

Poly(ester urethane urea) PolyHIPEs as High Porosity Bone Grafts

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Statement of Purpose: Engineered bone grafts have the potential to repair critical size defects when traditional transplants are unavailable or fail. It is widely recognized that scaffold architecture can profoundly influence the success of these construct. Scaffold architecture (porosity, pore size, interconnectivity) and the scaffold properties that result from that architecture (e.g. biodegradation rate, mechanical properties) are dictated by the fabrication process. Emulsion templating is a relatively new method for the production of highly porous scaffolds and involves the template polymerization of high internal phase emulsions (HIPEs). HIPEs are characterized by a droplet phase volume fraction of at least 74%. The continuous phase contains a monomer that is polymerized and locks in the emulsion geometry at the gel point. The droplet phase is then removed, and the resulting porous scaffold is known as a polyHIPE. The control of scaffold architecture afforded by emulsion templating makes polyHIPE materials attractive candidates for tissue engineering scaffolds. Traditional polyHIPEs have been fabricated with chain growth or radical crosslinking processes. In the present study, we utilized a step-growth polymerization mechanism that expands the range of monomers and resulting properties available to this fabrication strategy. Poly(ϵ -caprolactone) (PCL), a well-established biodegradable polymer, was functionalized with isocyanate end groups to create polyHIPEs with interconnected porosity that cure at body temperature.

Methods: Synthesis: All chemicals were purchased from Sigma-Aldrich (Milwaukee, WI, USA) and used as received. PCL-triol (300 g/mol) was endcapped with hexane diisocyanate (HDI) in dimethylformamide at 80°C using stannous octoate as a catalyst under anhydrous conditions.[1] The solution was then purified by washing with water and the solvent removed by rotary evaporation, leaving a viscous, colorless PCL-triisocyanate (PCL-TI) product.

HIPE formation: A series of polyHIPEs were fabricated using established emulsion templating protocols.[2] The organic phase consisted of HDI and PCL-TI (1:1, 2:1, 3:1, 6:1) with toluene as the diluent (40, 50, 60%). Span 80 (20 wt% of the organic phase) was used as the surfactant. These components were mixed thoroughly in a 3 neck round bottom flask with a mechanical stirrer at 300 rpm. An aqueous solution (1 wt% CaCl₂) was then added at a rate of 1mL/min to a ratio of 80:20 while stirring. The HIPE was cured at 37°C for at least 12 hours. After cure, samples were dried for 24 hours under vacuum. Gravimetric analysis was utilized to measure porosity and scanning electron microscopy (SEM) was used to characterize architecture of cryo-fractured specimens.

Results: Synthesis: Successful synthesis of PCL-triisocyanate was confirmed with FTIR and NMR spectroscopy, **Figure 1**. The FTIR spectrum of PCL-TI revealed a peak at 2270cm⁻¹ not present in the spectrum of

PCL-triol indicative of isocyanate endgroups, **Figure 1**. In addition, a broad absorption peak typical of OH stretching at 3383 cm⁻¹ in the PCL-triol shifted to the NH stretching at 3332cm⁻¹ as a result of urethane bond formation after functionalization.

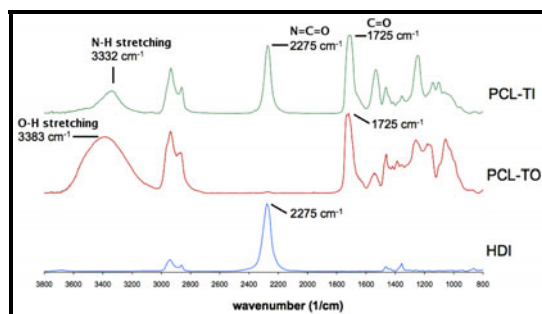


Figure 1. FTIR spectra of PCL-TI functionalization.

PolyHIPE Formation: HIPEs based on HDI:PCL-TI cured at 37°C via reaction of isocyanate end groups with water which liberated carbon dioxide to form amine end groups. Subsequent reaction of these amine end groups with the remaining isocyanate end groups resulted in a poly(ester urethane urea) network which locked in the emulsion geometry. The resulting grafts were characterized by open pores on the order of 5-40 microns, **Figure 2**, and typical porosity values greater than 90%. Foam properties ranged from rigid to elastomeric in nature based on the resultant network structure. Specifically, higher HDI concentration resulted in an increase in the distance between crosslinks.

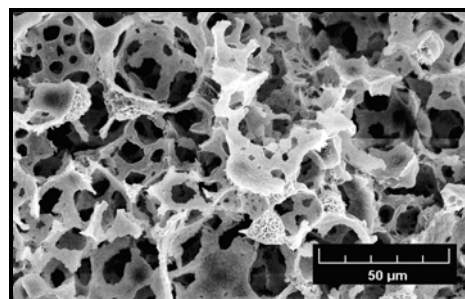


Figure 2. SEM of polyHIPE with interconnected porosity.

Conclusions: Emulsion templating of multifunctional polyester prepolymers was utilized to generate a new class of step-growth polyHIPEs. These high porosity scaffolds are of particular interest in bone tissue engineering due to the rigidity of the resulting foams, ease of fabrication, and control over architecture. Current studies are focused on cell behavior on these novel 3D scaffolds including mesenchymal stem cell viability, differentiation, and extracellular matrix deposition.

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References: [1] Skarja et al. *Journal of Biomaterials Science, Polymer Edition*, **9**(3), 271-295 (1998).

[2] Christenson et al. *Biomacromolecules*, **8**(12), 3806-3814 (2007).