# STUDIES ON HYBRID NANOSYSTEMS FOR MULTIMODAL BIOMEDICAL APPLICATIONS

## Abstract

Nanoscience in the 21st century is leading towards developing new engineered nanostructure with multifunctional attributes. The aim of research in this area is to achieve superior technological solutions on different issues like health, energy, environment, etc. of our life [1, 2]. In recent times, nanotechnology has emerged with tremendous potential and possibilities for its applications in the biomedical field. The new generation biomedical applications will be based on multimodal or multifunctional nanosystems [3, 4]. These nanosystems were developed by integration of more than one functional component in a template or through conjugation to make them superior as compared to the individual system. The multimodal biomedical imaging is conceptualized based on hybrid probes of magneto-fluorescent, $T_1$-$T_2$, multimetallic etc. [5-7]. As no single imaging modality can provide all necessary information in the imaging application, hence the concept of multimodal molecular imaging agents have been conceived. Considering the unique characteristics of magnetic nanoparticles and quantum dots; we have been integrated both the aforesaid system in the present study, for the development of magneto-fluorescent hybrid nanomaterials. Magnetic nanoparticles can serve as contrast agent for magnetic resonance imaging (MRI) technique whereas fluorescent nanoparticles can be used in imaging as well as monitoring of disease state.

In brief, chapterôs content included in the thesis are explained below.

**Chapter 1** reveals the general as well as the background information about scientific research of magnetic nanoparticles, quantum dots, and multifunctional or multimodal hybrid nanosystems. Different synthetic approaches for the preparation of magnetic and quantum dots are also described. The idea behind the development of hybrid nanosystems is also discussed in this chapter. The wide range of applications, based on these nanosystems and their properties are also highlighted in this chapter. Finally, the

objectives of the thesis are defined at the end of this chapter based on the literature review.

In **Chapter 2** the experimental details of the thesis work are described. All the chemicals and reagent used, the synthetic routes or methodologies/approach applied and analytical techniques for characterizing the samples are detailed in this chapter.

**Chapter 3** reports the synthesis and characterization of magnetic nanoparticles (MNPs) and is divided into three parts. In **Part A,** synthesis of stearic acid capped superparamagnetic iron oxide nanoparticles (SPION) by a non-aqueous method, involving thermal decomposition of a precursor followed by ligand exchange by tetramethylammonium hydroxide (TMAOH) has been detailed. The M-H and ZFC curve of so prepared MNPs exhibit superparamagnetic behavior at room temperature. XPS characterization reveals that there is no crystallographic phase change in magnetite after surface modification. The transverse relaxivity reveals the efficiency in contrast property of MR imaging.

In **Part B** of Chapter 3, synthesis of oleic acid and oleylamine capped paramagnetic Fe-rich, FePt nanodots followed by ligand exchange with tetramethylammonium hydroxide (TMAOH) has been described. The cytotoxicity assay study establishes biocompatibility of the nanodots. M-H curve of the FePt nanodots shows paramagnetic behavior and transverse relaxivity reveals the efficiency in contrast property of MR imaging.

In **Part C** of Chapter 3, one pot synthesis of thioglycolic acid capped superparamagnetic, hydrophilic FePt nanoparticles by polyol method has been reported. The sulfur atom from thiol group is attached on the surface of FePt whereas the carboxylic group projects outward from the surface. The FePt has an equiatomic composition of Fe and Pt atoms. Superparamagnetic behavior is ensured at room temperature from M-H and M-T characterizations. The transverse relaxivity exhibited by this particle ensure its suitability for contrast agent in MR imaging application. This projected carboxylic group provides hydrophilicity and also acts as a linker molecule in the development of hybrid nanosystem.

The detail microstructural and compositional properties of the magnetite ($Fe_3O_4$) and FePt nanodots/nanoparticles were studied with the aid of X-ray diffraction (XRD), high

resolution transmission electron microscopy (HR-TEM) and electron dispersive X-ray (EDX) techniques. The surface chemistry of nanosystems was analyzed by Fourier transform infrared spectroscopy (FTIR), and thermogravimetric analysis (TGA). Detailed magnetic and contrast properties of the nanoparticles were studied with the aid of vibrating sample magnetometer (VSM), and nuclear magnetic resonance (NMR) micro imager.

