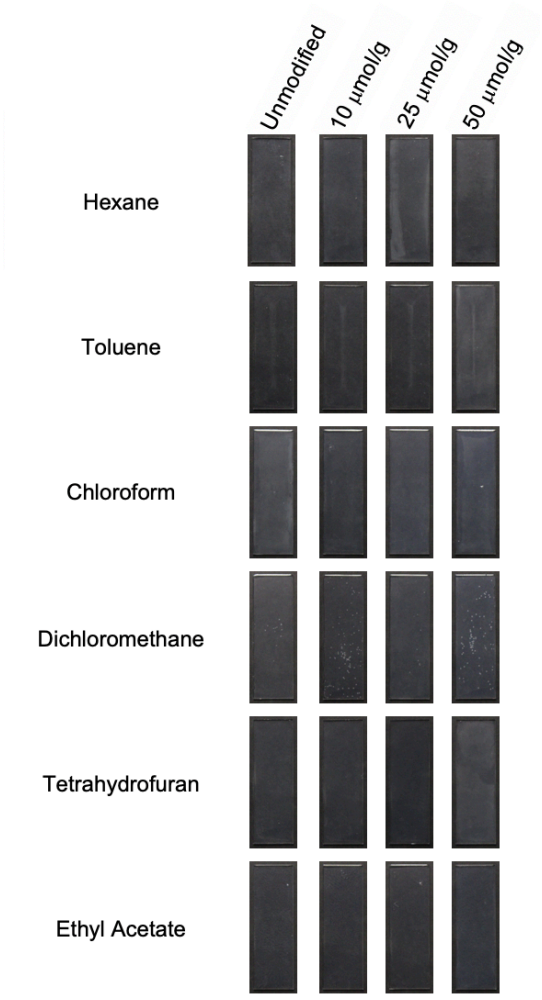

Figure A1. Photoseries of films in silicone solvent study.

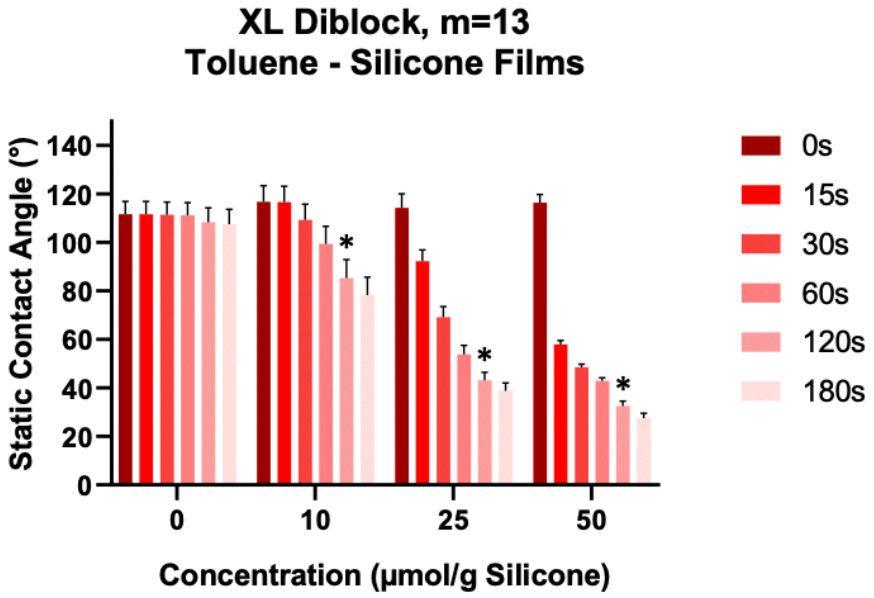

Figure A2. θ_{static} was measured for "XL diblock, m=13" modified silicones prepared via solvent-casting in Toluene. Statistical analysis ($p < 0.05$): **120s, unmodified* v. *120s, sample*.

