https://doi.org/10.48047/AFJBS.5.4.2023.178-206

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Magnetic Iron Oxide Nanoparticles: Synthesis, Stabilization, Characterization, and Biological Applications

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Volume 5, Issue 4, Oct 2023

Received: 15 Sep 2023

Accepted: 05 Oct 2023

Published: 25 Oct 2023

doi: 10.48047/AFJBS.5.4.2023.178-206

Abstract

Magnetic iron oxide nanoparticles (IONPs) have garnered significant academic attention due to their unique properties, which make them highly versatile for a range of applications, especially in catalysis and biomedicine. This review comprehensively examines the synthesis, stabilization, characterization, and biomedical applications of iron oxide nanoparticles, with a particular emphasis on maghemite and magnetite. These nanoparticles exhibit distinctive magnetic properties that enhance their utility in various fields, including targeted drug delivery, magnetic resonance imaging (MRI), and cancer hyperthermia. A key focus of this research is the magnetic behavior of IONPs in fluidic environments, crucial for processes such as high-gradient magnetic separation (HGMS) from non-magnetic fluids like blood. The study proposes a two-dimensional model to illustrate a cross-section of a spherical nanoparticle in a fluid, considering only drag and magnetic forces. The drag force is calculated using the Navier-Stokes equation, and magnetization is determined with the Langevin function. The model provides precise trajectory functions for nanoparticles under these forces, which is essential for fine-tuning their application in biomedical settings where control over particle dynamics in biological fluids is vital. In summary, this study enhances the understanding of IONP behavior in complex fluid systems and highlights their potential in advancing biomedical technologies.

Keywords: Iron Oxide, nanoparticles, magnetic resonance imaging, high gradient magnetic separation.

1. Introduction

The diameters of iron oxide nanoparticles represent an exceptionally expansive range, featuring measurements that span from as minuscule as 1 nanometer to a remarkable 100 nanometers, which effectively underscores their inherent nanoscale characteristics. In light of their unparalleled and distinctive magnetic properties, coupled with the extensive array of applications they offer across numerous contemporary scientific fields, it is not at all surprising that iron oxide nanoparticles have attracted considerable attention and fascination from a diverse group of researchers and scientists across the globe. Among the various forms of iron oxides that are predominantly applied within the realm of biomedical applications, two primary varieties distinctly emerge magnetite and maghemite. (Abd Elrahman andMansour 2019)Magnetite is recognized as a notably dark magnetic mineral, scientifically designated as iron (II, III) oxide or ferrous ferrite, and it holds significant importance in a multitude of technological applications due to its unique properties. (Ajinkya et al. 2020)The chemical formula that represents magnetite, which frequently appears in various representations, incorporates elements such as wüstite and hematite, thereby revealing its intricate and complex nature. (Al-Alawy and Kadhim 2018) This particular mineral exhibits the minerals that manifest the most potent and formidable magnetic characteristics found in nature, exhibiting a remarkable ability to interact with magnetic fields in a manner that is unparalleled by other naturally occurring substances, have been the subject of extensive academic inquiry and explorationthat can be found within the Earth's crust, which significantly enhances its utility in various applications (Ansari et al. 2019). In contrast, maghemite is characterized by its distinctive brown magnetic mineral features and is typically located within soil matrices, where it plays a crucial role in several environmental processes that are essential for soil health. (Baabu et al. 2022) This mineral demonstrates substantial magnetic characteristics and is classified as metastable when compared to hematite, which means it possesses the capability of forming a continuous metastable solid solution alongside magnetite, thereby further augmenting its versatility in various applications. (Tanvir et al. 2023) The stabilizzazione di nanoparticelle magnetiche di ossido di ferro (MIONs) emerges as an essential aspect that significantly influences their functionality, particularly within biological environments where the stability of such nanoparticles is of paramount importance (Bhattacharya et al. 2011). To improve the stability, dispersibility, and biocompatibility of MIONs, researchers frequently implement a multitude of surface modifications that incorporate polymers, surfactants, and inorganic coatings, including innovative materials such as silica and gold. (Hernández-Hernández et al. 2020) These sophisticated coatings serve a dual function; they not only alleviate the challenges associated with agglomeration but also introduce functional groups that facilitate subsequent conjugation with targeted ligands, pharmaceuticals, or imaging agents, thereby broadening their potential applications in medical and clinical settings. (Hussain et al. 2023) It is crucial to acknowledge that the strategies employed for stabilization are fundamentally important for preserving both the magnetic and structural integrity of MIONs throughout their storage and application processes, which, in turn, significantly enhances their efficacy when employed in biological systems. (Kumar and Singh 2021)For example, polymer-coated MIONs exhibit prolonged circulation times in the bloodstream and demonstrate reduced toxicity levels, which positions them as exceptional candidates for a variety of in vivo applications that require biocompatibility. The effective stabilization of these nanoparticles ensures the retention of their advantageous properties under physiological conditions, thus facilitating their widespread application in clinical settings, ultimately leading to improved patient outcomes that are essential in modern medicine (Ogbezode et al. 2023).

(Rukhsar et al. 2022)The characterization of magnetic iron oxide nanoparticles (MIONs) employs a range of sophisticated analytical techniques that provide critical insights into their properties. Key methods include transmission electron microscopy (TEM), dynamic light scattering (DLS), X-ray diffraction (XRD), and vibrating sample magnetometry (VSM). Each technique offers detailed information on different aspects of the nanoparticles, such as their morphology, size distribution, surface charge, crystallinity, and magnetic properties. Understanding these characteristics is essential for optimizing the application of MIONs across various fields, including biomedicine and materials science (Sheha et al. 2023).

2. METHODOLOGY

2.1 Techniques for preparing particles through experimentation

The multifaceted dimensions, diverse morphological characteristics, intricate size distributions, distinctive surface chemical properties, and the potential applications associated with magnetic nanoparticles are profoundly shaped and influenced by the specific methodologies and techniques that are meticulously employed throughout their preparation processes, which can significantly modify their fundamental properties and functionalities in ways that are critical to their overall performance and practical use. The synthesis of magnetic nanoparticles that demonstrate particular dimensions and morphologies has consistently presented a multitude of challenges and obstacles to researchers actively engaged in this specialized field, thereby necessitating the development of innovative and creative approaches to effectively overcome these complex difficulties and enhance nanoparticle fabrication. In order to successfully achieve the desired nanoparticles that possess optimal characteristics and attributes, a diverse array of synthesis methodologies has been painstakingly developed and refined over the course of time; as illustrated in Figure 1, the three most prominent and widely reported pathways for the preparation processes are depicted for the purposes of clarity and comparative analysis, thereby providing a comprehensive overview of the current landscape in nanoparticle synthesis. The most dominant strategy that has emerged in the academic literature is undoubtedly chemical synthesis, which has accounted for an impressive approximate 90% of all scholarly articles published on this subject to date, thereby underscoring its critical importance and relevance in the rapidly evolving field of nanotechnology. Furthermore, within the comprehensive context of these diverse methodologies, the coprecipitation technique that employs various iron salts has emerged as the most extensively utilized fabrication method, indicating its widespread acceptance, effectiveness, and reliability among researchers who seek to produce high-quality magnetic nanoparticles.

This predominant preference for the coprecipitation method can be attributed to its relative simplicity, cost-effectiveness, and inherent ability to yield nanoparticles that possess desirable properties, which are essential for various applications in technology and medicine. Consequently, the continued exploration, advancement, and optimization of these crucial synthesis techniques remain imperative for the ongoing development of the field and for enhancing the practical applicability of magnetic nanoparticles across a myriad of technological domains, including electronics, environmental remediation, and biomedical applications. The intricate interplay between the methodologies employed in synthesis and the resultant attributes of magnetic nanoparticles underscores the complex nature of this research area, necessitating further investigation and innovation. As researchers diligently strive to refine and expand the methodologies available for nanoparticle synthesis, the potential for groundbreaking advancements in the functionality and applicability of these materials continues to grow, highlighting the importance of sustained academic inquiry in this dynamic field. Ultimately, the future of magnetic nanoparticles and their contributions to various scientific and technological advancements will depend heavily on the commitment to rigorous research and the relentless pursuit of novel synthesis strategies that can effectively address the challenges presented in this evolving domain.

