Journal of Basic and Applied Engineering Research
p-ISSN: 2350-0077; e-ISSN: 2350-0255; Volume 3, Issue 8; April-June, 2016, pp. 681-685
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http://www.krishisanskriti.org/Publication.html

Review: Synthesis and Applications of Magnetic Nanoparticles

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Abstract—*The research on superparamagnetic iron oxide nanoparticles has increased over the last years. Due to finite size effects, such as the high surface-to-volume ratio and different crystal structures, magnetic nanoparticles exhibit interesting and considerably different magnetic properties. Magnetic nanoparticles (NPs) have many unique magnetic properties such as superparamagnetic, high coercivity, low Curie temperature, high magnetic susceptibility, etc.*

In the last decade, increased investigations with several types of iron oxides have been carried out in the field of magnetic NPs (mostly includes the Fe_3O_4 magnetite, when the size is less than 15 nm), $\gamma -Fe_2O_3$, FeO, among which magnetite and maghemite are the most promising and popular candidates since its biocompatibility have already proven.

This review focuses on the unique properties of magnetic NPs which make them desirable materials for various biological and industrial applications. The paper covers various important features related to the magnetic nature of Iron Oxides, their structure and characterization. Finally, this paper addresses the applications of magnetic NPs. In this work, we will also summarize the routes for the synthesis of iron oxide NPs and the surface modification of these superparamagnetic NPs.

1. INTRODUCTION

The term NPs is used to describe materials that fall in the dimension of approximately 1 to 100 nanometers (nm). Nanotechnology allows scientists and engineers to prepare nano size systems where the classic laws of physics are different at that small scale. As the size of the NPs decreases, the surface-to-volume ratio (and consequently the fraction of the surface atoms with respect to the bulk ones) increases. The large surface-to-volume ratio of the NPs is the key factor to the novel physical, chemical, and mechanical properties compared to those of the corresponding bulk material [1]. NPs exhibit optical, electric and magnetic properties. As mechanical properties NPs show great strength and hardness.

Magnetic particles respond to an applied magnetic field. In the presence of an external magnetic field the atomic current loops created by the orbital motion of electrons oppose the applied field. All materials display this type of weak repulsion to a magnetic field known as diamagnetism. However, diamagnetism is very weak and therefore any other form of magnetic behavior that a material may possess usually overpowers the effects of the current loops. Magnetic NPs have many unique magnetic properties such as superparamagnetic, low Curie temperature, high coercivity and magnetic susceptibility, etc. They are divided into five main types namely; ferromagnetic, paramagnetic, diamagnetic, antiferromagnetic, and ferrimagnetic [2].

In the last decade, increased investigations with several types of iron oxides have been carried out in the field of magnetic NPs (mostly includes the Fe_3O_4 magnetite, Fe_2O_3 (hematite,weakly ferromagnetic or antiferro- magnetic or maghemite which is ferrimagnetic), FeO (wu stite, antiferromagnetic), among which magnetite and maghemite is the very promising and popular candidates since its biocompatibility have already proven [3].

1.1 Iron oxide nanoparticles

Iron oxides are chemical compounds composed of iron and oxygen. Ferrites were discovered thousands of years ago. The first compass was made of magnetite (Fe_3O_4). Magnetic properties are interesting from the fundamental and technological points of view.

1.2 Structure of Fe_3O_4

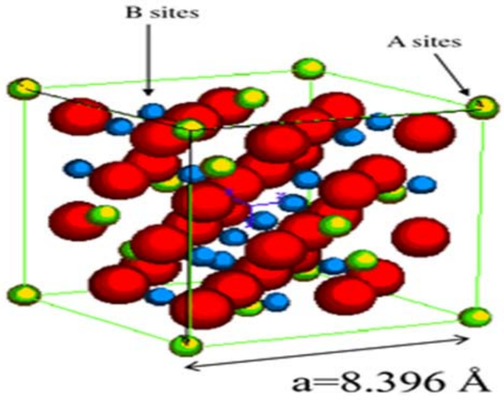

Fig. 1: Crystal Structure of Iron oxide

In magnetite and maghemite, the oxygen ions are in a cubic close-packed arrangement. Magnetite has an inverse spinel structure with Fe(III) ions distributed randomly between octahedral and tetrahedral sites, and Fe(II) ions in octahedral sites.

