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Development of siloxane-based amphiphiles as cell stabilizers for porous shape memory polymer systems

Sayyeda M. Hasan, Alexandra D. Easley, Mary Beth Browning Monroe, and Duncan J. Maitland*

Department of Biomedical Engineering, Texas A&M University, College Station, TX 77843-3120, United States

Abstract

Hypothesis—Polyurethane foaming surfactants are cell stabilized at the polymer-gas interface during foam blowing to prevent bubble coalescence. Siloxane-based surfactants are typically used to generate a surface tension gradient at the interface. The chemical structure of the hydrophobic and hydrophilic units affects surfactant properties, which can further influence foam morphology.

Experiments—Siloxane-polyethylene glycol (PEG) ether amphiphiles were synthesized in high yield via hydrosilylation to serve as surfactants for shape memory polymer (SMP) foams. Hydrophobic units consisted of trisiloxane and polydimethyl siloxane, and PEG allyl methyl ether ($n = 8$ or 25) was the hydrophilic component. Upon confirming successful synthesis of the surfactants, their surface tension was measured to study their suitability for use in foaming. SMP foams were synthesized using the four surfactants, and the effects of surfactant structure and concentration on foam morphology were evaluated.

Findings—Spectroscopic data confirmed successful siloxane-PEG coupling. All surfactants had a low surface tension of 20–21 mN/m, indicating their ability to reduce interfacial tension. SMP foams were successfully fabricated with tunable cell size and morphology as a function of surfactant type and concentration.

Graphical abstract

*Corresponding author at: Texas A&M University, Department of Biomedical Engineering, 5045 Emerging Technologies Building, 3120 TAMU, College Station, TX 77843-3120, United States. djmaitland@tamu.edu (D.J. Maitland).

Keywords

Silicone surfactants; Polyurethane foam; Shape memory polymers; Amphiphiles; Cell stabilizers

1. Introduction

Shape memory polymers (SMPs) are “smart” materials that have the capability of shape change from a programmed secondary shape to a primary shape upon the input of an external stimulus, such as heat, light, or electricity [1–3]. For thermal actuation, the polymer can be synthesized in a primary shape, heated above its transition temperature (T_{trans}), and mechanically programmed into a secondary shape [4]. Once cooled below T_{trans} , the material will remain in the secondary shape until it is heated again to return to its original shape [4]. Shape fixity occurs when the polymer chains are forced to align into conformations with net orientation and cooled below the actuation transition to restrict chain mobility [5]. Entropic recovery to the polymer chain equilibrium random orientation then drives the return to original shape [5]. Due to this shape memory behavior, SMPs have a wide range of uses in medical and industrial applications, such as vascular stents, occlusion devices, and self-controlled actuators [1,6].

Polyurethanes make up an extremely versatile class of polymers that have the capability to be biocompatible and biodegradable and to have tunable mechanical properties [7]. These characteristics make polyurethanes optimal for use *in vivo*. Wilson et al. developed highly crosslinked, amorphous SMPs using aliphatic polyurethanes for use in medical devices [5]. These materials have high recovery stresses due to a high level of crosslinking, tunable glass transition temperatures (T_g 's), and good shape recovery [5]. In an effort to increase the surface area, Singhal et al. synthesized foams with low density and high porosity from the polyurethane SMPs developed by Wilson et al. [8]. Open-celled SMP foams provide a substrate for increased cellular infiltration and adhesion, as well as flow stagnation and recirculation zones, resulting in rapid formation of a stable thrombus upon contact with blood [6,9]. Rodriguez et al. evaluated the biocompatibility of the SMP foams in a porcine model and observed minimal inflammation at 90 days [10]. These properties make SMP foams ideal for use as three-dimensional tissue scaffolds for biomedical applications.

Surfactants allow spreading at the polymer-air interface *via* the Gibbs-Marangoni effect [11,12]. Namely, surfactants lower the surface tension at the polymer interface, thereby inducing flow from high surface tension areas to low surface tension areas. In polyurethane foaming, surfactants stabilize individual foam cells through a change in the surface tension gradient [11]. Polyurethane foams are fabricated by additional polymerization of diisocyanates with alcohols [13,14]. This foaming process occurs in four steps: (i) bubble generation and growth, also known as the cream time; (ii) bubble packing and cell stabilization; (iii) polymer stiffening and cell opening, or gel time; and (iv) final curing, or tack-free time. Typically, surfactants used in flexible polyurethane foaming systems do not alter the reaction kinetics of the process. However, in the absence of surfactants, the foaming system will experience coalescence and eventual collapse [13]. During foaming, the bubbles introduced into the system by mechanical mixing will grow. As the volume fraction of the

gas bubbles exceeds 74%, the spherical bubbles distort into multi-sided polyhedrals with struts. Due to capillary pressure, the pressure within the struts is lower than that in the cells. This pressure difference causes the polymer liquid in the struts to drain. Without surfactants, this drainage rate will be very fast, causing cell rupture and bubble coalescence. The surfactants are adsorbed at the air-alcohol interface and have a significant effect on bubble generation, cell stabilization, strut thickness, final cell size, and foam porosity. These physical foam properties ultimately affect shape memory and/or mechanical properties of the resulting polymer scaffold.