2.1 Method of Co-Precipitation

The co-precipitation approach is recognized as one of the most effective and straightforward methods accessible for application across a multitude of scientific disciplines, particularly when one takes into account the numerous and diverse advantages it presents in terms of both simplicity and operational efficiency during execution. In light of its extraordinary ease of implementation, combined with a significantly reduced requirement for the use of hazardous chemicals and convoluted procedural steps, this technique has garnered considerable acceptance and is routinely utilized within the biomedical field, where the principles of safety and reliability hold paramount importance. This specific methodology not only facilitates the successful synthesis of iron oxide nanoparticles but also accomplishes this through the meticulous aging of a carefully balanced stoichiometric mixture comprising ferrous and ferric salts, all conducted within a meticulously controlled aqueous environment that guarantees optimal conditions conducive to particle formation. Consequently, the co-precipitation method emerges as an indispensable instrument in the ongoing development of nanoparticles, thereby promoting advancements in the realm of nanotechnology and its diverse applications within medicine and other related fields.

In addition to its practical applications, the co-precipitation process also exemplifies a significant intersection of chemistry and engineering, as it requires an intricate understanding of the underlying principles governing solubility and precipitation dynamics. Ultimately, this method not only enhances the efficiency of nanoparticle production but also serves as a cornerstone for future innovations in various scientific and technological arenas. The selection of salts involved, the molar ratio of Fe^{3+} to Fe^{2+} the operational temperature, the pH levels the characteristics of the solution, along with the ionic strength of the medium, significantly influence the ultimate dimensions, morphology, and chemical composition of the resultant particles.

The synthesis of $\mathrm{Fe_3O_4}$ can be articulated through the following (1-3) chemical reaction.

$$\mathrm{Fe}^{2+} + 2\mathrm{OH}^- \rightarrow \mathrm{Fe(OH)_2} \quad (1)$$

$$\mathrm{Fe}^{3+} + 3\mathrm{OH}^- \rightarrow \mathrm{Fe(OH)_3} \quad (2)$$

$$\mathrm{Fe(OH)_2} + 2\mathrm{Fe(OH)_3} \rightarrow \mathrm{Fe_3O_4} + 4\mathrm{H_2O} \quad (3)$$

Thermodynamic principles predict that $\mathrm{Fe_2O_3}$ precipitation should be complete within a pH range of 9 to 14, provided the molar ratio of Fe^{3+} to Fe^{2+} is maintained at 2:1 in an oxygen-free, non-oxidizing environment. However, $\mathrm{Fe_2O_3}$ is relatively unstable and susceptible to oxidation; in the presence of oxygen, it can transform into $\gamma\text{-}\mathrm{Fe_2O_3}$.

The thermodynamics of this reaction predict that, in a non-oxidizing, oxygen-free environment, a full precipitation of $\mathrm{Fe_3O_4}$should occur between pH 9 and 14, preserving a molar ratio of $\mathrm{Fe^{3+}:Fe^{2+}}$of 2:1. The unstable compound $\square^{8}\mathrm{Fe_3O_4}$can undergo oxidation to become $\gamma-\mathrm{Fe_2O_3}$when exposed to oxygen (table 1).

Table 1. characteristics of iron oxides physically.

characteristics	**Maghemite** $(\gamma-\mathrm{Fe_2O_3})$	**Magnetite** $(\mathrm{Fe_3O_4})$
Color	Black to reddish-brown	Black to dark brown
Crystal System	Cubic	Cubic
Density	5.0 g/cm³	5.18 g/cm³
Magnetic Properties	Generally magnetic	Strongly magnetic
Melting Point	1200-1500°C (varies)	1590°C
Structure	Spinel-type	Spinel-type

$$\mathrm{Fe_3O_4 + 0.25O_2 + 4.5H_2O \rightarrow 3Fe(OH)_3} \ (4)$$

$$\mathrm{2Fe(OH)_3 \rightarrow \gamma - Fe_2O_3 + 3H_2O} \ (5)$$

The creation of an environment that is completely devoid of oxygen is of utmost importance for the effective prevention of oxidation processes that may transpire within the surrounding atmospheric conditions, which can lead to detrimental effects on various materials. In order to attain and sustain such an immaculate environment, the strategic introduction of nitrogen gas into the solution is executed, which significantly contributes to the successful establishment of this oxygen-free milieu that is fundamentally necessary for an array of chemical and physical processes to occur without interference. Beyond its essential function in obstructing oxidation reactions, the incorporation of nitrogen within the solution also plays a crucial role in minimizing particle size, which consequently enhances the overall properties and characteristics of the final materials that are generated as a result of these meticulously controlled conditions.

Therefore, the careful regulation of the nitrogen concentration within the solution not only serves to inhibit harmful oxidation but also aids in the optimization of material qualities, thereby emphasizing the critical importance of maintaining an oxygen-free environment in diverse industrial and scientific applications that demand high precision and reliability. This multifaceted approach underscores how the interplay between nitrogen and the solution can lead to superior outcomes in material science, as well as in various technological innovations that rely heavily on the integrity of the substances involved. In conclusion, the strategic management of gaseous environments, particularly through the utilization of nitrogen, is indispensable for advancing our understanding and capabilities in fields that require rigorous control over oxidation and material properties, ultimately fostering progress across a broad spectrum of scientific endeavors.

The intricate and highly nuanced phenomenon that is commonly designated as coprecipitation can be thoroughly and comprehensively elucidated as being constituted of two separate yet intricately interconnected stages, both of which hold significant importance for the proficient and effective application of this advanced and sophisticated methodological framework. In the initial segment of this elaborate procedure, as the concentrations of the diverse chemical species present within the aqueous solution reach a critical threshold recognized as the point of supersaturation, tiny nucleation sites begin to manifest within the liquid environment, and these nascent nuclei subsequently act as the foundational and indispensable loci from which the process of crystalline growth can ultimately commence and take place.

The ensuing phase that follows this preliminary stage of nucleation is predominantly influenced by the advanced principles of mass transport, which intricately govern the diffusion dynamics of solute molecules as they navigate toward the surface of the developing crystal, thereby enabling and encouraging its ongoing evolution and maturation. It is of utmost significance that these two distinct stages be clearly and unmistakably demarcated from one another in order to effectively produce nanoparticles with the desired properties; for instance, it is critically important that the nucleation process does not occur simultaneously during the designated phase that is explicitly allocated for the growth and development of the crystals. Furthermore, the successful management and orchestration of these two phases can yield remarkable advancements in the field of material science, particularly in the synthesis of nanoparticles with tailored functionalities and characteristics that can be applied across a variety of disciplines. Ultimately, the understanding and manipulation of the coprecipitation process, through the careful regulation of nucleation and growth conditions, can lead to innovative solutions and breakthroughs in various technological applications.

In particular contexts where the nuclei are formed concurrently within a supersaturated solution, the resultant particles that arise after the preliminary stages of crystal formation tend to manifest a remarkably narrow size distribution, highlighting the precision of the nucleation process. Consequently, this observation leads to the conclusion that in order to attain a reasonably a uniform distribution of the resultant particle dimensions is often essential for the nucleation process to be concluded within an abbreviated time frame, thereby emphasizing the temporal aspect of nucleation. Furthermore, it is of considerable significance to note that during the following phase of crystal growth, the total number of particles present does not undergo any alterations; instead, this quantity remains constant and firmly established at the conclusion of the nucleation phase, reinforcing the stability of the system. This stability is crucial for understanding the dynamics of crystal growth and the factors influencing particle size distribution (table 2). Thus, the interplay between nucleation and growth phases is vital for the advancement of crystallography and material science.

