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Lipid-induced degradation in biocompatible poly(Styrene-Isobutylene-Styrene) (SIBS) thermoplastic elastomer

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ABSTRACT

The thermoplastic elastomer Poly(Styrene-block-Isobutylene-block-Styrene) (SIBS) is highly biocompatible, which has led to its use in several commercially-available implants. However, lipid-induced degradation has been previously identified as a primary cause of failure in long-term SIBS implants subject to mechanical loading. Thus, understanding the mechanisms and extent of lipid-induced damage and the role of styrene-isobutylene ratio and molecular weight is critical to improving longevity of SIBS-based implants in order to fully exploit the biocompatibility advantages. Samples of four different SIBS formulations were fabricated via compression molding, immersed to lipid saturation contents from 5 to 80% by weight, and tested in uniaxial tension, stress relaxation, and dynamic creep modes. Degradation mechanisms were investigated via infrared spectroscopy, chromatography, and microscopy. No evidence of lipid-induced chemical interactions or chain scissoring was observed. However, a decrease in tensile strength, loss of dynamic creep performance and faster relaxation with increasing lipid content is attributed to strong internal straining. The magnitude of these losses is inversely proportional to both molecular weight and styrene content, suggesting that selection of these variables during the design phase should be based not only on the mechanical requirements of the application, but the expected degree of lipid exposure.

1. Introduction

Poly(Styrene-*block*-Isobutylene-*block*-Styrene) (SIBS) is a thermoplastic elastomer with a phase-separated morphology that shows a very high degree of biocompatibility. With almost no foreign body reaction produced when implanted in the human body, SIBS is an ideal candidate for uses in biocompatible coatings and/or as the load-bearing structure in implantable devices (Pinchuk et al., 2008; Boden et al., 2009; Strickler et al., 2010; El Fray et al., 2006; Kamath et al., 2006). The high compatibility and *in vivo* stability is attributed to the absence of cleavable moieties and lack of groups that suffer oxidation, hydrolysis or enzymatic cleavage such as esters, amides, ethers, carbamates, urea, and others. In addition to this excellent biocompatibility, SIBS can be tailored to achieve different mechanical properties based on styrene/isobutylene ratio and molecular weight. The styrene phase and isobutylene phase are incompatible, and the resulting morphology is a separated styrene domain that varies in shape and size depending on composition (El Fray et al., 2006; Antony et al., 2004; Crawford et al., 2001; Storey et al., 1996). Varieties with lower relative styrene content have a mechanical response similar to that of a rubber, whereas formulations with a higher relative styrene content behave like a toughened plastic (Crawford et al., 2001; Storey et al., 1996; Puskas et al., 2003; St. Lawrence et al., 2001; Fittipaldi et al., 2015). As a result, SIBS is suitable for a wide range of applications with different mechanical requirements without sacrificing biocompatibility. Further, thermoplastic elastomer materials like SIBS are not vulcanized and can be thermoformed via standard molding processes, thereby significantly reducing manufacturing cost. Together, these characteristics form a strong argument for the use of SIBS *in vivo*, regardless of the mechanical requirements of any particular application. However, the long-term performance of SIBS in the *in vivo* environment is a necessary component in assessing the practical benefit of the material.

There are many different aspects of the *in vivo* environment that can affect the longevity and strength of polymeric materials, and in some cases lead to failure of implants. A characteristic of nearly all implant environments is the presence of lipids in location-dependent concentrations. The overwhelmingly negatively effect of lipids on many polymers used in biomedical applications is well-documented. Consequently, much effort has gone into understanding the mechan-

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isms of this damage in order to predict material properties during long term *in vivo* use. To that end, microstructural changes in a common implantable polymer, ultra-high molecular weight polyethylene (UHMWPE), were studied by accelerated aging in lipid-rich environments. It was found that lipids triggered an oxidative degradation in polyethylene (Puppulin et al., 2015). Another study on UHMWPE showed that synovial fluid lipids can initiate and accelerate oxidation even without the presence of free radicals. Furthermore, it was found that the crosslink density is significantly affected by the presence of lipids in the network, and this can negatively affect the mechanical properties of polyethylene (Oral et al., 2012). Sakoda *et al*. also studied the lipid induced degradation on UHMWPE and found that elastic modulus and elongation decreased, with maximum degradation occurring in locations of maximum lipid concentration (Sakoda and Niimi, 2016). Lipid induced degradation has also been studied in other systems, showing very similar results as those in UHMWPE. Thomas et al. studied *in vitro* ageing of polyurethane urea in a palm oil solution and found that mechanical properties decreased with exposure to the lipid-rich medium (Thomas and Jayabalan, 2009). SIBS has also been observed to deteriorate in the presence of lipids. Specifically, a SIBS trileaflet heart valve was tested in a sheep model to assess the feasibility of using SIBS in artificial heart valves. However, the study revealed that SIBS suffered lipid-induced plasticization that led to creep and surface cracking during implantation, and ultimately the death of the test animals (Wang et al., 2010). Though this failure was well-reported, no comprehensive study was performed in order to fully explore the mechanisms of degradation or identify potential solutions.