Silicone surfactants were first introduced in the 1950s for the development of industrial-grade polyurethane foam [15]. They are surface active agents that lower the interfacial surface tension and allow spreading [15,16]. Typically, surfactants contain a hydrophobic siloxane group attached to a hydrophilic polar molecule [13,17,18]. Siloxane-based surfactants have three unique properties: (i) they maintain surface activity in both water and non-aqueous systems, such as oil and polyols; (ii) they are able to lower surface tension to as low as 20 mN/m; and (iii) they remain liquid at very high molecular weights [15]. These unique properties are imparted by the siloxane backbone due to its low T_g and the presence of methyl groups that reduce surface tension. In comparison, hydrocarbon surfactants containing alkyl hydrophobic groups with primarily $-CH_2-$ groups only lower surface tension to 30 mN/m, making them less effective in allowing spreading at the interface [15]. Additionally, silicone surfactants have different aggregation properties from those of hydrocarbon surfactants, such that they form bilayer phases and vesicles rather than micelles and gel phases [15,19].

This research focuses on the development of linear surfactants for reliable production of SMP foams with reproducible thermomechanical properties and cell structure. Siloxane units served as the hydrophobic components, and polyethylene glycol (PEG) allyl methyl ether acted as the hydrophilic constituent. Hydrosilylation was used to synthesize the amphiphiles, which were then chemically and physically characterized [15,20–23]. Reliable production of SMP foams with reproducible thermo-mechanical properties and cell structure is important for the utilization of the foams for a variety of medical applications, such as vascular occlusion devices for use in aneurysm treatment. Our current foam composition relies upon a single supplier for surfactants. Thus, commercialization of SMP foams would be significantly hindered if this supplier chose to change the surfactant formulation or stop surfactant production. In this study, polyurethane foams were fabricated with various surfactant concentrations, and the effects of surfactant structure on foam morphology and thermal properties were evaluated. Control over the foam morphology and thermomechanical properties is critical for their application, specifically for their use as tissue scaffolds for embolic devices. Pore size, strut thickness, and cell isotropicity play key roles in cell infiltration and tissue ingrowth following implantation. The intended use of these SMP systems is in biomedical devices for vascular occlusion; hence, controllable foam morphology is desired to target a variety of vasculature, including cerebral and peripheral.

2. Materials and methods

1,1,1,3,5,5,5-heptamethyltrisiloxane (TS, 97%; Sigma-Aldrich Inc., St. Louis, MO); poly(dimethylsiloxane), hydride terminated (PDMS, $M_n \sim 580$ Da; Sigma-Aldrich Inc., St. Louis, MO); toluene (anhydrous, 99.8%; Sigma-Aldrich Inc., St. Louis, MO); chloroform-d ($CDCl_3$, 100%; Sigma-Aldrich Inc., St. Louis, MO); polyethylene glycol allyl methyl ether – Polyglykol AM 350 (PEG-350, $n = 8$; Clariant, Charlotte, NC); polyethylene glycol allyl methyl ether – Polyglykol AM 1100 (PEG-1100, $n = 25$; Clariant, Charlotte, NC); platinum(0)-1,3-divinyl-1,1,3,3-tetramethyldisiloxane complex solution (Karstedt's catalyst, Pt; Sigma-Aldrich Inc., St. Louis, MO); tris(triphenylphosphine)rhodium(I) chloride (Wilkinson's catalyst, Rh; Sigma-Aldrich Inc., St. Louis, MO); Fisherbrand™ activated carbon charcoal, 6–14 mesh (Fisher Scientific, Pittsburgh, PA); N,N,N',N'-tetrakis(2-hydroxypropyl)ethylene diamine (HPED, 99%; Sigma-Aldrich Inc., St. Louis, MO); triethanolamine (TEA, 98%; Sigma-Aldrich Inc., St. Louis, MO); trimethyl-1,6-hexamethylene diisocyanate, 2,2,4- and 2,4,4-mixture (TMHDI; TCI America Inc., Portland, OR); hexamethylene diisocyanate (HDI; TCI America Inc., Portland, OR); T-131 (Air Products and Chemicals, Inc., Allentown, PA); BL-22 (Air Products and Chemicals, Inc., Allentown, PA); Enovate 245fa blowing agent (Honeywell International, Inc., Houston, TX); 2-propanol 99% (IPA; VWR, Radnor, PA); and deionized (DI) water (>17 M Ω cm purity; Millipore water purifier system, Millipore Inc., Billerica, MA) were used as received.

All reactions were conducted under a N_2 atmosphere with a Teflon-covered stir bar to agitate the reaction mixture. Chemical structures were confirmed using proton nuclear magnetic resonance (1H NMR) spectroscopy using a Mercury 300 MHz spectrometer operating in the Fourier transform mode with $CDCl_3$ as the standard.