Maghemite has a spinel structure that is similar to that of magnetite but with vacancies in the cation sublattice. Two-thirds of the sites are filled with Fe(III) ions arranged regularly, with two filled sites being followed by one vacant site [4]. Fe_3O_4 is ferromagnetic in nature.

1.3 Properties

The functional activities of iron oxide NPs are influenced largely by their size. Fe_3O_4 NPs are reported to possess the following unique features:

i. Large surface to volume ratio
ii. High surface reaction activity
iii. High catalytic efficiency
iv. Strong adsorption ability
v. Biocompatibility
vi. Strong super paramagnetic behavior
vii. Low toxicity

However, magnetite (Fe_3O_4) is not very stable and is sensitive to oxidation. Magnetite is transformed into maghemite (γFe_2O_3) in the presence of oxygen as in Equation 1

$Fe_3O_4 + 2H^+ \rightarrow \gamma Fe_2O_3 + Fe^{2+} + H_2O$ (1)

2. SYNTHESIS OF MAGNETIC NANOPARTICLES

The synthesis of superparamagnetic NPs is a complex process because of their colloidal nature. The most common methods to prepare iron oxide NPs are

1. Co-precipitation [5].
2. Green synthesis
3. Microemulsion [6]
4. Hydrothermal [7,8]
5. Sol-Gel Reaction [9]
6. Electrochemical Method [10]
7. Thermal Decomposition

2.1 Co-Precipitation

The co-precipitation method is a conventional synthetic paradigm where Fe(II) and Fe(III) salts are co-precipitated in a basic solution in the presence of coating materials such as polymer or dextran (or its derivatives).The first controlled preparation of superparamagnetic iron oxide particles using alkaline precipitation of $FeCl_3$ and $FeCl_2$ was performed [11]. In the original synthesis, magnetite (Fe_3O_4) particles were roughly spherical, and their diameter measured by XRD was 8 nm [12]. The precipitates of MNPs were produced according to the reaction as given in Equation 2

$$2\ FeCl_3 + FeCl_3 + 8\ NaOH \rightarrow Fe_3O_4 + 8NaCl + 4H_2O \qquad (2)$$

According to the thermodynamics of this reaction, complete precipitation of Fe_3O_4 should be expected at a pH between 8 and 14, with a stoichiometric ratio of 2:1 (Fe^{3+}/Fe^{2+}) in a non-oxidizing oxygen environment [13]. The main advantage of the coprecipitation process is that a large amount of NPs can be synthesized.

2.2 Green Synthesis

A facile, rapid and green method is also practiced to prepare magnetite (Fe_3O_4) NPs in one step reaction. In this method, an aqueous solution of ferric chloride hexahydrate, ferrous chloride tetra hydrate (2/1 molar ratio) was mixed with carob leaf extract and heated for 5 minutes at 80℃ [14].

2.3 Micro emulsion

Microemulsion is a thermodynamically stable isotropic dispersion of two immiscible phases (water and oil) under the surfactant present. As in the binary systems (water/surfactant or oil/surfactant), self-assembled structures of different types can be formed, ranging, for example, from (inverted) spherical and cylindrical micelles to lamellar phases and bicontinuous microemulsions, which may coexist with predominantly oil or aqueous phases [15].

Particularly, water-in-oil (w/o) microemulsions are formed by well-defined nanodroplets of the aqueous phase, dispersed by the assembly of surfactant molecules in a continuous oil phase.The water-in-oil emulsions lead to the formation of SPIONs with water solubility.

Scientists have proposed a new method [16] to prepare in situ magnetic chitosan/Fe_3O_4 NPs composite in microreactors of tiny water pools of water-in-oil emulsion. When the basic solution of NaOH was added into the emulsion containing chitosan and ferrous salt, the magnetic Fe_3O_4 and chitosan NPs were precipitated from the system.