**Chapter 4** describes the synthesis and characterization of quantum dot (QD) systems. The QD systems were synthesized through polyol process using glutathione (GSH) as a capping agent to render hydrophilicity. It is divided into two parts. **Part A** describes the synthesis and characterization of cadmium telluride (CdTe) and cadmium selenide (CdSe) QDs. The emission wavelength of both the systems is varying between 390 to 466 nm.

**Part B** of **Chapter 4** describes a facile one-pot synthesis of hydrophilic cadmium sulfur (CdS) quantum dot using a polyol method with glutathione as a capping agent. Here, glutathione acts both as a capping agent and sulfur source. The emission wavelength is in the range 390 to 485 nm.

The detail microstructural, compositional and surface characteristics of the glutathione (GSH) capped CdTe, CdSe, and CdS quantum dots were studied with the aid of XRD, HR-TEM, EDX, FTIR and TGA techniques. The surface characterization of these QDs shows that the sulfur atoms are attached to the surface, whereas the carboxylic groups are projected outward rendering hydrophilic characteristics. The zeta potential study reveals negatively charged surface potential in wide pH range and the stability of QDs in water is found to be pH sensitive. The optical properties of CdTe, CdSe and CdS quantum dots had been realized from UV-Visible absorption and time-resolved photoluminescence spectroscopy studies. The *in vitro* cytotoxicity and fluorescence imaging were carried out using the RAW macrophage cell line. These QDs are biocompatible and exhibit fluorescence in the visible spectrum, making it suitable for fluorescence imaging.

**Chapter 5** describes a facile one-pot polyol synthesis of core/shell magneto-fluorescent hybrid nanosystems capped with GSH molecules. The FePt NPs capped with thioglycolic acid (In **Part C** of **Chapter** 3) was used as the core and the fluorescent

QDs were attached to it as a shell (**Chapter 4**). The microstructural study ensures the formation of these nanosystems. The optical and magnetic properties are getting modified due to the integration of magnetic and fluorescent components. This **chapter** is divided into two parts.

**Part A** of **chapter 5** describes a one pot facile synthesis of hydrophilic FePt@CdX (X= Te or Se) core/shell multimodal hybrid nanosystem. In these hybrid nanosystems, emission wavelengths are varying between 405 to 535 nm.

**Part B** of **chapter 5** describes a one pot facile synthesis of hydrophilic FePt@CdS core/shell multimodal hybrid nanosystem, where glutathione is used as a sulfur source as well as the capping agent. The emission wavelength is varying between 398 to 484 nm.

The physio-chemical properties of FePt@CdTe, FePt@CdSe, and FePt@CdS core/shell multimodal hybrid nanosystems were studied in contrast to the pristine magnetic nanosystem and quantum dots. The zeta potential study showed negative charge for all the hybrid systems and hydrophilic stability. The contrast properties of the multimodal hybrid nanosystems were studied and showed the almost similar magnitude to pristine magnetic nanosystem. The optical properties of FePt@CdTe, FePt@CdSe, and FePt@CdS core/shell multimodal hybrid nanosystems has been realized from UV-Visible absorption and time-resolved photoluminescence spectroscopies.

**Chapter 6** describes the multimodal application of magneto-fluorescent hybrid nanosystems in imaging. The magnetic (MRI contrast) and fluorescent imaging property of aforementioned hybrids were characterized by NMR micro imager and fluorescence microscopy respectively. The *in vitro* cytotoxicity and fluorescence imaging of the systems were carried out using the RAW macrophage cell line. The observed transverse relaxivity and the fluorescence property are comparable to the pristine magnetic nanosystems and QDs.

**Chapter 7** explains about the comprehensive conclusion drawn from the complete thesis work and future projection of it.