2.1. Synthesis of siloxane-polyethylene glycol ether amphiphiles

Siloxane-PEG amphiphiles were synthesized using the protocol detailed by Murthy et al. [24] Fig. 1 shows the reaction mechanism for the two siloxane units with the appropriate synthetic parameters. Equimolar ratios of TS and PEG allyl methyl ether ($n = 8$ or 25) were reacted to yield a siloxane-PEG amphiphile using Pt-catalyzed hydrosilylation. Similarly, equimolar ratios of PDMS and PEG allyl methyl ether ($n = 8$ or 25) were reacted using Rh-catalyzed hydrosilylation. The reaction components were added to a round-bottom flask equipped with a rubber stopper and heated to 80 °C. The reaction progressed for 12 h, after which its completion was monitored with Fourier transform infrared (FTIR) spectroscopy. An aliquot of the reaction solution was placed on a KBr plate, and the FTIR spectrum was obtained. The disappearance of the si-H peak at 2155 cm^{-1} suggested complete functionalization. The catalyst was removed from the product by refluxing the reaction mixture with activated charcoal for 12 h. The final product was isolated by vacuum filtration and removal of volatiles under reduced pressure.

TS (1 mol eq.), PEG allyl methyl ether ($n = 8$) (1 mol eq.), and 0.003 mol eq. of Karstedt's catalyst were reacted using hydrosilylation in toluene. The final liquid product, TS-PEG(350), was purified with a yield of 93%. 1H NMR (δ , ppm): -0.2 to 0.26 (m, 3H, $SiCH_3$), 0.42 (m, 2H, $SiCH_2CH_2$), 1.59 (m, 2H, $SiCH_2CH_2$), 3.4 (t, 3H, OCH_3), 3.5 – 3.8 (m, 2H, OCH_2CH_2).

TS (1 mol eq.), PEG allyl methyl ether ($n = 25$) (1 mol eq.), and 0.004 mol eq. of Karstedt's catalyst were reacted using hydrosilylation in toluene. The final solid product, TS-PEG(1100), was purified with a yield of 93%. ^1H NMR (δ , ppm): -0.01 to 0.26 (m, 3H, SiCH_3), 0.42 (m, 2H, SiCH_2CH_2), 1.59 (m, 2H, SiCH_2CH_2), 3.4 (t, 3H, OCH_3), 3.5 – 3.8 (m, 2H, OCH_2CH_2).

PDMS (1 mol eq.), PEG allyl methyl ether ($n = 8$) (1 mol eq.), and 0.0007 mol eq. of Wilkinson's catalyst were reacted using hydrosilylation in toluene. The final liquid product, PDMS-PEG(350), was purified with a yield of 93%. ^1H NMR (δ , ppm): -0.15 to 0.65 (m, 3H, SiCH_3), 0.95 (m, 2H, SiCH_2CH_2), 1.6 (m, 2H, SiCH_2CH_2), 3.4 (m, 3H, OCH_3), 3.5 – 4.6 (m, 2H, OCH_2CH_2).

PDMS (1 mol eq.), PEG allyl methyl ether ($n = 25$) (1 mol eq.), and 0.0007 mol eq. of Wilkinson's catalyst were reacted using hydrosilylation in toluene. The final solid product, PDMS-PEG (350), was purified with a yield of 97%. ^1H NMR (δ , ppm): -0.18 to 0.56 (m, 3H, SiCH_3), 0.50 (m, 2H, SiCH_2CH_2), 1.59 (m, 2H, SiCH_2CH_2), 3.4 (m, 3H, OCH_3), 3.5 – 4.34 (m, 2H, OCH_2CH_2).

2.2. FTIR spectroscopy

1–2 drops of the product were placed on a KBr plate, and FTIR spectra were collected using a Bruker ALPHA Infrared Spectrometer (Bruker, Billerica, MA). Thirty-two background scans of the blank KBr plate were taken followed by sixty-four sample scans of the various surfactant compositions. FTIR spectra were collected in absorption mode at a resolution of 4 cm^{-1} . OPUS software (Bruker, Billerica, MA) was utilized to subtract the background scans from the spectra, to conduct a baseline correction for IR beam scattering, and to perform an atmospheric compensation to remove carbon dioxide peaks. Each composition was measured three times.

2.3. Mass spectrometry

Matrix-assisted laser desorption ionization (MALDI) experiments were performed on a Voyager DE-STR mass spectrometer (Applied Biosystems, Foster City, CA) under optimized conditions in positive linear mode. Ions were generated by a pulsed nitrogen laser at 337 nm and accelerated through 25 kV. 100 laser shots were used per spectrum. *trans*-2-[3-(4-*t*-Butylphenyl)-2-methyl-2-prope nyridene]malononitrile (DCTB) and potassium trifluoroacetate (KTFA) were used as matrix and cationization reagents, respectively. The sample, KTFA, and matrix were prepared at concentration of 1, 10, and 20 mg/mL, respectively. The sample solution was mixed with the matrix and KTFA at a volume ratio of 1:5:1. Approximately $0.5\text{ }\mu\text{L}$ of this mixture was deposited on a stainless steel sample holder. After air-drying, the surfactant samples were analyzed using MALDI-TOF MS.

