Poly(ε-caprolactone) Homo-Blends with Controllable Properties and Cell Behavior

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Statement of Purpose: Poly(ε-caprolactone) (PCL), an FDA-approved biodegradable polymer with excellent biocompatibility and flexibility, can be degraded by hydrolysis of its ester linkages in physiological conditions.[1] PCL has received extensive attention in biomedical applications.[1] PCL is a semi-crystalline polyester with a glass transition temperature (T_g) of around -60 ^oC and molecular-weight-dependent melting point (T_m) and crystallinity.[1-3] In this study, we report the physical properties of a series of PCL binary homo-blends consisting of a higher-molecular-weight PCL and a lower one with different compositons. Using this series of PCL homo-blends, we have investigated the roles of PCL molecular weight and the blend composition in regulating material properties and mouse MC3T3 cell responses.

Methods: PCLs with three different nominal molecular weights used in this study were purchased from the Sigma-Aldrich Co. PCL2K with a nominal molecular weight of 2,000 g/mol and PCL530 with a nominal molecular weight of 530 g/mol were selected as the shorter components to form binary homo-blends with the longer component PCL80K having a nominal molecular weight of 80,000 g/mol. Using gel permeation chromatography (GPC) and standard monodisperse polystyrene samples for calibration, M_n and M_w for PCL80K, PCL2K and PCL530 were determined to be 98,000 and 144,000 g/mol, 3500 and 5200 g/mol, 1080 and 1180 g/mol, respectively. The blends of PCL80K/PCL2K or PCL530 with PCL80K compositions of 100%, 75%, 50%, 25% and 0% were prepared by dissolving them in a co-solvent, methylene chloride. After solvent evaporation, round disks with a diameter of 9.8 mm and a thickness of 1.5 mm were prepared from the blend melts on a heating stage set above the sample's T_m. Tensile measurements were performed at a strain rate of 0.001 s^{-1} on a dynamic mechanical thermal analyzer (DMTA) at both room temperature and 37 ^oC. Compression testing was processed on an Instron Universal Testing Machine at room temperature with a rate of 0.1 mm/min. Polymer disks were loaded into 48-well cell culture plate and mouse MC3T3 cells were used to examine cytocompatibility and cell responses to these homo-blends. After 4 hr, 1, 2 and 4 days, MC3T3 cells were fixed using 16% paraformaldehyde solution and stained using rhodamine-phalloidin (RP) solution before photographing on a Zeiss fluorescent microscope. The average area per cell at 4 hr and day 1 post seeding was measured on non-overlapping attached cells using the software ImageJ from the National Institutes of Health.

Results: Because of a high crystallinity and a T_m greater than 37 ^oC, PCL80K behaved as a rigid material at both room temperature and body temperature. In contrast, PCL2K and PCL530 were much weaker, especially at 37 ^oC. As expected, tensile and compressive moduli dropped as the composition of PCL80K in the homo-blends decreased (Figure 1). The mechanical properties of the blends at 37 ^oC were significantly lower than those at room temperature. Except PCL80K and PCL80K/PCL2K (75/25), other blends showed little cell attachment and proliferation (Figure 2). When the composition of PCL2K was 25%, cell numbers at all time points were less than those on pure PCL80K (Figure 2). The average cell area at 4 hr post seeding decreased significantly from that on PCL80K to PCL80K/2K (75/25), as shown in the lower inset of Figure 2 and Figure 3. The distinct cell responses to the PCL homo-blends at different compositions suggest that low molecular weight component may influence surface morphology and physicochemical characteristics significantly at 37 ^oC as well as mechanical properties.[4]

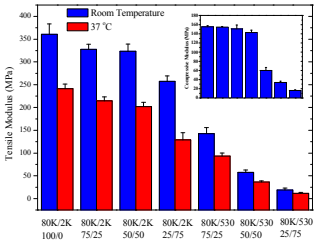

Figure 1: Tensile and compressive (inset) moduli of the PCL homo-blends at room temperature and 37 ^oC.

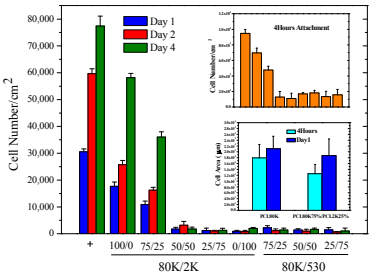

Figure 2: MC3T3 cell attachment (upper inset), proliferation, and cell area (lower inset) on the PCL homo-blends.

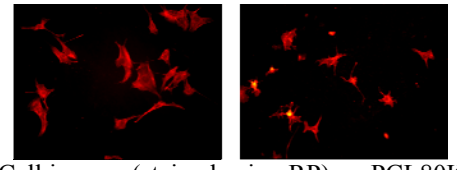

Figure 3: Cell images (stained using RP) on PCL80K (left) and PCL80K/PCL2K (75/25) at 4 hr post seeding.

Conclusions: Molecular weight plays a critical role in determining cell responses to PCL samples through varying surface physicochemical properties. By blending the long chains and short chains of PCL, material properties and cell responses can be modulated using the blend composition.

References:

1. Engelberg I. Biomaterials 1991;12:292.
2. Wang S. Macromolecules 2005;38:7358.
3. Wang S. Biomaterials 2006;27:832.
4. Discher DE. Science 2005;310:1139.