Tailoring Degradation Rate and Mechanical Properties of Modified Poly(ε-caprolactone)

Ting-Yu Shih, Jean-Dean Yang, Jui-Hsiang Chen
Industrial Technology Research Institute, Taiwan.

Statement of Purpose: Molecular design and modification allow the properties of degradable materials to be suited for specific requirements of biomedical applications. In this study, a novel urethane linkage containing poly(ε-caprolactone) (PCL) was first synthesized by solution polymerization. By using ε-caprolactone precursors with different molecular weights and ratios, a series of modified poly(ε-caprolactone) (mPCL) were obtained via ring opening polymerization with diisocynate as a coupling agent. The chemical structures of mPCL were characterized by ^{1}H NMR. The effect of PCL block length on thermal behavior has been investigated using DSC. Physical properties such as mechanical properties and invitro/invivo degradation rate were evaluated. The results suggest that urethane linked PCL exhibit tailoring degradation rate that is manipulated by the PCL block length.

Methods: Poly-ε-caprolactone (PCL), Poly-ε-caprolactone diol (PCL diol) with a molecular weight of 530, 2000, and 10000, 4,4-Methylenebis(cyclohexyl isocyanate) (H_{12}MDI), dibutyltin dilaurate (T_{12}), and dimethyl- d6 - sulfoxide (DMSO-d6) were supplied by Aldrich. The synthesis of modified poly(ε-caprolactone), was polymerized by a one shot synthesis. The reaction was carried out for 8 hours under stirring and extra amount of H_{12}MDI、DMAc and T_{12} were added into the reactor according to the real time viscosity. The resulting mPCL resin was purified for further characterization after adding butylamine to terminate the reaction. Molecular weights (Mw, Mn) and molecular weight distribution were determined by GPC with DMAc as the mobile phase. ^{1}H and ^{13}C NMR spectra were recorded with a 500 MHz Varian Unity Inova NMR spectrophotometer. Tensile and elongation strength tests which follow ASTM D638 were performed using an universal material testing machine equipped with a maximum 500N load cell. The in vitro degradation of both PCL and mPCL were performed in accordance with ISO 10993-9 standard. The in-vivo degradation study was carried out in the rat model of nerve injury. GPC was also used to determine molecular weight changes during one year period.

Results: The series of mPCL with various block length and ratio of block composition were successfully polymerized using HDI as a coupling agent with polydispersities (PDI) between 2.0~2.6. Mechanical properties of modified PCL were measured and compared to those of homogeneous PCL. The tensile strength of these polymers presented in Figure 1. The tensile strength of amorphous mPCL dropped which exhibits typical mechanical properties of non crystalline materials. Noticeably, while PCL homopolymer and mPCL (PCL530/PCL10000, ratio 25/75, crystallinity 44.8%) display similar crystallinity, the mPCL exhibited remarkably high tensile strength up to 36MPa, whereas homopolymer only reaches approximately less than half of the value (16MPa), which may be due to strong inter molecular hydrogen bonds of the urethane linkages forming among polymer chains.

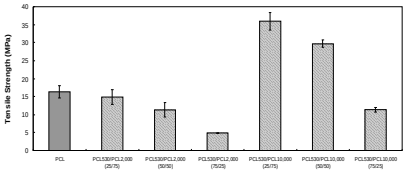

Figure 1 The tensile properties of PCL and modified PCLs

The In-vivo results are as shown in Figure 2. The porous PCL (area porosity 71%) and mPCL (area porosity 73%) were subsequently implanted into sciatic nerve for a year to investigate the biodegradation behavior. For the implanted period over three months, the molecular weight of mPCL decreased to 47.3% while PCL residue shows only 0.7% changed in molecular weight. Within six months, the mPCL was found nearly degraded completely and PCL showed that over 91.1% of the weight remained. The data shown here indicates the tendency of faster hydrolysis with MDI coupling agent applied than that of homogeneous PCL. The possible reason might be that higher ratio of urethane linkage causes limited crystalline nature which promotes degradation.

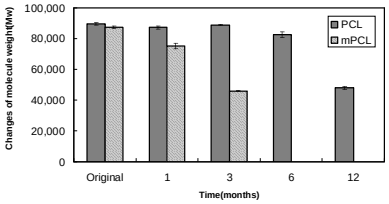

Figure 2 In vivo study degradation profile of PCL and mPCLs

Conclusions: A new strategy for synthesizing novel urethane linked biodegradable poly-caprolactone with tunable mechanical properties and fasten hydrolytic degradation process comparable to PCL is reported here. The modified polycaprolactone with urethane linkage introducing into polymer chain exhibited high flexibility and remarkable tensile strength above 200%. By tailoring the ratio and linkage between different molecular weights of PCL, these modified polyesters performed not only superior mechanical properties, but also speedy degradation rate. Our results reveal that urethane linked polycaprolactone could serve as tunable materials for a variety of medical implants, and therefore broaden PCL's applications. Furthermore, besides PCL, the same strategy to alter the materials' characteristics and performance such as PLA, PGA and PLGA, could be also possible.

References:

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