Table 2 Numerical Parameters in the Coprecipitation Process for Nanoparticle Synthesis

Parameter	**Concentration (mol/L)**	**Temperature (°C)**	**Time (seconds)**	**Particle Size (nm)**	**Size Distribution (nm)**
Growth Stage	0.05 - 0.1	50 - 70	300 - 600	10 - 50 (final nanoparticles)	05-Oct
Nucleation Stage	0.1 - 0.5	20 - 30	Oct-60	1 - 5 (initial nuclei)	02-Mar

Significance	Higher concentrations lead to rapid nucleation; lower concentrations favor growth without new nucleation.	Lower temperatures control nucleation rates; higher temperatures promote growth dynamics.	Short nucleation time ensures uniform size; extended growth period stabilizes size.	Initial nuclei size influences final particle dimensions; controlled growth maintains uniformity.	Narrow size distribution in nucleation leads to uniform particle sizes after growth.

A valuable method for regulating the dimensions of particles generated during the fabrication of magnetite nanoparticles involves the intentional incorporation of chelating organic anions, including α-hydroxy or carboxylate ions derived from compounds such as oleic acid, citric acid, or gluconic acid. Additionally, the incorporation of polymer surface complexing agents, which may comprise compounds such as dextran, polyvinyl alcohol, or starch, further contributes to this size modulation. The outcome of introducing these organic ions is contingent upon the specific ratio of these ions to iron salts; this ratio ultimately dictates whether the addition of organic ions will either impede the nucleation process or hinder the growth of the crystals, resulting in the formation of larger or smaller particles, respectively.

In the synthesis of magnetite nanoparticles, controlling particle size can be effectively managed through the deliberate addition of chelating organic anions, such as carboxylate or α-hydroxy carboxylate ions from gluconic acid, citric acid, or oleic acid. Furthermore, the use of polymer surface complexing agents, including dextran, polyvinyl alcohol, or starch, enhances this control. The effect of these organic ions depends on their ratio to iron salts, which influences whether they will inhibit nucleation or slow crystal growth, thereby affecting particle size.

Massart's original method produced spherical magnetite particles with a diameter of 8 nm (table 3). The study explored various factors impacting particle size, including the type of foundation (NaOH, ammonia, or methylamine), pH, added cations (Na^+, Li^+, K^+, NH_4^+, $N(CH_3)_4^+$, and $CH_3NH_3^+$), and the Fe^{3+} to Fe^{2+} ratio. Massart's research meticulously examined the relationship between these variables and the resulting nanoparticle dimensions.

Table 3Effect of Fe^{2+}/Fe^{3+} Ratio on Particle Size and Phase at Various x Values

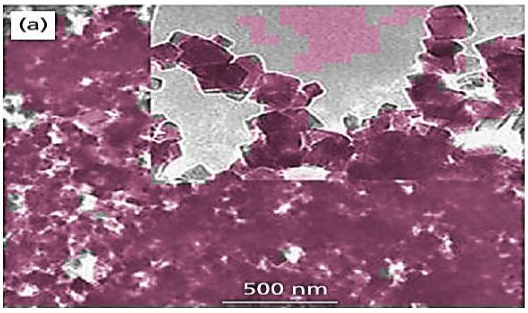
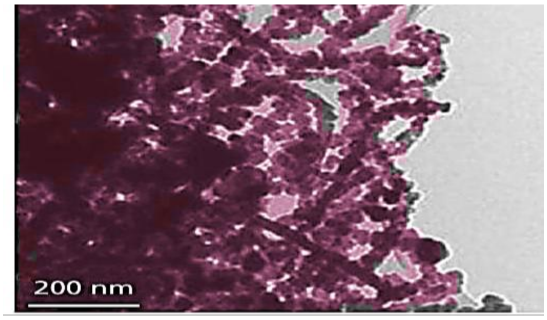
Phase	**x Value**	**Fe^{2+}/Fe^{3+} Ratio**	**Particle Size**
Coexisting Phase 1	0.3	0.07	4 nm
Coexisting Phase 2	0.3	0.33	Larger than 4 nm
Single Phase	0.35	0.5	Variable
Single Phase	0.5	0.7	Larger than at x = 0.3

Through a systematic alteration of various parameters, it was possible to synthesize particles exhibiting a size range that notably spanned from 4.2 nanometers to 16.6 nanometers, thereby highlighting the versatility inherent in the experimental methodology employed. In the context of other academic investigations, it has been documented that particles with sizes falling between 2 nanometers and 15 nanometers were also successfully produced, wherein the researchers meticulously scrutinized the influences exerted by both pH levels and ionic strength on the resultant nanoparticle characteristics. Moreover, it is essential to recognize that these two critical parameters significantly affect the surface composition of the nanoparticles, which subsequently implies that they also play a pivotal role in determining the electronic surface charge of the particles in question.

The correlation observed between the electrical surface density of the nanoparticles and their respective morphologies indicates that the medium utilized for their synthesis can vary, encompassing either aqueous solutions or non-polar liquids such as oils or organic solvents, thus demonstrating the adaptability of the synthesis process. In a separate experimental procedure documented by Massart, the nuances of nanoparticle synthesis were further elucidated, contributing to the broader understanding of this fascinating area of nanotechnology research.$\gamma - \mathrm{Fe_2O_3}$the fabrication of the material in question was accomplished through the employment of a rapid synthesis methodology that facilitated the incorporation of a variety of coatings, which included but were not limited to amino acids, α-hydroxy acids, hydroxamate, phosphoryl choline, and dimercaptosuccinic acid, thereby enhancing the functional versatility and applicability of the resultant magnetic iron oxide nanoparticles: an area of significant interest in both synthesis and practical applications.

The influence of Fe^{2+} to $\mathrm{Fe}^{3+}$the intricate relationship, often referred to as the ratio (x), concerning the various aspects of particle size, geometric configuration, compositional elements, as well as the magnetic characteristics, has been the subject of extensive scholarly investigation and research within the field of material science. It has been observed that, in instances where the ratio is diminished to an excessively low level, there can be significant adverse effects on the overall properties and behaviors of the particles in question, which may lead to unintended consequences in practical applications. Furthermore, this phenomenon underscores the critical importance of maintaining an optimal ratio to ensure the desired performance and functionality of materials, thereby highlighting the necessity for a thorough understanding and precise control of these parameters in experimental and industrial settings., $\mathrm{FeO(OH)}$ forms in the solution. When $\mathrm{x} = 0.3$, there are two coexisting phases. One has a Fe^{2+} and Fe^{3+} ratio of 0.07 and produces 4 nm particles; the other has a ratio of 0.33 and produces larger particles. When $x = 0.35$, only one phase exists. When $x = 0.5$, the particles exhibit a remarkable uniformity, both in terms of their dimensions and their chemical composition, which contributes to their overall functional properties. Moreover, the concentration of iron within the system emerges as a crucial determinant that significantly influences the synthesis process of these particles. It has been established that the optimal concentration range for iron lies between 39 and 78 millimolar, a range that has been meticulously determined through extensive experimentation. Additionally, the parameters of pH and ionic strength are found to exert considerable influence over the resultant size of the particles produced during synthesis. This influence is particularly pronounced due to their role in modulating the electrostatic surface charge of the particles significantly affects their agglomeration behavior. A notable correlation exists whereby both the particle dimension and the breadth of the size distribution augment with increasing pH and ionic strength. diminish, indicating a refinement in the particle characteristics. Thus, it is imperative to carefully control these parameters to achieve the desired particle morphology and functionality in various applications.

