3D Printing of Poly(glycerol sebacate) Elastomeric Scaffolds via Thiol-Norbornene Photochemistry

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Statement of Purpose: 3-dimensional (3D) polymeric scaffolds present great potential in tissue engineering applications; however, polymers with diverse properties and a wide range of processing options are still limited. Few materials combine the mechanical properties of elastomers and the ability to be processed through 3D printing.[1] Here, we utilized thiol-norbornene photochemistry to form poly(glycerol sebacate) (PGS) networks from norbornene functionalized-PGS (Nor-PGS), where the mechanical properties can be simply controlled by the amount of thiolate crosslinker. Additionally, the thiol-ene reaction is insensitive to oxygen and the step-growth mechanism results in a uniform network,[2] forming controlled and functional networks. We then illustrated the 3D printing of macroporous scaffolds with photocrosslinking of Nor-PGS macromers and thiolate crosslinkers.

Methods: PGS was synthesized *via* a polycondensation reaction.[3] Nor-PGS was prepared by the reaction of the prepolymer with 5-norbornene-2-carbonyl chloride (Fig. 1a). Nor-PGS macromers with 15% modification were mixed with 0.1 wt% of the photoinitiator 2,2-dimethoxy-2-phenylacetophenone (DMPA) and varying amounts of pentaerythritol tetrakis(3-mercaptopropionate) (PETMP) added for thiol-norbornene crosslinking (Fig. 1b). The polymerization of Nor-PGS polymers was measured using photorheometry and mechanical properties determined with tensile testing. Mixtures of Nor-PGS macromers and PETMP crosslinkers were used as elastomeric inks to print designed constructs, where the materials were extruded from a syringe on a standard 3D printer and cured by immediate exposure to UV light (365 nm, 10 mW/cm^2) upon extrusion. Scaffolds were imaged with scanning electron microscopy (SEM). NIH 3T3 fibroblasts were used to probe scaffold cytocompatibility.

Results: Nor-PGS macromers were crosslinked by PETMP quickly as the storage modulus (*G'*) increased orders of magnitude in seconds after light exposure (Fig. 1c). The rheological properties of Nor-PGS crosslinked networks can be fine-tuned by introducing different amount of PETMP, where the *G'* values ranged from 17 kPa to 96 kPa (results not shown). Tensile testing also showed the mechanical tunability of Nor-PGS, where the % elongation of Nor-PGS was modulated by the PETMP amount used for photocrosslinking, showing ~170%, 200%, 250% for thiol/norbornene ratios of 1, 0.75, 0.5, respectively (Fig. 1d).

We applied Nor-PGS as a printing ink to fabricate a porous cube structure through a layer-by-layer process (Fig. 1e), and the porous structure was imaged using SEM (Fig. 1f). To demonstrate Nor-PGS's utility as a biomaterial, the cytocompatibility of the scaffolds was assessed with 3T3 fibroblasts. The fibroblasts were viable and spread into confluent layers when seeded onto the printed Nor-PGS filaments (Fig. 1g).

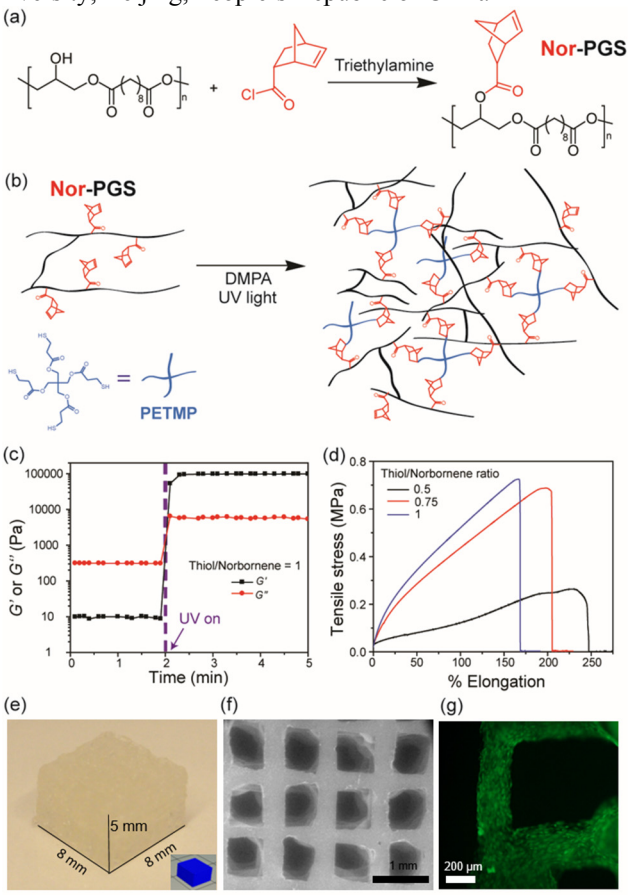

Figure 1. (a) Synthesis scheme of Nor-PGS macromers and (b) the formation of Nor-PGS networks. (c) Rheology of the crosslinking of Nor-PGS using PETMP and UV exposure. *G'* and *G''* are storage and loss moduli, respectively. (d) Representative tensile stress vs. elongation plots for Nor-PGS networks with varied crosslinker amount. (e) 3D-printed cube structure and (f) SEM image of porosity. (g) 3T3 fibroblasts cultured on Nor-PGS printed scaffolds and imaged with calcein-AM (green) for viability.

Conclusions: We developed a reactive norbornene functionality to PGS to facilitate the processing through techniques such as 3D printing. Nor-PGS exhibits tunable mechanical properties in the presence of different crosslinker amounts, allowing the use of the same functionalized Nor-PGS to attain varied mechanics. We also demonstrated the utility of Nor-PGS in the fabrication of 3D-printed elastomeric and biocompatible scaffolds. Taken together, we synthesized a new class of functionalized PGS, where the robustness of the thiol-norbornene photochemistry makes Nor-PGS a valuable biomaterial for scaffold processing.

References:

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