Biostable Multiblock Thermoplastic Polyurethanes Incorporating Poly(ε-caprolactone) and Polyhedral Oligomeric Silsesquioxane (POSS)

Jian Wu, Xinzhu Gu and Patrick T. Mather*
Department of Biomedical and Chemical Engineering and Syracuse Biomaterials Institute, Syracuse University, Syracuse, NY 13244

Statement of Purpose: Thermoplastic Polyurethanes (TPUs) are ideal for many implantable devices due to their great versatility in chemical composition and excellent performance in mechanical properties and biocompatibility. Biostability is a great challenge and of critical importance for polyurethanes materials applied as long-term medical implants, including artificial hearts components, valves, and small bore vascular grafts. Recently, our research group discovered that covalently bonded polyhedral oligomeric silsesquioxane(POSS), an inorganic silicon-oxygen(Si-O) cage and up to eight organic groups pendant to each corner of the cage with the size of 1~3 nm, dramatically suppresses the enzymatic degradation of poly(ε-caprolactone) (PCL)-polyethylene glycol (PEG) based multi-block TPUs hydrogels following a surface passivation mechanism.[1] To further engender oxidative stability, we have extended this PCL-PEG-POSS TPUs architecture to include PEG-free, PCL-based multi-block thermoplastic polyurethanes incorporating POSS. In this paper, we systematically assessed the dependence of enzymatic and oxidative stability on the chemical structures of hard-blocks (POSS) and chain extenders (diisocyanates).

Methods: Multi-block TPUs were synthesized from PCL-diol (1.25 kg/mol) alternating with polyhedral oligomeric silsesquioxane (POSS) diols and diisocyanates following our previous report.[2] The feed ratio of PCL-diol to POSS-diol is 70:30 in weight. The two POSS-diols used were 1,2-PropaneDiolIsobutyl POSS®(PP-POSS) and Trans-CyclohexaneDiolIsobutyl POSS®(TCH-POSS). The four diisocynates we compared are hexamethylene (HDI), lysine-derivated (LDI), isophorone (IPDI) and 4,4'-methylenediphenyl (MDI) diisocyanates. The yielded products were hot-pressed into the flat sheets with around 0.3 mm thickness, and cut into dog-bone shape samples for testing. The bulk structures of all samples were characterized by differential scanning calorimetry (DSC) and wide angle X-ray diffraction (WAXD). Enzymatic degradation experiments were carried out at 37 °C in a 0.05M pH=7.4 PBS (Phosphate Buffered Saline) solution with 0.4 mg/ml Lipase PS (enzyme). Oxidative degradation tests were conducted in 0.1M $CoCl_2$/20% H_2O_2 aqueous solution at 37 °C[3]. Biodegradation *in vitro* was assessed by measuring mass loss and conducting tensile mechanical tests with cross-head speed of 10 mm/min.

Results: WAXD patterns of the multi-block TPUs indicated one prominent peak centered at *d*-spacing: 10.7 Å (101 reflection peak of POSS rhombohedral unit cell), and an amorphous halo centered at 4.2 Å. The melting behavior of the crystalline domain observed in WAXD was revealed by DSC tests. DSC heating traces revealed only one melting peak attributed to crystalline POSS moieties, which strongly depends on the chemical structures of POSS and diisocyanate. PCL is thus amorphous in these samples. For PP-POSS based TPUs, the melting point is in the range 108 °C- 126 °C, while for TCH-POSS-based TPUs, it is in the range from 62 °C to 94 °C. The melting enthalpy of PP-POSS-based TPUs is higher than their TCH-POSS counterparts. Also, the melting point and latent heat follow the diisocyanate dependence: MDI > HDI > LDI > IPDI. Figure 1 showed the mass remaining of PCL-based multi-block TPUs after 30-day enzymatic and oxidative incubation. As compared with pure PCL[1], the multiblock TPUs tethered with POSS moieties show remarkable mass stability for 30-day enzymatic and oxidative degradation tests. Tensile testing indicated that for the samples enduring 30-day enzymatic degradation, none fractured (>1250% strain) when the elongation reaches the limitation of tensile test system (Linkam TST350). For those after 30-day oxidative degradation, the elongation at break strongly depends on the POSS-diol and diisocyanate. Importantly, those samples incorporating PP-POSS and aliphatic diisocyanates (i.e. HDI, LDI and IPDI) preserved their elongation-at-break values, >1250%.

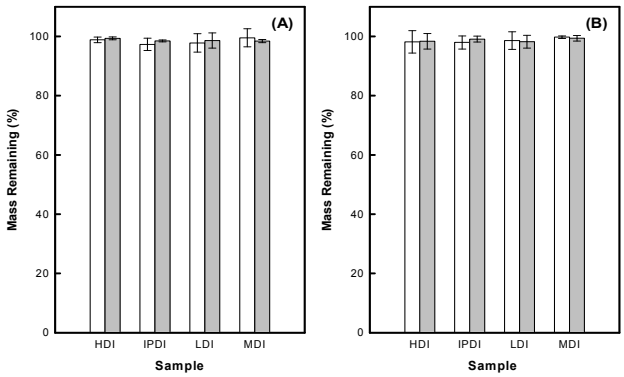

Figure 1. Mass remaining of multiblock TPUs after 30-day (A) enzymatic and (B) oxidative incubation varying with POSS-macromers: (blank bar) TCH-POSS and (gray bar) PP-POSS.

Conclusions: The incorporation of POSS moieties can significantly suppress the enzymatic hydrolytic degradation of micro-phase separated PCL-POSS multi-block TPUs. The oxidative stability strongly depends on incorporated POSS-diol and disocyanates. Those TPUs incorporating PP-POSS and aliphatic diisocynates show the excellent biostability *in vitro*. These striking results make PCL-POSS TPUs potentially applicable as long-term biostable surgical implants.

References: [1] Gu, X.Z. et al. Transaction of Society for Biomaterials 33rd Annual Meeting 2009, Paper 174; [2]Knight P.T. et al. Biomacromolecules 2008, 9:2458-2467. [3] Schubert, M.A. et al. Journal of Biomedical Materials Research, 1995, 29:337-347