In the comprehensive report, a meticulous examination of the impact that ionic strength exerts on the behavior and characteristics of nanoparticles was conducted with great attention to detail and precision. This investigation into ionic strength was facilitated through the systematic introduction of a 1 M NaCl solution, which served as a means to modulate the ionic concentration in the experimental environment. The study specifically focused on magnetite particles, which were characterized by a remarkably small size of 1.5 nanometers, thereby highlighting the significance of size in the context of nanoparticle behavior under varying ionic conditions. Overall, the findings presented in this report contribute valuable insights into the fundamental relationship between ionic strength and nanoparticle dynamics, which may have profound implications for various applications in nanotechnology and materials science.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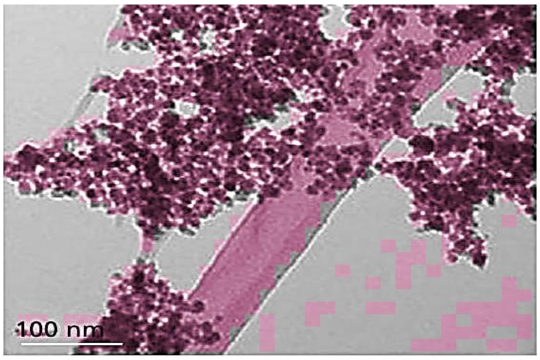	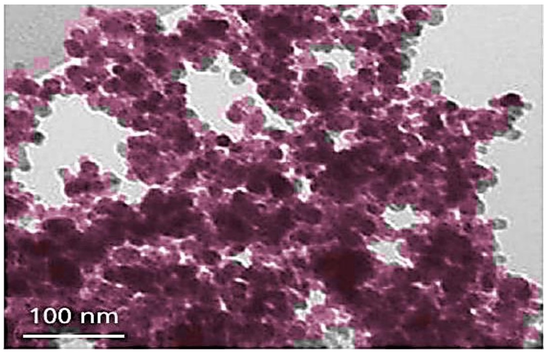
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Figure 1. Micrographs obtained from a transmission electron microscope depicting magnetite nanoparticles

Figure 1 (a) Synthesized through the Sugimoto method utilizing an excess of reagents.$[\mathrm{OH}^{-}]$; (b) Synthesized via Sugimoto's methodology under conditions devoid of agitation and without surplus of $[\mathrm{OH}^{-}]$or $[\mathrm{Fe}^{2+}]$; (c) Synthesized utilizing Massart's methodological approach via a reaction conducted in the presence of $\mathrm{NH_4OH}$; (d) Formulated utilizing the

Massart methodology involving a reaction facilitated by the dispersing agent TMAOH and in its absence. NH_4OH.[14]

The findings of this research indicate that the particles produced are smaller than those generated in the absence of added NaCl. Furthermore, in solutions characterized by elevated ionic strength, the resultant particles exhibit a reduced saturation magnetization compared to standard particles. The rate of mixing also plays a crucial role in determining particle size; as the mixing rate escalates, a corresponding decrease in particle size is generally observed. For instance, a reduction in particle size is noted when a base is introduced to the reactants, in contrast to the reverse scenario. Additionally, the effect of temperature has been examined in various studies. It has been established that, for the synthesis of magnetite nanoparticles, an increase in temperature correlates with a decrease in the quantity of particles formed.

2.2 Hydrothermal methods

Hydrothermal synthesis techniques have been extensively documented for the production of magnetite nanoparticles. In these techniques, chemical transformations take place in aqueous environments within specialized reactors or autoclaves, necessitating temperatures that surpass predetermined thresholds and pressures exceeding 2000 psi.

The synthesis of ferrite under hydrothermal conditions is predominantly executed through two distinguished methodologies: the process of hydrolysis and the alternative process involving the oxidation or neutralization of mixed metal hydroxides, which are both integral in the production of ferrite materials in a controlled environment. While these two approaches share similarities in their overarching principles, they primarily diverge in their specific use of ferrous salts in the hydrolysis technique, which plays a crucial role in the resultant chemical reactions. Various key factors, including but not limited to the choice of solvent, the temperature at which the reactions are conducted, and the duration of the reaction time, exert a significant influence on the physicochemical properties of the ferrite particles that are ultimately produced. Generally speaking, it has been observed that as the reaction time is extended and the volume of water utilized in the process is increased, there is a corresponding increase in the size of the particles that are formed. The particle formation process can be dissected into two distinct stages: the initial phase known as nucleation, followed by the subsequent phase which is characterized by crystal growth. At elevated temperatures, the rate of nucleation tends to surpass that of crystal growth, which consequently results in the formation of smaller particles that are less desirable in certain applications. Conversely, when the reaction time is prolonged, the conditions favor the process of crystal growth, which leads to the generation of larger particles that may possess advantageous properties for specific uses. Through the implementation of the hydrothermal method, researchers have successfully synthesized magnetite nanoparticles that exhibit a diameter of approximately 27 nanometers, a feat that signifies the efficacy of this synthesis approach. To enhance the stability and dispersion of these nanoparticles, bis (2-ethylhexyl) sulfosuccinate sodium salt has been utilized effectively as a surfactant, demonstrating the importance of surfactants in modifying the surface properties of nanoparticles during synthesis.

2.3 Decomposition of organic precursors at high temperatures

The meticulous and highly controlled synthesis of iron oxide nanoparticles, characterized by an exacting size regulation, a tightly constrained size distribution, exceptional crystallinity, and optimal dispersion properties, can be effectively achieved through the innovative method of thermal decomposition of various iron precursors when utilized in conjunction with activated organic surfactants. Among the commonly employed iron precursors in these synthesis processes are notable compounds such as iron pentacarbonyl ($Fe(CO)_5$), iron(III) acetylacetonate ($Fe(acac)_3$), and iron(III) cupferronate ($Fe(Cup)_3$). To illustrate this process in detail, the thermal decomposition of iron carbonyl when executed in the presence of octyl ether and oleic acid at an elevated temperature of 100°C results in the production of iron oleate, which is a significant intermediate compound.

Upon allowing the mixture to cool down to ambient room temperature, it is crucial to treat the resultant composition with trimethylamine, followed by subjecting it to reflux conditions to facilitate further reactions. Additionally, the further decomposition of iron pentacarbonyl when performed in the presence of oleic acid, accompanied by a maturation phase at a temperature of 300°C, yields magnetite nanoparticles that exhibit remarkable crystallinity and dimensions that typically range from 4 to 16 nanometers. It is imperative to note that the size and morphology of these nanoparticles are profoundly influenced by a variety of factors, including but not limited to the duration of the reaction, the temperature at which it is conducted, the types of precursors used, their concentrations, the ratios of the reactants involved, and the specific choice of solvent utilized in the process.

The surfactant coating plays an essential role in stabilizing the nanoparticles within a colloidal suspension, thereby enhancing their usability and performance in various applications. The method of thermal decomposition of iron carbonyl, particularly when conducted with octyl ether and oleic acid, in conjunction with a sequential aeration process, culminates in the formation of hydrophobic magnetite nanoparticles that possess a narrowly defined size distribution, a characteristic that is highly desirable in many advanced technological applications.

2.4 Sol-gel techniques

The sol-gel methodology commences with the formulation of a sol, which constitutes a colloidal suspension of solid particulates dispersed within a liquid medium. This sol is generally comprised of metal alkoxides or metal chlorides that are solubilized in a solvent. These precursors engage in hydrolysis and condensation reactions, thereby generating a gel framework.

