CHAPTER-1.0

INTRODUCTION
1.1 IRON OXIDE NANOPARTICLES

Iron Oxide Nanoparticles are an excellent material, which is highly preferred for many biomedical applications such as therapeutic agents for Hyperthermia, Drug Carriers for drug delivery, contrast agent for magnetic resonance imaging (MRI) and magnetic probes for biosensors. It exhibits excellent magnetic properties with good biocompatibility [1, 2]. In general, Iron Oxide Nanoparticles are categorized into two forms such as magnetite (Fe$_3$O$_4$) and maghemite (γ-Fe$_2$O$_3$). Both magnetite and maghemite have their own uniqueness in magnetic properties especially in the saturation magnetization ($M_s$) and remanent magnetization ($M_r$) values [3]. These two magnetic properties determine the type of iron oxide nanoparticles for specific biomedical application. Iron Oxide Nanoparticles have attracted a greater interest due to their superparamagnetic properties and it is termed as superparamagnetic iron oxide nanoparticles (SPION) with particle size larger than 50 nm and amply smaller particles less than 50 nm is termed as ultrasalm superparamagnetic iron oxide nanoparticles (USPIO) [4]. This property in iron oxide nanoparticles arises due to single magnetic domain and the magnetization of nanoparticles is the effect of single giant magnetic moment orchestrate by atoms of the nanoparticles [5].

The two forms of iron oxide nanoparticles exhibit unique crystal structure, magnetite (Fe$_3$O$_4$) has inverse spinel pattern with face-centered cubic crystal system, Fe$^{3+}$ occupy all the tetrahedral sites and both Fe$^{3+}$, Fe$^{2+}$ occupy the octahedral sites. Maghemite (γ-Fe$_2$O$_3$) vary from magnetite by occurrence of cationic vacancies inside octahedral site [1, 6]. The structure of both magnetite and maghemite is shown in Figure. 1.1.
Iron oxide is preferred over Cobalt and Nickel nanoparticles, since Cobalt and Nickel are more toxic to bio systems and easily oxides compared to iron oxide nanoparticles [8]. There are other forms of iron oxide materials such as hematite (α-Fe₂O₃) and hydroxide materials such as lepidocrocite (γ-FeOOH) which are also used for bio applications [9, 10].

Iron oxide nanoparticles have created a huge interest among researchers from various areas due to their unique magnetic properties and biocompatibility. Iron oxide nanoparticles exhibit a strong magnetic moment due to the presence of four unpaired electrons in 3d shell; there are four unpaired electrons present in Fe²⁺ and five unpaired electron in Fe³⁺ in 3d shell. Due to the alignment of these electrons, they can form multiple magnetic states such as ferromagnetic, ferrimagnetic etc. In case of ferromagnetic state atomic moments are aligned without an external magnetic field and in case of ferrimagnet there are two different atoms, which exhibits opposing magnetic moments. When the magnetic field is applied to a ferromagnetic material the magnetization increases with field strength until saturation. In case of paramagnetic state, the atomic magnetic moments are randomly oriented and exhibit zero net magnetic moment in the absence of magnetic field. Superparamagnetic state contains single magnetic domain, which do not exhibit hysteresis loop. In general, ferromagnetic and ferrimagnetic materials undergo transition to paramagnetic state above its curie

Figure. 1.1: Crystal Structure of magnetite and maghemite (maghemite structure adapted from [7]).
temperature; in case of superparamagnetic materials the transition occurs below Curie temperature. Both magnetite (Fe$_3$O$_4$) and maghemite (γ-Fe$_2$O$_3$) exhibit ferrimagnetic state at room temperature and unstable at higher temperatures. Since, the particle size plays an important role in magnetic properties, magnetite and maghemite with particle size less than 20 nm exhibit superparamagnetic states at room temperature [3, 11]. The magnetic domain of each system and effect of magnetic field on ferromagnetic and superparamagnetic system are shown in Figure. 1.2 (a, b).

Figure. 1.2: (a) Domain of various magnetic states, (b) effect of magnetic field on ferromagnetic and superparamagnetic nanoparticles.

