Control of Network Structure of Photopolymerized Poly(ethylene glycol) Diacrylate Hydrogels

Georgia Papavasiliou[1], Megan Morris[2] Fouad Teymour [1]and Eric M. Brey[1].
Illinois Institute of Technology Chicago, IL[1] University of Utah, Salt Lake City, UT [2]

Statement of Purpose:
Poly(ethylene glycol) diacrylate (PEG-DA) hydrogels have been utilized for a variety of tissue engineering applications. A critical factor determining successful use of these materials is the crosslink density which is related to the transport and mechanical properties of the resultant hydrogel. Experimentally, a variety of parameters such as the duration of photopolymerization, and the chemical composition of the polymerization system affect the hydrogel crosslink density. Experimental and theoretical sensitivity analyses of the key parameters of hydrogel formation based on the kinetics of the polymerization process has been conducted to control the crosslink density of PEG-DA hydrogels. The capability to control and optimize the network structure of these materials will contribute significantly to the development of tissue engineered substitutes.

Methods:
PEG-DA hydrogel formation was accomplished via free-radical photopolymerization in the presence of the co-initiator triethanolamine (TEA) and N-vinyl-Pyrrolidinone (NVP) using eosin as the photoinitiator followed by exposure of the pre-polymer solution to visible light (λ = 514nm). Prior to photopolymerization the precursor solution was adjusted to pH 8 with 6M HCl and filter sterilized using a 0.2 µm syringe teflon filter. To control the crosslink density as a function of laser exposure time of the resultant hydrogels formed, the concentrations of each of the components of the precursor solution were varied individually. Precursor solutions were prepared with (a) varying percentages of PEG-DA (25%, 40% and 50% w/v) and fixed concentrations of 225mM TEA, 37mM NVP and 0.09mM eosin, with (b) varying NVP concentrations (19mM, 37mM and 74mM) and fixed concentrations of 0.09mM eosin, 225mM TEA and 25% w/v PEG-DA, with (c) varying TEA concentrations (113mM, 225mM and 450mM) and fixed concentrations of 37mM NVP, 0.09mM eosin and 25% w/v PEG-DA and with (d) varying eosin concentrations (0.05mM, 0.1mM and 0.09mM) and fixed concentrations of 225mM TEA, 37mM NVP and 25% w/v PEG-DA. In each case polymerization times were varied from 2-20 minutes. Hydrogels were weighed in their relaxed state immediately following polymerization, in their swollen state after immersing the hydrogel in water for twelve hours, and in their dried state following drying for 72 hours in vacuum. This data was used to quantify the crosslink density using the Flory-Rehner equation. A computational model predicting the crosslink density of PEG-DA hydrogel formation based on the kinetics of the free-radical polymerization process has been developed. The mechanism of gel formation results from crosslinking due to the propagation of radicals through pendant double bonds induced by the presence of the PEG-DA monomer. The computational model utilizes the Numerical Fractionation technique (NF)[1] and circumvents the issue of numerical divergence of the polymer weight-average chain length at the gel point allowing for the prediction of the gel properties and the gel crosslink density.

Results/Discussion: An experimental sensitivity analysis based on variation of the concentration of components in the precursor solution indicates that the crosslink density of the hydrogels can be controlled. Figure 1 shows that increasing the percentage of PEG-DA (w/v) in the precursor solution increases the polymer crosslink density since this increases the number of pendant acrylate groups resulting in more highly crosslinked hydrogel structures. Experimental results also indicate a decrease in crosslink density with increasing TEA and eosin concentrations.

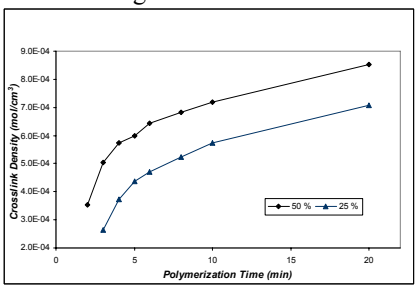

Figure 1. Effect of PEG-DA % (w/v) on Crosslink Density as a Function of Time

Similar trends in crosslink density were observed from computational model predictions with increasing percentages of PEG-DA in the polymer formulation. Experimental results from this study are currently being used to validate computational model predictions as the key parameters of the polymerization process are varied.

Conclusions: This experimental and theoretical investigation indicates that hydrogel crosslink density can be controlled based on the polymerization kinetics. Future work focuses on validating the computational model's predictions of crosslink density as a function of polymerization time with experimental measurements. Computational model predictions will be used as a guide to experimental design and contribute significantly towards the optimization of network structure of PEG-DA hydrogels in tissue engineering applications.

References:
1. (Teymour F. Macromolecules. 1994; 27: 2460-2469)

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