Accelerated Thermoplastic Polyurethane Hydrolytic Stability Screening

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Statement of Purpose: Thermoplastic polyurethanes (TPUs) have been used in several long term medical device applications due to their excellent mechanical properties, established biocompatibility and reliable fatigue strength. Numerous *in vitro* methods of screening TPUs have been developed over the years to help predict biostability of these materials. In recent years, evidence comparisons with results from *in vivo* studies have been used to evaluate the effectiveness of *in vitro* enzymatic hydrolysis and oxidative stability screening methods to predict material biostability[1,2]. Furthermore, recent investigations utilizing accelerated *in vitro* screening methods to evaluate the hydrolytic stability of commercially available TPUs has been the subject of some discussion.[3,4] In this study, we examined the hydrolytic stability of poly(ether urethanes) (Elasthane™ 80A TPU, Elasthane™ 55D TPU, PurSil® 20 80A TSPU, PurSil® 35 80A TSPU) and poly(carbonate urethanes) (Bionate® 80A PCU and CarboSil® 20 80A TSPCU) extruded films using several different methods of standard and accelerated *in vitro* treatments. The results of the test methods were compared to publications of *in vivo* testing to evaluate the overall effectiveness of those models.

Methods: *In Vitro* Hydrolytic Treatment: Unstrained films were tested in three different solutions: phosphate buffered saline (PBS) at 37°C (standard hydrolysis rate), PBS at 70°C (heat accelerated rate), and 0.5 M sodium hydroxide (NaOH) at 37°C (alkaline accelerated rate). All three test groups received weekly solution changes to maintain relatively consistent levels of water, buffer and base concentrations. Samples were removed and washed thoroughly at 0, 2, 4, 16, and 32 weeks before characterization. ***Material Characterization:*** Surface chemistry changes were monitored using attenuated total reflectance-Fourier transform infrared (ATR-FTIR) spectroscopy. Soft segment loss was quantified by determining the 1253 cm^{-1} or 1110 cm^{-1} peak height (C-O of soft segment carbonate or ether respectively) relative to the internal aromatic ring reference peak at 1598 cm^{-1}. The 1702 and 1730 cm^{-1} peak heights (hydrogen bound and non-bonded C=O of hard segment urethane) were also analyzed to monitor changes in hard segment content and hard domain interactivity. Scanning electron microscopy (SEM) was used to look at physical damage on the surface of all unstrained specimens. Strained-to-failure specimens were examined to determine chance of environmental stress cracking. Tensile strength and percent elongation were determined from stress vs. strain curves. Finally, molecular weight changes were monitored using gel permeation chromatography (GPC).

Results: Specimens subject to treatment in PBS at 37°C showed minimal changes in both surface and bulk properties throughout the full 32 week period, Figure 1. Specimens treated in PBS at 70°C all exhibited significant decreases in molecular weight after the 32 week treatment period, Figure 1. In addition, most tensile testing results showed a loss of tensile strength accompanied by an effect on percent elongation and stress-strain curve shape. Elasthane™ 55D TPU, the hardest material evaluated in this study, demonstrated the most resistance to heat accelerated treatment, where the lowest losses of both molecular weight and tensile properties were observed. Despite significant losses in bulk properties, surface chemistry remained unchanged throughout treatment for all materials, and no effects to the surface topography of any of the films was observed. Samples subject to the 0.5 M NaOH alkaline medium exhibited a very different pattern when compared to the heat accelerated group. Molecular weight changes were minor and tensile property changes were minimal. Minor losses of soft segment ether and silicone were observed in the PurSil® 35 80A TSPU specimens, while major losses of soft segment carbonate were seen in both the Bionate® 80A PCU and CarboSil® 20 80A TSPCU specimens. No effect on surface chemistry was observed in the remaining polyurethanes. Finally, SEM analysis depicted pitting and cracking in the poly(carbonate urethane) specimens.

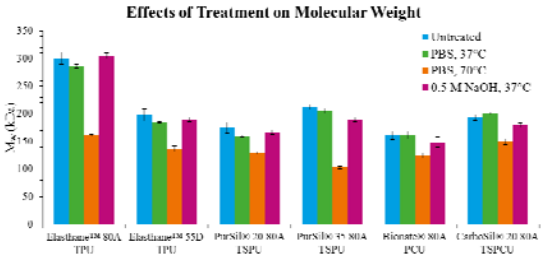

Figure 1. Changes to molecular weight after 32 weeks treatment in all three hydrolytic environments. (n=4)

Conclusions: The two accelerated test methods produced very different TPU degradation profiles when subject to both bulk and surface characterization techniques. Ultimately, the purpose of these *in vitro* accelerated tests is to project long term *in vivo* performance. While the heat accelerated test shows significant losses in molecular weight and tensile properties, no effects on surface chemistry were observed, contrary to results observed in the literature from previous *in vivo* studies on the same materials. The alkaline accelerated method shows greater evidence of surface degradation prior to effects in the bulk, which is more in line with results from *in vivo* studies.

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