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Thermoresponsive Magnetic/Polymer Composite Nanoparticles for Biomedical Applications

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ABSTRACT

Thermoresponsive magnetic/polymer composite nanoparticles possess unique properties for combined simultaneous application of magnetically targeted drug delivery, hyperthermia, controlled drug release and Magnetic Resonance Imaging (MRI). Magnetic nanoparticles (MNPs), in particular Fe_3O_4 and γ-Fe_2O_3, are widely employed as magnetically targeted drug carriers, hypothermic therapeutics, MRI contrast agents due to their apparent biocompatibility and unique size-dependent properties. Thermoresponsive polymers provide controlled release of drugs with the temperature stimulus above their lower critical solution temperature (LCST). Incorporation of MNPs into the thermoresponsive polymers structure provide combined benefits: (i) the magnetic component acts as an internal heat source as a result of magnetically induced heating, which could trigger shrinking of polymer shell to release the drug; (ii) preferential accumulation of drug loaded composite nanoparticles to the targeted locations is achieved by utilizing an external magnetic field; (iii) imaging and diagnostic can be done by MRI. In this article, formulation of a drug delivery system based on γ-Fe_2O_3 MNPs and thermoresponsive polymer Poly(N-isopropylacrylamide) (PNIPA) is presented. γ-Fe_2O_3 MNPs were synthesized by wet chemical methods. γ-Fe_2O_3–PNIPA composite nanoparticles were synthesized by dispersion free-radical polymerization of NIPA monomers. The synthesized magnetic/polymer composite nanoparticles were characterized by transmission electron microscopy (TEM), X-ray diffraction (XRD), thermal gravimetric analysis (TGA), UV-visible spectroscopy (UV-Vis), vibrating sample magnetometry (VSM) and dynamic light scattering (DLS) techniques. Anti-cancer drug, doxorubicin, was loaded into composite nanoparticles. The drug release profile was tested *in-vitro* under magnetically induced heating conditions, and therapeutically significant amount of drug release was observed. Furthermore, *in-vivo* magnetically targeted drug delivery was studied using buffalo rat model in which drug loaded particles were injected through the main hepatic artery. MRI and histology studies have shown efficient localization of the particles in the tumoral region. ***Therefore, multimodal cancer therapy using drug loaded thermoresponsive magnetic/polymer composite nanoparticles via magnetic drug targeting, simultaneous hyperthermia and controlled drug release can improve the efficacy of present cancer treatment.***

Keywords: Biomaterials, Drug Delivery, Composite Nanoparticles