Hydrogel Nanocomposites for Remote Controlled Drug Delivery Applications

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Statement of Purpose: Hydrogels and hydrogel composites are currently being extensively studied for various high interest biomedical applications including drug delivery, tissue engineering, and microfluidic valves. The incorporation of magnetic nanoparticles into a hydrogel matrix can provide unique properties including ability of remote actuation by application of alternating magnetic field (AMF). In this study, development and characterization of magnetic hydrogel nanocomposites, demonstration of remote controlled (RC) pulsatile drug delivery, and soft actuator applications will be highlighted.

Methods: Magnetic nanocomposites of negative temperature responsive poly (N-isopropylacrylamide) (PNIPAAm) hydrogels were developed by incorporation of superparamagnetic Fe_3O_4 nanoparticles. NIPAAm content and nanoparticle loadings in the system were varied to get the desired temperature and AMF response. Heating and collapse of application of AMF and subsequent recovery was studied and a model was proposed to predict this process for varying hydrogel geometries.
AMF was applied to show pulsatile release of different model drugs for varying ON-OFF cycles. The hydrogel nanocomposite was incorporated as a valve in a ceramic microfluidic device with channel dimensions of 600X700 µm. The flow through channel was remotely regulated using AMF.

Results: The temperature sensitivity and swelling transition temperature of nanocomposite was controlled by composition of PNIPAAm in the hydrogel system. When exposed to AMF, heating of superparamagnetic Fe_3O_4 particles led to rise in temperature of the nanocomposite system. When temperature increased above the lower critical solution temperature (LCST), the hydrogel collapsed. Increasing particle loadings and nanocomposite thickness resulted into higher temperatures and faster collapse. However, more thickness also implies slower recovery because it is controlled by diffusion. Other factors that influence the heating and collapse process include properties of the surrounding fluid such as heat transfer coefficient and temperature.
The unique property of remote heating and collapse was used to obtain RC pulsatile drug release from matrix type systems (Fig 1). The pulse of AMF leads to squeezing out of drug and corresponds to a pulse in drug release. Important factors that influence release profile are drug molecular weight and AMF ON-OFF durations. The model drug with higher molecular weight showed more control on release than smaller drug because of its slower diffusion in OFF state.

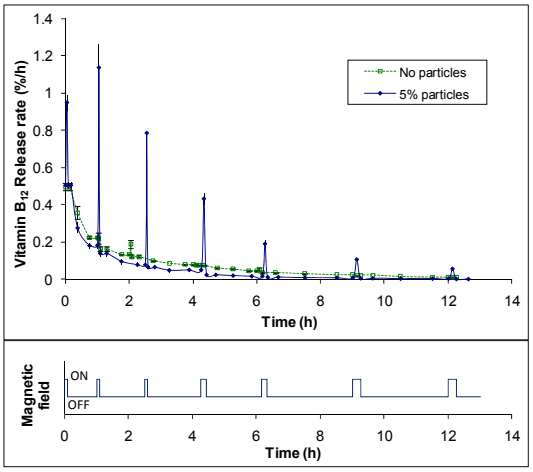

Fig. 1.Release of vitamin B_{12} on AMF application

A hydrogel nanocomposite disc was placed in the channel of a ceramic microfluidic device. RC heating and collapse of the gel led to opening of the valve and control on flow using AMF was observed for multiple cycles (Fig 2). Present studies are underway to further study this device and demonstrate drug delivery applications.

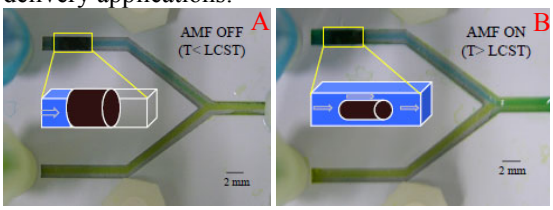

Fig. 2. Hydrogel nanocomposite valve in microfluidic device for flow control with a point heater (A) Closed (B) Open

Conclusions: Magnetic hydrogel nanocomposites were successfully synthesized and their temperature and AMF response was tailored using the composition and geometry. The rate of hydrogel collapse and recovery are key parameters in design of hydrogel as a component of drug delivery device. A model was developed to predict the RC heating, collapse, and recovery process. The accelerated RC collapse of hydrogel nanocomposites in matrix resulted into pulsed release. Hydrogel nanocomposite was incorporated as a valve in a microfluidic device and ON-OFF control was demonstrated. Future studies include demonstration of hydrogel nanocomposite as a valve in an implantable drug delivery device for precise dose control using AMF.

References: Satarkar NS, Hilt JZ. Acta Biomater 2008 (4) 11
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