Superparamagnetic property strongly dependent on particle size, coercivity (H$_c$) becomes zero when the size of single domain particles decreases below critical diameter. Below critical particle size the coercivity becomes zero and exhibits nil hysteresis, also the nanoparticles become magnetic only in the presence of external magnetic field and switches back to non-magnetic state when external magnetic field is not applied. This particular behavior plays an important role for the selection of superparamagnetic materials for many biomedical applications [12]. The effect of particle size on coercivity for single and multi-domain systems is shown in Figure. 1.3.
1.1.1 Synthesis of Iron Oxide Nanoparticles

Iron oxide nanoparticles can be synthesized using several techniques; each technique has unique advantage over another method. The synthesis method has strong effect on significant properties like particle size, shape, magnetization and surface effects for biocompatibility. Another important aspect is particle size distribution and structural defects, which play vital role especially for biomedical applications. In general, the iron oxide nanoparticles were synthesized using techniques such as coprecipitation, microemulsion, hydrothermal, thermal decomposition and sol-gel technique [1, 13]. There are many challenges exist among these techniques such as control of particle size, size distribution and morphology. Also, on another side there is a requirement to synthesize these nanoparticles using simple techniques at low-cost and large scale production is required for various applications [13].

Hydrothermal method involves reaction of precursor material in autoclaves which is maintained around 2000 psi pressure at 200°C temperature. In this method, the particles will experience an effect during the increase in reaction time and quantity of water content [1]. At higher temperatures, the nucleation will be faster resulting in the decrease of particle size [14]. During this process, type of solvent, reaction temperature and duration plays an important role on tuning the particle size and shape [15]. High level of monodispersity can be achieved in nanoparticles using thermal decomposition method. In addition, the particle size
and morphology can be tuned by controlling reaction time and temperature along with type of solvent and precursors etc [16]. Sol-gel technique is suitable for wet synthesis process of nanoparticles [17]. Since the reactions were undertaken at room temperature, heat treatment is essential to obtain required crystalline state [18]. Type of solvent, salt precursor, temperature, pH and agitation time are the important parameters that controls the structure and properties of materials [19]. The advantage of this method is the control of particle size and maintains homogeneity of the reaction [20]. Microemulsion technique involves dispersion of two immiscible liquids with nanosized domains of either one or both liquids that is stabilized by an interfacial film of the surface-active molecules. This technique is generally categorized as oil-in-water or water-in-oil depending on dispersed and continuous phases [6], the surfactant will reduce the surface tension between oil and water. Hence, the water droplet acts as nano reactors for synthesizing nanoparticles, the size of nanoparticles strongly depends on this factor [21].

Coprecipitation method is mostly preferred by many researchers for synthesis of iron oxide nanoparticles. This technique is considered as simple and efficient method for preparation of iron oxide nanoparticles. Both magnetite (Fe₃O₄) and maghemite (γ-Fe₂O₃) were prepared by a stoichiometric combination of ferric and ferrous salts in aqueous medium [1, 22]. A classical chemical reaction for synthesis of magnetite and maghemite is shown below equation 1.1,

\[
\text{Fe}^{2+} + 2\text{Fe}^{3+} + 8\text{OH}^- \rightarrow \text{Fe}_3\text{O}_4 + 4\text{H}_2\text{O} \tag{1.1}
\]

\[
\text{Fe}_3\text{O}_4 + 2\text{H}^+ \rightarrow \gamma-\text{Fe}_2\text{O}_3 + \text{Fe}^{2+} + \text{H}_2\text{O} \tag{1.2}
\]

The stoichiometric ratio of [Fe²⁺/Fe³⁺] plays an important role in synthesis of magnetite and maghemite nanoparticles, magnetitie is highly sensitive to oxidation and transforms into maghemite in the presence of oxygen. The main advantage in coprecipitation process is that a larger quantity of nanoparticles can by produced but control of particle size distribution is critical. Parameters such as pH, temperature, selection of salts (chlorides, sulfates), Fe²⁺/Fe³⁺ ratio plays an significant role for controlling the size and shape of particles [23].
Addition of chelating agents such as (citric, oleic acid) or polymer agents such as (polyvinyl alcohol, dextran) during the synthesis process can control the size of the nanoparticles [1]. In this process, Fe$^{2+}$ and Fe$^{3+}$ ions are allowed to react in alkaline solution like sodium hydroxide or ammonium hydroxide, in most of the cases ammonium hydroxide is preferred as an alkali during the synthesis reaction, since ammonia evaporates within shorter duration and it is simple process to separate iron oxide nanoparticle from the solution [24, 25].

