SYNTHESIS AND CHARACTERIZATION OF MAGNETICALLY RESPONSIVE HYDROGEL COMPOSITES

Reynolds A. Frimpong and J. Zach Hilt
University of Kentucky, Department of Chemical and Materials Engineering
177 F. Paul Anderson Tower, Lexington, KY 40506-0046

INTRODUCTION

Hydrogels are three dimensional networks of mainly hydrophilic polymer chains and have been used as biomaterials for many biological applications due to their biocompatibility. Environmentally responsive hydrogels can be made to trigger their swelling response due to changes in their ambient conditions such as pH, ionic strength and temperature [1].

Magnetic micro- and nanoparticles have unique properties that are different from their bulk properties. They can be coated with biological molecules and be made to interact with or bind to biological entities and have been used in many biomedical applications. They can be manipulated from a distance by an applied magnetic field and in addition be made to generate thermal energy via an oscillating magnetic field [2], which is a property specifically harnessed in magnetic hyperthermia treatment.

Hydrogel composites containing magnetic particles were studied that exploit the swelling response of N-isopropylacrylamide, a temperature responsive hydrogel, and the heating capabilities of magnetic particles. Their swelling dependence on temperature, crosslinking length, crosslinking percentage and the presence of magnetic particles were analyzed.

EXPERIMENTAL METHODS

Synthesis of Magnetically Responsive Hydrogel Composites

Network systems of crosslinked poly(N-isopropylacrylamide) (PNIPAAm) containing ethylene glycol of different crosslinking lengths and at various crosslinking percentages were prepared and examined. Microscale magnetic particles were incorporated in some of these systems. Equilibrium swelling studies were done on these thermally sensitive hydrogels to characterize their swelling response with varying temperature and also investigate their dependence on crosslinker length and percentage.

The monomer used was N-Isopropylacrylamide (NIPAAm). The crosslinkers used were ethylene glycol dimethacrylate (EGDMA), tetraethylene glycol dimethacrylate (TEGDMA) and poly(ethylene glycol) 400 dimethacrylate (PEG400DMA). The initiator used for the UV free radical polymerization was 2, 2-dimethoxy-2-phenyl acetophenone (DMPA). Carboxylated paramagnetic polystyrene particles (1 – 2 μm in diameter, 2.65 vol%) contained in an aqueous suspension were used. These particles are iron containing (Fe_2O_3, Fe_3O_4) microspheres with a functionalized polystyrene surface. The NIPAAm and DMPA were obtained from Aldrich. EGDMA, TEGDMA, PEG400DMA and carboxylated paramagnetic polystyrene particles were obtained from Polysciences, Inc. (Warrington, PA).

The monomer mixtures were prepared with 20 mol% EGDMA, 10%, 20% and 30 mol% TEGDMA, and 20 mol% PEG400DMA. Ethanol solvent was added to the mixtures prepared on a 1:1 vol% basis to speed up the dissolution of the NIPAAm in these crosslinkers. The 20 mol% EGDMA, 20% and 30 mol% TEGDMA were similarly prepared and 25 vol% of the micro magnetic particles added. Since the micro magnetic particles were contained in an aqueous solution the corresponding amounts of additional water present in these mixtures were also added to their respective systems without particles. This was to ensure the additional water did not contribute to any differences in the swelling studies. A summary of the formulated systems is given in Table 1.

Table 1 Crosslinker types and percentage crosslinking used with NIPAAm

Mole Percent Crosslinking	***Ethylene Glycol DMA***	***Tetra ethylene Glycol DMA***	***Poly(ethylene Glycol) 400 DMA***
10		O	
20	**X**	**X**	O
30		**X**	
X - systems with and without magnetic particles O - systems that did not include magnetic particles			

A 1 wt % DMPA initiator (of weight of NIPAAm and crosslinker) was added to the mixtures. The monomer mixtures were pipetted between two clamped 6" by 6" glass plates with a Teflon spacer that was about 750 μm thick. The glass assembly plate was placed under a UV source (Lesco Exposure Lamp System) and exposed to UV light of wavelength 365 nm with an intensity of 30.0 mW/cm^2 for 5 minutes to initiate the free radical polymerization. The polymer films were washed with deionized water for several days to remove excess solvent and any unreacted monomers and initiators. The water was changed several times during the washing process.

Methods for Equilibrium Swelling Studies

Equilibrium swelling characteristics were obtained by placing polymer discs in a phosphate buffered saline (PBS) solution of pH 7.4 at different temperatures and measuring the swelling ratios. After the polymer films were completely washed, polymer discs of about 1.5 cm in diameters were cut. The discs were dried and their dry weights measured in air. Their weights were also measured in a non-solvent, heptane using a Mettler Toledo density kit. The discs were then placed in 50 ml centrifuge tubes filled with PBS in water baths maintained at set temperatures for study. The temperatures used were 20, 25, 27.5, 30, 33.5, 37 and 40 ^{o}C. The samples were taken out periodically, wiped, and weighed until they reached an equilibrium point. At equilibrium, the weights of the samples are again measured in heptane. Three samples were used and responses averaged for each system. The weight swelling ratio, q, was calculated for each sample from the ratio of the weight of the swollen sample to the weight of the dry sample. The volume, V, of each sample was determined from its weight in air and in heptane.

$$V = \frac{W_a - W_h}{\rho_h} \qquad (1)$$

where W_a is the weight of the sample in air and W_h is its weight in heptane. The volume swelling ratio, Q, was then determined from the relation:

$$Q = \frac{W_a{}^s - W_h{}^s}{W_a{}^d - W_h{}^s} \qquad (2)$$

with the superscripts s and d representing the swollen and dry forms respectively.