Hydrolysis and Condensation:

Hydrolysis: When exposed to water, metal alkoxides or chlorides experience hydrolysis, wherein the alkoxy or chloride moieties react with water molecules to yield hydroxyl groups along with byproducts of alcohol or hydrochloric acid.

Condensation: The hydroxyl groups produced during the hydrolysis phase subsequently participate in condensation reactions, wherein they interact with one another to form metal-oxygen-metal linkages, culminating in the establishment of a three-dimensional network structure. This progression gradually transitions the sol into a gel.

Gel Formation:

The resultant gel manifests as a porous, three-dimensional architecture of interconnected metal oxide particulates. This gel configuration arises as the sol solidifies, encapsulating solvent within its matrix. The metamorphosis from sol to gel is delineated by the emergence of a continuous network of metal-oxygen linkages.

Aging and Drying:

The gel undergoes an aging process, during which the network structure persists in evolving, and additional condensation reactions fortify the gel matrix. In the drying phase, the solvent sequestered within the gel evaporates, resulting in a porous, solid entity referred to as a xerogel.

Heat Treatment (Sintering):

To enhance the material's attributes, including its crystallinity and mechanical robustness, the xerogel is frequently subjected to heat treatment or sintering. This stage eradicates any residual organic materials and facilitates the development of a dense, well-crystallized substance.

The sol-gel technique is esteemed for its adaptability, permitting the synthesis of a diverse array of materials, encompassing ceramics, glasses, and thin films. It affords meticulous control over the composition, microstructure, and characteristics of the final product, rendering it advantageous for implementations in electronics, catalysis, optics, and materials science.

2.5 Tiny emulsions

A microemulsion can be comprehensively defined as a thermodynamically stable isotropic dispersion that consists of two immiscible liquids, wherein nanoscale domains of one or both of these liquids are meticulously stabilized by a surfactant layer that resides at the interface between the two phases. In the specific case of water-in-oil microemulsions, one observes that aqueous phase microdroplets are finely dispersed within a continuous oil phase, with surfactant molecules effectively surrounding and stabilizing these microdroplets. This stabilization is critical as it plays a significant role in the control of nucleation, growth, and agglomeration of particles within the microemulsion system. When a solution containing iron salts is introduced into the microemulsion, the iron salt seamlessly integrates into the aqueous microdroplets present in the system. These droplets are in a constant state of motion, as they continuously collide, coalesce, and fragment, which ultimately leads to the formation of a precipitate as the reactants engage in interaction with one another. The growth of the particles occurs through the exchange of material between the droplets and the subsequent aggregation of nuclei that are formed during the process. Following this intricate interaction, the precipitate can be effectively separated from the surfactants that facilitated its formation.

The utilization of an aqueous core in conjunction with aerosol-OT/n-hexane reverse micelles within a microemulsion system has notably advanced the synthesis of iron oxide nanoparticles characterized by an exceptionally narrow size distribution, as evidenced in Figure 4. The aqueous core serves a pivotal role by solubilizing the reactants necessary for the synthesis process. In this particular study, a combination of iron and other salts was dissolved in a carefully controlled 2:1 ratio within the aqueous core, after which precipitation was induced through the introduction of a deoxygenated sodium hydroxide solution. The magnetite nanoparticles that emerged from this process, which were synthesized under a nitrogen gas atmosphere at significantly reduced temperatures, typically measure less than 15 nanometers in diameter and are observed to exhibit a remarkably narrow size distribution, as illustrated in Figure 6. The primary advantage of employing the microemulsion technique lies in its inherent ability to precisely control the size of the particles by making adjustments to the dimensions of the aqueous core, thereby allowing for a high degree of customization in the synthesis of nanoparticles.

2.6 Sonolysis

Sonolysis, which refers to the intricate process of breaking down organometallic precursors through the application of acoustic wave energy, has emerged as a highly effective technique for facilitating the synthesis of iron oxide nanoparticles, thus garnering significant attention in the field of nanomaterials. In order to achieve precise control over the growth of these particles, researchers frequently incorporate various additives such as polymers, organic stabilizers, or even structural frameworks, which serve to modulate the characteristics of the resulting nanoparticles. The phenomenon of rapid collapse of bubbles induced by sound waves generates localized zones of remarkably high temperatures, which plays a crucial role in the conversion of ferrous salts into nanoparticles that exhibit magnetic properties. As an illustrative example, the hydrosol method has been successfully utilized to produce well-defined superparamagnetic iron oxide nanoparticles through the mechanism of sonolysis, showcasing the versatility of this technique. In this particular method, the nanoparticles are meticulously coated with oleic acid, which acts as a surfactant that significantly enhances their dispersion within a chitosan matrix, thus improving their overall stability and functionality. The nanoparticles that are ultimately produced, characterized by a size of approximately 65 nanometers, exhibit a notable degree of stability, which is essential for their practical applications. The performance and effectiveness of these nanoparticles are critically influenced by a range of factors, including their size, distribution, morphology, and inherent magnetic properties, all of which can exhibit considerable variability depending on the specific synthesis techniques employed (figure 2). In addition to sonolysis, various other deposition methodologies are also utilized in the synthesis of nanoparticles, which encompass polyol synthesis, electrochemical processes, as well as aerosol and vapor deposition techniques, each offering unique advantages and challenges in the fabrication of nanostructures.

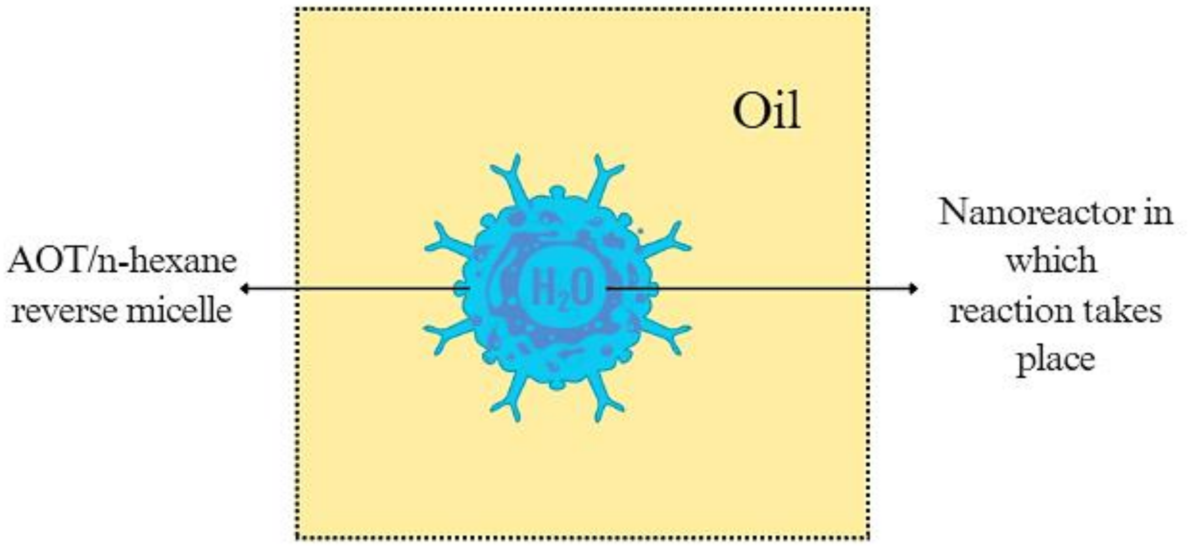

Figure 2Architectural arrangement of a hydrous core encapsulated

3. Features of the particles

3.1 Consistency of colloids

It is essential to recognize that iron oxide nanoparticles are generally synthesized and preserved in a colloidal state, which underscores the critical importance of their stability in various applications. The stability of these nanoparticles is primarily influenced by three significant factors: the presence of hydrophobic interactions, the impact of magnetic forces, and the effects of Van der Waals forces. The occurrence of hydrophobic interactions can initiate a clustering phenomenon among the nanoparticles, ultimately leading to the development of larger aggregates that can reach micron-scale dimensions. Furthermore, the magnetic dipole-dipole interactions that exist between the individual iron oxide nanoparticles serve to further exacerbate the aggregation process, contributing to the continuous formation of these micron-sized clusters over time. It is imperative to understand that these interactions are not merely incidental; rather, they play a fundamental role in determining both the stability and dynamic behavior of the nanoparticles within various colloidal systems. Consequently, a comprehensive examination of these factors is vital for optimizing the performance and reliability of iron oxide nanoparticles in practical applications. Therefore, the intricate interplay among hydrophobic interactions, magnetic forces, and Van der Waals forces must be thoroughly investigated to enhance our understanding of the stability mechanisms at work in colloidal nanoparticle systems.