Literature reports conclude that iron oxide nanoparticles with narrow particle size distribution can be achieved by several methods including coprecipitation technique [12, 26, 27]. Coprecipitation method has incredible benefits for large scale synthesis of iron oxide nanoparticles with tunable size, morphology and magnetic properties. Aggregation of nanoparticles and biocompatibility were the major challenges faced in several biomedical applications. Co-precipitation technique is considered as an advantage to overcome this issue by introducing suitable surfactant, polymers or dispersion agent directly during the synthesis process to avoid aggregation and maintain biocompatibility [7]. Coprecipitation is a simple method for the synthesis of magnetite and other ferrite based nanoparticle using ferrous and ferric salts. Also, with by tuning the Fe$^{2+}$/Fe$^{3+}$ ratio, it is possible to control the size and shape of nanoparticles. Figure 1.4 shows the particle size distribution plot of iron oxide nanoparticles synthesized by various methods [13].
1.1.2 Effect of Particle Size on Magnetic Properties

There are several properties like particle size, shape and chemical composition that can alter the magnetic properties of nanoparticles. Particle size has significant effect on magnetic properties; magnetic nanoparticles can be controlled using a suitable applied magnetic field. Magnetic nanoparticles exhibit different magnetic state such as ferromagnetic and ferrimagnetic state with the application of external magnetic field [28, 29]. Superparamagnetism generally appears in small ferromagnetic or ferrimagnetic systems and typically occur in single-domain nanoparticles system. Superparamagnetism is highly dependent on size of nanoparticles in the range less than 50 nm [11]. Several literatures have reported the effect of particle size on variation in the magnetic properties. This magnetic property is unique in nanoscale particles which has high surface-to-volume ratio [30, 31].
Different types of magnetic behavior (magnetic hysteresis) with the effect of applied magnetic field are shown in Figure 1.5. Superparamagnetic materials do not exhibit any hysteresis, since their magnetic moments will be aligned along the direction of applied magnetic field leading to net magnetization [32].

![Magnetic Behavior Diagram](image)

Figure 1.5: Magnetic behavior with applied magnetic field (Ref.[32]).

The net magnetization will be affected by presence of multiple superparamagnetic particles in clusters; saturation magnetization ($M_b$) is dependent on the bulk magnetization of the material, mass of individual particle and size of the particle [33]. The relationship between particle size and the net saturation magnetization is given in the equation (1.3) where, $M_{sat}$ is the net saturation magnetization, $M_{so}$ is the saturation magnetization of the bulk material, $m$ is the mass of the individual particle, $r$ is the particle radius and $d$ is the shell thickness.

$$M_{sat} = m M_{so} \left(\frac{r-d}{r}\right)^3 \quad (1.3)$$

It is evident from the literature that broad particle size distribution will have larger effect on blocking temperatures ($T_b$). Superparamagnetism is based on size effect and coercivity values that change with respect to particle size. Superparamagnetic particles fluctuate randomly by thermal effects at high temperature, if the temperature is low then the effect of thermal energy will
become less significant and the net magnetic moment will be blocked, this specific point is termed as blocking temperature ($T_b$), below this point superparamagnetic material loses its preferred magnetization direction when the field is removed [34]. Particle size is also a crucial parameter like temperature that alters the magnetic properties of materials. Magnetic hysteresis will exhibit variation in saturation magnetization ($M_s$) even with small difference in the particle size; it is important that coercivity ($H_c$) should be least in the superparamagnetic materials, decrease in particle size will eventually reduce coercivity and increase in saturation magnetization values [35, 36]. Figure. 1.6 shows the effect of particle size on coercivity and saturation magnetization even with minor variation in particle size.

![Figure 1.6](image)

Figure. 1.6: Effect of particle size on (a) coercivity and (b) saturation magnetization in the nanoparticles (Adapted from [35, 36]).