RESULTS

Figure 1 below shows the temperature effect on the equilibrium volume swelling (Q) for different network systems which were either incorporated with magnetic particles or had none present. In the figure, 20 and 30 represent mol% crosslinking. E and T represent ethylene glycol dimethacrylate and tetraethylene glycol dimethacrylate, respectively, and M indicates the presence of magnetic particles in the network. Highest equilibrium volume swelling was observed at the lower temperatures. PNIPAAm has a lower critical transition temperature around 32 – 35 ^{0}C [1, 3] and is more hydrophilic below the critical temperature.

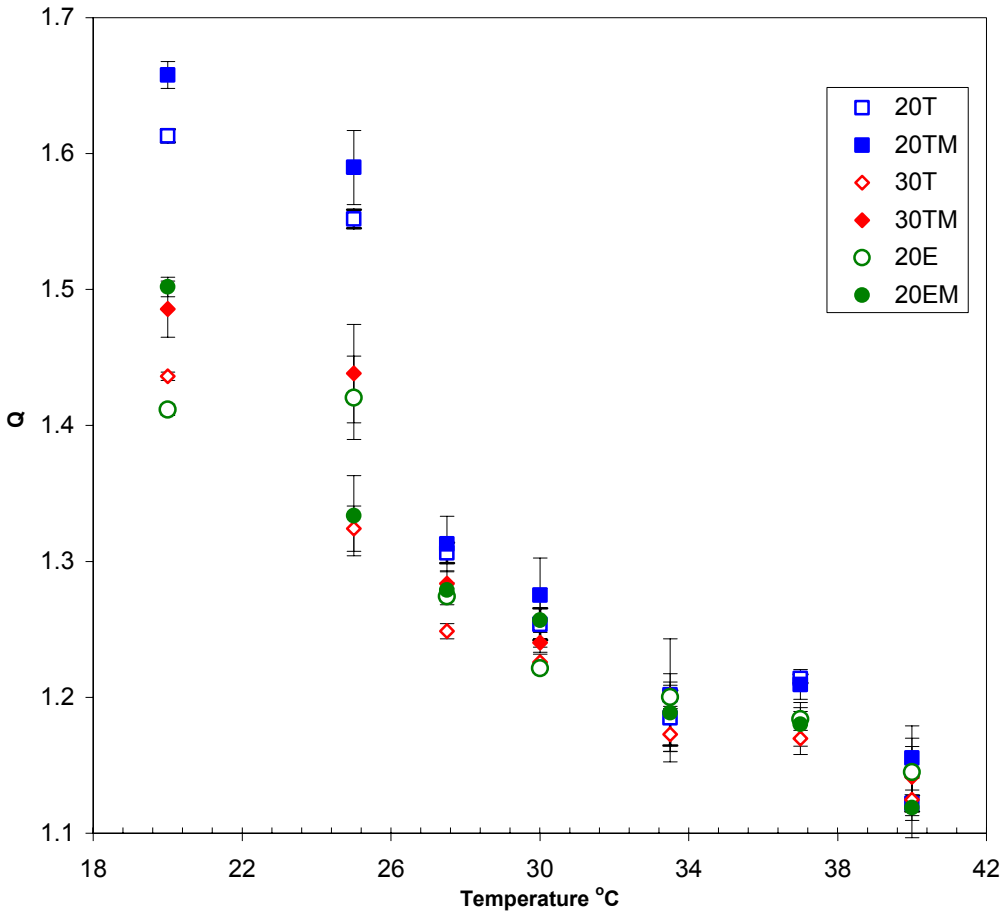

Figure 1 - Effect of temperature on volume swelling ratio

The presence of the magnetic particles caused slight increases in Q for the TEGDMA samples at all the temperatures studied but for the EGDMA samples decreased Q was observed for some. The magnetic particles create voids in the polymer which should allow more water to be absorbed and an increase in the volume swelling as observed for the TEGDMA systems. This, however, does not explain the different trend observed for the EGDMA system which had a different interaction with the magnetic particles.

The highest equilibrium volume swelling was obtained for PEG400DMA while EGDMA showed the least swelling. The greater the percentage of crosslinking, the less equilibrium swelling was obtained for the various systems. EGDMA has shorter chain lengths TEGDMA and PEGDMA and thus forms tighter networks which limit swelling. Increased crosslinking percentages also lead to tighter networks.

DISCUSSION

Different hydrogel systems of NIPAAm have been characterized by establishing their swelling dependence on crosslinking length, crosslinking percentage, temperature, and the effect of the presence of magnetic particles. Longer crosslinkers have loose networks and swell more than shorter crosslinkers. Increased percentage of crosslinking lowers swelling as network chains become tighter. Increased swelling is also observed at reduced temperatures which are lower than the LCST (32 – 35 ^{o}C) of NIPAAm. The presence of magnetic particles caused increased swelling in TEGDMA systems but reduced swelling was observed for the EGDMA system. The presence of the magnetic particles however, did not introduce any significant change in trend of the dependence of Q on temperature. The different interactions have to be examined further to understand the mechanisms involved.

REFERENCES

1. Peppas, N.A., Bures, P., Leobandung, W., Ichikawa, H., Hydrogels in Pharmaceutical formulations, European Journal of Biopharmaceutics 50 (2000) 27-46.
2. Rosenweig, R., Heating magnetic fluid with alternating magnetic field, Journal of Magnetic Materials 252 (2002) 370-374.
3. Zhang, J., Huang, S., Zhuo, R., Preparation and characterization of novel temperature sensitive Poly(N-isopropylacrylamide-co-acyloyl beta-cyclodextrin) hydrogel with fast shrinking kinetics, Macromolecular Chemistry and Physics 205 (2004), 107-113.