Magnetic iron oxide nanoparticles, when subjected to the influence of an external magnetic field, undergo a notable increase in their magnetization levels as a direct consequence of the intricate interactions that occur with adjacent clusters of nanoparticles, a phenomenon that ultimately culminates in the enhanced aggregation of these particles into larger conglomerates. Furthermore, when these nanoparticles are suspended in a medium, they possess a propensity to aggregate as a result of the attractive Van der Waals forces that operate between them, which contributes to a reduction in their overall surface energy, thereby facilitating the formation of larger aggregates. This process of aggregation leads to the emergence of clusters that exhibit a limited surface area relative to their substantial volume, and intriguingly, these clusters demonstrate pronounced ferromagnetic properties that are characteristic of iron oxide nanoparticles. However, it is important to note that such aggregation can considerably impede the functional utility and effectiveness of the iron oxide nanoparticles in various applications.

In order to ensure the long-term stability and functionality of these nanoparticles, the incorporation of protective coatings or stabilizers during their synthesis is of paramount importance. These stabilizers, which encompass a diverse array of materials such as surfactants and polymers, are meticulously introduced into the synthesis process with the primary goal of preventing excessive agglomeration of the nanoparticles, which can compromise their performance. In the context of biomedical applications, it becomes critically important that the coatings applied to these nanoparticles are not only biocompatible, ensuring that they do not provoke adverse biological reactions, but also biodegradable, allowing for safe degradation within biological systems. The polymers used in this stabilization process typically adhere to the surfaces of the nanoparticles in a highly specific manner that is tailored to the particular substrate, thereby ensuring that the stability and functionality of the nanoparticles are preserved over time.

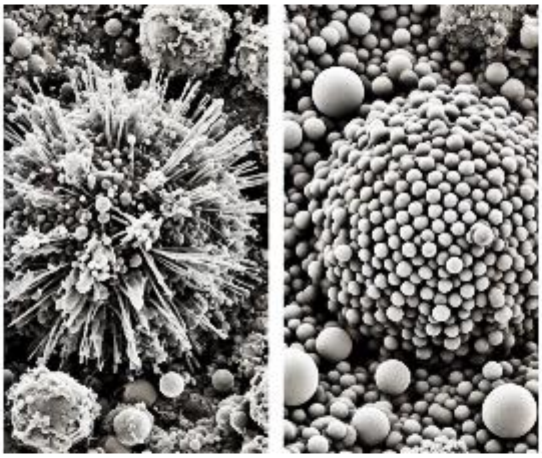

Figure 3Transmission electron micrographs illustrating magnetic nanoparticles synthesized in (a) bulk solutions and (b) water-in-oil microemulsions.

The coatings also serve to shield the particles from subsequent oxidative deterioration. The stabilization can be attributed to two primary mechanisms: electrostatic and steric repulsions. The electrostatic interactions are influenced by the pH and ionic strength of the medium. Conversely, steric repulsion poses a more complex challenge for assessment and, particularly in the context of polymeric coatings, is contingent upon the polymer's molecular weight and density (figure 3). It is crucial to carefully select the coating materials for the nanoparticles. These coating materials may encompass both inorganic and polymeric substances. A comprehensive list of the materials utilized as coatings along with their corresponding applications.

3.2 The colloids' magnetic characteristics

The dimensions of magnetic iron oxide nanoparticles must be significantly minimized to enable the development of a colloidal suspension. Typically, these dimensions fall within the range of 4 nm to 18 nm, remaining beneath the threshold of a singular magnetic domain. As a result, all magnetic moments within a nanoparticle attain optimal alignment, leading to complete magnetization.

In the specialized domain of nanoparticle magnetism, it has been established that the extent or degree of magnetization exhibited by a particular nanoparticle is intricately connected to the anisotropy energy associated with that particle. This specific form of magnetic energy is significantly influenced by the orientation of the magnetization vector, which is a critical factor in understanding the magnetic properties of nanoparticles. The particular orientation that leads to the minimization of magnetic energy is commonly referred to as the anisotropy direction, or more colloquially, the easy axis, and it is fundamentally dictated by the crystalline structure inherent to the nanoparticle itself. As the angle that exists between the magnetization vector and this designated easy axis increases, there is a corresponding rise in the magnetic energy, indicating a direct relationship between these two parameters. This specific correlation between the orientation of the magnetization vector and the resultant magnetic energy is quantitatively expressed through the concept of anisotropy energy.

Furthermore, it is important to note that anisotropy energy exhibits a proportional relationship with the volume of the nanoparticle, a relationship that can be articulated mathematically through the use of (Equation 6), thereby providing a precise quantitative framework for understanding these phenomena.

$$\mathrm{E}_a = \mathrm{K}_a \mathrm{V} \; (6)$$

where Ea represents the anisotropy energy, Ka is the anisotropy constant, and V denotes the volume of the particle.

The Néel relaxation time is notably influenced by the anisotropy energy. As shown in Figure 7, the anisotropy energy reaches its minimum at the easy axes, which are the two preferred orientations. These antiparallel configurations correspond to the lowest magnetic energy and represent stable states for the nanoparticle. Consequently, the magnetic moment in an isolated domain nanoparticle typically aligns with these orientations, constrained by anisotropy energy barriers. At temperatures above absolute zero, there is a non-zero probability for the magnetization to overcome these barriers and shift its orientation. This process is known as Néel relaxation, and the average time required for the nanoparticle to transition between different easy axes is termed the Néel relaxation time, which can be mathematically represented by (Equation 7).

$$\tau_N = \tau_0 \exp \frac{\mathrm{E}_a}{\mathrm{kT}} \; (7)$$

where Ea denotes the anisotropy energy, k is the Boltzmann constant, T represents the absolute temperature, and τo is a characteristic time period. The value of τo depends on the anisotropy energy.

4. Applications in biomedicine

Magnetic iron oxide nanoparticles have been utilized in the domain of in vitro diagnostics for an impressive duration of nearly four decades, a testament to their remarkable and distinctive physical, chemical, thermal, and mechanical properties which set them apart from other materials. The exceptional versatility exhibited by these nanoparticles has led to their extensive application across a multitude of biomedical fields, as illustrated in the accompanying Figure 9, which highlights their diverse roles and functionalities within these sectors.

The extensive utilization of magnetite and its corresponding nanoparticles within the realm of biomedicine can primarily be attributed to their inherent biocompatibility and the remarkably low toxicity they exhibit when interacting with human tissues. These nanoparticles fulfill a variety of important functions, such as acting as contrast agents in magnetic resonance imaging (MRI), enabling the precise and targeted delivery of pharmaceutical drugs, participating actively in immunoassays, and contributing significantly to the process known as magnetic hyperthermia. It is of paramount importance to maintain their superparamagnetic characteristics at physiological temperatures, as this is essential for ensuring optimal performance while concurrently minimizing the risk of particle aggregation that could potentially obstruct blood vessels and impede normal physiological processes. Moreover, the stability of these nanoparticles in aqueous environments at a neutral pH is a critical factor that influences their effectiveness, as the colloidal stability of the nanoparticles is significantly affected by the selection of coating materials and the dimensions of the particles themselves.

