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Synthesis, Characterizations, and Challenges of Magnetic $Zn_xFe_{2-x}O_3$ Nanoparticles

Gizachew Diga Milki*

Abstract

Diluted magnetic semiconductors comprising magnetic nanoparticles are a driving force in a variety of applications, including biomedicine, bioelectronics, photocatalytic activities, and nanosensors. However, the functionality of these nanomaterials can be influenced by several factors such as synthesis route, characterization procedures, source, crystal size, and morphology. In this research, emphasis is devoted to synthesizing and characterizing magnetic nanoparticles. Most importantly, it is focused on biological methods, Co-precipitation methods, hydrothermal Gravity methods, solid-state reaction methods, sol-gel method, solvothermal method, methods, Polyol method, and pulsed laser deposition method. The research also underpins the impact of rheological conditions, including pressure, temperature, magnetic fields, and concentration, on the choice, cost, quality, and production yield. Herein, the synthesis process, significance, and challenges associated with each synthesis method are discussed. Moreover, the potential role of these synthesis methods and characterization methods, including EDX, XPS, FIB-SEM, and HRTEM, was presented. Moreover, magnetic nanoparticles, primarily $Zn_xFe_{2-x}O_3$ *nanoparticles and their functionality as therapeutic agents, Hyperthermia, diagnosis, imaging, biosensing, and drug delivery systems are discussed.*

keywords: Magnetic nanoparticles, synthesis route, characterization methods, rheological conditions, biosensors, therapeutic agent, hyperthermia, diagnosis

INTRODUCTION

Currently, nanotechnology is a big area of investment in developed nations, namely Japan, Europe, the United States, China, India, and Korea. Nanotechnologies open cutting-edge research in theranostics and nanomedicine. As Zijun Jiang et al. (2021) [1] explained, nanomedicine enables effective tumor treatment with improved photothermal therapy, nanoparticle-based drug delivery, and release. Nanomedicine is a combination of skills, knowledge, and techniques targeted to diagnosis, detection, protection, prevention, and treatment of diseases using nanoscale materials and devices. It is an innovative technology comprising applied nanotechnology, bio-nanotechnology, green nanotechnology, and their potential role in areas of medicine, biotechnology, electronics, energy, and agriculture. It enables controlling the transmission, duplication, and treating disease using nanoparticles and its counterpart. It incorporates the use of magnetic nanoparticles, lipid nanoparticles, DNA therapy, genomics, and multi-omic technologies based on DNA nanotechnology. Consequently, it revolutionalize medical procedure from microfluid technology to nanomedicine, personalized medicine, and nanotheranostics by improving medical imaging, diagnosis, therapeutics, and targeted drug delivery.

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The purpose of engineering nanomaterials is not to get matter to a relatively small size. But it is aimed at fabricating materials at the nanoscale with desired bio-chemical, physio-chemical, and bio-physical properties. These properties influence the durability, speed, performance, quality, and functionality of magnetic nanoparticles.

The sensitivity, stability, quality, biocompatibility, and functionality of magnetic nanoparticles are greatly influenced by early synthesis and characterization techniques. To improve these requirements, strategies are designed. As Kefeni K. K. et al. (2015) [2] stated, key strategies for improving such requirements are using appropriate surfactants (oleic acid/oleylamine), increasing temperature/pH, and surface coating. Moreover, AI-based detecting, monitoring, and optimizing biophysical properties and the choice of raw materials for the synthesis will influence stability, sensitivity, biocompatibility, crystallinity/homogeneity, functionality, and surface properties.

Nanotechnology involves the synthesis of materials, such as nanocomposites, nanoparticles, nanorods, and monohybrids, that foster nanomedicine and precision medicine. In this manuscript, some selected nanoparticle synthesis methods are discussed. These methods are preferred based on their effectiveness, including response to external rheology, toxicity of product, yield, quality, cost, and impact on ecosystems. Some of these methods are Pulsed laser deposition, Polyol Methods, Solid-state reaction, Sol-gel method, Co-precipitation, hydrothermal, high gravity method, Solvothermal, and Biological (Green) method (Figure 1). These methods are first discussed. Then, some suitable characterization techniques for magnetic nanoparticles are assessed. Finally, some of the most dominantly suspected challenges of both synthesis procedures and characterization methods are enumerated.

METHODS OF SYNTHESIZING

Pulsed Laser Deposition (PLD)

While growing nanoparticles using the PLD technique, it is important to analyze and visualize the substrate conditions such as texture and substrate temperature. The settlement and nucleation of the particles promote the nature of film formation, whether dense or smooth. The nucleation of nanoparticles is dependent on the substrate temperature, pressure, and catalytic layer. $Zn_xFe_{2-x}O_3$ nanoparticles can be synthesized by using a KrF laser, the sapphire, Al_2O_3 (0001) as a substrate. Trang Minh Nguyen Thai et al. (2014) [3] synthesized Fe_2O_3 thin films by using the pulsed laser on α-Al_2O_3 (0001), MgO (001), and fused quartz. Piotr Kupracz et al. (2020) [4] also revealed that the metastable suspension of FeO, Fe_3O_4, and Fe_2O_3 nanoparticles can be synthesized by Pulsed Laser for decorating anodized TiO_2 nanotube. Pulsed lasers can also create homogeneous particles without temperature segregation in high-temperature processes. It is a very rapid synthesis method and can be used as an alternative method of synthesizing $Zn_xFe_{2-x}O_3$ nanoparticles.