Previously, we have reported and characterized lipid diffusion behavior in SIBS. It was observed that lipid diffusion kinetics conform to Fickian diffusion behavior very closely. Additionally, lipids were observed to severely plasticize the isobutylene phase, leading to blistering and surface cracking. Prominent swelling was also observed for all different formulations of SIBS studied, with increased swelling in formulations with higher relative volume of isobutylene (Fittipaldi and Grace, 2016). However, the underlying reason for the deleterious effect of lipids in SIBS has not yet been fully understood or modeled, and its early effects on mechanical and viscoelastic properties have not been determined. In this study, the mechanical and viscoelastic properties of four different formulations of SIBS are evaluated at different lipid contamination levels in order to determine the effect of lipid-induced softening and network relaxation. These results, coupled with Fourier transform infrared spectroscopy (FTIR), Gel Permeation Chromatography (GPC), and Scanning Electron Microscopy (SEM) analysis, contribute to a better understanding of the long-term performance of SIBS in lipid-rich environments and identification of potential degradation mitigation methods.

2. Materials and methods

KANEKA Corporation provided four types of SIBS (SIBSTAR 103, 102, 73 and 72) in pellet form. Table 1 shows the composition of SIBS as determined by GPC, along with the diffusion coefficient and the saturation lipid (equilibrium) content obtained via gravimetric analysis (Fittipaldi and Grace, 2016). To ensure all residual moisture was removed from the SIBS pellets, they were dried in a vacuum oven until constant weight measurements were recorded over a 12 h interval. SIBS 102, 73, and 72 pellets were compression molded using 8 MPa of pressure at 193 °C for 10 min, then folded and compressed again for another 10 minutes, and allowed to slowly cool to room temperature in order to fabricate SIBS sheets with no weld or flow lines. SIBS 103 was compressed at 220 °C because of its higher melting temperature, while all other process parameters remained the same as the other formulations. All SIBS sheets had dimensions of 300 by 300 mm and a thickness of approximately 0.5 mm. Tensile and stress relaxation specimens were cut using an arbor press and a die in accordance with ASTM D412 Type C, and dynamic creep specimens were cut using a rectangular die to prepare 6.35 by 33 mm specimens. All weights and dimensions were recorded using a high precision analytical balance and a rubber thickness gauge for consistent measurement.

Table 1
SIBS formulation and diffusion parameters.

	Styrene content (wt. %)	M_w (g/mol)	Diffusion coefficient (mm^2/hour)	Lipid saturation content (wt. %)
SIBS 103	30	106,000	1.42×10^{-4}	44.8
SIBS 102	15	117,000	1.24×10^{-4}	59.3
SIBS 73	30	76,000	1.44×10^{-4}	54.3
SIBS 72	22	75,000	1.65×10^{-4}	62.8

Samples were immersed in glass jars filled with palm oil at 37 °C and kept in constant temperature water baths until target saturation contents were reached (5%, 10%, 15%, 20%, 30%, 40%, 60% and 80% of the lipid saturation content). Palm oil was chosen because it is mainly composed of palmitic acid, oleic acid, and linoleic acid in triglyceride form (Tan and Che Man, 2000; Haryati et al., 1998). These triglycerides can be found in human plasma, adipose tissue, the stratum corneum, and in many other areas (Kingsbury et al., 1961; Lampe et al., 1983; Hodson et al., 2008), making it a suitable simulant of human body lipids. Lipid concentration *in vivo* is variable, and lower than the conditions described here. However, palm oil was used in its undiluted form for this first-of-its-type analysis in order to establish a baseline, worst-case exposure condition and to isolate the effect of lipids on degradation. After each immersion period, specimens were removed from the oil and cleaned by dabbing with oil absorbent towels. To ensure the full removal of all surface lipids, the specimens were rinsed in acetone for twenty seconds, removed and allowed to fully dry before weighing and measuring dimensional changes. Acetone was chosen because it is non-aggressive to SIBS and it is volatile, ensuring that all surface acetone was quickly evaporated.

Dumbbell specimens were tested in a universal testing frame in accordance with ASTM D412 at a rate of 500 mm/min, utilizing self-tightening roller grips to ensure all specimens would break in the narrow section. Stress relaxation experiments were performed for 16 minutes with an initial stress of 5 MPa for all types of SIBS. Rectangular specimens were fatigued for 10,000 cycles in tension using a DMA Q800 (TA Instruments®) at a stress level of 100 kPa for SIBS 72 and 102 and 250 kPa for SIBS 73 and 103. Different stress levels were used in order to accommodate the different strain levels based on relative styrene content. FTIR was performed using a PerkinElmer® Frontier instrument.

3. Results and discussion

3.1. FTIR and GPC

Fig. 1 shows the results of FTIR performed on all samples of uncontaminated SIBS, saturated SIBS and undiluted palm oil. Palm oil showed no broad peak corresponding to the O–H stretch at around 3300 cm^{-1} that would be present for the carboxyl group in free fatty acids. This indicates that all fatty acids are bound to glycerol forming ester bonds, which is identical to how it would be present in blood plasma. The spectra does not show any evidence of chemical interaction between the polymer specimen and the absorbed oil, nor any degradation of the polymer due to environmental aging. Further inspection reveals that the spectra of saturated SIBS appears to be a linear combination of the uncontaminated SIBS and palm oil spectra. In the region of 1800–1700 cm^{-1} a strong peak corresponding to the C=O stretch can be observed, and is attributed to the ester group in the triglycerides (Rohman and Man, 2010). This peak can be observed for the palm oil spectra and the palm oil saturated sample due to the absorption of triglycerides in SIBS.