Nanocomposite Hydrogels as Remote Controlled Drug Delivery Systems

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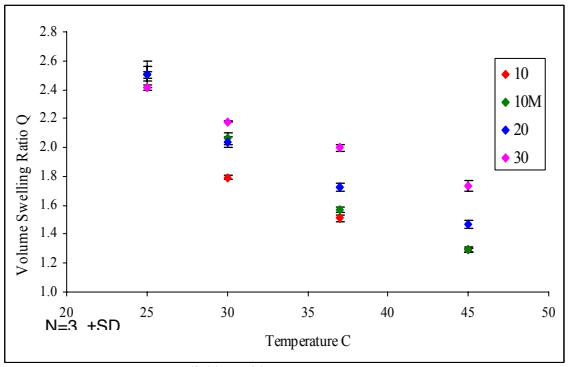
Statement of Purpose: Hydrogel nanocomposites have potential applications as functional components of microdevice (e.g. valves, sensors) because they can respond to specific external stimuli. Hydrogel nanocomposites with and without magnetic nanoparticles were prepared and characterized for swelling behavior, morphology, and electromagnetic field effect. Drug release behavior from nanocomposite was studied to demonstrate remote controlled (RC) drug delivery.

Methods: Hydrogel nanocomposites with and without iron oxide (Fe_3O_4) nanoparticles, were synthesized by UV photopolymerization with various crosslinking densities and nanoparticle loadings. The hydrogel systems were based on N-isopropylacrylamide (NIPAAm) as temperature sensitive monomer with various crosslinkers like tetraethylene glycol dimethacrylate (TEGDMA) and polyethylene glycol 400 dimethacrylate (PEG400DMA).

The hydrogel films were cut into circular discs and dried. Kinetic and equilibrium swelling studies were performed on hydrogel discs at different temperatures to characterize the effect of crosslinking density, type of crosslinker, and particle loading on swelling transition temperature. Morphology of the nanocomposites was analyzed to characterize the dispersion of magnetic nanoparticles in the hydrogel matrix. Dry hydrogel nanocomposite discs with varying particle loadings were subjected to electromagnetic field of strength 0.41 kA/m and frequency 297 kHz to demonstrate the heating effect. Nanocomposites were loaded with pyrocatechol violet dye as a model drug and release studies were conducted with one set of discs placed in alternating electromagnetic field of strength 0.85 kA/m and frequency 297 kHz, while another set outside the field.

Results/Discussion: The swelling studies on NIPAAm-PEG400DMA system with varying crosslinker density at various temperatures show that as temperature increases, the volume swelling ratio of the hydrogels decreases (fig. 1). This trend is expected since NIPAAm is negative temperature-sensitive hydrogel.



10, 20, 30 represent % crosslinking with PEG400DMA
M represents magnetic nanocomposite

Figure 1. Effect of temperature on equilibrium swelling

The swelling studies also show that magnetic particles do not have significant effect on swelling behavior.

When the dry hydrogel nanocomposite discs were subjected to electromagnetic field, gels with no particles showed negligible heating, while increase in particle loading increased the maximum temperature achieved in field (fig. 2). Initial temperature rise is fast followed by slow continuous increase in temperature later on. Apart from particle loading, temperature rise also depends on heat transfer aspects as the disc was open to air.

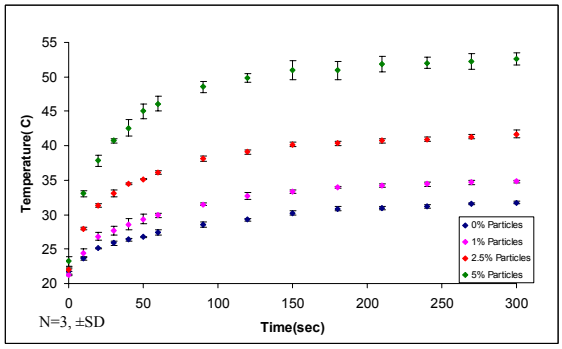


Figure 2. Heating effect of nanocomposites in electromagnetic field

The dye release studies showed that when alternating electromagnetic field was applied, nanocomposites with 5% particles show about 25% reduction in dye release, while pure hydrogel was unaffected (fig. 3). This suppression in release is a result of the collapse of the hydrogel network in field. High temperatures generated at nanoscale cause negative temperature sensitive network of NIPAAm to collapse, shrinking the mesh size.

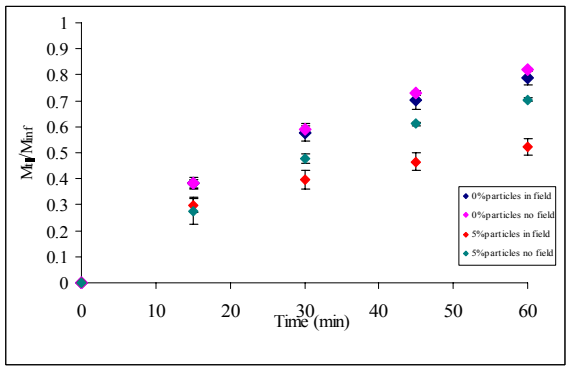


Figure 3. Controlled drug release from nanocomposites in electromagnetic field

Conclusions: Magnetic nanocomposites of N-isopropylacrylamide show negative temperature sensitivity. Rise in temperature of nanocomposite on application of electromagnetic field can be controlled by nanoparticles loading. Controlled drug release was obtained from magnetic nanocomposites on application of electromagnetic field, which demonstrates RC drug delivery.