Polyol Methods

The polyol method is a liquid-phase synthesis route for the synthesis of nanoparticles, which involves separating metal nanoparticles from their host hydroxide, salts, or polyalcohols. This route is also used to synthesize metal oxides, fluorescent and luminescent materials, and nanomaterials. It can be extended for the preparation of Nanosized $Zn_xFe_{2-x}O_3$ particles. As Hoang Nguyen et al. (2019) [5] realized, the Polyol method enables to soliloquize many metallic precursors and activates the reactions, favoring particles with a high crystallinity and a narrow size distribution. $Zn_xFe_{2-x}O_3$ can be synthesized with a Zn:Fe molar ratio of 1:10–1:1 by Polyol methods. The polyol method is advantageous since it enables the possibility to control nucleation and synthesis procedures.

Solid-State Reaction Methods

The solid-state reaction method is the synthesis of poly-crystalline nanoparticles from a solid mixture. It is done by mixing together powdered reactants and pressing them into pellet shape and then heating them in a furnace for prolonged periods. This method is also known as shaking in bake or beating in heat. Using this method, chemical reaction routes can be carried out, and the compound of interest can be obtained by balancing the chemical reaction using the electron method. The skeletal reaction is presented as follows.

$Fe(NO_3)_3.9H_2O + Zn(NO_3)_2.6H_2O \frac{Glycine \rightarrow}{water} Zn_{1-x}Fe_{2-x}O_3$ + Gaseous product.

Balancing the skeletal equations and taking x = 0, will give the following product:

$$4Fe_3O_4 + 6ZnO + 4H^+{}_2 \rightleftharpoons 6(ZnFe_2O_3) + 4H^+{}_2O.$$

Alternatively, sulfides are used for the synthesis of $Zn_{1-x}Fe_{2-x}O_3$ nanoparticles by solid-state reaction methods.

$$4FeCl_2.3H_2O + 4ZnO + O_2 \rightarrow 2ZnFe_2O_4 + 4ZnCl_2 + 12H_2O.$$

Balancing the given skeletal equation gives:

$$2FeCl_2.4H_2O + 2ZnO \rightarrow ZnFe_2O_4 + 2ZnCl_2 + 6H_2O$$

Taking the first term on the right-hand side and reducing it to a small definite proportion, the required $ZnFe_2O_3$ is obtained. As Lee S. et al. (2024) [6] revealed, heat treatment is important in solid state chemical reaction methods and recommended for mass production, and cost effectiveness. In the solid-state reaction process, the mixture must be heated up to 800–1000 degrees Celsius, while Fe^{2+} in the $FeCl_2$ is oxidized to Fe^{3+}. The challenge of this synthesis method is the slow reaction rate at room temperature. Hence, high temperatures are needed to speed up the rate of chemical reaction.

Sol-Gel Method

The sol-gel method is a wet-chemical, bottom-up approach designed to synthesize solid materials, including metal oxides, semiconductor nanoparticles, and magnetic nanoparticles, from small molecular precursors. Sol-gel is a chemical process that involves the incorporation of metal nanoparticles into the organic phase. It involves the conversion of monomers into a colloidal solution. In this process, gelatin is used as a polymerizing agent. The sample is usually dried and calcined at low temperature up to 875 k on average. This process has the advantage of high purity and uniform crystal nanoparticles. The preparation process takes place comparatively at a low temperature, so that the mixing process is held at an atomic scale.

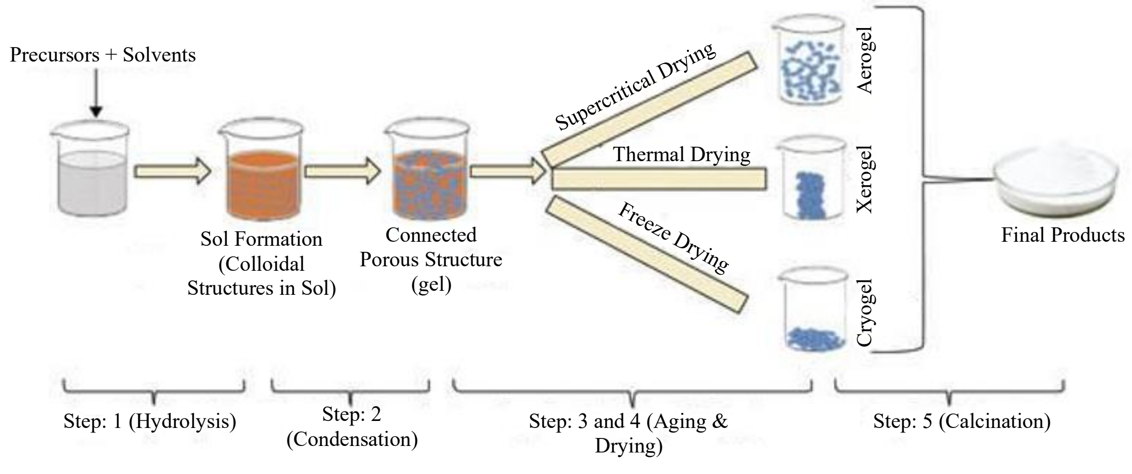

Figure 1. Key procedure for synthesizing nanomaterials by the Sol-gel method (Bokove D., et al. (2021) [7]). The key procedures involved are: (1) precursor solution, (2) hydrolysis & condensation (sol-formation), (3) Gelation, (4) aging, and (5) drying and heat treatment.

Magnetic nanoparticles, such as Ferric oxides, can be synthesized by the Sol-gel route. Besides, it can be used for the synthesis of amorphous nanoparticles such as ceramic and SiO_2. However, it is limited to a certain extent since sol–gel methods involve two distinct phases: Solution formation and gelation. It is also time-consuming and expensive.

Co-Precipitation Method

The co-precipitation method is the most powerful method for the synthesis of iron oxide nanoparticles. The reason is that this method is suitable for fine Stoichiometric management. The co-precipitation method enables a greater probability of obtaining ultra-fine particles in the nanoscale with high crystal quality and uniform particle distribution. It takes place when any solution is supersaturated to form precipitates with another substance. Any change in the rheological condition, such as Concentration of solute or PH, produces precipitations. Another factor influencing this method is the ratio of hydroxide ion to iron ion, the Fe^{3+} to Fe^{2+} ratio, temperature, and Pressure.

