PEGylated poly(ester amide) elastomers with tunable physico-chemical, mechanical and degradation properties

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Statement of Purpose: Biodegradable synthetic elastomers such as Poly(1,3-diamino-2-hydroxypropane-co-polyol sebacate)s (APS) are gaining importance in soft tissue engineering applications due to their biocompatibility and mechanical compliance. However, APS-based thermoset elastomers exhibit poor solubility and low viscosity in commonly used organic solvents, limiting their processability. Moreover, APS elastomers has a relatively narrow (less than 8 fold difference) range of elastic modulus (0.56-4.34 MPa) and tensile strength (0.24-1.69 MPa. This study is aimed to synthesize and characterize a class of PEGylated poly(ester amide) elastomers to broaden the property spectra of APS and overcome these limitations of APS elastomers by incorporating biocompatible polyethylene glycol (PEG) in the polymer backbone to modify physicochemical and functional properties.

Methods: A series of novel APS-co-PEG copolymers was synthesized by varying PEG mole percentage (15-40%) and PEG molecular weight (400Da to 4kDa) to widely tune the physicochemical, mechanical and degradation properties. APS-co-PEG pre-polymers were synthesized via one-pot two-step condensation polymerization. The first step is the polycondensation between SA and PEG. In the second step, specific amounts of G and DAHP were added the reactants. APS-co-PEG pre-polymers were chemically and thermally characterized by nuclear magnetic resonance (^{1}H NMR), Fourier transform infrared spectroscopy (FTIR), gel permeation chromatography (GPC) and differential scanning calorimetry (DSC). The pre-polymers obtained under different synthetic conditions were thermally crosslinked into copolymer films and characterized for mechanical properties by uniaxial tensile pull assay. *in vitro* degradation properties was assessed by mass loss, change in film thickness, FTIR, mechanical testing and scanning electron microscope (SEM) imaging .

Results: We synthesized a series of APS-co-PEG pre-polymers by changing PEG mole % (15, 25 and 40% of PEG1K) and PEG molecular weight (400Da, 1kDa, 2kDa and 4kDa at 25% PEG). Incorporation of PEG in the APS polymer structure significantly improved its solubility in common organic solvents. FTIR spectra of APS-co-PEG showed increase in ester bond formation suggested that PEG was covalently bonded to SA and not physically blended in the copolymer structure. With the increase of PEG concentration from 0% to 40%, Tc shifted to higher temperatures and higher ΔHc indicated improved crystallization capacity. Also, there is a decrease in Tg with increase in PEG ratio. APS-co-PEG pre-polymers were thermally cured into elastomers. The crosslinking process was also confirmed by comparing the FTIR spectra of the pre-polymer and cured film samples. APS-co-PEG elastomers have a wide range of mechanical properties that could be carefully tuned to suit the desired application by tuning curing time, PEG ratio as well as monomer feeding ratio. Compared to the benchmark thermoset elastomers such as PGS and APS, APS-co-PEG polymers possessed wider range of the mechanical property spectrum. APS-co-PEG possessed wide range of ultimate tensile strength (0.07-2.38 MPa), elastic modulus (0.02-3.0 MPa) and elongation (93-993%) in crosslinked elastomer films (Fig. 1). Moreover, PEG incorporation increased the hydration of APS-co-PEG elastomer films leading to tunable degradation rate in phosphate buffered saline (10-40% mass loss over 14 days) (Fig. 2). Of note, the degradation is via surface erosion and preferential hydrolysis at the ester bonds in the APS-co-PEG backbone.

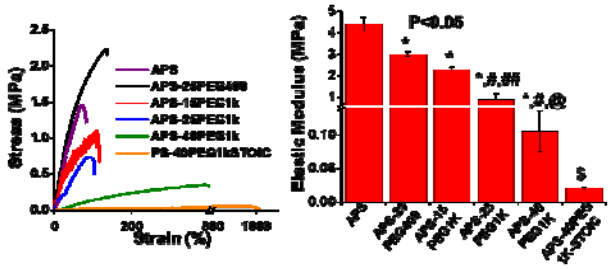

Figure 1. Mechanical properties of APS-co-PEG elastomers

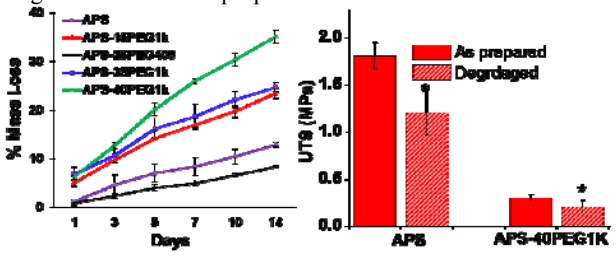

Figure 2. Degradation profiles of APS-co-PEG

Conclusions: We successfully synthesized a series of novel APS-co-PEG elastomers by tuning the molar ratio and molecular weight of PEG. The physicochemical, mechanical and degradation properties could be successfully tailored by altering the amount and length of PEG segments within the APS backbone. APS-co-PEG showed increased hydrophilicity and wide range of mechanical and degradation properties. Importantly, these elastomers degraded by surface erosion. We envision that these elastomers will broaden the property spectrum of currently available elastomers and will allow fine-tuning of physicochemical, mechanical and degradation properties to match that of a wide range of tissues to facilitate their regeneration.

References: 1 Bettinger, C. J.; Bruggeman, J. P.; Borenstein, J. T.; Langer, R. S., Biomaterials 2008, 29, (15), 2315-2325.

2 Bettinger, C. J.; Bruggeman, J. P.; Borenstein, J. T.; Langer, R., J Biomed Mater Res A 2009, 91A, (4), 1077-1088.