Mechanical and Biological evaluation of Poly(glycerol sebacate) microfibrous scaffolds

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Statement of Purpose:

Biomaterial for tissue engineered (TE) scaffolds should provide desired chemical, physical and mechanical properties. In addition, designed scaffold should have topographical features mimicking native ECM to provide contact guidance, a phenomenon regulating cell behavior and cell functions *in vivo*. Amongst various polymers, collagen mimicking biodegradable Poly- (glycerol-sebacate) (PGS) was synthesized with elastomeric mechanical properties and has shown great promise in microfabricated scaffolds. However, its use is limited by its solubility and ability to cast nano-/microfibrous structures. For its superior mechanical properties, thermal or UV crosslinking of pre-polymer is required under high temperatures and vacuum. Here, we report fabrication of electrospun PGS fibers by simply blending it with biodegradable polycaprolactone (PCL) polymer without any post-processing. It was hypothesized that microfibrous structures of PGS polymer could provide contact guidance to the cells in addition to its mechanical properties.

Methods:

PGS: PCL hybrid scaffolds were prepared by blending the two polymers in various ratios (PGS:PCL = 0:1, 2:1, 3:1, 5:1, 0:1). Effect of PGS: PCL ratio and voltage (12-20kV) on fiber morphology and fiber diameter was studied. Surface morphology was observed with SEM and mechanical properties were studied using uniaxial tensile testing. HUVEC attachment and proliferation were studied up to 8 days with alamar blue assay on PGS: PCL scaffolds and compared with PCL-only scaffolds.

Results/Discussion:

Fiber formation showed a very random trend dependent on both PGS concentration as well as applied voltage. At the same PGS: PCL ratio, increased voltage resulted in reduced fiber diameter due to stretching of polymer jet. Further increase to 20 kV led to fiber fusion and increased fiber diameter. Similarly, increase in PGS amount resulted in increased fiber diameter form 2.76 ± 0.03 µm for PCL to 6.77 ± 0.26 µm for 5:1 PGS: PCL scaffolds. This was attributed to lower solution viscosity and waxy nature of PGS prepolymer. Mechanical properties (Fig. 1A and B) showed higher elastic modulus and ultimate tensile strength for 5:1 PGS: PCL scaffolds. Interestingly, increase in the modulus did not compromise on the ultimate elongation of the scaffold, suggesting its improved toughness while retaining its elasticity. Also, PGS: PCL scaffolds showed mechanical properties comparable to native human aortic heart valve leaflet, suggesting its potential application in heart valve tissue engineering. It should be noted that such improved mechanical properties could be achieved without any further thermal or UV crosslinking unlike other methods. Fabricated scaffolds were stable with thickness ranging from approximately 100-400 microns.

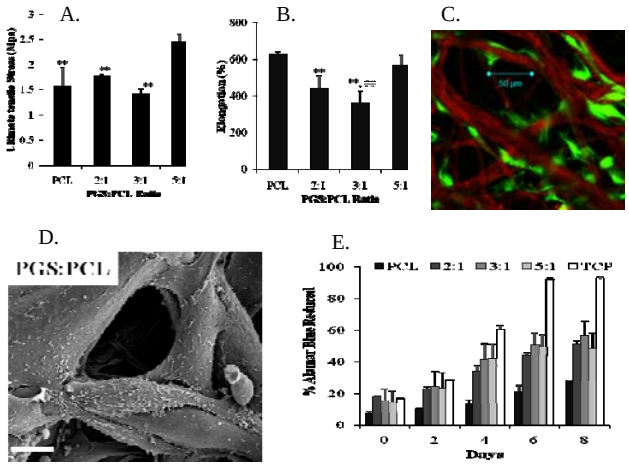

Figure 1: A. Ultimate tensile strength, B. % elongation at break, C. Cells attached to and aligned on fibers, D. SEM of cells on fiber, E. Cell proliferation on fibrous scaffolds.

HUVEC cells seeded on the PGS scaffolds showed significantly improved attachment and spreading (Fig. 2C and D) whereas cells remained rounded on PCL-only scaffolds. Addition of PGS also resulted in significantly higher cell proliferation (Fig 2E) compared to PCL scaffolds ($p < 0.05$). Thus, As-spun PGS scaffolds did not only improve mechanical properties but also showed better cell attachment and proliferation.

Conclusions:

We have fabricated microfibrous scaffolds from difficult to electrospin PGS polymer without any thermal or UV crosslinking. Scaffolds showed improved mechanical properties with higher PGS concentration. We also demonstrated improved cell attachment and proliferation on PGS scaffolds as compared to pure PCL scaffolds.