As J. K. Furdyna (1988) [8] revealed, α-Fe clusters can be oxidized and converted to precipitates of $ZnFe_2O_4$ at high temperatures and for sufficiently long annealing time. Wojciech Szczerba et al. (2016) [9] synthesized zinc-doped iron oxide nanoparticles by conducting two different bases, namely sodium hydroxide (NaOH) and aqueous ammonia (NH_3 (aq.)), by dissolving an adequate amount of $FeCl_3.6H_2O$, $FeCl_3.4H_2O$, and $ZnCl_2$ in deionized water in air at 20°C. On the other hand, J. Grotel et al. (2018) [10] prepared Fe-doped ZnO by the Co-precipitation method by using $ZnSO_4.7H_2O$, Fe $(NO_3)_3.9H_2O$, and NaOH.

As Cristina Blanco Andujar et al. (2014) [11] noted, the function of nanoparticles can be exploited by the incorporation of biomolecules and improving the stability of colloids. Therefore, it is important to figure out the role of alcohol-based ligands to improve the exchange between bonds in the synthesis of $Zn_xFe_{2-x}O_3$ ferrite. Co-precipitation method is advantageous since it can be extended to the synthesis of calcites and radio nuclides in addition to magnetic nanoparticles such as Zn-doped Fe_2O_3.

Hydrothermal Method

The hydrothermal method involves the incorporation of an aqueous solution as a reaction system in confined vessels by creating high pressure and temperature as governed by the equation of state. By using Zinc nitrate hexahydrate, iron (II) chloride tetrahydrate, and iron (III) chloride hexahydrate as precursors, Chan Oeurn Chewy (2015) [12] prepared $Zn_x(\alpha Fe_{2-x}O_3)$ nanoparticles without morphology deformation. Hence, the qualities of the magnetite are controlled by monitoring the iron chloride tetrahydrate. As M. Mohapatra and S. Anand (2010) [13] stated, high temperature decomposition of iron precursors shows that Zn-doped alpha iron oxide has a high level of mono disparity and manageable size.

Why is the hydrothermal method preferred? This method is used for synthesizing advanced nanomaterials as well as ZnFeO nanocomposites exhibiting tailored properties. In addition, it is used to produce nanostructures which are undoubtedly applicable for electronics and Optoelectronics, Nanozymes, biomedicine, biophotonics, etc.

The hydrothermal method is carried out in a pressure furnace (autoclave) at controlled pressure and temperature. Usually, the autoclave is coated with Teflon coatings. The process is carried out in an aqueous solution. By varying temperatures beyond 100°C, one can attain the saturation vapor pressure governed by the statistical equation of states. This pressure is referred to as internal pressure and depends on the concentration of the input solution.

The hydrothermal method is advantageous since it can be carried out anywhere. It is also advantageous because it is used for recycling nano waste. Besides, in the hydrothermal synthesis process, it is possible to control many physical parameters, such as concentration, pressure, temperature, and even particle morphology, by noting statistical thermodynamic laws. Hiromichi Hayashi et al. (2010) [14] verified that Hydrothermal synthesis has advantages for the synthesis of multi-metal oxides at the supercritical point of water. Yong X. Gan et al. (2020) [15] demonstrated that the Hydrothermal synthesis method can generate nanomaterials that are not stable at elevated temperatures and maintain minimum material loss. It enables particle production in a highly controlled diffusivity in a strong solvent medium in a closed system. Moreover, Nanoparticles synthesized by Hydrothermal techniques can be characterized by X-ray diffraction (XRD), Mossbauer spectroscopy, and transmission electron microscopy (TEM).

Gravity Methods

The gravity method is another physical method that is designed to synthesize magnetic nanoparticles with high yield, purity, and stability. Most often, high-gravity methods involve mass transfer or chemical transfer. Thus, the high gravity method enables particle control and monitoring and maintains uniform particle size and shape. Consequently, it maximizes magnetic nanoparticle production and yield. As Qi G. et al. (2019) [16] explained, a high gravity reactive precipitation enables impinging streamlined-rotating packed bed (IS-RPB) reactors.

The rotating packed bed (RPB) is designed to generate a centrifugal field exceeding the Earth's gravitational field by ~10N. The high gravity provides a suitable ecosystem for rapid micro mixing and accelerates the rate of mass transfer. Magnetic nanoparticles produced in this way are highly monodispersed, highly stable, and smaller in size. As Wang A, S. et al. (2025) [17] reported, high gravity technology enables precise control over multiphase flow and synthesis procedures with superior mixing capability.

Solvothermal Method

Solvothermal synthesis is a versatile, nanomaterial synthesis route that uses non-aqueous solvents. It takes place in an autoclave (sealed vessels) to produce high-quality, crystalline nanoparticles at an extreme temperature and pressure. It offers excellent control over particle size, shape, and composition, often resulting in narrow size distributions. The solvothermal method is used to synthesize both elemental and compound nanostructures. It is applicable in the synthesis of magnetic nanoparticles, metal oxides, chalcogenides, and alloys (Figure 2). As Haloing Hu et al. (2020) [18] noted, the simple Solvothermal method has proven to be an excellent route to synthesize iron oxide nanorods. The Zn-doped iron oxide nanorods prepared in this way exhibit different magnetic properties. These properties with proper thermal conditions enable $Zn_xFe_{2-x}O_3$ nanoparticles for the applications of biomedicine, magnetic recording materials, gas sensors, and catalysts. It is mainly applied for the synthesis of $Zn_xFe_{2-x}O_3$ and metal nanoparticles, such as Au or Ag, which are outstanding candidates in biomedical applications.

