In vitro Biostability of Segmented Polyisobutylene-Based Thermoplastic Polyurethanes

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Statement of Purpose: Thermoplastic polyurethanes (TPUs) are the most commonly used biomaterials in the production of blood contacting biomedical devices and increased biostability is a coveted quality.[1] Conventional polyether- or polyester-based polyurethanes are susceptible to oxidative and hydrolytic degradation *in vivo*, respectively.[2] Recently there have been attempts to increase the biostability of TPUs by incorporating stable elastomeric components such as poly(dimethylsiloxane) soft segments.[3] Limiting the syntheses of such polyurethanes are miscibility issues between polar hard segment (HS) and nonpolar soft segment (SS).[3] Incorporation of poly(hexamethylene oxide) (PHMO) was necessary to produce TPUs with adequate mechanical properties. The resulting polyurethanes have shown retarded degradation.[4] Polyisobutylene (PIB) has excellent biostability as demonstrated by the application of a PIB copolymer as polymer coating in Taxus™ (Boston Scientific Corp.) drug eluting coronary stent system. Previous attempts to synthesize PIB-based TPUs with adequate mechanical properties were unsuccessful.[5] Recently we have reported that incorporation of 10-30% poly(tetramethylene oxide) (PTMO) diol in the SS significantly improved the mechanical properties of PIB-TPUs.[6] This study observed the resistance of said TPUs to *in vitro* accelerated metal ion oxidative (MIO) degradation.

Methods: Pellethane™ 2363-55D and Pellethane™ 2363-80A used as controls, were obtained from Dow Chemical Co. The PIB-PTMO polyurethanes of varying hardness and compositions were synthesized as reported previously.[5] Polyurethane films were placed in vials and soaked in a 20% H_2O_2 in aqueous 0.1 M $CoCl_2$ solution and at 50 °C. The solutions were changed every other day to ensure a constant concentration of radicals. At time points after 1, 2, 4, 6, and 12 weeks, dedicated samples were removed from the oxidative environment, washed, and dried for analysis. Dry samples were characterized by weight loss, ATR-FTIR (Thermo Electron Corp. Nicolet 4700 FT-IR with a Thermo Electron Corp. Smart Orbit attachment for ATR with a diamond crystal) spectroscopy, tensile strength (Instron Model Tensile Tester 4400R), elongation at break, SEM (JEOL model JSM 7401F FE-SEM), and gel permeation chromatography (MiniDawn, Wyatt Technology Inc.).

Results/Discussion: The PIB-based TPUs showed significant oxidative stability as compared to the commercial controls such as Pellethane™ 2686-55D and 2686-80A. After 12 weeks *in vitro* (equivalent of ~ 10 years *in vivo*) the PIB-PTMO TPUs with 10-20% PTMO in the SS showed 6-15% weight loss whereas the Pellethanes degraded completely in about 9 weeks (Figure 1). The weight loss was linearly proportional to the PTMO content in the PIB-PTMO TPUs. ATR-FTIR spectroscopy confirmed the degradation of Pellethanes via MIO by the consistent disappearance of aliphatic C-O-C stretching frequency at ~1110 cm^{-1}, and appearance of a crosslinking C-O-C frequency at ~1174 cm^{-1}. However, no such absorption band was apparent in the spectra of the PIB-based TPUs. The PIB-based TPUs exhibited 10-30% drop in tensile strength compared to 100% for the Pellethanes after 12 weeks. The drop in tensile strength correlated approximately with PTMO content in the TPU. Molecular weight results correlated well with tensile strength, showing a slight decrease 10-15% at 12 weeks. The Pellethanes showed a dramatic decrease in M_n as well as an increase in low molecular weight degradation product. SEM showed severe cracking in the Pellethanes after two weeks, whereas the PIB-based TPUs exhibited a continuous surface morphology at least up to six weeks. Some small shallow craters were observed in some of the softer samples after 12 weeks that maybe attributed to processing issues. The weight loss, tensile, and SEM data correlate well with each other and indicate excellent biostability of these materials.

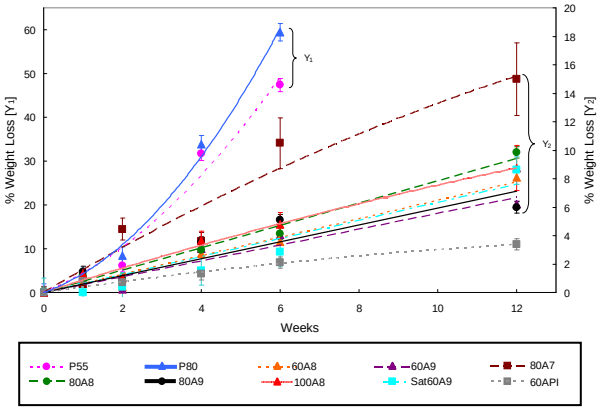

Figure 1. Weight Loss vs. Degradation time

Conclusions: PIB-based TPUs containing 10-20% PTMO in the SS exhibit excellent stability against MIO. The amount of PTMO diol used in the polyurethane dictates the degradation rate. These TPUs are highly promising candidates for biomedical device applications requiring long-term *in vivo* biostability.

References:

[1] Ciardelli G. Macromol Symposia 2004; 218: 261-271
[2] Stokes K. J Biomater Appl. 1995; 9: 321-354
[3] Gunatillake PA. J Appl Polym Sci. 2000; 76:2026-2040
[4] Simmons A. Biomaterials 2004; 25: 4887-4900
[5] Speckhard TA. Polymer 1985; 26: 55-68
[6] Ojha U. Polymer 2009; 50: 3448-3457

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