2.4 Hydrothermal Technique

This technique has also been used to grow dislocation-free single crystal particles and grains. Several authors have reported the synthesis of iron oxide NPs by hydrothermal method [17].The syntheses of Fe_3O_4 NPs by hydrothermal technique is performed in aqueous media in reactors or autoclaves where the pressure can be higher than 2000 psi and the temperature can be above 200°C. During the reaction method, the NH_4OH performs in major rules, like control the pH value of the solution as well as resource to supply hydroxyl ions to the solution. The $FeCl_3$ reacts with NH_4OH and forms FeO(OH), which, upon heating, further produce into Fe^{2+} and OH^- ions, which consequently assists in the development of Fe_2O_3 ions according to the following chemical reactions:

$NH_4OH\ (aq) \rightarrow NH4\ (aq) + OH^-\ (aq)$

$FeCl_3\ (s) \rightarrow Fe^{2+}\ (aq) + 3Cl^-\ (aq)$

$Fe^{2+}\ (aq) + 2OH^-\ (aq) \rightarrow FeO(OH)\ (aq) + H^+$

The FeO(OH) finally, however dissociates to the formation of Fe_2O nuclei according to the reactions

$FeCl_3$ (aq) + $2NH_4OH$ (aq) → FeO OH (aq) + $2NH_4$ +(aq) $+H^+$ (aq) + $3Cl^-$ (aq)

FeO OH (aq) → Fe_2O_3 (s) + H_2O (l)

The initially formed Fe_2O_3 nuclei perform as building blocks for the development of final products.

2.5 Sol-Gel Reaction

The sol-gel process is a suitable wet route to the synthesis of nanostructured metal oxides [18].

This process is based on the hydroxylation and condensation of molecular precursors in solution, originating a “sol” of nanometric particles. Further condensation and inorganic polymerization lead to a three-dimensional metal oxide network denominated wet gel. Because these reactions are performed at room temperature, further heat treatments are needed to acquire a crystalline state [19].

2.6 Electrochemical Methods

On the basis of an electrochemical method developed and published in a literature [20] Scientists [21] have prepared 3-8 nm maghemite particles from an iron electrode in an aqueous solution of DMF and cationic surfactants. Adjustment of the current density controls the particle size. Electrochemical deposition under oxidizing conditions has been used to prepare NPs of Fe_2O_3 and Fe_3O_4 [22].

2.7 Thermal Decomposition

Thermal decomposition of organometallic precursors where metal is the zerovalent in their composition (such as $Fe(CO)_5$) initially leads to a formation of metal NPs but if followed by oxidation can lead to a high in quality monodispersed metal oxides.

Reports have been publishes [23] where a general decomposition approach for the synthesis of size-controlled monodispersed magnetite NPs based on high temperature (265^o C) reaction of $Fe(acac)_3$ in phenyl ether in the presence of alcohol, oleic acid, and oleylamine.

The five above mentioned synthetic methods have several advantages and disadvantages for preparing iron oxide NPs, respectively.

In terms of size and morphology control of the iron oxide NPs, thermal decomposition and hydro- thermal synthetic route seems the optimal method. For obtaining the water-soluble and biocompatible iron oxide NPs, co-precipitation often was employed, but this method presents low control of the particle shape, broad distributions of sizes and aggregation of particles. As a time- competitive alternative, sonochemical route can also be used to synthesis iron oxide NPs with unusually magnetic properties. Also inlet of nitrogen into the reaction system that protects against critical oxidation of the magnetite also reduces the particle size when compared to methods without oxygen removal [24].

3. APPLICATIONS OF FE_3O_4

Iron oxide NPs have numerous applications in medicines due to their magnetic, physical, chemical and effective biological properties. The recent development of functionalized NPs is expected to bring a break-through to the possibilities in several biomedical application, e.g. targeted drug delivery, tissue engineering, MRI techniques as well as monitoring mental or neurodegenerative diseases.

Superparamagnetic iron oxide NPs with appropriate surface chemistry can be used for numerous in vivo applications, such as MRI contrast enhancement, tissue repair, immunoassay, detoxification of biological fluids, hyperthermia, drug delivery, and cell separation [25].