2.4. Critical micelle concentration (CMC) determination via UV transmittance

20 wt% surfactant solutions were prepared in ethanol. An iodine (I_2) solution was made in ethanol at $3.35 \times 10^{-3}\text{ M}$. Two hundred microliters of each 20 wt% surfactant solution was pipetted into a clear 96 well flat bottom plate. Serial dilutions ($n = 3$) of each solution, along with a blank control (ethanol only), were conducted to attain a concentration range of 20–0.3

wt%. Ten μL of the I_2 solution was pipetted into each well. All measurements for this study were made with a Tecan Infinite 200Pro multimode microplate reader (Tecan Group Ltd., Männedorf, Switzerland). Absorbance was acquired at 460 nm for all samples using the Tecan i-control software (Tecan Group Ltd., Männedorf, Switzerland). Transmittance (%) was calculated and plotted with respect to concentration for each surfactant.

2.5. Rheometry

A simple shear test was conducted on 1 mL of each surfactant type using a Physica MCR 301 (Anton Paar USA Inc., Ashland, VA). Viscosity was measured under a controlled shear rate of 50 s^{-1} for 120 s (6 s intervals, 20 points) for each surfactant. For solid surfactants, the rheometer plate was heated to $40 \pm 0.03 \text{ }^\circ\text{C}$ during each run. Viscosity (η) was evaluated using the RheoCompass software (Anton Paar USA Inc., Ashland, VA).

2.6. Surface tension

Hydrostatic surface tension measurements of the neat surfactants were carried out using a KSV CAM-2008 Contact Angle Analyzer (KSV Instruments, Ltd., Helsinki, Finland). A 5 μL drop of surfactant was ejected from the tip of the syringe. The drop was allowed to reach equilibrium for 60 s, and surface tension was measured using an Attension Tensometer and the Attension Theta software package (Biolin Scientific, Stockholm, Sweden). Surface tension measurements were collected and presented as the measurement average ($n = 3$).

2.7. Synthesis of SMP foams

SMP foams were synthesized using the three-step protocol described in previous work [25,26]. First, an isocyanate (NCO) prepolymer was synthesized with appropriate molar ratios of HPED, TEA, HDI, and TMHDI. These prepolymers were allowed to react for 32 h with a temperature ramp from room temperature to $50 \text{ }^\circ\text{C}$ and back to room temperature. Next, a hydroxyl (OH) mixture was blended with the remaining molar equivalents of HPED and TEA. This mixture also contained DI water and catalysts. The NCO prepolymer and the OH mixture were combined along with a physical blowing agent, Enovate, and one of the newly synthesized surfactants, TS-PEG(350), TS-PEG(1100), PDMS-PEG(350), or PDMS-PEG(1100). The siloxane surfactants appeared to solubilize well with the NCO and OH components. This mixture was mixed in a FlackTek speedmixer (FlackTek, Inc., Landrum, SC) and poured into a mold. The foam was allowed to cure at $90 \text{ }^\circ\text{C}$ for 20 min before cooling to room temperature for further processing. Table 1 shows the weight percentage of each component used for foam synthesis. Multiple foams were synthesized with varied concentrations of each surfactant type. Lower surfactant concentrations ($<0.5 \text{ wt}\%$) were selected for PDMG-PEG(350) based on the poor foam morphology observed with surfactant concentrations $>0.5\%$.

Foams were mechanically programmed by heating to $90 \text{ }^\circ\text{C}$ and compressing using a Carver press (Carver, Inc., Wabash, IN). Once cooled, the foams were cleaned using two 15 min cycles of isopropyl alcohol and four 15 min cycles of reverse osmosis water under sonication. The foams were placed in aluminum pans and frozen overnight at $-20 \text{ }^\circ\text{C}$. A FreeZone 6 (Labconco, Kansas City, MO) freeze-dryer was used to remove all water from

the cleaned foams, after which they were dried overnight under vacuum at 50 °C prior to characterization.

2.8. Density

Density measurements were conducted on foam blocks acquired from the top, middle, and bottom sections of foams, as outlined in ASTM standard D-3574 [27]. The length, width, and height of the cube were measured, the mass of the sample was recorded, and density was calculated in g cm^{-3} . Each foam block was measured three times.

2.9. Scanning electron microscopy (SEM)

Cell structure was determined by cutting thin slices of the bulk foam in the transverse direction, as indicated by ASTM standard D-3576-15 [28]. Samples were acquired from the top, middle, and bottom sections of each foam to enable imaging throughout the foam bulk. The samples were mounted onto a stage and sputter coated with gold for 60 s at 20 mA using a Cressington sputter coater (Ted Pella, Inc., Redding, CA). The samples were then visualized using a Joel NeoScope JCM-5000 scanning electron microscope (Nikon Instruments, Inc., Melville, NY) at 15 $\times$ magnification under high vacuum and 5–10 kV. SEM images were analyzed using Image J software to quantify pore sizes. An average of pore diameter acquired from each of the three sections (top, middle, and bottom) was used to provide representative pore size estimations for all foam compositions.

