

Preface

Magnetic iron oxide nanoparticles have been investigated for various bioapplications such as: (a) cellular therapy involving cell labeling and targeting as a tool for cell-biology research to separate and purify cell populations, (b) tissue repair, (c) targeted drug delivery, (d) magnetic resonance imaging (MRI), (e) hyperthermia for cancer treatment, etc.

In recent studies, magnetite and maghemite are the most favourable candidates due to their biocompatibility and non-toxic nature. For various bioapplications, in particular areas of magnetic hyperthermia and drug delivery etc., need a stable and homogenous suspension of magnetic particles in carrier solvents. So, the preparations of the ferrofluids are an important part in magnetic hyperthermia. PVA (poly vinyl alcohol), oleic acids etc. are generally used as capping agents for the magnetic nanoparticles which help in preparation of ferrofluids. Without surface modifications, they get agglomerated and thus the preparation of ferrofluids becomes difficult. Researchers are using pure and substituted iron oxides MNPs such as $M_xFe_{3-x}O_4$ or $\gamma-M_xFe_{2-x}O_3$ where $M = Zn, Bi, Ti, Al, Ca, Mn, Mg$ etc. for magnetic hyperthermia.

Despite these, researchers are searching for magnetic material which can be used for *in-vivo*, *in-vitro* studies with controlled heating in the range of 42 - 46 °C. It could minimize the side effects associated with unwanted death of normal cells during therapy. For this, we need MNPs which have their Curie temperature near 42 - 46 °C. They could be transformed from ferromagnetic/ferrimagnetic to paramagnetic states and may stop heating in presence of AC magnetic field. A few materials ($ZnGd_xFe_{2-x}O_4$, $Zn_xGd_{1-x}Fe$, $Ni_{1-x}Cr_x$, Cu-Ni alloy and $La_{1-x}Sr_xMnO_3$ nanoparticles) have their T_C near therapeutic temperature. But, the low specific magnetization and inferior biocompatibility limit their applications in magnetic hyperthermia. To achieve the desired T_C value, several substituted magnetites (such as $M_xFe_{3-x}O_4$ where $M =$

Al, Zn, Ni, Mg, Cu, Mn or Co etc. & $0 \leq x \leq 1$) are prepared. However, none of them had their T_C near 50 °C. This doctoral thesis presents the systematic investigation of the heating ability of the tetravalent ions (Zr or Hf), trivalent (Al), divalent (Zn) and monovalent (Li) substituted magnetite nanoparticles at different fields and frequencies of the AC magnetic field. The thesis comprises of seven chapters. Chapter 1 describes literature on the structural and magnetic properties, synthesis procedure and bioapplications of pure and substituted Fe₃O₄ nanoparticles. Chapter 2 gives procedure for the synthesis of the substituted Fe₃O₄ nanoparticles, preparation of ferrofluids and various characterization techniques which were used during this doctoral work.

Chapter 3 presents the systematic study of structural and magnetic properties of tetravalent doped Fe₃O₄ nanoparticles. The nanoparticles of Zr_xFe_{3-x}O₄ ($0.01 \leq x \leq 1.0$) and Hf_xFe_{3-x}O₄ ($0.01 < x \leq 0.8$) were produced by microwave refluxing method. The substitutions of Zr or Hf-ions over the whole range were confirmed by XRD and TEM analyses. The M_S value was continuously varying with respect to Zr substitutions. This was due to the substitutions of Zr⁴⁺ ions at both tetrahedral and octahedral sites. On the other hand, the M_S value was 51.07 Am²/kg for $x = 0.06$ sample which decreased continuously with increased substitutions. The preferred substitutions of Hf-ions are at octahedral sites at lower concentrations. It however does go to tetrahedral sites at higher concentration. This was confirmed by XRD, Mössbauer spectra and magnetization results. The ferrofluids of the single phase M_xFe_{3-x}O₄ ($0.01 \leq x \leq 1.0$, M = Zr or Hf) system displayed temperature stability ($T_S \sim 42\text{--}46$ °C) during hyperthermia at suitable combinations of frequency and amplitude of the field.

Chapter 4 describes the study of structural and magnetic properties of trivalent doped Fe₃O₄ nanoparticles. Single phase was observed for all nanocrystalline Al_xFe_{3-x}O₄ ($0.01 \leq x \leq 1$) samples. There were continuous decrement in lattice parameters after Al³⁺ substitution in Fe₃O₄

beyond for $x = 0.1$ sample. Ferrimagnetic and superparamagnetic components were observed in the sample due to particle of different sizes which was confirmed through hysteresis loops. The stabilizations of temperature at different combinations of frequencies and fields were observed during magnetic hyperthermia.

Chapter 5 focuses on the structural and magnetic properties of divalent doped Fe_3O_4 nanoparticles. The nanoparticles of $\text{Zn}_x\text{Fe}_{3-x}\text{O}_4$ ($0.01 \leq x \leq 0.8$) have displayed spinel type structure and a continuous increase in the lattice parameter value with increased Zn content. The size of the particles was found to be between 3 - 11 nm from TEM analysis. The XPS analysis suggests the presence of Fe^{2+} , Fe^{3+} and Zn^{2+} ions in the sample. Due to the occupancy of Zn^{2+} and Fe^{2+} ions at tetrahedral sites of spinel structure, the M_S value initially rises slightly and then decreases with increased Zn content. The presence of both ferrimagnetic and superparamagnetic component was suggested from hysteresis loops and Mössbauer spectra. Like, tetravalent or trivalent substituted magnetites, Zn substituted samples also displayed AC field dependent controlled heating during magnetic hyperthermia.

Chapter 6 deals with the structural and magnetic properties of monovalent doped Fe_3O_4 nanoparticles. Nanoparticles of $\text{Li}_x\text{Fe}_{3-x}\text{O}_4$ ($x = 0.06, 0.1$ and 0.3) samples were of spherical morphology and size was in the range of 4 to 22 nm. The monovalent ions substitution has continuously decreased the M_S value of magnetite. This could be due to the occupancy of the Li-ions in octahedral sites of Fe_3O_4 . All the samples exhibited stabilization temperature at various field and frequencies of AC magnetic fields. The SAR values of the samples were relatively larger than that of tetravalent, trivalent and divalent substituted magnetite samples.

Chapter 7 presents a summary and all major conclusions drawn from the present investigation. The suggestions for future scope of the work are given at the end.

