Abstract

The main goal of the thesis is to fabricate smart, and multi-responsive nanogels based on branched Penta-erythritol-polycaprolactone-b-polyacrylic acid (Pe-PCL-b-PAA) ornamented with functionalized superparamagnetic nanoparticles. The work describes the preparation, fabrication, characterization, application, and future prospective of nanogel based nano-carriers for targeted and multiple stimuli-responsive drug delivery. The contribution and future prospects of the thesis are also carefully presented at the end. Superparamagnetic nanoparticles (Fe_3O_4 and $MnFe_2O_4$) with 5±2nm particle size and narrow distribution were prepared by the solvothermal process. To improve colloidal stability and to impart functional groups on the surface of the nanoparticles, those were modified with aminopropyl trimethoxy silane (TMAS). The pristine and modified nanoparticles were characterized by FTIR, XRD, XPS, SQUID Magnetometer, EDX, and HRTEM. In both cases, the extent of TMAS modification is found to be about 9 wt% however, the colloidal stability of Fe_3O_4 based nanoparticles are higher and magnetization is significantly higher for $MnFe_2O_4$ based particles. Cytotoxicity, as assessed by MTT assay using L929 cells, shows more than 90% cell viability up to 20 µg/mL concentration. Based on colloidal stability, TMAS functionalized Fe_3O_4 was taken up for further studies. Besides, the branched block copolymer Pe-PCL-b-PAA of variegated molecular weight and PAA content was synthesized by using ring opening polymerization (ROP) and atom transfer radical polymerization (ATRP) techniques. The structure of the polymer was established by FTIR, ^{1}H NMR, and GPC. Coining the synthesized polymer with functionalized Fe_3O_4, the hybrid nanogels were synthesized, purified (by dialysis) and characterized by FTIR, FESEM, HRTEM, DLS, and by rheometry. Nanogels with size range 65 to 616nm display porous structure showing a maximum 20 % loading of DOX. Out of these magnetic nanogels with size scales around 145 nm with a zeta potential of -35 mV were carefully evaluated *in-vitro* drug release studies utilizing magnetic field as well as pH as stimuli. The magnetic nanogels display 73 % release of DOX within 24h at pH 5 in the absence of magnetic field; however, the release rate is dramatically increased to 56 % in 1h in the presence of dynamic magnetic field where the device was fabricated in-house. Increase cell uptakes, as well as cytocompatibility, establish the proof of the concept of magnetically stimulated drug delivery system. Remarkably, these nanogels give rise to an unforeseen tubular self-assembled structure over time, which was characterized to understand the mechanism of formation and their future applications is envisaged. Further with higher acrylic acid containing polymer analogs as described above were tested for triple (namely redox, magnetic and pH) responsive nanogel augmented with both physical and chemical crosslinks containing nano-carriers for advanced drug delivery system. The magnetic nanogels display 91 % release of DOX within 24h at a pH 5, and with 10 mM glutathione concentration in the absence of magnetic field, however, the release rate is dramatically increased to 65 % in 1h in the presence of a dynamic magnetic field. These significant findings have opened the paths for the future studies on *in-vivo* animal models and subsequently, that may potentially direct to foundation of a novel nano-carrier for future cancer therapy.

Keywords: ROP, ATRP, magnetic gel, biocompatibility, drug delivery, multi-stimuli responsive, superparamagnetism

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