Abstract

Iron oxide nanoparticles are becoming technologically important materials because of their wide spectrum of biological applications such as bioseparation, MRI contrast agent, site specific drug delivery and hyperthermia. Particularly nanomagnetite is desirable for biomedical applications as it shows high saturation magnetization, less sensitive to oxidation than magnetic transition metals such as cobalt, iron, and nickel and has well-established biocompatibility. However its efficiency in such applications depends upon a number of parameters such as small particle size with uniform particle morphology and narrow size distribution, high saturation magnetization and tailored surface chemistry. Proper manipulation of the surface in order to obtain stable magnetite particles with pendant functional groups is a flourishing contemporary research in nanobiotechnology.

The present thesis entitled "***Syntheses and Characterizations of Functionalized Iron Oxide Nanoparticles for Biological Applications***" includes the preparation of magnetite nanoparticles by controlled coprecipitation of Fe^{3+} and Fe^{2+} from aqueous medium at room temperature and functionalization of their surfaces with various modifiers aiming at different biological applications. Magnetite nanoparticle surface is modified by either *in-situ* coating or post grafting and the resulting functionalized nanoparticles have been systematically characterized by X-ray diffraction analysis (XRD), Transmission Electron Microscopy (TEM), Dynamic Light Scattering (DLS), Fourier Transform Infrared Spectroscopy (FTIR) and X-ray Photoelectron Spectroscopy (XPS). The impact of modifying agents on magnetic properties has been investigated by vibration sample magnetometry (VSM). The *in-vitro* applications of some functionalized magnetite nanoparticles have also been studied.

The present thesis has been divided into eight chapters.

Chapter 1 contains a brief review on type of iron oxides, main synthetic methods for iron oxide nanoparticles, biomedical applications of iron oxides, and surface functionalization of magnetic iron oxides in view of its biological applications.

Chapter 2 describes *in-situ* synthesis of amine derivatised magnetite nanoparticle by co-precipitation of Fe^{2+}/Fe^{3+} in presence of water-soluble 3-aminopropyltriethoxysilane (APTS). The quantity of surface adsorbed APTS during the formation of magnetite particle was determined by C, N and thermal analysis. The effect of APTS concentration of particle size and stability of the colloid was studied and it has been found that the particles with highest density of surface active $-NH_2$ groups have > 70% protein coupling efficiency.

Chapter 3 includes the preparation of superparamagnetic Fe_3O_4@silica core shell nanoparticle with surface-active iminodiacetate groups, which after chelation with Ni^{2+} can be used as a binder and carrier for 6xHis-Tagged proteins. A thin layer of silica was coated on coprecipitated magnetite nanoparticle surface from tetraethyl orthosilicate precursor following a sol-gel route which was subsequently functionalized with iminodiacetate through a silane coupling agent. These Ni^{2+}-charged Fe_3O_4@silica core shell nanoparticles were successfully used for isolation of recombinant protein histidine-tagged nitroreductase from total cell lysate.

Chapter 4 describes preparation of boronic acid-functionalized superparamagnetic magnetite nanoparticles for the first time. Boronic acid has been successfully attached to the surface of the magnetite nanoparticle through 3,4-dihydroxy benzaldehyde. The synthesized boronic acid immobilized magnetite particles show highest sugar loading capacity at pH 8.5 at 25°C.

Chapter 5 describes preparation of stable magnetite nanoparticles with pendant functional groups like $-NH_2$ and -COOH using some tailor made phosphonic acids. The extent of surface coverage by different phosphonic acids has been investigated by BET surface area measurement and elemental analysis. The colloidal stability of these functionalized magnetite nanoparticles in aqueous medium have been of extensively studied by dynamic light scattering and zeta potential measurement.

Chapter 6 includes synthesis of highly hydrophilic poly(vinylalcohol phosphate) coated magnetite nanoparticles by coprecipitation of Fe^{2+} and Fe^{3+} in dilute aqueous solution of poly(vinylalcohol phosphate). A cubic magnetite nanoparticle of average 5.8 nm was produced when only 1% PVAP solution was used during coprecipitation.

Chapter 7 describes preparation of novel folic acid conjugated magnetite nanoparticles of size < 60 nm and investigation of their cell-targeting capacity taking B16 F0 (mouse epithelial) and HeLa (human cervical) cancer cell lines. Due to reasonably good intracellular uptake behavior these folate conjugated magnetic particles may find potential biomedical applications.

Summary, conclusion and future scope of the present work are described in **chapter 8**.