2.10. Strut thickness

Strut thickness was measured by cutting thin slices of bulk foams in the axial direction and imaging the samples in the bright-field mode using a Leica MZ8 microscope (Leica Microsystems, Wetzlar, Germany) with RSImage software (Photometrics, Tucson, AZ). Foam images were analyzed using Image J software (NIH, Bethesda, MD), where strut thickness was measured in microns for each foam composition.

2.11. Thermal transitions

The T_g of the foams ($n = 5$) was determined under dry and wet conditions. For dry T_g , foam samples (3–8 mg) were stored in a dry container with desiccant prior to analysis. A Q-200 differential scanning calorimeter (DSC) (TA Instruments, Inc., New Castle, DE) was used to obtain foam thermograms. The first cycle consisted of decreasing the temperature to $-40\text{ }^{\circ}\text{C}$ at $10\text{ }^{\circ}\text{C min}^{-1}$ and holding it isothermally for 2 min. The temperature was then increased to $120\text{ }^{\circ}\text{C}$ at $10\text{ }^{\circ}\text{C min}^{-1}$ and held isothermally for 2 min. In the second cycle, the temperature was reduced to $-40\text{ }^{\circ}\text{C}$ at $10\text{ }^{\circ}\text{C min}^{-1}$, held isothermally for 2 min, and raised to $120\text{ }^{\circ}\text{C}$ at $10\text{ }^{\circ}\text{C min}^{-1}$. T_g was recorded from the second cycle based on the inflection point of the thermal transition curve using TA Instruments software (TA Instruments, Inc., New Castle, DE). The aluminum tin was not vented during this step. For wet T_g , foam samples (3–8 mg) were submerged in RO water at $50\text{ }^{\circ}\text{C}$ for 5 min to allow full plasticization. After the samples were removed from water, they were pressed dry with Kimwipes (Kimberly-Clark Professionals, Roswell, GA), weighed, and placed in an aluminum pan sealed with a vented aluminum lid. A Q-200 DSC was used to cool the samples to $-40\text{ }^{\circ}\text{C}$, hold them isothermally for 2 min, and heat them to $80\text{ }^{\circ}\text{C}$ at $10\text{ }^{\circ}\text{C min}^{-1}$. TA Instruments software (TA

Instruments, Inc., New Castle, DE) was used to generate the thermogram and acquire the T_g after water plasticization using the average inflection point of the thermal transition.

2.12. Actuation studies

Actuation studies were performed on the following foam compositions: 100 HDI 7% TS-PEG(350), 100 HDI 7% TS-PEG(1100), 100 HDI 0.5% PDMS-PEG(350), 100 HDI 7% PDMS-PEG(1100), and 100 TMHDI 7% PDMS-PEG(1100). The foam compositions were selected to allow comparison of each surfactant at a concentration that is comparable to that used previously with commercial surfactants (7%), except in the case of PDMS-PEG(350), where the maximum surfactant concentration that resulted in stable foams was 0.5%. The use of 100HDI and 100 TMHDI foams with PDMS-PEG (1100) provides information on the ability to control actuation with foam hydrophobicity. Cylindrical foam samples ($n = 3$) with a diameter of 4 mm and a height of 1 cm were cut. A 203.20 μm diameter nickel-titanium (Nitinol) wire (NDC, Fremont, CA) was inserted through the center of the sample along its length to serve as a stabilizer. The foam samples were radially compressed to their smallest possible diameter using a ST 150-42 stent crimper (Machine Solutions, Flagstaff, AZ) by heating the material to 100 $^{\circ}\text{C}$, holding it isothermally for 15 min, and programming the foams to the crimped morphology. Initial foam diameter was measured and recorded for each sample using Image J software. The foams were placed in a water bath at 37 $^{\circ}\text{C}$, and images were taken at 30 s, 1 min and every minute thereafter until 15 min, followed by one image every 5 min thereafter until 30 min. Foam diameter was measured at each time point using Image J software. The final diameter of the samples was measured and recorded using Image J software. Percent volume recovery was calculated using Eq. (1), and volume expansion was calculated using Eq. (2).

$$\% \text{ Volume Recovery} = \left(\frac{\text{Recovered diameter}}{\text{Original diameter}} \right)^2 * 100 \quad (1)$$

$$\% \text{ Volume Expansion} = \left(\frac{\text{Recovered diameter}}{\text{Compressed diameter}} \right)^2 \quad (2)$$

3. Results and discussion

3.1. Siloxane-PEG ether amphiphiles

Four surfactants were successfully synthesized with high yield and appropriate siloxane to PEG coupling, as demonstrated by ^1H NMR, FTIR, and MALDI (Supplemental Information). Evaluation of CMC of the siloxane-PEG surfactants and commercial surfactants is presented in the Supplemental Information. Characterization of the rheological changes for each amphiphile is shown in Table 2. Molecular weight played a major role in changing the surfactant viscosity. Lower molecular weight amphiphiles, TS-PEG(350) and PDMS-PEG(350), had lower viscosities of 9.60 ± 0.02 mPa s and 66.27 ± 0.03 mPa s, respectively. The sharp increase in viscosity for PDMS-PEG(350) compared to its TS

counterpart is attributed to the high molecular weight of (~580 Da) PDMS relative to that of TS (222 Da). Furthermore, TS-PEG(1100) and PDMS-PEG(1100) had higher viscosities of 75.69 ± 0.10 mPa s and 169.00 ± 0.12 mPa s, respectively. The long chain lengths of PEG (1100) and PDMS contributed to the higher viscosities compared to lower molecular weight counterparts. Relative to commercial products, the siloxane-based surfactants had low viscosities, which is likely due to the linear and branched structure of the surfactants as compared to the graft-type commercial surfactants.

