Synthesis, processing and characterization of a biodegradable, elastomeric poly(ester-carbonate urethane) urea (PECUU) for soft tissue engineering

Yi Hong[1,2], Jianjun Guan[1,2], Kazuro Fujimoto[1,2], Ryotaro Hashizumi[1,2], Anca Peclinescu[3], William R. Wagner[1-4]
[1]McGowan Institute for Regenerative Medicine, Departments of [2] Surgery, [3] Bioengineering and [4] Chemical Engineering
University of Pittsburgh, Pittsburgh, PA 15219, USA

Introduction

Biodegradable elastomers are of increasing interest for regenerative medicine applications in soft tissue repair and regeneration. We have previously developed a series of poly(ester urethane)ureas (PEUUs) and poly(ether ester urethane)ureas that act as thermoplastic elastomers and provide tunable increases in degradation rates with increasing ether content.[1,2] For some applications it would be desirable to have slower degradation, which might be achieved by partially substituting polyester with polycarbonate segments in the polymer backbone. Specifically we investigated different molar ratios of polycaprolactone diol (PCL) and poly(hexamethylene carbonate) diol (PHC) as soft segments incorporated in thermoplastic poly(ester-carbonate urethane) urea (PECUU) elastomers. PECUU chemical structure, mechanical properties, degradation and cytocompatibility were investigated and porous scaffolds were generated. These scaffolds were implanted subcutaneously in rats to assess differential in vivo degradation and tissue response.

Materials and Methods

PECUUs were synthesized from PCL (M_n=2000) and PHC (M_n=2000) reacted with 1,4-diisocyanatobutane (BDI) and chain extended with putrescine. PCL:PHC ratios examined were 100/0 (PEUU), 75/25, 50/50, 25/75 (PECUUs) and 0/100 (PCUU). Films were cast from hexafluoroisopropanol (HFIP) solutions. PECUU structure was confirmed by FTIR, glass transition (T_g) and melting (Tm) temperatures by DSC, and tensile properties using ASTM D638-98. Inherent viscosity was tested with an Ubbelohde viscometer. Rat smooth muscle cells (SMCs) were seeded onto polymer films to quantify cell adhesion and growth with tissue culture polystyrene (TCPS) as a control.

To form porous scaffolds, 20% PECUU/HFIP solution and 100-150 μm salt particles were blended and placed in a cylindrical mold. After solvent evaporation, the mixture was immersed in 30% ethanol to remove salt particles and lyophilized. Scaffold mechanical properties and porosity were measured and the growth of SMCs seeded into scaffolds assessed. PEUU, PECUU 50/50 and PCUU scaffolds were subcutaneously implanted into a rat model. At 8 wk, expants were histologically evaluated.

Results and Discussion

Polyurethane structure was verified by specific peaks at 1738 cm^{-1} and 3335 cm^{-1} from C=O and N-H bonds respectively. PECUUs and PCUU had a specific peak at 1266 cm^{-1} assigned to O-C-O bonds.[3]

All polymer T_gs were <-46°C. T_ms ranged from 40°C (PEUU) to non-detectable (PCUU) dependent on PHC content. Inherent viscosities ranged from 0.8 to 1.38 dL/g. PECUUs generally had tensile strength, breaking strain and initial modulus values between those of PEUU (34±6 MPa, 660±85 % and 24±2 MPa) and PCUU (14±2 MPa, 875±83% and 8±2 MPa), along with 100% strain recovery after 10% stretch. After 8 wk in PBS at 37°C, PECUUs had ~1% mass loss while PEUU and PCUU had 8% and 0% loss, respectively. However, degradation at 8 wk evidenced by the residual inherent viscosities ranged from 78-97% depending on carbonate amount. Differences in thermal and mechanical properties and degradation rates between the five polymers were attributed to the molar ratio between semi-crystallized polyester and non-crystallized slowly degradable polycarbonate. SMC adhesion at 24 h onto films of all polyurethanes was >100% of TCPS with proliferation evident at 4 days. PECUU scaffolds possessed high distensibility (>100% strain) and interconnected pores with ~85% porosity. SMCs proliferated within all scaffolds after 7 days of spinner flask culture. Subcutaneous scaffold implants of PEUU, PECUU and PCUU exhibited differential degradation rates consistent with in vitro behavior (**Fig.**).

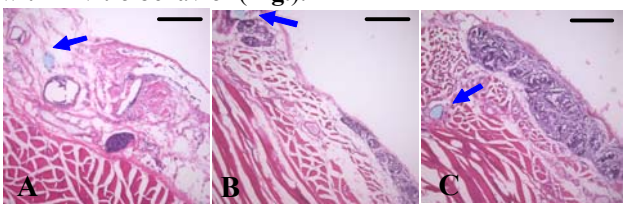

Fig. Histologic images of the scaffold implant area for (A) PEUU, (B) PECUU 50/50, and (C) PCUU demonstrate differential degradation behavior at 8 wk. Scale bar = 200μm. Blue arrows indicate suture line. Scaffold residue is seen within purple areas near the surface in (B) & (C).

Conclusions

PECUUs were successfully synthesized from PCL, PHC, BDI and putrescine and shown to possess attractive mechanical properties and cytocompatibility. In vitro hydrolysis studies and in vivo subcutaneous implantation demonstrate that the PECUUs exhibit obviously slower degradation rates than the PEUUs previously reported[2]. These new thermoplastic elastomers might find future application where slower degradation rates coupled with strong elastic behavior is desirable.

References

[1] Guan J et al. *Biomaterials* 25:85 (2004).
[2] Guan J et al. *J Biomed Mater Res* 61:493 (2002).
[3] Szelest-Lewandowska A et al. *JBMR* 82A:509 (2007).