In the realm of MRI, superparamagnetic iron oxide nanoparticles are employed as contrast agents with the specific purpose of enhancing the contrast between healthy tissues and pathological conditions, thereby facilitating an improvement in imaging resolution to a level that is microscopic and highly detailed. When it comes to drug delivery applications, these nanoparticles possess the capability to be loaded with pharmaceutical agents either on their surfaces or sequestered within their cores, which allows for innovative therapeutic strategies. Upon exposure to an external magnetic field, these nanoparticles can be effectively directed towards specific sites within the body, which enables the controlled release of drugs at targeted locations and significantly reduces the likelihood of adverse side effects that often accompany traditional drug delivery methods.

In the specialized field of hyperthermia as a treatment modality for cancer, superparamagnetic nanoparticles are known to generate localized heat when subjected to an alternating magnetic field, which selectively inflicts damage on malignant cells while ensuring that healthy tissues experience only reversible damage, thus optimizing therapeutic outcomes. Furthermore, iron oxide nanoparticles that are equipped with polymeric coatings find application in a variety of processes such as cell separation, protein purification, and biochemical syntheses, wherein these coatings serve to enhance the stability and overall functionality of the nanoparticles in question.

Each of these diverse applications necessitates the presence of specific attributes pertaining to the nanoparticles, including but not limited to size, size distribution, morphology, structural integrity, chemical composition, and the nature of the coating materials employed, all of which are determined by the synthesis methodologies utilized. As a result, fabrication techniques are meticulously tailored to align with the unique requirements of particular applications, ensuring that the nanoparticles exhibit the desired characteristics for optimal performance. A particularly significant area of research and study pertains to the magnetic properties of iron oxide nanoparticles in fluidic environments, especially in relation to high-gradient magnetic separation processes from non-magnetic liquids such as blood, which serves as a foundational principle underlying a broad spectrum of biomedical applications. These applications encompass drug delivery, cell separation, protein purification, and even extend to industrial processes such as ore processing and water treatment, illustrating the extensive impact of these nanoparticles across various sectors.

5. Two-dimensional model of magnetic iron oxide nanoparticles in fluids

In the current segment of this analysis, a fundamental two-dimensional representation is thoroughly scrutinized, which effectively depicts a cross-sectional view traversing the central axis of a spherical particle that is submerged within a fluid medium, as illustrated in Figure

10. Within this scenario, the fluid is meticulously channeled through a designated pathway, while concurrently, a magnetic field is strategically applied in a direction that is perpendicular to the boundaries of this channel. The presence of the magnetic force engenders an attractive interaction that draws the particle towards the wall of the channel, consequently leading to its confinement at the inner surface of that particular wall. In the context of this model, the superparamagnetic nanoparticle is characterized by a singular domain crystalline core that is completely enveloped by a protective coating layer, which plays a crucial role in its stability and functionality (Figure 4). Furthermore, the origin of the coordinate system is judiciously established at the base of the channel, providing a foundational reference point for all subsequent measurements and calculations. This meticulous setup not only facilitates a clearer understanding of the particle's behavior under these specific conditions but also lays the groundwork for more complex analyses in future studies. Ultimately, the integration of these elements contributes significantly to the overall comprehension of the dynamics at play within the system being examined.

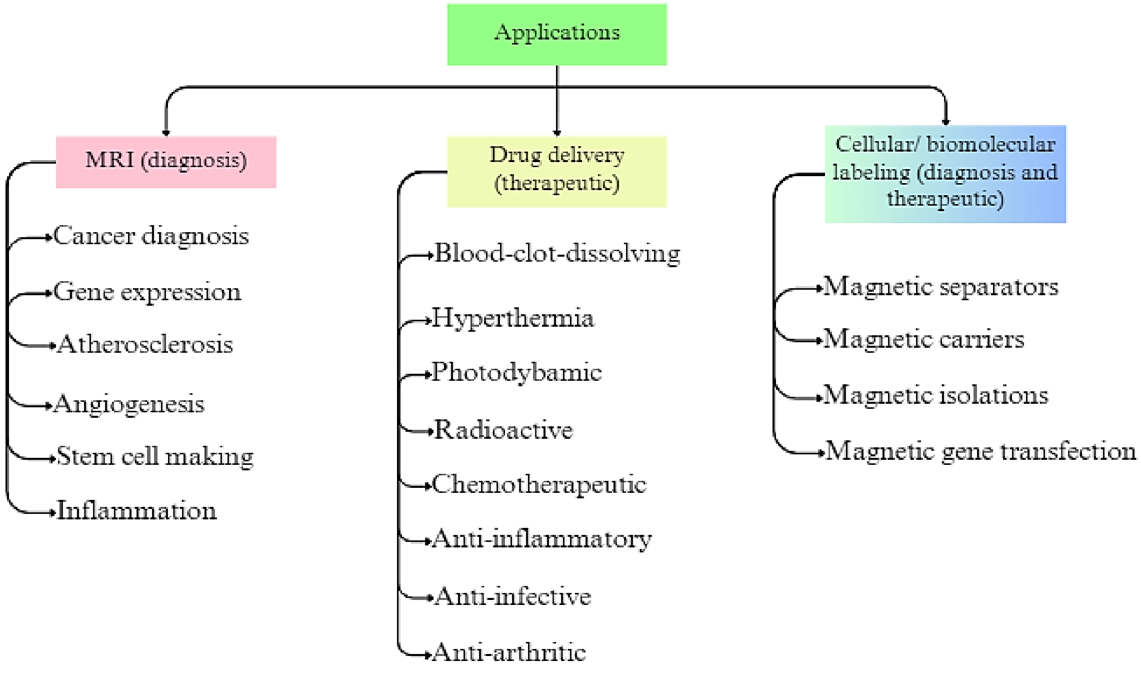

Figure 4. Current uses of magnetic iron oxide nanoparticles in medicine.

6.RESULTS

In the context of numerous biomedical applications, the conduit within the model serves as a representation of blood vessels, while the fluid medium is indicative of blood. Table 3 delineates the parameters' values pertinent to this simulation. By incorporating these values into the trajectory function, the function is subsequently transformed into equation 8:

$$2y^3 - 150y^2 - 1557.8x - 2h^3 + 150h^2 = 0 \ (8)$$

wherein, the variables and encompass the measurement of. Thus, the trajectory delineated by the particle within the circulatory system is dependent on the initial elevation, h, of the particle. Figure 5 depicts the trajectories of the particle at different altitudes.

Current approaches for the synthesis of iron oxide nanoparticles not only enable the creation of superparamagnetic entities that demonstrate an exceptionally uniform size distribution but also allow for the modification of their surfaces for a variety of applications. The effectiveness of these nanoparticles is profoundly influenced by their magnetic characteristics, which are intrinsically linked to the particle dimensions. Therefore, the synthesis techniques employed are vital for the successful implementation of diverse applications. The biomedical potential of magnetic nanoparticles offers significant prospects for the advancement of diagnostic methods and therapeutic interventions, thereby enhancing overall quality of life.

The magnetic characteristics of iron oxide nanoparticles dispersed in a fluid medium represent a critical area of research for numerous applications, especially in relation to the extraction of particles from a non-magnetic liquid environment. Within the framework outlined in this study, only the magnetic force and viscous drag force are taken into account. The magnetization of the nanoparticle is calculated utilizing the Langevin function, while the fluid drag force is determined via the Navier-Stokes equations. The behavior of the particle within the fluid is affected by variables such as the magnetic field gradient, the diameter of the channel, the size of the particle, and the viscosity of the fluid medium (table 3). This model holds potential applications across various fields, including drug delivery, cellular separation, protein purification, mineral processing, and water treatment.