Considering the above criteria, it is essential to tune the particle size to control the magnetic behavior of iron oxide nanoparticles. This property plays a major role among nanoparticles to generate a suitable thermal energy during hyperthermia process, and to produce suitable magnetic field strength for drug delivery and release applications [37, 38, 39].
1.1.3 Colloidal Stability of Nanoparticles

Stability of magnetic nanoparticles is very important for biomedical applications; major challenge is to maintain these particles in stable form and prevent agglomeration. Due to high surface-to-volume ratio they tend to agglomerate with nearby particles with large surface energy, also if the magnetic particles are not stabilized properly then they will exhibit internal magnetic effects that leads to rigorous agglomeration. A strong and sufficient repulsive force should be created over the surface of the particles to prevent the desirability to agglomerate with nearby particles. Such forces were acheived by introducing strong electrostatic or steric repulsion. Both methods have their own advantages, but steric repulsion is widely followed for its simple and effective mechanism. Such forces are created by coating the particles with a polymer agent or surfactants with long hydrocarbon chains [40]. Biocompatible surfactants and polymers were coated over iron oxide nanoparticles to maintain stability in dispersion medium as shown in Figure. 1.7. [41, 42].

![Figure 1.7](image)

Figure. 1.7: Magnetic nanoparticles were treated with (a) surfactant and (b) polymer agent prior to several biomedical applications (Adapted from [41, 42]).
Magnetization of the iron oxide nanoparticles will be altered after treating with surfactant or polymer agent, since the [nanoparticle core+ polymer coated over the surface of the nanoparticle] will increase overall size of sample that reduces the magnetization value. Figure 1.8 shows the effect of polymer coating over the magnetic nanoparticles, the magnetization values decrease drastically after the polymer coating, this process is very important and it should be analyzed to determine the required magnetization values for specific biomedical applications.

![Figure 1.8](image)

Figure 1.8: (a) Polymer coating over iron oxide nanoparticles and (b) Effect of polymer on magnetization ($M_s$) values (Adapted from [43, 44]).

It is important to understand the mechanisms of relaxation of magnetic moments in the nanoparticles, and capacity to swap magnetic properties. The mechanism occurs at micro- and submicro- second timescales, which have been studied extensively [45]. There are two mechanisms for relaxation of magnetic moments in nanoparticles, viz., the rotation of the magnetic moment about the crystallographic anisotropy axes (characterized by the Néel relaxation time, $\tau_N$) or thermally-induced Brownian rotational motion of the nanoparticle [46] (characterized the Brownian relaxation time, $\tau_B$). As the particle size increases, the relaxation mechanism of magnetic moments becomes hard, and the nanoparticle tends to exhibit ferromagnetic behavior.
Suspension stability of iron oxide nanoparticles are characterized using different techniques such as Zeta Potential, Dynamic Light Scattering (DLS), AC susceptibility measurements, fluorescence spectroscopy and UV-Visible spectroscopy techniques [47-50]. Zeta potential is based on the electrokinetic potential in colloidal dispersion; zeta potential values indicate the level of electrostatic repulsion between particles with identical charge in liquid medium. Higher zeta values indicate that the particles are more stable and lower values indicate rapid coagulation, the values are represented in millivolts [mV] and it varies from 0 to ± 5 mV for poor stability and values more than ± 61 mV for excellent stability [51, 52].

The stability of the particles is also determined by their particle size distribution; to analyze this part, particles are dispersed in liquid medium and characterized by techniques such as dynamic light scattering and laser diffraction. Particles with larger size distribution remain unstable in most of the samples, proper surfactant or chemical agent is utilized to obtain monodispersed particles, thus the size distribution of particles were controlled to maintain better stability in liquid medium [1, 53].

![Figure 1.9: Schematic diagram of (a) DLS with particle size distribution plot and (b) Zeta potential (Adapted from [54]).](image)

DLS involves mathematical analysis to obtain information on particle size from light scattering technique. Schematic representation of DLS set up with
interpretation of data and zeta potential is shown in Figure. 1.9. Spectroscopic techniques are utilized to obtain data on stability of particles in liquid medium. Suspension stability and settling behavior of nanoparticles can also be studied for longer duration using UV-Vis spectroscopy techniques. Stability of silver and iron oxide systems with the effect of particle size and surface coating at different durations were studied using spectroscopic techniques. Chemical agents have significant effect on stabilization of the nanoparticles for longer duration [55-57]. In such conditions, UV-Vis spectroscopy technique can be utilized to study stability of nanoparticles with the effect of chemical agent over the nanoparticles for longer duration.