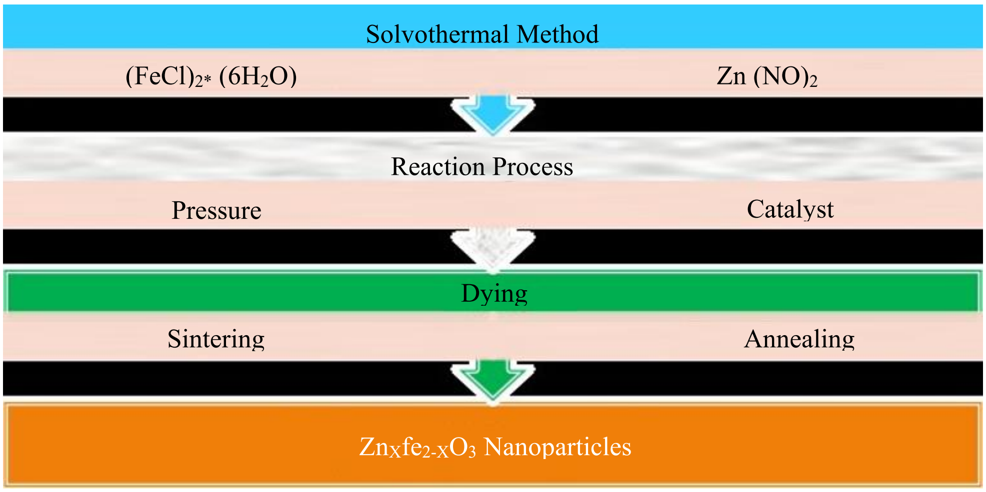

Figure 2. Synthesis of $Zn_xFe_{2-x}O_3$ nanoparticles by the Solvothermal method.

Not only Zn-doped iron oxide nanoparticles but also more complex transition metal, alkaline metal, and rare earth metal-doped iron oxide compounds can be synthesized by this method. As a prime example, A. Manohar and C. Krishnamurthy (2017) [19] synthesized $Mg_{1-x}Zn_xFe_2O_4$ with (x = 0.2, 0.4, 0.5, 0.8) by the Solvo thermal flux method. Hence, upon Mg and Zn doping, the resulting crystal appears cubic spinal structures. Reviews, including Lagerkvist U et al. (2016) [20], discussed the possibility of preparing single-phase ZnO (0% Fe), $ZnFe_2O_4$ (67% Fe), and α-Fe_2O_3 (100% Fe) using nitrates and acetates precursors.

Biological Methods of Synthesis

The biological method of synthesizing nanomaterials, particularly nanoparticles, is referred to as green chemistry. This method involves the utilization of plants, animals, and microorganisms belonging to lower and higher taxonomy. Green synthesis of nanomaterials is expected to have a high commitment to environmental security and health. It is proven by R. K. Das et al. (2017) [21] that the biologic method of synthesizing magnetic nanoparticles is practically applicable for the synthesis of gold (Au), silver (Ag), copper oxide (CuO), Zinc oxide (ZnO), Fe_2O_3, palladium (Pd), platinum (Pt), nickel oxide (NiO), and magnesium oxide (MgO).

This method is very important because it is cost-effective, environmentally friendly, and has the least toxic effect. Fe_2O_4 Nanoparticles are composed of green algae and Cyanobacteria. It is possible to synthesize $Zn_xFe_{2-x}O_3$ nanoparticles by catalytic (enzymatic) activation. As demonstrated by the research group, Jag prêt Singh et al. (2018) [22], Green synthesis of metallic nanoparticles accommodates various biological materials such as bacteria, fungi, algae, and plant extracts (Figure 3).

F.I. Bassey et al. (2014) [23] determined different transition metals, namely Fe = 7.8, Zn = 4.45, and Mn = 4.47 in the samples of tomato leaves and Fe = 5.5, Zn = 2.85, and Mn = 3.03 in the tomato fruit (Figure 3(a)).

(a) Tomato (b) Spinach

Figure 3. (a) Tomato leaves and (b) fruit and spinach for transition & metal oxide extraction.

This evidence reveals that both tomato leaves and fruits contain important elements, which are essential to human body cells and tissues. These garden plants have high promise for the synthesis of magnetic nanoparticles like ZnO, Fe_2O_3, and $Zn_xFe_{2-x}O_3$ nanoparticles. Other fruits, such as melon, spinach, banana, mango, and mango fruits, contain important elements, like Cu, Zn, Co, Ni, and Cd, which are helpful for the synthesis of ZnO and $Zn_xFe_{2-x}O_3$nanoparticles (Figure 3(b)).

These plants are frequently used as a source of medicine due to their important metals and nutrient constituents. On the other hand, Moringa is enriched with the most important vitamins, including vitamin A, vitamin B_1 (thiamine), B_2 (riboflavin), B_3 (niacin), B-6, folate, and Ascorbic acid (vitamin C). It also contains important cations, which are composed of human body organs (Figure 4). The cations include calcium (Ca), potassium (K), iron (Fe), magnesium (Mg), phosphorus (P), and zinc (Zn). It also contains extremely low fats and has no harmful cholesterol. Nanoparticles synthesized by green methods are applicable for painting sprays, perfume with natural flavor, and good aroma.

Figure 4. *Tephrosia purpurea* for Nano flavonoids.

The bark & other parts of *Taxus brevifolia* contain an anticancer drug, Taxol. It is active against lung cancers, ovarian cancers, breast cancers, and brain cancers (Figure 5). However, its seeds are poisonous to humans, cattle, and horses. However, birds consume a great deal of it. These are all wild plants used in the green synthesis of $Zn_xFe_{2-x}O_3$ nanoparticles (Figure 5). Particularly, spinach is enriched with high levels of iron, calcium, and many important vitamins.

(a) *Astragalus membranaceus* to strengthen immunity, to treat hepatitis, and for cancer therapy.

