Poly(N-isopropylacrylamide-co-PEG Acrylate) Simultaneously Physically and Chemically Gelling Polymer Systems

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Statement of Purpose: A thermosensitive physically and chemically cross-linking poly-N-isopropylacrylamide based polymer system was developed and then evaluated against purely physical cross-linking gels for lower critical solution temperature (LCST), as well as creep, rheological and swelling properties. Because of its improved mechanical properties and self-assembling behaviour, this material could be useful in functional embolization and other microsurgical applications.

Methods:

Materials employed include poly(ethylene glycol) monoacrylate(PEG), pentaerythritol tetrakis 3-mercaptopropionate (QT), phosphate buffered saline, Poly-N-isopropylacrylamide (pNIPAAm), and acryloyl chloride. pNIPAAm was initially copolymerized with PEG and further modified to form poly(NIPAAm-co-PEG)-acrylate with acylate terminated pendant groups.
The copolymer was then chemically cured by mixing with QT, a tetrafunctional thiol containing compound.
LCST of the material was determined using differential scanning calorimetry (DSC) and rheology. The effect of mixing time on the polymer's gelation kinetics was investigated through rheometry. A separate rheometry study examined the frequency dependence of the polymer gel at different temperatures. Swelling tests were conducted on chemically cured polymer samples at temperatures of 5, 20, and 37 C to determine temperature dependant swelling. Swelling kinetics were also evaluated for the temperature-dependent swelling.

Results/Discussion:

For poly(NIPAAm-co-PEG) at 95:5 feed ratio , the real ratio was 94.6:5.4 and NMR data exhibited that the ratio of PEG to PEG- acrylate was 1.6:3.5, giving approximately a 69 % conversion. When poly(NIPAAm-co-PEG)-acrylate was mixed with a multifunctional thiol compound, chemical cross-linking occured between the acrylate and thiol groups through a Michael-Type Addition reaction. Figure 1 shows the chemical cross-linking network that is formed during this reaction.
Rheological data shows that the polymer exhibits frequency dependence when not chemically cured with QT at both 5°C and 20°C. It should also be noted that the physically gelling polymers exhibit low-frequency strength loss, while the chemically cured polymers consistently have a higher dynamic moduli in both the low and higher frequency regions.

Swelling of the chemically cross-linked polymer was found to be temperature dependent, as seen in Figure 2.

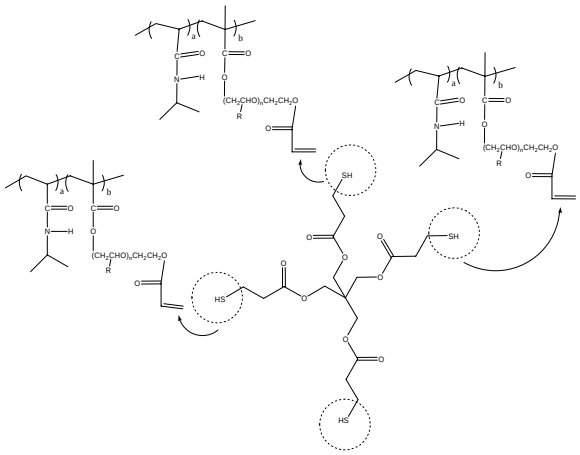

Figure 1. Chemical cross-linking network between functionalized copolymer and QT through Michael Type reaction

At 4˚C, the polymer demonstrated a high degree of swelling, at 456%. However, as temperature increased to 20˚C and 37˚C, the polymer swelling decreased to 387% and 319%, respectively indicating that this chemical gel remains temperature sensitive due to physical interactions between the temperature-dependent hydrophobicity of the N-isopropylacrylamide chains.

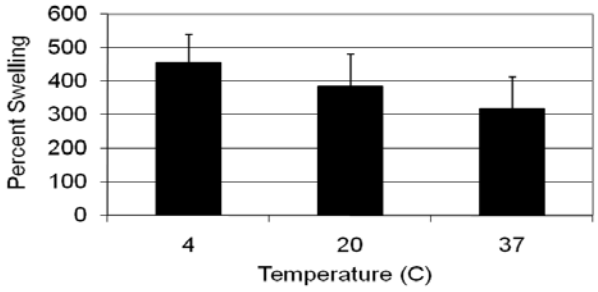

Figure 2. Temperature-dependent swelling of gelled polymer (pH 7.4), n=3;

Conclusions: A simultaneously physical and chemical crosslinking polymer was developed by modifying NIPAAm with PEG and acrylate and mixing it with a tetrafunctional thiol containing compound. The combination of physical and chemical gelation provides a curing capability not found in other physical gels under study for use in microsurgical applications.

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