Surfactant surface tensions were comparable to those of commercially available surfactants utilized in polyurethane foam synthesis, with values ranging between 20 and 21 mN/m (Table 2). These surface tension values are indicative of the ability of these surfactants to generate a surface tension gradient and thereby serve as cell stabilizers for polyurethane foam blowing.

3.2. Morphology of SMP foams

Qualitatively, SEM micrographs of the various SMP foams show changes in pore uniformity with different surfactant types (Fig. 2). TS-PEG(350) and TS-PEG(1100) yielded foams with uniform pores and some open pores (Fig. 2a and b). PDMS-PEG(350) yielded foams with non-homogenous pores with both large and small bubbles (Fig. 2c). The pore irregularity further suggests the role of CMC in foam morphology, as small bubbles coalesced to form larger, irregular pores. As shown in Fig. 2d, PDMS-PEG(1100) also yielded uniform pores with mostly closed cells. Surfactants that resulted in smaller pores provided more consistent bulk foams. Smaller pores are potentially a result of improved cell stability during foam blowing, as the surfactant stabilizes the small pores upon generation and prevents them from coalescing into larger pores. Specifically, TS-PEG(1100) yielded more isotropic pores with the isotropicity of 0.89 compared to PDMS-PEG(1100), where the pore isotropicity was 0.77. Increased isotropicity generally resulted in smaller pore sizes. Due to the desirable foam morphology of PDMS-PEG(1100)-based foams, alternative polymer compositions containing 100% TMHDI were pursued to test surfactant viability for different systems. Ultra-low densities are maintained with the TMHDI foam compositions, and SEM images demonstrate uniform pores (Table 3, Fig. 2e). These results indicate the suitability of PDMS-PEG(1100) as a surfactant for varied polyurethane systems. Foam pore sizes were also affected by surfactant type and concentration (Fig. 3). At low TS-based surfactant concentrations (0.5–1%), the foam pore sizes are larger (>3000 μm) compared to higher concentrations of 4% and 7%, where the pore sizes decrease to approximately 2000 μm (Fig. 3a and b). Alternatively, for PDMS-based surfactants, the pore sizes remain fairly consistent around 1500–2000 μm with no discernable trend (Fig. 3c and d).

Strut thickness of the porous SMP systems was also dependent on the surfactant type and concentration. Controlling the strut thickness could provide an alternative route to tuning the mechanical properties of the scaffolds, as thicker struts are hypothesized to result in more mechanically robust systems. Quantitative results in Fig. 3 demonstrate changes in strut thickness, and visual assessment of strut thickness is shown in the microscopic images in Fig. 4. Lower concentrations of TS-based surfactants resulted in thicker pore struts due to the lack of polymer spreading at the air-liquid interface. As surfactant concentration

increased, the struts became thinner due to polymer mixture stabilization during bubble growth. Namely, low surfactant concentrations (0.5% and 1%) (Fig. 3a) of TS-PEG(350) yielded foams with strut diameters of $70 \pm 5 \mu\text{m}$ and $42 \pm 8 \mu\text{m}$, respectively. At higher concentrations of 4% and 7%, the strut thicknesses were reduced to approximately $30 \mu\text{m}$ (Fig. 4a). Similar trends were noted with TS-PEG(1100) foams. At 0.5% PDMS-PEG(350), the strut thickness increased due to cell destabilization; however, no definite trend could be established (Figs. 3c and 4c). As shown in Figs. 3d and 4d, minimal changes in strut diameter were observed with increasing concentration for PDMS-PEG(1100), where struts were approximately $22 \mu\text{m}$ over the range of surfactant concentrations. There was no trend in strut thickness for SMP foams synthesized using PDMS-based surfactants.

SMP foams were synthesized using each of the four surfactants, and their physical properties were characterized, as shown in Table 3. Stable foam formulations with consistent densities of approximately $0.02\text{--}0.03 \text{ g cm}^{-3}$ were obtained for all surfactant types at varied concentrations. The SMP foams had minimal variation in density, which indicates the crucial role of cell stabilizers in developing homogenous, ultra-low density porous systems. However, higher concentrations of TS-PEG surfactants generally resulted in increased densities due to smaller pores. It should be noted that higher concentrations ($>0.5\%$) of PDMS-PEG(350) resulted in bubble coalescence and foam collapse. It can be hypothesized that PDMS-PEG(350), at above 0.5% concentration, reached the critical micelle concentration (CMC). Above the CMC, surfactant/polymer interactions are disrupted, and surfactant molecules interact with each other, causing micelle formation that prevents the surfactants from providing phase stability.