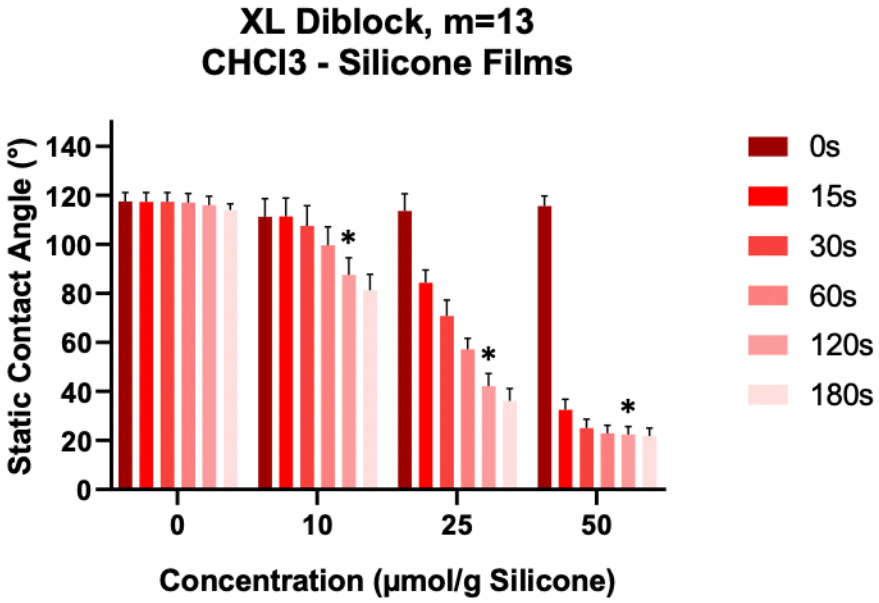

Figure A3. θ_{static} was measured for "XL diblock, m=13" modified silicones prepared via solvent-casting in $CHCl_3$. Statistical analysis ($p < 0.05$): **120s, unmodified* v. *120s, sample*.

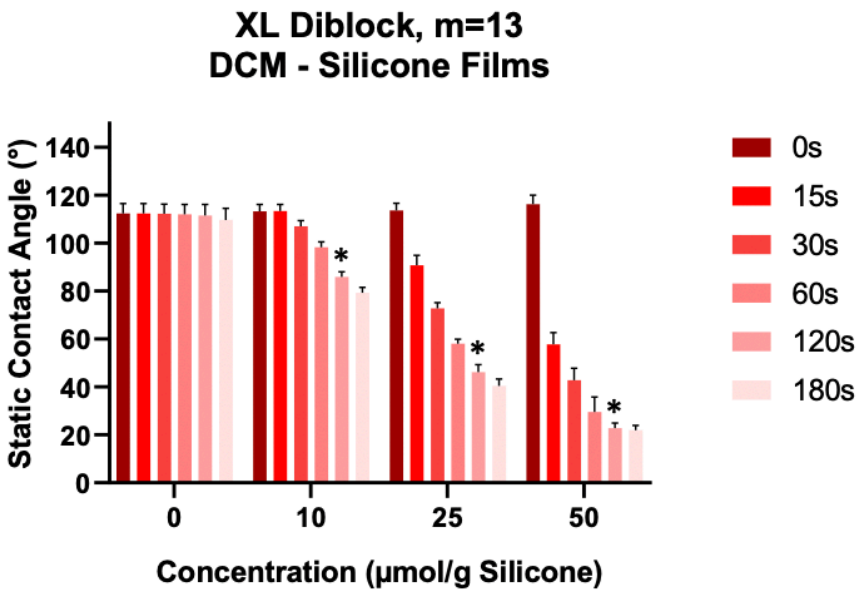

Figure A4. θ_{static} was measured for "XL diblock, m=13" modified silicones prepared via solvent-casting in DCM. Statistical analysis ($p < 0.05$): **120s, unmodified* v. *120s, sample*.