(b) *Moringa* plant: antioxidant, protects cells from damage, decreases inflammation, diabetes, and anticancer.
Figure 5. Green plants for extracting ZnO, Fe_2O_3, and used for developing immunity & therapy.

Cheruth et al. (2017) [24] nutritional composition of Tephrosia Apollonian analyzed based on micro and macro elemental analysis reveals that T. Apollonian contains Fe, Ca, Mg, Na, and Zn in appreciable quantities and phosphorous, copper, and potassium in lower amounts. Pollen grains are good candidates for synthesizing nanomaterials using biological methods.

As S. K. Hosseinihashemi, 2020 [25] verified, *T. bacata* leaves contain sugars, acids, alkane, alcohols, aldehydes, ether, esters, flavonoid, phenol, and Steroids. Flavonoids are believed to be a good anti-inflammatory and wound-healing substance.

Magnetic $\alpha Fe_2O_3/Zn_xFe_{2-x}O_3$ nanoparticles can also be synthesized by using the *Sida cordfolia* Plant. As Shamaila Sajad et al. (2018) [26] discussed, spherical magnetic Fe_3O_4 nanoparticles (SMNPs) can also be synthesized from Syzygium cumin seed extract with an inverse spinel cubic structure.


(a) *Taxus brevifolia* blue Mts WA.


(b) *Taxus baccarat*.

(c) *Taxus cuspidata* for anticancer.

Figure 6. Different types of Taxus leaves for synthesizing metal oxide nanoparticles and medicines for cancerous cells.

Astragalus membranaceus is a medicinal plant that is significantly used for immunomodulation, anti-tumor, anti-inflammatory, and antioxidant properties. It has an anti-aging effect. However, upon enzymatic activity and combining Zn/Fe-bearing oxides, it modifies its functional properties and helps to synthesize $Zn_xFe_{2-x}O_3$ nanoparticles.

$Zn_xFe_{2-x}O_3$ Nanoparticles can also be synthesized in biological processes using magnetotactic bacteria. Magneto-tactic bacteria are enriched with iron oxide, particularly hematite nanoparticles. The magnetotactic bacteria bear organelles called magnetosomes, which contain magnetic crystals. These crystals are critically important in the synthesis of magnetic ZnFeO nanoparticles.

The following is the pictorial representation of green synthesis of nanoparticles of $ZnxFe_{2-x}O_3$ using Astragalus Plant and Magnetotactic bacteria.

The bacteria possess Fe_3O_4, which possesses Zn-bearing compounds that are decomposed into $Zn_xFe_{2-x}O_3$ Nanoparticles by a photo-catalytic process. Mycobacteria (MTB) are Gram-negative prokaryotes. They can be used as target materials for detecting medical or sensitivity of nanodevices such as biosensors. In addition to synthesizing $Zn_xFe_{2-x}O_3$ nanoparticles (Figure 7), magnetotactic bacteria are guided by magnetic fields in medicine and biotechnology, for cell separation, targeted drug delivery, and magnetic fluid hyperthermia. Dudchenko N. et al. (2022) [27] & Shimoshige H. et al. (2017) [28] revealed that magnetite (Fe_3O_4) and Magnetite (Fe_2O_3) synthesized from magnetotactic bacteria are biocompatible and used for targeted cancer therapy. Moreover, Mai Abdeen (2016) [29] and Vargas G. et al. (2018) [30] noticed that magnetic nanoparticles synthesized from the magnetotactic bacteria can also be used for magnetic fluid hyperthermia, magnetic resonance imaging (MRI), and drug delivery. Dasdag S et al. (2014) [31] illustrated the potential applications of magnetotactic bacteria in chemiluminescence enzymes, immunoassays, nanorobotics, and purification of DNA & RNA.

What advantages do biological (green) synthesis methods have? It is preferred since it is environmentally friendly, with the least toxic effect; the raw materials (magneto tactic bacteria, leaves, roots, stems, or fruit) have their own medical value, particularly for cancerous cells. For example, in the setup above, magnetotactic bacteria are used for generating magnetic nanoparticles, which is quite used for magnetic resonance imaging and magnetic fluid hyperthermia, while *Astragalus membranaceus* is significantly important to strengthen the immune system, to treat hepatitis, and for cancer therapy. It also produces tunable optical wavelengths in the visible electromagnetic spectrum such as green, red, blue, and yellow. Green synthesis methods are also an alternative means of waste treatment since some Kitchen wastes and peels are used for the green synthesis of magnetic nanoparticles & quantum dots. In addition, nanoparticles prepared in this way are good indicators of PH value when tested by methyl blue.