1.1.4 Hydrodynamic behavior of Iron oxide nanoparticles

Magnetic nanoparticles are efficient candidate for magnetic drug targeting and hyperthermia applications. Iron oxide nanoparticle is considered as more suitable system for such application compared to other magnetic nanoparticles like Cobalt and Nickel [8]. The magnetic properties of iron oxide nanoparticles are more compatible and feasible for such application. Hence, iron oxide nanoparticles are preferred for Phase-1 human clinical trials [58]; during such trials the magnetic particles are introduced into bloodstream and magnetic field is utilized to control or deliver the magnetic particles at required locations. Main issue during this procedure is to identify the exact quantity of particles required at targeting locations during to continuous blood flow. Identifying the efficiency of magnetic field on the magnetic nanoparticles is important to hold the particles in blood flow for required duration. Parameters like particle size, size distribution, shape, effects of surface agents, distance of magnet for effective generation of field etc. play an important role for the effective magnetic drug targeting process [59]. Ferrofluids has major role in several applications such as liquid seals, switches, micro scale pumps and valves; it is significant that magnetic particles in fluidic system should be stable to counteract the various forces during flow condition.
Ferrofluids contain magnetic nanoparticles suspensions that are efficient as contrast agent for magnetic resonance imaging (MRI) and magnetically guided applications. These particles have a capacity to act as a carrier vehicle to deliver the drug at required locations. During such occasion, the concentration and retention time of particles during continuous flow is important to determine the withstanding capacity of the nanoparticles to overcome such force in flow conditions [60]. Figure 1.10 shows the mechanism of magnetic drug delivery and hyperthermia procedures.

Figure. 1.10: Images of (a) magnetic drug delivery mechanism and (b) magnetic hyperthermia in mouse; tumor is destroyed 30 days after the treatment (Adapted from [61, 62]).
The key challenges during motion of the nanoparticles in real-time conditions are listed below.

- Consistency in size, shape of nanoparticle in order to pass conveniently through several capillaries with different diameter without disturbing the environment.
- Magnetic nanoparticles should exhibit sufficient magnetization even with therapeutic agents.
- The particles must able to deliver the required quantity of drug at the target site.
- The particle should be biocompatible or biodegradable and it should be easily removed from the system after the treatment procedure.

The variation in particle size and its distribution will eventually make them to settle under the effect of gravitational and magnetic field. Parameters like magnetization of particles, viscosity, velocity of fluid in medium and applied magnetic field strength play vital role for efficient drug targeting and other magnetically guided applications [63].

Theoretical interpretation and simulation studies of these vital parameters are very important to acquire more clarity on the magnetic drug targeting. Analysis of particles in suitable blood flow velocity and the effect of applied magnetic field strength are prominent factors, which determines the motion of nanoparticles in blood vessel. Also, this analysis should be carried out in blood vessels with various sizes to get broader picture.

The main purpose is to determine the effect of magnetic field strength on nanoparticles, which may dominate over blood velocity in flow, or washaway of particles even under the presence of the magnetic field. It is necessary to determine the types of forces acting over the magnetic nanoparticles during its motion in fluid medium under the effect of magnetic field.
There are four important fundamental forces that seem to dominate these particles in flow conditions. The fundamental forces are magnetic \( (F_m) \), gravitational \( (F_g) \), buoyant \( (F_b) \) and drag resistance force \( (F_d) \). Figure. 1.11(a) shows the simulated blood vessel as straight channel and effect of magnetic field over the magnetic nanoparticles (b) shows the effect of various forces acting on the magnetic nanoparticles in a solution under magnetic field \([64, 65]\).

Figure. 1.11: Schematic diagram of (a) simulated blood vessel with an entrance for magnetic nanoparticles and effect of field, drag force over particles (b) Effect of various forces over magnetic nanoparticles in a microcapillary model (Adapted from \([64, 65]\)).

