Synthesis and Characterization of *in situ* crosslinkable polyester elastomer

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Statement of Purpose: Typical thermoset polyester elastomers employ harsh processing conditions (>80º C, <5 pa, and >24h) and sacrifice all their available functional groups to construct three dimensional networks.[1,2] Furthermore, these polyesters show poor solubility towards water that limits their use for an injectable tissue engineering scaffold. Herein, we acknowledges the need for a biomaterials with 1) good range of mechanical properties for soft tissue engineering, 2) can be crosslinked under mild condition and in a short period of time, 3) saturated with surface chemistries such as hydroxyl and carboxylic acid for potential further bioconjugation, 4) can be dissolved in wide range of solvents including water in its pre-polymeric state, and 5) can serve as a injectable or *in situ* crosslinkable material. Structural analysis, mechanical properties, swelling ability, sol content, degradation profile, and the processability of the elastomer Poly (poly(ethylene glycol) maleate citrate) (PPEGMC) have been thoroughly investigated in order to meet the specific requirement of various soft tissue engineering.

Methods: poly(ethylene glycol) (PEG 200), Citric acid, Maleic acid, Acrylic acid, 2,2'-Azobis(2-methylpropionamidine) dihydrochloride (ABDH) are purchased from Sigma-Aldrich (Milwaukee, WI) and used as received. Citric acid, PEG 200, Maleic acid were added into a round bottom flask and allowed to react at temperature of 135º C under nitrogen flow and stirring condition until the desired viscosity was achieved. Synthesized pre-polymer was dialyzed with 500 Da cutoff molecular weight dialysis tube to remove unreacted monomers. Various bonds contents of the pre-polymer were evaluated using FTIR and composition ratios of all the monomers in the pre-polymer were evaluated by ^{1}H-NMR. Furthermore, the pre-polymer was dissolved in water and photocrosslinked in presence of ABDH and acrylic acid under 365 nm ultraviolet light. Comparison of pre-polymer and crosslinked polymer in their functionality was made using AT-IR. Tensile mechanical properties of the crosslinked polymers were evaluated by using MTS Insight II mechanical tester. Swelling ratios of the polymer were evaluated by soaking in water and PBS until it reaches equilibrium state. Degradation of the polymers were evaluated in PBS at 37º C. Scaffolds were fabricated using gas foaming technique where calcium carbonate was used as a gas foaming agent. Nanogels were fabricated using precipitation technique. Dynamic Laser scattering test was used to measure the size distribution of the obtained nanoparticles.

Results: The pronounced peak in FTIR spectra within 1690–1750 cm^{-1} suggests the presence of carbonyl (C=O) groups from the ester bond and pendent carboxylic acid from citric acid. The shoulder peak of lower wavelength at 1650 cm^{-1} proves the presence of double bond from maleic acid. Hydrogen bonded hydroxyl functional group showed absorbance as a broad peak centered at 3570 cm^{-1}. ^{1}H-NMR conforms that composition of the polymer can be controlled by the feeding ratio of all the monomers. Tensile mechanical tests on polymer samples shows that PPEGMC is a soft and elastic polymer with the initial modulus (150 ±25.54 to 777.2 ± 109.36), ultimate tensile stress (304.39 ± 13.39 to 702.37± 62.11) and elongation (131.40 ± 17.77 to 685.06 ± 40.97) which is suitable for soft tissue engineering. It was observed that soft and elastic polymer can be achieved if the molar ratio of citric acid precedes maleic acid as seen in strain-stress curve in Figure 1.

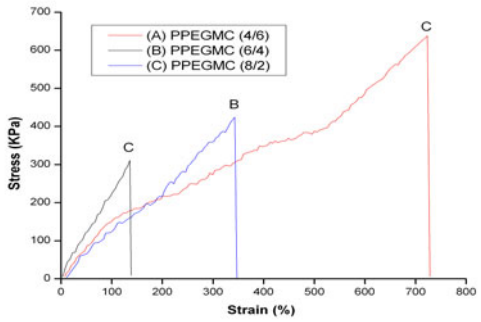

Figure 1: Tensile stress–strain curves of the different PPEGMC polymers

Water uptake ability of the polymer (103 ±23 % to 270.53 ± 25%) shows that it behaves as a hydrogel when in the hydrated condition. Interestingly, swelling ability of polymer increases by 10 folds if soaked in PBS (539.8 ± 46.67 % to 1908.5± 88.29%). More than 70% of the polymers mass were lost within 30 days of incubated time in PBS. Nanogels fabricated using PPEGMC were observed in the range of 200-500 nm.

Conclusions: In this work, we have evaluated a new class of synthetic, elastomeric, biodegradable polyester that can be crosslinked under mild conditions within a short period of time. the pre-polymer is in viscous state and can also be dissolved in water to show its potential in applications for an injectable tissue engineering scaffold. Available –COOH and –OH chemistries of scaffolds and nanogels can be further conjugated with various biomolecules for targeted drug delivery and tissue engineering applications. Biocompatibility evaluation, bioconjugation, drug delivery, and cell encapsulation ability of the polymer are the subjects of future study of the polymer. In the quest of designing soft and biodegradable elastic materials for soft tissue engineering, POMC meets general requirement of various soft tissue engineering.

References:

1. Nijst, C. L. *Biomacromol.* **2007**, *8*, 3067-73.
2. Dey J. Biomaterials **2008**, 29, 4637-4649