Physical properties of the SMP foams fabricated with the four siloxane-based surfactants had minimal variation as a function of surfactant type (Table 3). 100% HDI foams had a dry and wet T_g of approximately 50°C and 17°C , respectively, for all surfactant types. The T_{trans} of 100% HDI SMP foams synthesized using commercial surfactants, DC 4000 and DC 5169, was reported by Singhal et al. to be 55°C under dry conditions for H60 compositions [8]. Lack of variation in T_g with varied surfactant structure indicates that the surfactants serve only as cell stabilizers without added plasticization of the polymer. The 100 TMHDI foams, synthesized using PDMG-PEG(1100), maintain a T_{trans} value of $57 \pm 1^\circ\text{C}$, which is close to the T_g reported in literature ($58 \pm 1^\circ\text{C}$ for 100% TMHDI formulations with commercial surfactants) [29]. The siloxane-PEG surfactants generated in this study had a minimal effect on thermal properties of SMP foams and provided materials that are comparable to those synthesized with commercially available products.

Further characterization of the actuation profiles of the SMP foams showed that foams synthesized using TS-based surfactants actuated fully within the first 3 min of exposure to physiological temperatures in an aqueous environment (Fig. 5a). The volume recovery of these foam compositions was 100%, which is indicative of their rapid shape memory behavior (Table 3). Due to the relatively hydrophilic nature of HDI, the rapid actuation and high volume recovery are expected outcomes. In contrast, PDMS-PEG(350) SMP foams experienced slower recovery, with full actuation achieved after 10 min. Additionally, the volume recovery of the PDMS-PEG(350) foams was lower compared to other compositions, at only 77%. The irregular pore morphology of the SMP foams synthesized using PDMS-

PEG(350) could have a potential effect on reducing the shape memory behavior of the system. However, the total volume expansion ($21\times$) of these foams was similar to TS-based formulations. 100 HDI, PDMS-PEG(1100) foams also experienced rapid actuation, with volume recovery similar to that of TS-based foam formulation. The 100 TMHDI foam composition with PDMS-PEG(1100) experienced slower actuation, with full recovery achieved after 20 min (Fig. 5b). The presence of methyl groups on TMHDI increased the foam hydrophobicity; hence, slower water plasticization and recovery profiles were observed. However, the volume recovery of this system was 110%, indicating preservation of the shape memory behavior of the material. Both foam compositions had actuation profiles comparable to the SMPs synthesized using commercial surfactants. Controlling shape recovery of the SMP foams is important for modifying material properties to match application needs. For example, fast volumetric recovery is desirable for wound hemostatic treatments, while slow actuation would be optimal for aneurysm occlusion devices that require delivery through a micro-catheter.

4. Conclusions

Silicone surfactants are widely used as cell stabilizers in the polyurethane foam industry [13,15,19,30]. In this work, siloxane-PEG surfactants were successfully synthesized with high yield using hydrosilylation to serve as cell stabilizers during shape memory polyurethane foam synthesis. Traditionally, graft-type surfactants are used in polyurethane foam synthesis [31–33]. This work studies the development of branched and linear surfactants as cell stabilizers. The surfactants had low surface tension, similar to commercially available products [15]. Siloxane-PEG surfactants stabilized the foam cells during synthesis of porous SMPs. By lowering the surface tension within the struts, the surfactants allowed liquid polymer spreading at the interface. In addition to pore stability, the surfactants played a key role in tuning the pore size and morphology of the SMP foams. Furthermore, strut thickness of the foams was heavily dependent on surfactant type and concentration. Controlling the strut thickness also provides a means to control foam morphology and mechanical properties for a variety of applications.

Overall, surfactant properties and performance were similar to those of commercially available cell stabilizers, indicating their potential use in quality-controlled SMP foam synthesis. The effects of TS- and PDMS-based surfactants on the morphology of SMP foams must be evaluated to gain a full understanding of their utility as cell stabilizers. Surfactant interaction with the polymer is governed by the ionic nature of the two systems. Therefore, further studies will be conducted on SMP systems with varying polyol and polyisocyanate constituents to gain an improved understanding of these surfactant systems. It is key to note that the morphological properties of SMP foams synthesized here, using linear and branched surfactants, were similar to those synthesized with commercially available branched surfactants, such as Tegostab BF 2370, while their surface tension matches those of the graft-type surfactants, such as DABCO DC 198 and DABCO DC 5943. The ability to synthesize tunable surfactants in-house eliminates the reliance upon a single-source surfactant supplier to aid commercialization of SMP foams for use in biomedical applications. Additionally, synthesis of siloxane-PEG surfactants provided a means of

controlling the purity and manufacturing capabilities of individual components utilized in polyurethane foaming.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.jcis.2016.06.031>.

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HIGHLIGHTS

- PU foam surfactants were prepared by hydrosilylation of siloxanes to PEG.
- The surfactants were used as cell stabilizers for shape memory polyurethane foams.
- Surfactants controlled cell morphology and eliminated single-source reliance.

