

Controlling the Release of Cyt C and L- Dopa from pNIPAM-AAc Nanogel Based Systems

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Abstract : Release of drugs from nanogels and nanogel-based systems can occur under the influence of external stimuli like temperature, pH, magnetic fields and so on. pNIPAM-AAc nanogels respond to the combined action of both temperature and pH, the former being mostly determined by hydrophilic-to-hydrophobic transitions above the volume phase transition temperature (VPTT), while the latter is controlled by the degree of protonation of the carboxylic acid groups. These nanogels based systems are promising candidates in the field of drug delivery. Combining nanogels with magneto-plasmonic nanoparticles (NPs) introduce imaging and targeting modalities along with stimuli-response in one hybrid system, thereby incorporating multifunctionality. Fe@Au core-shell NPs possess optical signature in the visible spectrum owing to localized surface plasmon resonance (LSPR) of the Au shell, and superparamagnetic properties stemming from the Fe core. Although there exist several synthesis methods to control the size and physico-chemical properties of pNIPAM-AAc nanogels, yet, there is no comprehensive study that highlights the dependence of incorporation of one or more layers of NPs to these nanogels. In addition, effective determination of volume phase transition temperature (VPTT) of the nanogels is a challenge which complicates their uses in biological applications. Here, we have modified the swelling-collapse properties of pNIPAM-AAc nanogels, by combining with Fe@Au NPs using different solution based methods. The hydrophilic-hydrophobic transition of the nanogels above the VPTT has been confirmed to be reversible. Further, an analytical method has been developed to deduce the average VPTT which is found to be 37.3°C for the nanogels and 39.3°C for nanogel coated Fe@Au NPs. An opposite swelling-collapse behaviour is observed for the latter where the Fe@Au NPs act as bridge molecules pulling together the gelling units. Thereafter, Cyt C, a model protein drug and L-Dopa, a drug used in the clinical treatment of Parkinson's disease were loaded separately into the nanogels and nanogel coated Fe@Au NPs, using a modified breathing-in mechanism. This gave high loading and encapsulation efficiencies (L Dopa: ~9% and 70µg/mg of nanogels, Cyt C: ~30% and 10µg/mg of nanogels respectively for both the drugs. The release kinetics of L-Dopa, monitored using UV-vis spectrophotometry was observed to be rather slow (over several hours) with highest release happening under a combination of high temperature (above VPTT) and acidic conditions. However, the release of L-Dopa from nanogel coated Fe@Au NPs was the fastest, accounting for release of almost 87% of the initially loaded drug in ~30 hours. The chemical structure of the drug, drug incorporation method, location of the drug and presence of Fe@Au NPs largely alter the drug release mechanism and the kinetics of these nanogels and Fe@Au NPs coated with nanogels.

Keywords : controlled release, nanogels, volume phase transition temperature, l-dopa

Conference Title : ICNB 2016 : International Conference on Nanotechnology and Biotechnology

Conference Location : Melbourne, Australia

Conference Dates : February 04-05, 2016