

CHAPTER 7

COMPREHENSIVE CONCLUSION AND FUTURE PROJECTION

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In the present thesis, comprehensive studies on synthesis and structure-property correlation of pristine and magneto-fluorescent hybrid nanosystems have been reported. The modification of magnetic and optical properties of the pristine systems due to the hybrid formation has been investigated in this work. MRI relaxivity studies of the so prepared hybrid nanosystems were performed along with the pristine magnetic nanosystems to explore their applicability potentials.

Two pristine magnetic nanosystems, namely, Fe_3O_4 and FePt have been developed. A relatively simple, reproducible, and cost-effective method for the development of magnetite nanoparticles based on pyrolysis of iron (III) acetylacetonate in stearic acid was introduced. Stearic acid, second most abundant saturated fatty acid in nature, and also found in the lipids of most living organisms, enables controlled growth of nanoparticles and biocompatibility with living systems. On the other side, iron (III) acetylacetonate decomposition occurs at relatively low temperature. Monophasic replacement of fatty acid by TMAOH on the surface of NPs did not lead to any notable change in the microstructure and phase. Our results also revealed that the surface ligands of these magnetite nanoparticles can be readily replaced by TMAOH ligands, resulting in high solubility and extremely stable in a hydrophilic solvent. Magnetic measurements show the superparamagnetic characteristic of this system. A suitable transverse relaxivity has been obtained for this system, so making it a potential candidate of MRI contrast agent.

Another system of magnetic nanoparticles, iron-rich FePt capped with oleic acid and oleylamine was developed through a non-aqueous route. In this novel method, the synthesis of FePt at lower temperature than previously reported polyol method, was reported. This, in turn, prevented the thermo-aggregation typical to polyol processes and also facilitated the efficient capping of the nucleating FePt nanodots. These $\text{Fe}_x\text{Pt}_{1-x}$ ($x=0.7$) nanoparticles were also surface modified with TMAOH for phase transformation to hydrophilic phase. The surface modification allows for the assembly of nanodots and advantageous for applicability in biological requests. The system exhibits a narrow size distribution. The low coercivity and remanence is attributed to the

magnetically soft fcc FePt nanodots as well as its superparamagnetic characteristics. This Fe-rich FePt system exhibit high biocompatibility and notable MRI transverse relaxivity making it a potential candidate for MRI contrast agent.

Unlike these aforementioned two methods, a direct aqueous synthesis polyol method was used to synthesize FePt nanoparticles with the superparamagnetic property. So far we know, this is the first time in polyol process in which thioglycolic acid (TGA) was employed as the capping agent for FePt synthesis. A series of experiments were carried by polyol process to evaluate the role of the capping agent in the synthesis process of FePt nanoparticles. We have found that the surfactant concentration with respect to iron precursor plays a crucial role in the direct synthesis of water dispersible TGA capped superparamagnetic fcc-FePt MNPs. The surface characterization reveals the sulfur atom attached to the surface of the FePt nanosystem whereas the carboxylate group projected outward to the surface which will help in core/shell or hybrid formation further. The system exhibits narrow size distribution with an equiatomic ratio of Fe and Pt atoms. The increasing trend of FC moment below the blocking temperature corresponds to the superparamagnetic character. The relaxivity (r_2), a measure of the change in the spin-spin relaxation rate per unit concentration, is found suitable for biomedical applications. This FePt nanosystem was used as a core for the synthesis of multimodal magneto-fluorescent hybrid nanosystems like FePt@X (X= CdTe, CdSe, and CdS).