There are few governing mathematical equations, which play an important role for theoretical interpretation on control of magnetic nanoparticles in flow systems. Magnetic Richardson number is a prominent factor, which determines the governing force on nanoparticles; it is the ratio of magnetic force at the centerline in vessel to stokes drag force at the center line, as given in the equation (1.4). If the Richardson number increases to value greater than unity then it shows that the magnetic forces experience by particles dominate the drag forces and vice-versa.

\[
\psi = \frac{\text{magnetic force at centerline}}{\text{stokes drag force at centerline}} = \frac{|F_m|}{|F_g|} \quad (1.4)
\]
Mass-Peclet number determines the mechanism of nanoparticles advection with respect to their diffusion; it is shown in equation (1.5), if the peclet values $P_e$ are large then advection of nanoparticles is greater than their diffusion. 

$$P_e = \frac{\text{Blood vessel width} \times \text{Maximum blood velocity}}{\text{Total diffusion coefficient of particles}} = \frac{d_b V_{bmax}}{D_{tot}} \quad (1.5)$$

Where, $d_b$ is the blood vessel width, $V_{bmax}$ is the maximum blood velocity and $D_{tot}$ is the total diffusion coefficient of particles. Force on small sphere moving through viscous fluid is determined by stokes law, which is given in the equation (1.6),

$$F_d = 6\pi \mu a v \quad (1.6)$$

Where, $F_d$ is the frictional force, $\mu$ is the dynamic viscosity, $a$ is the radius of the particle which is assumed as sphere or equivalent sphere and $v$ is the flow velocity.

Even though several simulation studies have explained the transport mechanism of magnetic nanoparticles in flow systems, an exclusive experimental observation is required to identify the practical problems and understand the mechanism of magnetic nanoparticles in various flow conditions. Developing a hydrodynamic setup to study these parameters will be more constructive for effective handling of magnetic nanoparticles under flow condition.

A systematic investigation on the transport mechanism of magnetic nanoparticles is essential to understand the accumulation and wash away mechanism with the effect of applied magnetic field. Visualization of such mechanism in practical approach along with simulation studies should be taken into account to obtain better insight on the accumulation, dispersion and wash away mechanism. Visualization will also convey clear picture on the effect of various flow rates, distribution of particles at specific locations, effect of chemical agent such as surfactant and polymers, diffusion of particles at different conditions, effect of particle size and shape during flow analysis. During these experiments, ferrofluids will be injected into test section of wide range of flow
rates under various conditions and the behavior is photographed at various durations using CMOS/CCD cameras with proper illumination from test region. The recorded images were further processed using various image processing techniques for qualitative analysis. A quantitative analysis is also performed using advanced techniques such as particle image velocimetry (PIV) to capture the different patterns of ferrofluid behavior under flow conditions. Illumination of test sections was performed by focusing suitable light source with optical accessories. This study involves in quantification of samples from captured images with respect to space and time. Specific algorithms were also used to describe various behaviors of ferrofluids using processed frames of the image captured during experiments [66-68]. The simulation studies of this mechanism are reported in literatures, which describes the process of retention and washaway at different flow rates for various durations [69,70]. During hydrodynamic studies, there are two prominent regions which are focused to understand the flow mechanism of ferrofluids under various condition, they are (1) core region, where ferrofluid accumulates at larger extent and (2) wash away region, where the ferrofluid experience large force due to fluid flow in flow cycles. CFD simulations can also be utilized to generate similar behavior under different experimental conditions to study accumulation and wash away mechanisms of ferrofluid.

1.1.5 Electrospun nanofibers - Iron oxide nanoparticles composite

Biocompatible electrospun nanofibers are considered as prominent candidates for drug delivery applications. Recently, Electrospun nanofibers are used in tissue engineering as a small blood vessel graft, which is flexible and durable to survive in continuous blood flow conditions [71], such fibers are more suitable to release the drug or nanoparticles in tubular systems. The significance of nanofibers is their ability to trap and release the drug or nanoparticles at specific location. Hence, Controlled release of particles can be achieved using polymer nanofibers. Electrospun nanofibers can be utilized for various drug release or nanoparticle release applications. Nanofibers act as carrier medium
for release of drug or particles in crucial locations. The key challenge is to load the specific drug or particles into nanofiber and initiate the sustained release mechanism. Several types of bio agents, drugs, and nanoparticles were embedded with nanofibers for site specific release applications. Electrospinning is simple and efficient technique to embed different types of nanoparticles in polymer solution to develop nanofiber-nanoparticle composites [72]. Polyvinyl Alcohol (PVA) is familiar water soluble polymer and also bio-compatible and hemocompatible material [73, 74]. This polymer was used for encapsulation of various drugs and nanoparticles for sustained release mechanism, especially many literatures reported the encapsulation and coating of magnetic nanoparticles using PVA for bio applications [75-78].

