Development of biodegradable elastomeric polyurethanes with low initial moduli

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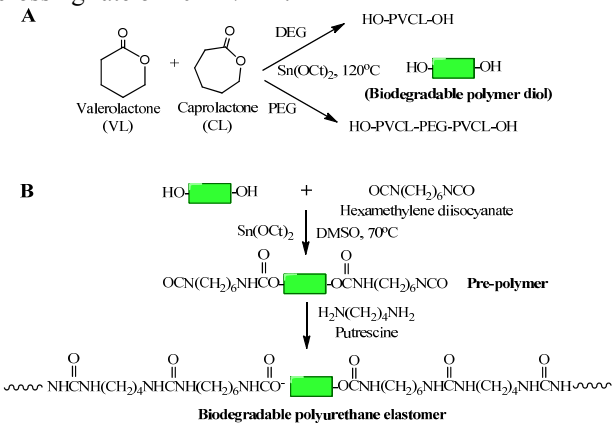
Statement of Purpose: Scaffold mechanical match with native tissue gains increasing attentions on tissue repair and regeneration [1-3]. For example, the mechanical mismatch of synthetic vascular grafts with native blood vessel would induce the intimal hyperplasia and lead to the graft failure. The synthetic cardiac patch's mechanical mismatch with native myocardium would result in the abnormal cardiac functions, such as blood output. Generally, native soft tissues show a J-shape stress-strain curve with a low initial modulus. However, the synthetic polymers exhibit much higher initial modulus compared to the native soft tissues. Hence, it is very important to develop a biodegradable robust polymer with a low initial modulus by molecular design. Polyurethane based polymers are usually synthesized from three "blocks", including soft segment, hard segment and chain extender. They have high elasticity and robust mechanical properties. It is notable that their mechanical properties can be tuned by flexibly altering the three blocks. It was found that polyurethane urea based on a soft segment of amorphous poly(δ-valerolactone-co-ε-caprolactone) (PVCL) had a low initial modulus (2.8±1.3MPa) [4]. To further reduce the polymer initial modulus under a physiological condition, we will incorporate hydrophilic poly(ethylene glycol) (PEG) into the soft segment to increase the polyurethane hydrophilicity.

Here, we synthesized series of amorphous copolymer PVCL, and triblock copolymer PVCL-PEG-PVCL with various total molecular weights and various PEG molecular weights. The polyurethanes were then synthesized from PVCL or PVCL-PEG-PVCL as a soft segment, hexamethylene diisocyanate (HDI) as a hard segment and putrescine chain extender. The chemical structure was confirmed by ^{1}H NMR. The mechanical properties at dry and wet state were measured.

Methods:

The PVCL and PVCL-PEG-PVCL copolymer diols were synthesized using δ-valerolactone (VL) and ε-caprolactone (CL) by ring-opening polymerization with diethylene glycol (DEG) or poly(ethylene glycol) (PEG, MW=1000 and 2000) as an initiator (**Scheme 1A**). The molar ratio of VL/CL was 50/50. We then synthesized a new family of biodegradable polyurethanes based on PVCL and PEG-VCL diols with 1,6-hexamethylene diisocyanate (HDI) and a chain extender putrescine using a two-step solution polymerization (**Scheme 1B**). The molar ratio of soft segment : hard segment:chain extender was set as 1:2:1. The polymer films were fabricated by solvent casting in hexafluoroisopropanol (HFIP). The molecular weights of PVCL and PVCL-PEG-PVCL were confirmed by ^{1}H NMR. The mechanical properties of the produced polyurethanes before and after water immersion were measured on a MTS workstation with a head crossing rate of 10mm/min.



Scheme 1. Synthesis of (A) biodegradable copolymer diols and (B) biodegradable elastic polyurethanes.

Results:

The ^{1}H NMR confirmed chemical structure and molecular weights of copolymer diols of PVCL2000 and PVCL 6000, and triblock copolymer diols of PVCL-PEG-PVCL(500-1000-500), PVCL-PEG-VCL(3000-1000-3000), and PVCL-PEG-PVCL(3000-2000-3000). The initial modulus was markedly reduced by increasing the molecular weight and hydrophilicity of the soft segment. When soft segment molecular weight of PVCL-PEG-VCL was 3000-2000-3000, the initial modulus measured at wet state was 1.2±0.4MPa, which value is comparable with heart muscle initial modulus (10-500KPa) [5,6].

Conclusions:

A series of biodegradable triblock copolymer diols based on PEG, VL and CL were synthesized for polyurethane synthesis. The new family of biodegradable elastic polyurethanes showed relatively low initial moduli, which decreased with molecular weight and hydrophilicity of the triblock copolymer. These biodegradable polyurethanes can provide opportunities to be applied as mechanical match scaffolds for repairing and regenerating soft tissues, such as myocardium and blood vessels.

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