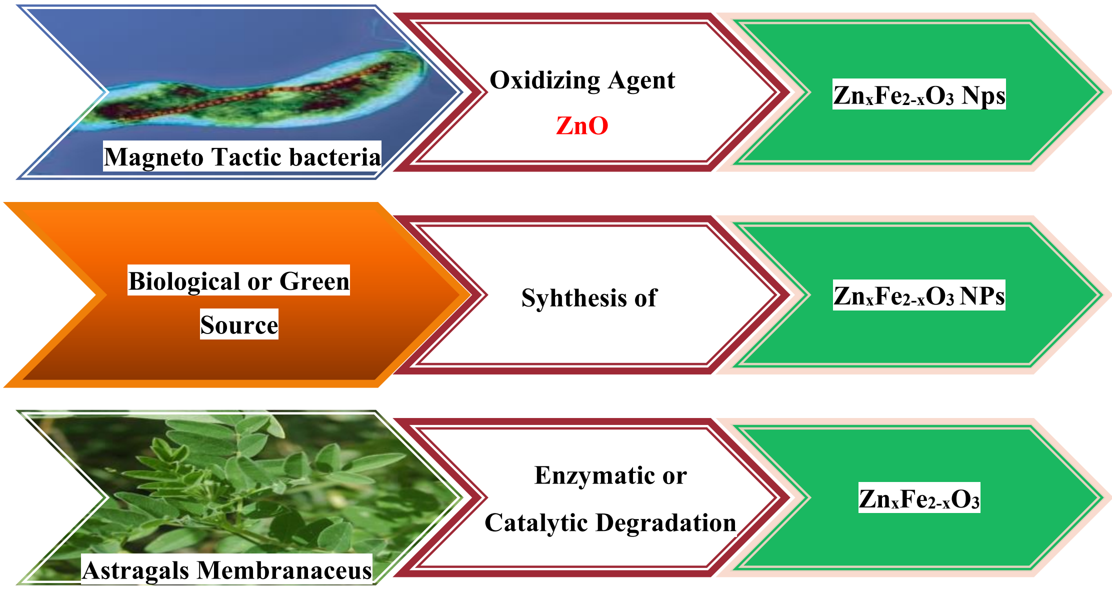

Figure 7. Green (biological) syntheses of $Zn_xFe_{2-x}O_3$ nanoparticles.

What are the challenges? The biological method of synthesizing nanoparticles is at least a two-step process. (1) It involves extractions of metals from biological matter by spectroscopic techniques. (2) Then requires the reactions of extracted transition metals, such as Zn, Mn, Ni, Fe, and Cr, etc., with metal oxides such as Fe_2O_3, ZnO, TiO_2, SnO_2, etc. In general, different methods can be incorporated to synthesize $Zn_xFe_{2-x}O_3$ Nanoparticles. However, most of the synthesis methods have both merits and demerits related to cytotoxicity, raw materials, energy expenditure, time, and cost. For this reason, emphasis is given to the hydrothermal method, Solvothermal method, and the green synthesis method. These methods are also preferred for the future focus areas of study.

In general, the variety of magnetic nanoparticle synthesis methods incorporated have their corresponding merits and demerits. However, further researching, revitalizing, and optimizing raw materials, reviewing the instruments, and monitoring the rheological conditions will improve the functionality.

CHARACTERIZATION TECHNIQUE

Most of the properties of diluted magnetic nanoparticles rely on growth, characterizations, annealing, substrate conditions, and concentrations of dopant. Advanced Nanoscale characterization techniques allow observing the location and distribution of magnetic ions, dopants, defects, and carrier types. As Somayeh Shams (2021) [32] experimentally verified, Zn dope αFe_2O_3 can be characterized by XRD, SEM, FTIR, UV-Visible spectroscopy, and VSM. Scientists, like Prof. Dr. Roland Wiesendanger et al. (2004) [33], realized that new analytical approaches had been developed to investigate Nanoscale properties of materials using scanning tunneling microscopy/spectroscopy and related techniques. M. Sharmila et al. (2022) [34] stated that the morphology of Zn-doped iron oxide can be characterized by Field Emission Scanning Electron Microscope (FESEM and Energy Dispersive Spectroscopy (EDS). The crystal structure of the compound can also be analyzed by X-ray diffraction, Neutron diffraction, Raman spectroscopy, and X-ray photoelectron emission spectroscopy (XPS). These characterization techniques not only demonstrate the crystal structure but also its electrical, magnetic, and optical properties. For example, the X-ray photoelectron emission spectroscopy (XPS) at the Fermi level demonstrates the metallic characteristics of $Zn_xFe_{2-x}O_3$. In this research, EDX, XPS, and HRTEM are discussed.

Energy Dispersive X-Ray (EDX)

The Energy Dispersive X-ray (EDX) is a technique of elemental analysis associated with electron microscopy based on the generation of characteristic X-rays. The finite element analysis methods aided by energy dispersive X-ray analysis can help to detect the nanoparticles embedded in body tissues. X-rays are electromagnetic waves and have finite wavelengths. It is useful in the study of drug delivery, in which the EDX is an important tool to detect nanoparticles. Joan Talibaw et al. (2022) [35] Characterized hydrothermally synthesized Zn and Ni co-doped hematite by Zeiss Crossbeam, which is connected directly with energy-Dispersive X-ray spectroscopy (EDS). The resulting crystal shows uniform homogeneity and absorbs UV light in the visible electromagnetic spectrum. Microanalysis of these nanoparticles using EDX can help in detecting metal contaminants in lung cancer.

X-Ray Photoelectron Emission Spectroscopy (XPS)

X-ray Photoelectron Spectroscopy (XPS) is a modern technique of chemical analysis. It is used to determine compositions, constituents, and chemical structure by irradiating the sample with monochromatic X-rays. These techniques enable emissions of energetic photo electrons with a characteristic frequency. X-ray photoelectron spectroscopy enables measuring the Kinetic energy of emitted electrons, which also helps to determine the temperature. The XPS core level and valence band (VB) photo emission spectra can help to determine the degree of iron oxidation. This is of fundamental importance to better understand the electronic structure of the obtained iron oxide nanoparticles to control and improve their quality for specific biomedical applications. Shuang Yang et al. (2017) [36] synthesized Zn (II)-doped magnetite nano rings of width 13–20 nm.

Based on the above discussion, the morphological evolution of nano rings from Nano plates is achieved by a combined effect of decomposition of the organic component and diffusion growth of the newly formed nano crystals. X-ray photoactive superlattices of $Zn_xFe_{2-x}O_3$ can be prepared on a silicon substrate. The difference in energy between Photon energy and optical band gap near the high absorbance region is given by Tauc and the Davis–Mott model.

$$\alpha h\nu = \beta\left(h\nu - E_g\right)^n \quad (1)$$

where α is the absorbance coefficient, β is a constant, h is the Planck constant, and v is the Photon frequency.