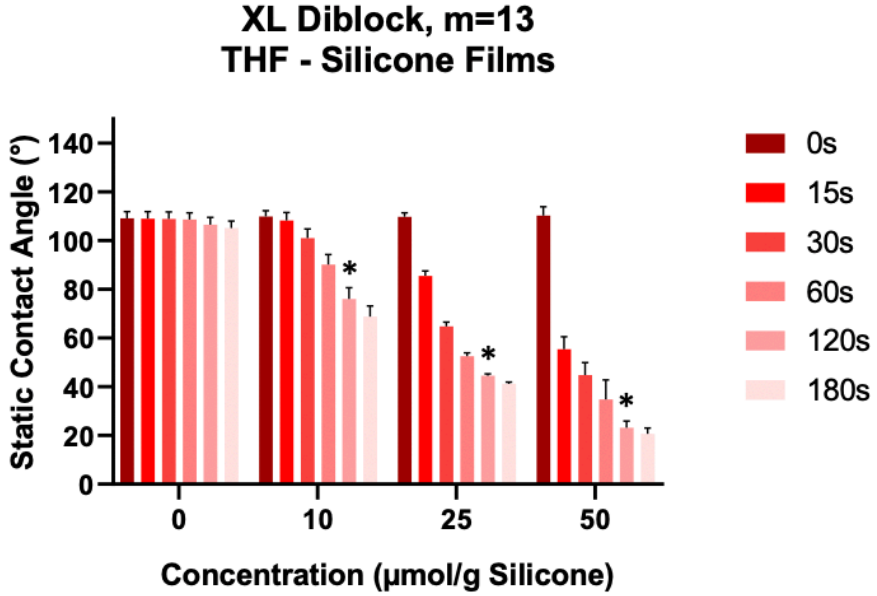

Figure A5. θ_{static} was measured for "XL diblock, m=13" modified silicones prepared via solvent-casting in THF. Statistical analysis ($p < 0.05$): **120s, unmodified* v. *120s, sample*.

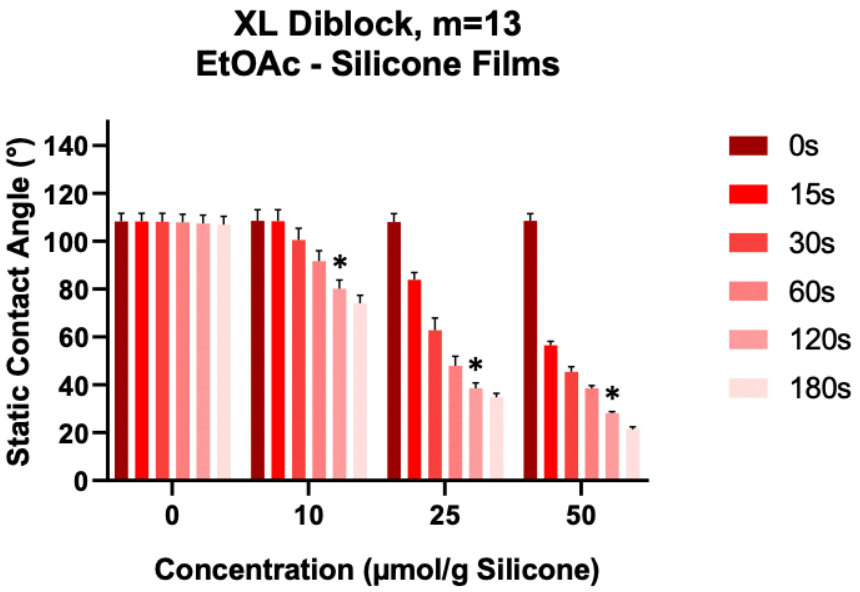

Figure A6. θ_{static} was measured for "XL diblock, m=13" modified silicones prepared via solvent-casting in EtOAc. Statistical analysis ($p < 0.05$): **120s, unmodified* v. *120s, sample*.