Fig. 1. Hydrosilylation reaction schematic of (a) trisiloxane and (b) poly(dimethylsiloxane) hydride terminated with poly(ethylene glycol) allyl methyl ether ($n = 8$ or 25).

Fig. 2. SEM images of SMP foams with varying pore sizes based on surfactant type. (a) 100 HDI 7% TS-PEG(350), (b) 100 HDI 7% TS-PEG(1100), (c) 100 HDI 0.5% PDMS-PEG (350), (d) 100 HDI 7% PDMS-PEG(1100), and (e) 100 TMHDI 7% PDMS-PEG(1100).

Fig. 3.

Pore size and strut thickness of SMP foams fabricated using the siloxane-PEG surfactants.

(a) TS-PEG(350), (b) TS-PEG(1100), (c) PDMS-PEG(350), and (d) PDMS-PEG (1100).

Fig. 4. Micrographs of SMP foams with varying strut thickness based on surfactant type and concentration. (a) TS-PEG(350), (b) TS-PEG(1100), (c) PDMS-PEG(350), and (d) PDMS-PEG(1100).

Fig. 5. Actuation profiles of (a) 100 HDI foams and (b) 100 TMHDI foams synthesized with siloxane-PEG surfactants.

Table 1

Composition of foams synthesized with 100% HDI or 100% TMHDI with various surfactant types and concentrations.

Foam composition	Surfactant type	Surfactant (wt%)	TMHDI (wt%)	HDI (wt%)	T-131 (wt%)	BL-22 (wt%)	HPED (wt%)	TEA (wt%)	DI H ₂ O (wt%)	Enovate (PPH)
100 HDI H67	TS-PEG(350)	0.5	–	65	0.4	1.0	23	8	3	4
		1	–	65	0.4	1.0	23	8	3	4
		4	–	63	0.4	1.0	22	7	3	4
		7	–	61	0.4	0.9	21	7	3	4
100 HDI H67	TS-PEG(1100)	0.5	–	65	0.4	1.0	23	8	3	4
		1	–	65	0.4	1.0	23	8	3	4
		4	–	63	0.4	1.0	22	7	3	4
		7	–	61	0.4	0.9	21	7	3	4
100 HDI H67	PDMS-PEG(350)	0.1	–	65	0.4	1.0	23	8	3	4
		0.25	–	65	0.5	1.4	23	8	3	4
		0.5	–	65	0.5	1.4	23	8	3	4
100 HDI H67	PDMS-PEG(1100)	0.5	–	65	0.5	1.3	23	8	3	4
		1	–	64	0.5	1.3	22	8	3	4
		4	–	62	0.5	1.3	22	7	3	4
		7	–	61	0.5	1.2	21	7	3	4
100 TMHDI H60	PDMS-PEG(1100)	6	66	0	0.3	0.7	17	8	2	1

Table 2

Rheological and surface tension properties of the various siloxane-PEG surfactants.

Surfactant	Viscosity (mPa s)	Surface tension (mN/m)
Dabco DC 198	2470.4 ± 17.3	20.0 ± 0.1
Dabco DC 5943	1277.2 ± 2.5	20.9 ± 0.1
TS-PEG(350)	9.6 ± 0.1	21.0 ± 0.1
TS-PEG(1100)	75.7 ± 0.1	20.1 ± 0.3
PDMS-PEG(350)	66.3 ± 0.1	21.3 ± 0.1
PDMS-PEG(1100)	169.0 ± 0.1	20.3 ± 0.1

Table 3

Key physical properties of SMP foams synthesized using siloxane-PEG surfactants.

Surfactant type	Foam composition	Surfactant (wt%)	Density (g cm ⁻³)	Dry T _g (°C)	Wet T _g (°C)	Volume recovery (%)	Volume expansion (x)
TSS-PEG(350)	100 HDI H67	0.5	0.017 ± 0.001	–	–	–	–
		4	0.024 ± 0.002	–	–	–	–
		7	0.028 ± 0.004	52 ± 2	16 ± 2	103 ± 11	23 ± 3
TSS-PEG(1100)	100 HDI H67	0.5	0.019 ± 0.001	–	–	–	–
		4	0.028 ± 0.002	–	–	–	–
		7	0.026 ± 0.004	51 ± 2	16 ± 2	100 ± 18	22 ± 4
PDMS-PEG(350)	100 HDI H67	0.1	0.018 ± 0.009	–	–	–	–
		0.25	0.025 ± 0.002	–	–	–	–
		0.5	0.019 ± 0.001	53 ± 3	17 ± 2	77 ± 5	21 ± 6
PDMS-PEG(1100)	100 HDI H67	0.5	0.022 ± 0.003	–	–	–	–
		4	0.016 ± 0.001	–	–	–	–
		7	0.017 ± 0.001	48 ± 1	17 ± 1	93 ± 14	32 ± 10
	100 TMHDI H60	7	0.024 ± 0.002	57 ± 1	32 ± 1	110 ± 1	17 ± 4