X-ray photoelectron spectra and optical property analysis determine valence bands, which indicate a shift in the Fermi level characteristic of a conversion from n-type in pure α-Fe_2O_3 to p-type with relaxation time less than 10s zinc-doped α-Fe_2O_3 (Figure 8). The data confirmed by X-ray photoelectron spectroscopy (XPS) shows that incorporation of Zn at the Fermi level increases the density of states (DOS). In case of iron doping ZnO, the band gap decreases from 3.24eV to 3.01eV. However, in case of Zn doped iron oxide, the band gap increased from 3.24 to 3.32eV. This is because the Fe has greater atomic radius than zinc on the periodic table.

Focused Ion-Beam Scanning Electron Microscope (FIB-SEM)

Focused Ion-Beam Scanning Electron Microscope (FIB-SEM) is a versatile, non-volatile device for characterizing magnetic nanoparticles (MNPs). It is designed for analyzing 3D structure, spatial distribution, for cross-sectional study, and surface and subsurface texture. As Gu L., et al. (2020) [37] FIB-SEM is used in 3D tomographic analysis bridges the gap between X-ray and transmission electron microscopic tomography technique. It combines site-specific milling with high-resolution imaging to enable detailed analysis, even for complex, heterogeneous, or embedded nanoparticle systems.

As Mura F., et al. (2023) [38], verified, the introduction of new models, such as plasma and cryo-FIB, machine learning, and deep learning systems, has improved the performance of FIB-SEM. It improves not only image resolution and the quality of the data output, but also the automation, efficiency, and real time monitoring.

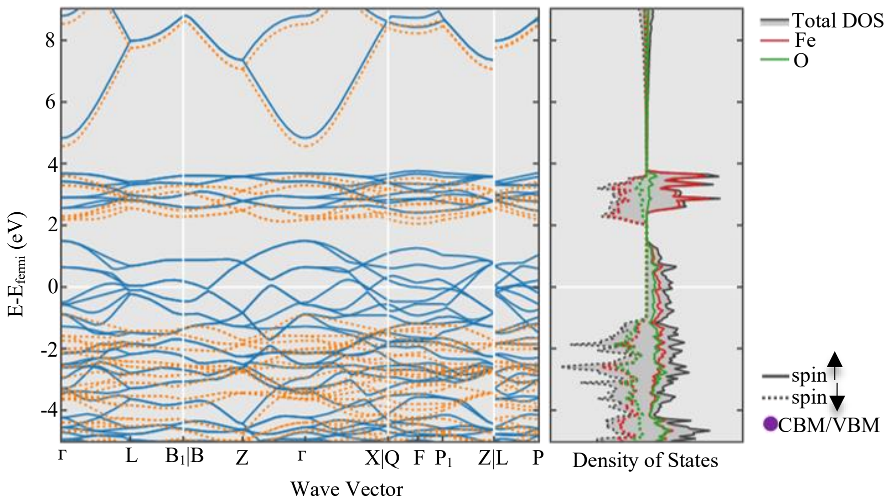

Figure 8. Energy band structure and density of states of αFe_2O_3.

High Resolution Transmission Electron Microscopy (HRTEM)

HRTEM is an imaging mode of specialized transmission electron microscope that allows direct imaging of the atomic structure of samples. It has high resolution in analyzing and characterizing metal nanoparticles, magnetic oxides nanoparticles, semiconductor nanoparticles, nanotube, and sp^2 hybridization. The interference of the electron wave in the image plane produces high contrast. It is also used as Phase contrast transmission electron microscopy.

The working principle of a high-resolution transmission microscope depends on the biocompatibility of the molecules or nanoparticles. It can perform the characterization process of more than three different accelerating voltages. Thus, it can produce good image viability and contrast. This technique is used to characterize the electrical and optical properties of the sample. It is also used to determine the lattice parameters of nanocrystals.

As Manish Kumar et al. (2019) [39] using a high-resolution transmission electron microscope observed, the average crystallite size of Zn doped iron oxide nanostructures is 20 nm. S. Ghosh and R N. Basu, (2019) [40] verified, HRTEM can also be used for characterization of core-shell metal oxide-coated noble metal particles, genetically coded multimeric nanoparticles, and asymmetric nanoparticles for the applications in photo catalysis, photo thermal therapy, molecular sensing, and Photo voltaic. In general characterizing Zn doped Fe_2O_3 nanoparticles with XRD, EDX, SEM, FTIR, and HRTEM will help to attain high crystal quality, homogeneity, reduced grain size, and high phase purity.

MAGNETIC NANOPARTICLE SYNTHESIS AND CHARACTERIZATION CHALLENGES

The scientific methods for synthesizing magnetic nanoparticles are widely studied and rated as the best alternatives. However, there are a variety of challenges associated with them. Some of the limitations of these techniques are briefly summarized in Table 1, below.

Although synthesizing magnetic nanoparticles (magnetosomes) from biological organisms, including magnetotactic bacteria (MTB) and green plant extract, is preferred due to its cost-effectiveness and ecofrindly in nature, there are some challenges associated with yield, scaling, and synthesis route. Particularly, synthesizing magnetic nanoparticles from magnetotactic bacteria encounters challenges, including scaling up cultivation, low yield, and complex purification processes. Because magnetotactic bacteria exhibit magnetic behavior, enumeration of magnetic interactions with magnetic nanoparticles requires an additional task. This interaction also caused nanoparticle aggregation and agglomeration. Consequently, magnetic nanoparticles synthesized in this procedure lack uniformity, size, shape, and even stability.

On the other hand, synthesizing magnetic nanoparticles by the Co-precipitation method encounters the same challenges. However, nanoparticles synthesized in Co-precipitation methods lack magnetic behavior/exhibit low coercivity and saturation magnetization, which are critically important in therapeutics, including hyperthermia and medical imaging. Moreover, synthesizing magnetic with pulsed laser deposition/and the Polyol method are challenging tasks. This is due to the high-power consumption (electric and heat), which can destroy samples due to thermal instability. Table 2 shows a summary of some of the widely studied and used synthesis methods and their underlying challenges to the synthesis roots.

