In vitro degradation of poly(DL/L-lactide-ε-caprolactone) biomaterials

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Statement of Purpose: Copolymers of DL and L-lactide andε-caprolactone have been examined as biodegradable materials in a variety of applications including tissue engineering scaffolds and pharmaceutical formulations. The aim of this study is to thoroughly examine the degradation kinetics of these polymers, which is useful in determining the appropriate biomaterial for a given application. The effects of polymer composition and the presence of unreacted monomer on the in vitro degradation of poly(DL-lactide-co-ε-caprolactone) and poly(L-lactide-co-ε-caprolactone) are examined.

Methods: *Polymers.* Lakeshore Biomaterials™ bioabsorbable polymers were obtained from SurModics Pharmaceuticals, Birmingham, AL. The materials examined here were ester end group copolymers with varying lactide-caprolactone compositions (Table 1). Both DL- and L-lactide were studied, where DL-lactide is a racemic mixture of the D & L stereoisomers, and L-lactide is the L stereoisomer only. Poly(caprolactone) was also examined as a control. In addition, purified versions of these polymers were examined, where purification produces lowered levels of residual monomer.

Degradation Studies. The polymers were melt-pressed at 80°C into films of a defined thickness, from which discs were punched to achieve a controlled surface area. Individual discs were placed into scintillation vials with 20 mL of Phosphate Buffered Saline, 6.7 mM, pH 7.4 (Fisher Scientific, Pittsburg, PA) containing 0.01% of the preservative ProClin 300 (Sigma, St. Louis, MO). The vials (n=3) were placed in a 37°C static incubator and pulled at 1, 2, 4, 8, 12, 16 & 24 weeks for analysis. Complete fluid changes were made at least every two weeks for all samples.

Analytical Methods. Molecular weight analysis was performed at each time-point by Gel Permeation Chromatography (GPC). Residual water content was determined by Karl Fisher. Nuclear magnetic resonance (NMR) spectroscopy was performed to determine polymer and monomer content. The total mass loss was determined after the samples were lyophilized to dryness.

Table 1: Description of Polymers

Polymer	Lactide Content, % (stereoisomer)	Caprolactone Content (%)	Average Molecular Weight (kDa)
1	10 (DL)	90	95
2	50 (L)	50	107
3	80 (L)	20	172
4	90 (DL)	10	94
5	n/a	100	80

Results: The degradation of the synthetic copolymers was tracked over a 24-week time period. The rate of degradation was found to increase with increasing lactide:caprolactone ratios. Figure 1 shows the degradation profiles for the polymers examined over time in terms of molecular weight average (Mw). Polymers having lower lactide content, Polymers 1 & 2 (Table 1) have similar profiles and degrade much slower than comparatively higher lactide content polymers, Polymers 3 & 4 (Table 1). Notably, these higher lactide content polymers experienced a much sharper decline in molecular weight after only 1 week of degradation time.

Mass loss was recorded at weeks 8 and 12 of the degradation study. Lower lactide content polymers (Table 1 – Polymers 1 & 2) retained more than 80% of their original mass after 12 weeks. Among the higher lactide content polymers, the Polymer 3 (Table 1) retained more than 70% of its original mass at 12 weeks, while Polymer 4 (Table 1) had retained less than 20% of its original mass at 12 weeks.

Degradation studies were performed on purified copolymers, and it was found that purification did not change the degradation profile of the material.

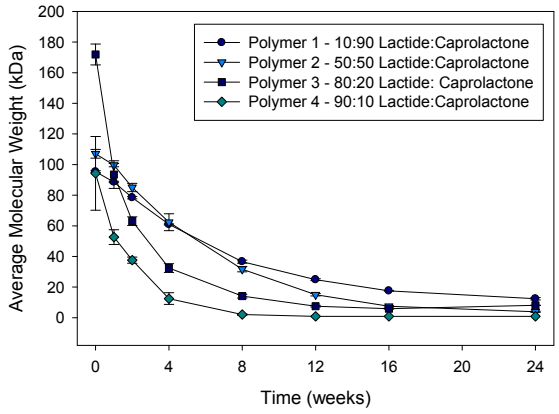

Figure 1. Molecular weight degradation of poly(DL/L-lactide-ε-caprolactone)

Conclusions: Poly(DL/L-lactide-ε-caprolactone) is a biodegradable material whose degradation kinetics may be tuned by adjusting the lactide:caprolactone ratios. A high lactide component will produce a faster degradation compared to lower lactide components that will allow for much slower degradation. Molecular weight changes and mass loss should be monitored in future degradation studies with these materials in order to gain a full understanding of the degradation kinetics.

References: Jung Y. Biomaterials. 2008;29(35):4630-6. Meek MF. J Biomed Mater Res A. 2004;68(1):43-51. Malin J Applied Polymer Science. 1996;59:1289-98