Similar to pristine magnetic nanosystems, we have developed a novel, cost-effective, environment friendly, glutathione (GSH) capped polyol approach for the one-pot open synthesis of highly luminescent biocompatible fcc-CdTe, hexagonal wurtzite CdSe and hexagonal wurtzite CdS QDs with high photostability. All the three systems exhibited good crystallinity. The coordination of the thiol group to QD surface and carboxylic group projected outward makes the QDs hydrophilic. Zeta potential measurements showed excellent stability at physiological pH, which is important for biomedical applications. The emission properties studied with PL and TRPL showed dominant band edge type emission for all three systems. The biocompatibility of GSH capped CdTe, CdSe, and CdS QDs were established using the Alamar Blue (AB) toxicity assay on RAW macrophage cell lines. Suitable fluorescence efficiency of all three quantum dot systems in the cellular environment was also confirmed from the fluorescence

micrographs of used cell lines for AB assay. These results indicate that the as-prepared CdTe, CdSe, and CdS QDs will have the potential as an alternative probe for *in vivo* imaging and biological tagging.

The integration of fluorescence imaging (FI) probe with MR imaging (MRI) probe is an attempt towards the development of innovative noninvasive imaging agents. We have developed a novel facile one-pot route, tripeptide glutathione (GSH) capped multimodal magneto-fluorescent hybrid nanosystems (FePt@CdX; X= Te, Se, S) through polyol process. Thioglycolic capped FePt nanoparticles were used as a seed for the development of GSH capped magneto-fluorescent hybrid nanosystems with CdTe, CdSe, and CdS quantum dots as the optical counterparts. The XRD peak of hybrid nanosystem shifted to higher values as compared to pristine systems, which indicate the crystal lattice disorder induced strain occurring at the time of hybrid formation. Zeta potential results showed negative charge on all three hybrid systems and hydrophilic stability. Interestingly, calculated quantum yields for all three hybrid nanosystems were obtained to be higher than that of the pristine quantum dot systems. The enhanced fluorescence efficiency of hybrid nanosystem can be due to more passivation effect of defects. HR-TEM micrographs shows the central darker region while peripheral lighter contrast in FePt@CdX in the hybrid nanosystem, affirm the core-shell structure formation. On the other side, magnetization values for the hybrid systems were also not much altered after hybrid formation. The reduction in M_s for hybrid nanosystems can be attributed to the surface spin disorder due to capping with the nonmagnetic shell (CdTe, CdSe, and CdS). It is also observed that high band gap semiconductor nanocrystals are not likely to be modified during the hybrid formation. Extremely low values of coercivity and remanence along with the obtained blocking temperature well below the room temperature signify the superparamagnetic characteristic of the developed hybrid nanosystems. Due to biocompatible tripeptide GSH coating, all three magneto-fluorescent hybrid systems also exhibited high biocompatibility and fluorescent efficiency after cellular uptake. The intensity of fluorescence of FePt@CdTe and FePt@CdSe is superior to the FePt@CdS system. This can be correlated to the higher band gap of CdS QDs. It is observed that there is a decrease in relaxivity of all hybrid nanosystems as compared to the pristine FePt, which is due to the nonmagnetic coating. Among all the hybrid nanosystems, FePt@CdTe has revealed the highest while

FePt@CdSe has shown the lowest value of relaxivity which may be due to the thicker nonmagnetic shell growth as revealed in HRTEM images. Thus, the developed hybrid nanosystems have fulfilled desire properties of a potential multimodal imaging probe that can be used for simultaneous fluorescence imaging and magnetic resonance imaging.

Hydrophilic nanoparticles below 35 nm diameter, exhibit much less uptake by the reticuloendothelial system (RES) i.e. spleen and liver. Hydrophilic surfactant reduces opsonization and minimizes the clearance by the RES, leading to longer blood circulation times and improved pharmacokinetic properties. The nanosystem described in the thesis are small in hydrodynamic diameter and hence lower probability of uptake by RES to achieve long blood circulation times. After achieving the desired properties, the imaging efficiencies of these hybrid nanosystems need to be evaluated under *in vivo* conditions i.e. in an animal model and clinical trials before recommending them for medical applications.

The present thesis has reported developing of a multimodal biomedical imaging probe and opened up a new area of imaging integrating magnetic and fluorescent imaging functionality for better imaging efficiency and resolution in diagnostics. However, future studies are required to ensure the applicability of this new generation of imaging probe into the clinical practice. Development of T₁-T₂ hybrid nanosystems can also be explored as the future study.