Table 1. Shows a summary of some of the widely studied and used synthesis methods and their underlying challenges to the synthesis roots.

S.N.	Method	Challenges	Reference
1	Biological Methods	Low yield, scaling difficulty, and complex purification procedures.	Jacob JJ, et al. (2016) [41]
2	Co-precipitation Method	Difficulty in controlling particle size and shape, particle aggregation, and low magnetic behavior.	Ali A, et al. (2016) [42]; Dudchenko N, et al. (2022) [43]
3	Hydrothermal Methods	High energy consumption, requirement of high pressure and temperature, difficulty in real-time monitoring and analysis, and scalability issues.	Vinukonda A, et al. (2025) [44]
4	Gravity Methods	Complexity in operating rotating machinery, need for precise process control, and challenges in nanoparticle management.	Ren G, et al. (2022) [45]
5	Solvothermal Methods	High cost, limited scalability, complex and lengthy procedures, and use of hazardous organic solvents.	Mahajan R, et al. (2021) [46]
6	Sol-Gel Method	Difficulty in controlling phase purity, particle agglomeration, requirement of high calcination temperatures, lengthy processing time, high cost, and lack of real-time monitoring and analysis.	Nassar KI, et al. (2025) [47]
7	Solid-State Reaction Method	Large particle size, poor homogeneity, requirement of high temperatures and prolonged reaction times, low surface area-to-volume ratio, and surface contamination.	Basha SA, et al. (2024) [48]
8	Polyol Method	Requirement of elevated temperatures leading to thermal instability and the use of flammable reagents.	Dudchenko N, et al. (2022) [43]
9	Pulsed Laser Deposition Method	Requirement of high-power laser ablation, low yield, scalability challenges, complex optimization processes, and high cost.	Kumar D, et al. (2004) [49]; Samani HN, Razavi RS. (2024) [50]

Table 2. Characterization methods and their associated challenges in nanoparticle analysis.

No	Characterization methods	Challenges	Reference
1	XRD	broadening of diffraction peak, present indistinguishable phases (e.g., Magnetite vs. Maghemite), cannot analyze particles with size less than 5 nm, etc. cannot analyze amorphous nanoparticles.	Holder C. F., and Schaak, R. E. (2019) [51]
2	EDX	Low signal generation and detection limit, long acquisition time, inefficient to characterize coatings, difficult to identify nanoparticle composition.	Scimeca M. et al. (2018) [52]
3	XPS	Accumulation of surface charges, complex data analysis process, cannot analyze nanoparticles with large core shell structure.	Tayefeh A. et al. (2019) [53]
4	FIB-SEM	Magnetic interaction with the beam, and preparation complexities, low space to analyze data, amorphization and damage	Gu L. (2020) [37] & Miller D. (2020) [54]
5	HR-TEM	Produce image distortion or astigmatic images, high voltages can destroy coatings or surfactants, Sample preparation requires drying artifacts, and motion (rotation) of magnetic moments.	Ali A. et al. (2021) [55] & Bian L. (2021) [56]

As depicted in the table and the former discussion, characterizing magnetic nanoparticles is not a simple task, but rather requires rigorous procedures. The characterization techniques have different responses to the particle size, shape, type (target), and rheological conditions. As the table reveals, FIB-SEM has better efficiency and performance compared to others. Particularly, FIB-SEM integrated with AI, including machine learning and deep learning, provides better performance. However, most FIB-SEM are based on Ga, which provides minimal space for data analysis as compared with the size. As Berger C. et al. (2025) [57] explained, very thin lamellae mostly < 50 nm, the high voltage can damage a significant portion of the material amorphously, reducing TEM image quality and resolution. Therefore, an in-depth understanding and further exploration of its new features is of prime importance.

On the contrary, HR-TEM produces the least image resolution, which makes it difficult to enumerate the features of magnetic nanoparticles completely. Moreover, EDX generates low signals, which limit data quality. Moreover, XPS is subjected to surface charge accumulation, which must be compensated for, reviewed during sample preparation, and the use of dual beam charge neutralization. Therefore, researchers working with magnetic nanoparticles are recommended to check their results with a specialized device such as “Apreo-chemi-SEM” or “AI-integrated FIB-SEM”.

CONCLUSION

In this research, the scientific method for synthesizing and characterizing magnetic nanoparticles is reviewed. Among these methods, the best candidates for synthesizing magnetic nanoparticles, such as Zn-doped Fe_2O_3 semiconductor magnetic nanoparticles, are the sol-gel method, solid state reaction methods, co-precipitation methods, hydrothermal methods, high gravity method, solvothermal methods, and biological (green) synthesis methods. These techniques are preferred depending on their potential to yield high-quality nanoparticles, functionality in medicine, environmental safety, and cost-effectiveness. Among the characterization methods, XXRD, EDX, FIB-SEM, and HR-SEM are studied. These instruments have been used by many scholars and researchers for characterizing not only magnetic nanoparticles but also dichalcogenides, metal oxides, quantum dots, and nanorods. In general, the preferred synthesis and characterization methods need careful adjustments to maintain stability & biocompatibility, control sensitivity, size, and shape. Moreover, adjustment is important for scaling the product, maximizing the yields, and improving quality. Particularly, in the case of FIB-SEM, high voltages can damage the lamella. Moreover, in the case of HR-TEM, moisture can damage it. Hence, the sample must be dried before characterization. Thus, in all cases, optimizing temperature, pressures, Power, sample concentrations, and review of setups and adjustments are advised. Moreover, monitoring and detecting the synthesis routes and integrating the characterization tools with AI devices can greatly reduce the burden.

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Conflict of Interest

The author declares that there is no conflict of interest due to funding opportunities, employment and personal interest.

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