

# “Design and Development of PEI Coated Iron Oxide Based Theranostic Nanoparticles for Targeting Brain Tumors”

## Abstract

The present work describes the developmental process of theranostic nanoparticles with diagnostic and therapeutic capabilities on a single platform. The diagnostic component consisted of the gadolinium doped iron oxide core which displayed dual contrast in MRI imaging along with hyperthermia in presence of alternating magnetic field. The particle size of the metallic core was less than 10 nm with spherical morphology as determined by TEM. The metallic core was carboxylated using citric acid to get aqueous dispersibility. The metallic core was coated with lenalidomide using PLGA and nanoprecipitation technique which yielded high entrapment efficiency of  $97.49 \pm 0.42\%$ . The modified PEI with folate and triphenyl phosphonium was synthesized and used in secondary coating for active targeting of glioma. The optimised formulation of theranostic nanoparticles had particle size of  $122.26 \pm 2.17$  nm with PDI of  $0.161 \pm 0.009$  and zeta potential of  $12.3 \pm 0.52$  mV. The drug coated core and theranostic nanoparticles showed drug release of  $97.54 \pm 2.01\%$  and  $92.428 \pm 4.52\%$  in 8 hours respectively by dialysis sac method using methanolic phosphate buffer saline pH 7.4. Cell line studies on U87MG glioblastoma cell lines showed the cytotoxic property of theranostic nanoparticles in MTT studies while mitochondrial function disruption was observed in case of TMRM and ATP level experiments. Confocal microscopy showed the localization of FITC tagged theranostic nanoparticles into mitochondria. The theranostic nanoparticles exhibited low toxicity profile as observed from mucosal toxicity and % hemolysis studies. *In vivo* biodistribution implied the brain penetration of theranostic nanoparticles after administration of  $I^{131}$  labelled theranostic nanoparticles by intranasal route. It can be concluded that the developed theranostic nanoparticles can serve as a diagnostic agent as well as active targeted drug delivery platform for treatment of glioma.

**Key words:** Theranostic, Iron oxide, Polyethylenimine, Lenalidomide, PLGA, Mitochondrial targeting, Biodistribution.