A Soft Biodegradable Elastomer Featuring a Dual Crosslinking Mechanism

Richard Tran[1], Dipendra Gyawali[1], Jung-Chih Chiao[2], and Jian Yang[1]
[1]Deptartment of Bioengineering and [2]Department of Electrical Engineering
The University of Texas at Arlington, Arlington, TX 76019

Statement of Purpose: The need for advanced materials in tissue engineering has prompted increased research to produce novel biomaterials with a wide range of controllable properties. Currently, there is a scarcity of research in developing new biodegradable elastomeric materials for soft tissue engineering.[1] Herein, we report the synthesis and evaluation of a novel elastomeric polymer from biocompatible monomers citric acid and maleic anhydride termed poly (octamethylene maleate (anhydride) citrate) (POMaC). This is the first time a dual crosslinking mechanism has been introduced for elastomer designs. The mechanical properties, degradability, and functionalities of POMaC can all be tuned through the dual crosslinking mechanism.

Methods: The synthesis of POMaC is shown in Fig. 1A.

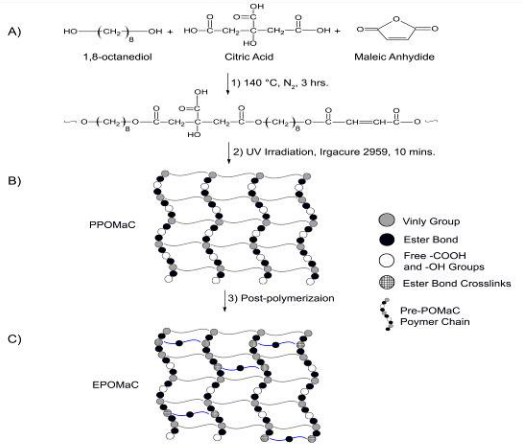

Figure 1. Schematic representation of POMaC A) synthesis, B) UV crosslinked networks, and C) dual crosslinking mechanism.

In order to remove any of the unreacted monomers and oligomers, the pre-polymer was dissolved in 1,4-dioxane, and purified by drop wise precipitation in deionized water. The undissolved pre-polymer was collected and lyophilized 3 days to obtain the purified pre-POMaC. ^{1}H-NMR and FT-IR spectra were obtained to verify the chemical composition of the pre-polymer, and the average molecular weight was characterized by MALDI-MS. POMaC networks were formed by crosslinking through free radical polymerization upon exposure to UV irradiation (Fig. 1B). POMaC has the option to be further crosslinked via post-polymerization at 80°C for pre-determined times to create ester-bond crosslinked POMaC (EPOMaC) (Fig. 1C). Tensile tests, swelling studies, *in-vitro* degradation, and *in-vitro* cell attachment and proliferation studies were also performed to evaluate the POMaC networks. In addition, POMaC polymers were combined with MEMS technologies to create unique scaffolds for soft-tissue engineering.

Results: The synthesis of POMaC was carried out under a controlled condensation reaction to yield a low molecular weight polymer with average molecular weights in the range of 701.23 to 1291.34 Da. The shoulder peak located at 1650 cm^{-1} in the FT-IR spectra, and the peaks located between 6-7 ppm in the ^{1}H-NMR spectra verify the successful incorporation of the vinyl group into the polymer chain. The presence of the olefin moiety allows POMaC to be crosslinked in the absence of harsh conditions through a free radical polymerization upon exposure to UV light or redox initiated systems. Crosslinking through this method allows for the preservation of valuable functional groups, which can be used for further crosslinking through ester bond formation to fine-tune the material properties or the bioconjugation of proteins into the bulk material.

The material properties of POMaC can all be controlled through the monomer ratios, initiator concentration, and dual crosslinking mechanism. Tensile tests show that the Young's modulus ranged from 0.041 to 1.54 MPa, and elongations from 76 to 441% for POMaC networks. The swelling ratio of the polymer in water was in the range of 76 to 211%. The degradation studies of the polymer in PBS (pH 7.4; 37°C) show that 18-77% of the polymer mass remained, which was dependent upon on the crosslinking density of the network and molar ratios of the monomers.

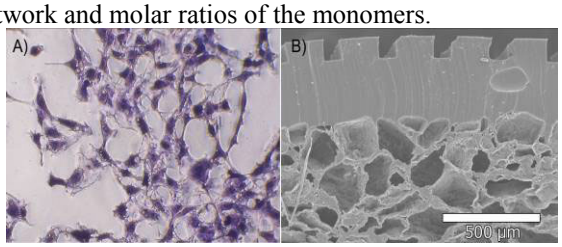

Figure 2. A) H&E stained 3T3 fibroblasts on EPOMaC 8 film and C) MEMS channeled salt leached scaffold

In-vitro cell culture evaluation indicates 3T3 cellular attachment and proliferation with normal morphologies on both film (Fig. 2A) and scaffold substrates. POMaC polymers can also be combined with MEMS technologies to create micro-channeled scaffolds for soft-tissue engineering purposes (Fig. 2B).

Conclusions: We have developed a new class of novel elastomeric biomaterials that are synthesized using inexpensive monomers and a cost-effective synthesis procedure. The dual crosslinking mechanism allows for the option of crosslinking the material through *in-situ* UV irradiation and/or polycondensation through the addition of heat, thus giving POMaC a wide range of material properties, excellent cytocompatibility, and great processability. Thus, POMaC may be a viable material to meet the versatile needs in soft-tissue engineering applications.

References:

1. Yang, J. *Biomaterials* **2006**, *27*, 1889-98.