The drug or nanoparticles embedded with nanofiber form matrix-type web structure. This process encapsulates the particles and prevents rapid reaction with external environment [79]. The key process in this technique is to regulate the release of the required quantity of drug or nanoparticles. Electrospun nanofiber has a major role for this release mechanism. Also, embedding nanoparticles with polymer nanofiber prevents the agglomeration of nanoparticles and it can be precisely released from nanofiber during flow condition. Thus, a polymer matrix is essential for effective release of drug or nanoparticles at required region [80]. This mechanism can be utilized for the release of Iron oxide nanoparticles at specific locations. Iron oxide nanoparticles can be tuned to maintain the required magnetic properties. The particles should be finetuned to experience the maximum effect of external magnetic field even if it is embed with nanofibers. This Iron oxide nanoparticles polymer nanofiber composite will be highly useful for magnetic nanoparticles mediated targeted drug delivery systems.
1.2 STRUCTURE OF THESIS

This thesis consists of nine chapters with introduction and literature part in Chapter 1 and Chapter 2. These chapters cover types of iron oxide nanoparticles, crystal structure, magnetic domain and magnetic properties, superparamagnetic property with respect to particle size. Comparisons were carried for certain properties with other magnetic nanoparticles such as cobalt and nickel. This also gives information on different approach for synthesis of iron oxide nanoparticles. Description on the effect of particle size on colloidal stability and hydrodynamics of iron oxide nanoparticles were discussed. Chapter 2 provides information from various literatures which throw light on different approach on the effect of synthesis parameters on particle size and magnetic nanoparticles and tuning the magnetic properties of nanoparticles by chemical synthesis method.

Chapter 3 deals with exclusive experimentation work carried to tune the magnetic properties of iron oxide nanoparticle with different particle size using chemical coprecipitation method. This chapter also covers the information on instrumentation developed and used to assess the suspension stability of iron oxide nanoparticles with different size in the presence of magnetic field in UV-Vis instrument. A detailed data analysis process to obtain required value from UV-Vis spectrum is described in this chapter. This chapter also describes about the hydrodynamic setup, which was designed and developed for the analysis of flow behavior of iron oxide nanoparticle fluidic systems, image processing techniques used to quantify the area of interest is also described in this chapter. Experimental work carried to assess the release of iron oxide nanoparticle from electrospun PVA nanofibers in hydrodynamic flow condition; quantification of released particles using in-line spectroscopic method.

Chapter 4 contains information on the synthesis of iron oxide nanoparticles by chemical co-precipitation technique. This chapter mainly focuses on the effect of particle size on tuning the magnetic properties of iron oxide nanoparticles. A detailed characterization and discussion on morphology, particle size, size
distribution, crystal phase, composition and magnetic properties of iron oxide nanoparticles are described in this chapter.

Chapter 5 delivers information on suspension stability studies of iron oxide nanoparticles with an effect of chelating agent and at two different magnetic fields. The effect of particle size, chelating agent and magnetic field on agglomeration and sedimentation of iron oxide nanoparticles in aqueous medium is explained using UV-Vis spectroscopy technique. The magnetic forces experienced on nanoparticles are presented and discussed in this chapter.

Chapter 6 deals with hydrodynamic studies of iron oxide nanoparticles with different particle size. The effect of chelating agent and magnetic field on accumulation and wash away of iron oxide particles is described in this chapter. Also, this chapter covers information on the hydrodynamics setup, image capture and processing techniques to study behavior of iron oxide nanoparticles under various conditions.

Chapter 7 describes the studies on release of iron oxide nanoparticles from electrospun PVA nanofiber in hydrodynamic condition. Electrospinning process of PVA nanofibers with iron oxide nanoparticles, fabrication of sandwich mesh assembly for nanofibers, introduction of mesh assembly into hydrodynamics setup and analysis on release of nanoparticles from nanofiber using in-line spectroscopy setup are described in this chapter.

Chapter 8 concludes the outcomes of this research work on tuning the magnetic properties of iron oxide nanoparticles by coprecipitation technique, suspension stability of nanoparticles under various conditions using UV-Vis technique, hydrodynamic studies of iron oxide nanoparticles and mechanism of iron oxide nanoparticles release from nanofiber in hydrodynamic condition.

Chapter 9 provides information on the scope of future work involved in this research work for specific applications and future perspectives and importance on hydrodynamic studies and in-line imaging of iron oxide nanoparticles.