3.1 Antimicrobial Activity

The antimicrobial activity of iron oxide NPs has largely been studied against different organisms [26] and has been shown to depend on three factors: size, stability, and concentration in the growth medium. The size of microbial cells is in the micrometer range while outer cellular membranes have pores in the nanometer range. Due to the smaller size of NPs compared to bacterial pores, they have the unique ability of crossing cell membranes.

3.2 Adsorption Agents

Due to the extremely small particle size, high surface-area-to-volume ratio, and more important the magnetism, Fe_3O_4 NPs have been widely used and have shown promising performance in environments treatment, including pollutant removal and toxicity mitigation [27].

Magnetic Fe $_3O_4$ NPs are good candidates for connecting chelating materials to their surfaces because of their inertness to surrounding environment, ease of surface modification with specific functional groups, and high surface area-to-volume ratio leading to enhancement of adsorption capacity [28].

3.3 Bioseparation

Another important kind of application of iron oxide NPs is the functionalization for in Vitro protein or cell separation. Magnetic separation is a commonly used technique for polypeptide/protein separation and cell separation.

Scientists have developed magnetic NPs coated with charged bipyridinium carboxylic acids and biotin. Such functionalized particles have been used for affinity isolation of fluorescein-labeled protein avidin [29].

3.4 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is a commonly used non-invasive medical imaging technique in clinical medicine to visualize the structure and function of tissues, which is based on the behavior, alignment and interaction of protons in the presence of an applied magnetic field.

NPs are used as Contrast Agents for MRI because of their very high transverse relaxivity [30]. Colloidal suspensions of superparamagnetic nanocrystals are very good candidates for the development of new smart contrast agents, allowing for an early detection of several pathologies.

3.5 Drug Delivery

Among various drug delivery systems, the magnetic targeted-drug delivery system [31] is considered the most popular and efficient. Compare to the conventional, non-targeted methods of drug delivery, magnetic Nps are promising drug carriers due to the better specificity to the target site and the reduced adverse effects. In this technique, the drug carrying magnetic materials like Fe_3O_4 will be led to the cancer areas by outside magnetic field after taken orally or injected through vein.

3.6 Hyperthermia

Magnetic induction hyperthermia means the exposition of cancer tissues to an alternating magnetic field, in which heat is generated due to magnetic hysteresis loss. Cancer cells exposed to magnetic particles will heat up to a temperature higher than 43 °C, at which the cancer cells are destroyed whereas the normal cells can survive. Scientists have shown that a strong magnetic field gradient at the tumor location induces accumulation of the NPs [32]. It has also been reported theat development of a biostable methotrexate-immobilized iron oxide nanoparticle drug carrier that may potentially be used for real-time monitoring of drug delivery through magnetic resonance imaging [33].

3.7 Protein Immobilization

Protein immobilization serves as a very effective tool to solve the difficulties encountered in the catalytic application of free enzymes, such as poor stability and hard recovery. Proteins could be immobilized onto Fe_3O_4 NPs in the manner of physical absorption, covalent bonding, and bioconjugation. Coupling reagents, such as glutaraldehyde, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) and sodium tripolyphosphate (TPP) [34], are often utilized to achieve much more stable immobilization.

4. CONCLUSION

Due to their unique properties Fe_3O_4 nanoparticles have emerged as ideal materials for generating functional materials, which have already displayed promising effects in practical applications in protein immobilization, bioseparation, biomedical science, environmental treatment, and food analysis. Substantial progress has been made in the synthesis of magnetic NPs for application in nanotechnology and biotechnology. Different kinds of monodisperse nanocrystals have been synthesized by a wide range of chemical synthetic procedures namely coprecipitation, thermal decomposition, sol-gel reactions, green synthesis, electrochemical and hydrothermal methods. Among the methods reviews, hydrothermal synthesis probably offers the most promising results with respect to size and stability of magnetic NPs.

5. ACKNOWLEDGMENT

The authors gratefully acknowledge the financial support provided by the DRDO, New Delhi, India and also express their sincere regards to Dr Jaswinder Singh, Principal of our college for providing the necessary infra structure and moral support.

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