Magnetothermally-Triggered Drug Delivery: Combining FePt and Co-γFe_2O_3 Nanoparticles with Thermosensitive Polymers

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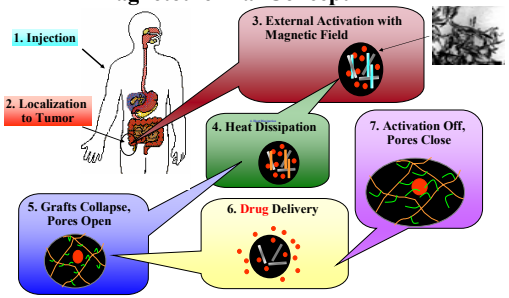
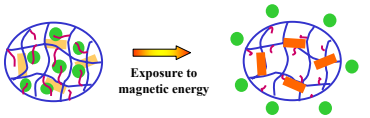
Abstract

Novel drug delivery systems that can be triggered by an alternating current magnetic were developed by incorporating magnetic FePt nanoparticles into hydrogels based on poly(N-isopropylacrylamide), PNIPAAm. Polymers were developed with both positive and negative thermally-activated release responses, using thermosensitive grafts to activate release at high temperatures. The stable inclusion of FePt nanoparticles in hydrogels was verified, as was the influence of the magnetic nanoparticles on polymer thermosensitivity.

Magnetothermal Concept



Objective: Magnetothermal Drug Delivery System



Grafted matrix with magnetic particles and drug entrapped

Drug releases as the temperature of the system rises due to heat dissipation from magnetic particles

External Triggered Delivery

Triggering Events:

Change in Environmental Conditions

Temperature, pH, Ionic Strength, Chemical Concentration, Pressure, Magnetic Field, Radiation/Light

Infrared or Light Energy

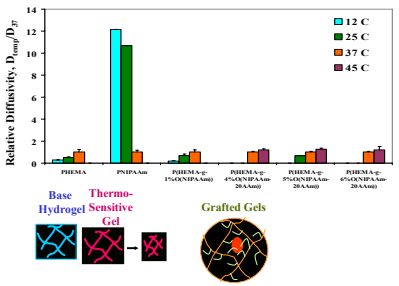
limited by light penetration through dermis/tissue or photoinitiated reaction during angioplasty {West and Hubbell, 1990s}

Magnetic Field

Placement/localization of particles (eg., blood brain barrier)
Pulsatile delivery by forcing/squeezing drug from gel {Edelman and Langer, 1980s}

Release using Grafted Gels

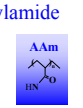
Diffusion Coefficient Increases with Temperature for Grafted System

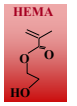


Materials

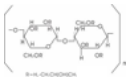
Polymers:

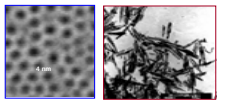
1. Base Polymer: poly(2-hydroxyethyl methacrylate), PHEMA
   Grafts: N-isopropylacrylamide-co-acrylamide (NIPAAm-co-AAm)





2. Hydroxypropyl Cellulose HPC





Magnetics: FePt Nanospheres
Co-γFe_2O_3 Maghemite Nanorods

Model Drug: Theophylline

Incorporating Nanoparticles

Certain Magnetic Nanoparticles Heat in an AC Magnetic Field

Curie Temperature (T_c): Temperature at which superparamagnetic materials stop heating (Project goal: 45 °C, to avoid tissue necrosis)
- T_c affected by composition and size of nanoparticles

Challenges:

1. Disperse magnetic nanoparticles in aqueous solution

stabilize dispersion with poly(acrylic acid), mercapto-undecanoic acid or other surfactant

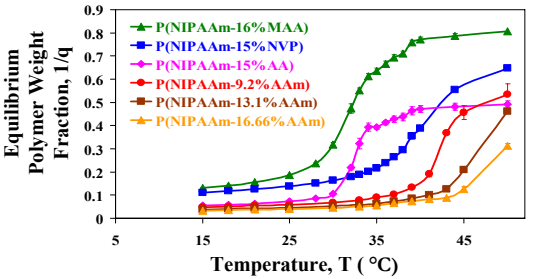
2. Maintain dispersion in hydrogel for uniform heating

agglomeration problem in PNIPAAm gels

FePt remains dispersed in HPC solution

Modifying LCST

Adding Hydrophilic Comonomers to NIPAAm Raises the LCST



Conclusions and Future Work

Grafted P(HEMA-g-NIPAAm) gels allow positive thermosensitive drug release, but need to optimize graft length and density

FePt and Co-γFe_2O_3 have been incorporated into PNIPAAm and HPC hydrogels with mixed success

Future work:
study the thermal response of magnet-loaded hydrogels when exposed to AC magnetic fields