Elastomeric Electrospun Poly(glycerol sebacate) via a Water-Soluble Carrier Polymer

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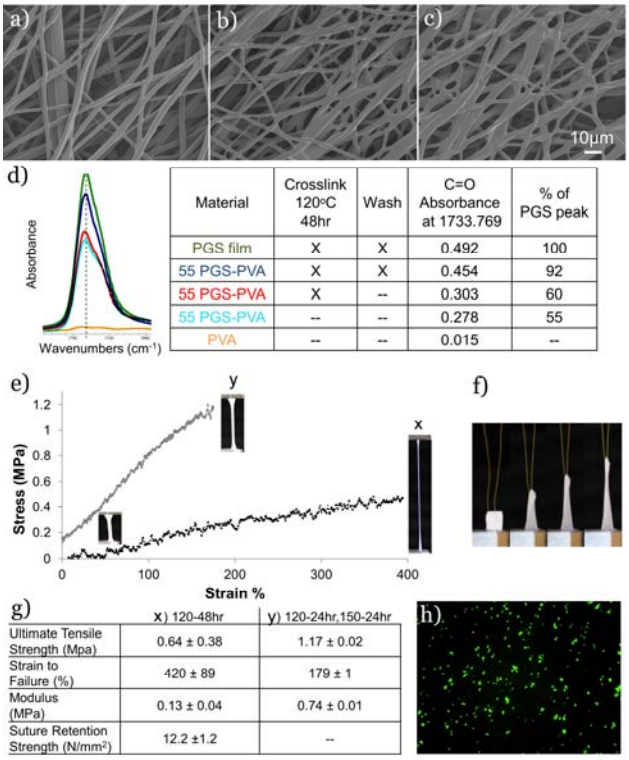
Statement of Purpose: Poly(glycerol sebacate) (PGS) is suitable for repairing many soft tissues due to its elasticity, rapid degradation, and minimal inflammation (Rai R. Prog in Poly Sci. 2012: 37:1051-1078). Yet, its use has been limited by available processing methods. Non-porous PGS films limit diffusion and cell infiltration while salt-leeched foams compromise strength. Electrospinning PGS has been challenging since low molecular weight necessitates a carrier polymer, which alters properties if not removed. Additionally, the low glass transition temperature results in poor fiber morphology and has led to potentially toxic crosslinking approaches. We report a standard electrospinning method to produce well-defined PGS fibers while maintaining the excellent mechanical and cytocompatible properties of thermally crosslinked PGS.

Methods: PGS prepolymer was synthesized as previously reported (Wang Y. Nat Biotech. 2002:20:602-606) and dissolved in hexafluoroisopropanol (HFIP) with polyvinyl alcohol (PVA). Fibers were collected around a rotating mandrel. Fiber sheets were removed from the mandrel and cured at 120°C for 48 hours under vacuum. PVA and unreacted monomer were removed by ethanol and water washes. Chemical composition was evaluated by Fourier transform infrared spectroscopy (FTIR). The mass of the scaffold and the absorbance at 1733 were quantified before and after washes to estimate PVA removal. Uniaxial tensile testing of hydrated PGS sheets was performed for two separate crosslinking regimens. Additionally, suture retention tests were performed. Cytocompatibilty was evaluated by culturing human umbilical cord vascular endothelial cells (HUVEC) cells on fibrous sheets and staining with Live/Dead kit.

Results: Scanning electron microscopy (SEM) images show defined electrospun PGS-PVA fibers of 2.8 ± 1.2µm diameter (Fig1a). Fibrous structure is retained after crosslinking (Fig1b) and washing (Fig1c) although minor fusion is observed. The absorbance of the carbonyl group for electrospun PGS-PVA is 55% of PGS film, matching the value predicted by the PGS:PVA(55-45) mass ratio (Fig1d). After washing, the signal increased to 92% of PGS film and 53% of the original mass remained, suggesting removal of most of the PVA. Mechanical testing produced results similar to those previously reported for PGS films. As previously demonstrated the mechanical properties can still be tailored by adjusting crosslinking regimen. Electrospun PGS also demonstrates suturability. Live/dead results for HUVECs show high viability.



Material	Crosslink 120°C 48hr	Wash	C=O Absorbance at 1733.769	% of PGS peak
PGS film	X	X	0.492	100
55 PGS-PVA	X	X	0.454	92
55 PGS-PVA	X	--	0.303	60
55 PGS-PVA	--	--	0.278	55
PVA	--	--	0.015	--

	x) 120-48hr	y) 120-24hr,150-24hr
Ultimate Tensile Strength (Mpa)	0.64 ± 0.38	1.17 ± 0.02
Strain to Failure (%)	420 ± 89	179 ± 1
Modulus (MPa)	0.13 ± 0.04	0.74 ± 0.01
Suture Retention Strength (N/mm²)	12.2 ±1.2	--

Figure 1. Characterization of electrospun PGS. a-c) SEM of 55 PGS-PVA fibers after a) electrospinning, b) curing at 120°C for 48hrs, c) washing/ lyophilization. d) FTIR absorbance at 1733 cm^{-1} is used to estimate percent PGS present after each processing step and demonstrate removal of PVA e) uniaxial tensile testing to failure of electrospun PGS crosslinked at 120°C-48 h (x) and 120°C-24h/150 °C-24hr (y). f) Suture retention. g) Modulus, strength, and strain are similar to cast PGS and can be tailored by adjusting the crosslinking conditions h) Live/Dead staining of HUVEC on fibrous PGS shows high viability in vitro.

Conclusions: We developed an electrospinning approach to obtain thermally crosslinked elastomeric PGS fibrous structures. The process does not require coaxial set-ups or chemical crosslinkers. Additionally, PVA is removed by aqueous washes, producing true PGS fibers that preserve the mechanical and cytocompatible properties of PGS sheet and foam. This fabrication method permits more complex structures to be fabricated by fibrous PGS. Future work will focus on optimizing the protocols and producing inductive scaffolds for in situ tissue engineering.