Table 3. Values of the parameters used in the simulations.

Parameter	**Symbol**	**Value**	**Unit**	**Description**

Temperature	T	300	K	Ambient temperature
Pressure	P	1	atm	Ambient pressure
Time Step	Δt	0.01	s	Simulation time step
Number of Steps	N_steps	10000	-	Total number of simulation steps
Grid Size	L	10	nm	Size of the simulation grid
Particle Mass	m	1.67 x 10^{-27}	kg	Mass of a single particle
Interaction Strength	ε	1	-	Strength of particle interactions
Diffusion Coefficient	D	2.0 x 10^{-11}	m^2/s	Coefficient of diffusion
Temperature Coefficient	α	0.01	K^{-1}	Temperature coefficient for expansion

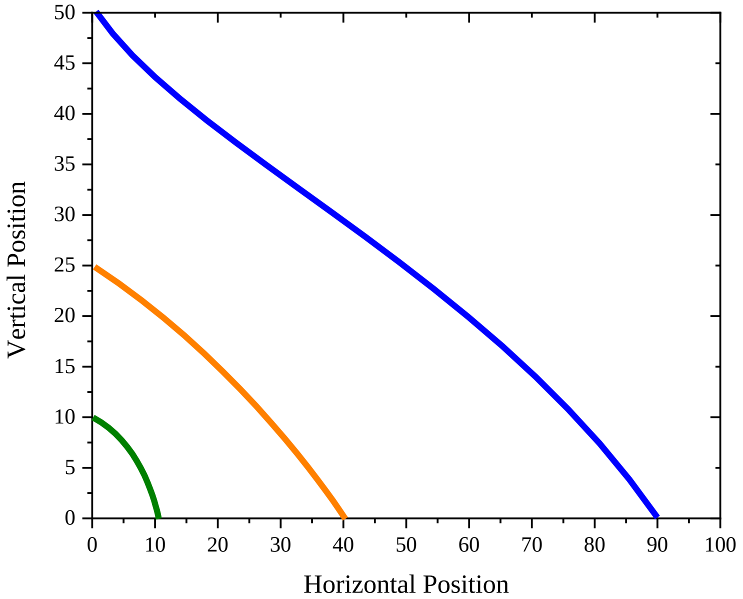

Figure 5. The paths of the particle initiating from elevations of 10, 25, and the y axes are measured in unit dimensions.

6. Conclusion

Magnetic iron oxide nanoparticles (MIONs) have surfaced as an extraordinarily versatile class of nanomaterials, owing to their unique magnetic attributes, compatibility with biological environments, and the ease of surface modification. The fabrication of MIONs, typically executed through methodologies such as co-precipitation, thermal decomposition, and hydrothermal synthesis, is crucial in determining their dimensions, morphology, and magnetic properties, all of which significantly influence their performance across a spectrum of applications. By adjusting the fabrication parameters, it is possible to engineer nanoparticles with tailored magnetic characteristics and a narrow size distribution, both of which are vital for specific uses including magnetic resonance imaging (MRI), targeted drug delivery, and magnetic hyperthermia. The ability to meticulously fine-tune these features has established MIONs as a prominent focus of research within the field of nanomedicine, where rigorous control over particle properties is essential for enhancing therapeutic efficacy and mitigating negative side effects.

REFERENCES

1 Abd Elrahman, A. A., & Mansour, F. R. (2019). Targeted magnetic iron oxide nanoparticles: Preparation, functionalization and biomedical application. Journal of Drug Delivery Science and Technology, 52, 702-712. https://doi.org/10.1016/j.jddst.2019.05.035

2 Ajinkya, N., Yu, X., Kaithal, P., Luo, H., Somani, P., & Ramakrishna, S. (2020). Magnetic iron oxide nanoparticle (IONP) synthesis to applications: present and future. Materials, 13(20), 4644. https://doi.org/10.3390/ma13204644

3 Al-Alawy, A. F., Al-Abodi, E. E., & Kadhim, R. M. (2018). Synthesis and characterization of magnetic iron oxide nanoparticles by co-precipitation method at different conditions. Journal of Engineering, 24(10), 60-72. https://doi.org/10.31026/j.eng.2018.10.05

4 Ansari, S. A. M. K., Ficiarà, E., Ruffinatti, F. A., Stura, I., Argenziano, M., Abollino, O., ... & D’Agata, F. (2019). Magnetic iron oxide nanoparticles: synthesis, characterization and functionalization for biomedical applications in the central nervous system. Materials, 12(3), 465. https://doi.org/10.3390/ma12030465

5 Baabu, P. R. S., Kumar, H. K., Gumpu, M. B., Babu K, J., Kulandaisamy, A. J., & Rayappan, J. B. B. (2022). Iron oxide nanoparticles: a review on the province of its compounds, properties and biological applications. Materials, 16(1), 59. https://doi.org/10.3390/ma16010059

6 Bhattacharya, D., Sahu, S. K., Banerjee, I., Das, M., Mishra, D., Maiti, T. K., & Pramanik, P. (2011). Synthesis, characterization, and in vitro biological evaluation of highly stable diversely functionalized superparamagnetic iron oxide nanoparticles. Journal of Nanoparticle Research, 13, 4173-4188. https://doi.org/10.1007/s11051-011-0363-7

7 Hernández-Hernández, A. A., Aguirre-Álvarez, G., Cariño-Cortés, R., Mendoza-Huizar, L. H., & Jiménez-Alvarado, R. (2020). Iron oxide nanoparticles: synthesis, functionalization, and applications in diagnosis and treatment of cancer. Chemical Papers, 74(11), 3809-3824. https://doi.org/10.1007/s11696-020-01289-7

8 Hussain, A., Yasar, M., Ahmad, G., Ijaz, M., Aziz, A., Nawaz, M. G., ... & Faisal, S. (2023). Synthesis, characterization, and applications of iron oxide nanoparticles. International Journal of Health Sciences, 17(4), 3. https://doi.org/10.53730/ijhs.v17n4.1

9 Kumar, S., Kumar, M., & Singh, A. (2021). Synthesis and characterization of iron oxide nanoparticles (Fe2O3, Fe3O4): a brief review. Contemporary Physics, 62(3), 144-164. https://doi.org/10.1080/00107514.2020.1870823

10 Ogbezode, J. E., Ezealigo, U. S., Bello, A., Anye, V. C., & Onwualu, A. P. (2023). A narrative review of the synthesis, characterization, and applications of iron oxide nanoparticles. Discover Nano, 18(1), 125. https://doi.org/10.1186/s11671-023-03718-3

11 Rukhsar, M., Ahmad, Z., Rauf, A., Zeb, H., Ur-Rehman, M., & Hemeg, H. A. (2022). An overview of iron oxide (Fe3O4) nanoparticles: From synthetic strategies, characterization to antibacterial and anticancer applications. Crystals, 12(12), 1809. https://doi.org/10.3390/cryst12121809

12 Sheha, M. M., Mostafa, A. M., Nasr, D. G., & Shahin, R. Y. (2023). Magnetic nanoparticles: Synthesis, characterization, biomedical applications and challenges. Sphinx Journal of Pharmaceutical and Medical Sciences, 5(1), 1-32. https://doi.org/10.53967/sjpms.v5i1.425

13 Tanvir, F., Sardar, N., Yaqub, A., & Ditta, S. A. (2023). Synthesis of iron oxide nanoparticles, characterization, uses as nanozyme and future prospects. Bioinspired,

Biomimetic and Nanobiomaterials, 11(4), 156-167. https://doi.org/10.1680/jbibn.22.00035