Development of Photocrosslinkable Urethane-Doped Polyester Elastomers for Soft Tissue Engineering

Yi Zhang, University of Texas at Arlington, USA
Richard T. Tran, University of Texas at Arlington, USA
Dipendra Gyawali, University of Texas at Arlington, USA
Jian Yang, University of Texas at Arlington, USA

ABSTRACT

Finding an ideal biomaterial with the proper mechanical properties and biocompatibility has been of intense focus in the field of soft tissue engineering. This paper reports on the synthesis and characterization of a novel crosslinked urethane-doped polyester elastomer (CUPOMC), which was synthesized by reacting a previously developed photocrosslinkable poly (octamethylene maleate citrate) (POMC) prepolymers (pre-POMC) with 1,6-hexamethylene diisocyanate (HDI) followed by thermo- or photo-crosslinking polymerization. The mechanical properties of the CUPOMCs can be tuned by controlling the molar ratios of pre-POMC monomers, and the ratio between the prepolymer and HDI. CUPOMCs can be crosslinked into a 3D network through polycondensation or free radical polymerization reactions. The tensile strength and elongation at break of CUPOMC synthesized under the known conditions range from 0.73±0.12MPa to 10.91±0.64MPa and from 72.91±9.09% to 300.41±21.99% respectively. Preliminary biocompatibility tests demonstrated that CUPOMCs support cell adhesion and proliferation. Unlike the pre-polymers of other crosslinked elastomers, CUPOMC pre-polymers possess great processability demonstrated by scaffold fabrication via a thermally induced phase separation method. The dual crosslinking methods for CUPOMC pre-polymers should enhance the versatile processability of the CUPOMC used in various conditions. Development of CUPOMC should expand the choices of available biodegradable elastomers for various biomedical applications such as soft tissue engineering.

Keywords: Biodegradable Elastomer, Polyester, Soft Tissue Engineering, Thermo-Crosslinking, UV-Crosslinking

1. INTRODUCTION

Finding an ideal biomaterial is one of the major goals in the field of tissue engineering. Many of the native tissues in the human body have elastomeric properties. Thus, the biomaterials selected to repair these tissues should have similar elastic properties in order to sustain and recover from multiple deformations without causing irritation to the surrounding tissues (Wang, 2002).
It has been proven that mechanical stimuli can enhance cellular growth, alignment, and extracellular matrix production. Previous research has also shown that the appropriate mechanical constraints can help yield both fibril alignment and the geometry of a native heart valve (Neidert & Tranquillo, 2006; Robinson, 2008). Moreover, the addition of mechanical stimuli has also been shown to have an influence on the stem cell differentiation (Engelmayer, 2006; Zhao, 2009). Mechanical mismatch between host blood vessels and vascular grafts may contribute to the development of myointimal hyperplasia, a major reason for graft failure (Yang, 2005). Therefore, a suitable biomaterial for soft tissue engineering should have the appropriate mechanical properties similar to the target tissue, and be capable of transmitting mechanical stimulus to the seeded cells.

Recently, many researchers have focused their work on the development of biodegradable polyester and polyurethane elastomers for soft tissue engineering. Biodegradable polyurethanes (BPUs) are a family of elastomers, which have been used in a wide variety of biomedical applications due to their good mechanical properties (up to 29 MPa tensile strength) and elasticity (up to 895% elongation) (Guan, 2002, 2004; Guan & Wagner, 2005; Guelcher, 2008; Zhang, 2008). However, due to their aliphatic nature BPUs are susceptible to permanent creep under cyclic mechanical loading. Therefore, the potential long-term success of polyurethanes as scaffold materials for dynamic tissues like blood vessels and ligament is still questionable (Dey, 2008).

Elastomeric polyesters are another family of polymers that have attracted interest due to the appropriate biodegradability, biocompatibility, and elasticity for various biomedical applications (Webb, 2004; Yang, 2009). Therefore, crosslinked polyester elastomers have attracted much attention recently due to their excellent elasticity without permanent deformation under cyclic deformation such as poly (glycerol sebacate) (PGS) and poly (octamethylene citrate) (POC) (Wang, 2002; Yang, 2004, 2006; Chen, 2008). PGS and POC have shown excellent biocompatibility in vitro and in vivo. The crosslinking nature of PGS and POC also confer excellent elasticity to these polymers. However, the mechanical strength of PGS and POC are still relatively weak which range from 0.5±0.2 MPa to 2.9±0.1 MPa, especially when they are made into porous scaffolds. The reported tensile mechanical strength of POC porous scaffolds are only 0.3±0.1 MPa (Yang, 2005). The processability of PGS and POC is also limited with only a salt-leaching method reported for this type of polymer. A commonly used thermally induced phase separation (TIPS) or freeze-drying method for scaffold fabrication cannot be applied to these polymers due to the sticky nature of their low molecular weight pre-polymers, which are the only processable forms for these polymers.

To improve the mechanical properties of POC but retain the excellent elasticity, we have recently reported a crosslinked urethane-doped polyester (CUPE) elastomer. 1,6-hexamethylene diisocyanate (HDI) is used to extend the POC pre-polymer chains to obtain a pre-CUPE polymer. Pre-CUPE can be further thermally crosslinked into a urethane-doped polyesters (CUPE) elastomeric network. The tensile strength of CUPE was as high as 41.07±6.85 MPa with corresponding elongation at break of 222.66±27.84% (Dey, 2008).

Given that there has been great interest in using photopolymerization techniques for various biomedical applications such as 3-dimensional (3-D) tissue construction and cell entrapment, (Khademhosseini et al., 2006; Du, 2008; Yu & Ding, 2008) an in situ crosslinkable biodegradable polyester network which was referred to as poly(octamethylene maleate citrate) (POMC) has been recently synthesized based on POC (Gyawali, 2010). Unsaturated maleic acid is reacted with citric acid and 1,8-octanediol to form a photocrosslinkable POMC pre-polymer (pre-POMC). However, similar to POC in addition to the photocrosslinkability, POMC is still relatively weak and the processability of pre-POMC is still limited due to its low molecular weight.
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