RESEARCH ARTICLE

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Magnetic Nanoparticles Synthesis, Surface Coating, and Biomedical Applications: A Review

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Abstract: In recent years, the development of magnetic nanoparticles (MNPs) has attracted the attention of users worldwide due to their potential for use in many fields, including biomedical applications. The unique properties of MNPs, such as superparamagnetism, high saturation magnetization, and biocompatibility, make them ideal for many biomedical applications, including cancer therapy, magnetic resonance imaging (MRI), and drug delivery. Synthetic methods include ball milling, gas phase condensation (GPC), sol-gel, and thermal decomposition. Surface coating of MNPs is important to improve their biocompatibility, stability, and targeting ability. Various coating materials are discussed, including organic polymers, inorganic silica, and gold. Using MNPs as a contrast agent in MRI improves image quality and allows imaging of small tumors. MNPs also show promise in cancer treatment, including chemotherapy and hyperthermia. Biocompatibility and toxicity of MNPs are important factors to consider in their biomedical applications. Surface coating of MNPs plays an important role in reducing their toxicity and increasing their biocompatibility. The use of biocompatible materials such as polyethylene glycol (PEG) increases the safety of MNPs in biomedical applications. Future research should focus on overcoming challenges associated with mass synthesis, coating, and biomedical applications of MNPs.

Keywords: Magnetic nanoparticles (MNPs), Synthesis, Surface Coating, Biomedical Applications, Cancer Treatment, Magnetic Resonance Imaging (MRI), Drug Delivery, Biocompatibility, Toxicity

1. Introduction

It is not necessary to have a vacuum system in order to generate cold plasma at atmospheric pressure, which is one of the reasons why working in an open environment is advantageous for this process. The domains of energy, environment, material preparation and

modification, biomedicine, and the development of the generation technology on atmospheric pressure plasma, in which the gas temperature is only non-thermal and safely and friendly contact with the human body, have all shown a great deal of interest in this topic. Because plasma medicine is an interdisciplinary field of study, it is primarily attracting an increasing amount of interest, particularly in the context of its applications in the treatment of cancer, skin diseases, and wound rehabilitation. The primary purpose of plasma medicine is to investigate the effects of microbial inactivation, blood coagulation, and chronic wound repair through the utilization of plasma techniques. Due to the unique properties that nanomaterials possess in comparison to bulk materials, they have garnered a great deal of attention over the course of the past several years. The production of various types of magnetic nanoparticles (MNPs) has continued to garner increasing attention, and numerous publications have been written about the very stable and shape-controlled nanoparticles that have limited size distributions. Nanoparticles have a wide variety of distinctive characteristics. The standard chemical methods for the synthesis of nanomaterials require the use of oxidants that are less harmful, and this is a logical justification for the conventional methods and reductants, which are necessary for the production of nanoparticles and their stability. The alternative method of synthesis that does not include the use of harmful chemicals is an important development in nanotechnology for the field of biomedical applications. Currently, plasma technology is garnering more and more attention as the most abundant green synthesis for the methods of magnetic nanoparticle formation and the nanomaterials in the biomedical applications.

Additionally, there are various synergistic effects that contribute to the higher treatment efficiency for medicine. Nanoparticles were developed with the intention of being utilized through the cold atmospheric pressure plasma approach in order to achieve the highest possible level of effectiveness in the treatment of biological applications. In the field of biomedical research, the magnetic materials family is a vast and captivating subject due to the enticing super paramagnetic properties that it possesses. Magnetic resonance imaging, medication delivery, and biomedicine are some of the fundamental qualities that MNPs possess. Given their high chemical stability, colloidal stability, and biocompatibility, the MNPs are being investigated for the applications of magnetic resonance imaging (MRI) contrast, magnetic hyperthermia, and targeted drug delivery structures.

The MNPs are some of the reasons why iron oxide (Fe_2O_3, α-Fe_2O_3) is the most popular material. Every single one of the biological applications that were addressed in the articles still contains some changelings. This review will focus on the reduction of the toxicity that is displayed by MNPs. The precise responsiveness and reproducible targeting control of magnetic nanostructures accomplished through the utilization of an external magnetic field, in conjunction with the optimization of the synthesis. Because the biological samples have a background that is almost magnetic, it is possible to do high-sensitivity measurements on biofluid samples that have been slightly treated and that have biological uses that are based on MNPs. Both the solubility

and the chemical stability of the magnetic nanoparticle ought to be subject to careful regulation in a variety of biological settings.

In order to prevent the MNPs from precipitating, the chemical stability and biocompatibility feature are indispensable. Magnetic nanoparticles that have a surface that has been correctly functionalized have the potential to be chemically and physically stable, biocompatible, and safe for the environment. In order to facilitate the practice of nanomedicine, the surface coatings of the MNPs are necessary. The behaviours of magnetic nanoparticles exhibit characteristics similar to those of the many forms of magnetism. The magnetism can be broken down into four distinct categories. There are four types of properties of nanoparticles that are being discussed: ferromagnetism, ferrimagnetism, para magnetism, and superparamagnetic qualities. In the field of biomedical applications, the magnetic susceptibility, relaxivity, and dipolar interactions amongst MNPs are extremely important. With the materials, the MNPs are covered with both single and multicore structures. Either organic or inorganic material comprises the single core that has been coated with the substance. In the MNPs, there are two different sorts of approaches. Approaches from the top down and from the bottom up are the two types. Following the Top-Down methodology, the bulk materials are created by the use of the lithography process and ball milling. The Bottom-Up method involves the synthesis of magnetic nanoparticles by the process of gas-phase condensation. In order to manage the magnetic nanoparticle stability and biocompatibility of the materials, the functionalization of the bulk materials that were evaluated should be controlled in a variety of biological settings. As a result of the ease of synthesis and the simple surface chemicals that are comparable in size to biological ligands, there has been an increase in the amount of attention paid to the application of MNPs in clinical diagnostics and rehabilitation.

In the field of magnetite bioassays, the MNPs have been effectively employed for the Giant Magneto Resistive (GMR) biosensors, Magnetic Tunnel Junction (MJT) based biosensors, Magnetic Relaxation Switching (MRSw), and Magnetic Particle Spectroscopy (MPS). Magnification of Magnetic Resonance Imaging (MRI) and Magnetic Particle Imaging (MPI) is achieved by the utilization of contrast. For the purpose of delivering drugs by magnetic hyperthermia, magnetic nanoparticles (MNPs) have been used in a wide variety of applications in the field of magnetic therapy. A significant amount of effort is being put into the development of the synthesis of superparamagnetic iron oxide and other magnetic nanoparticles in order to satisfy the fundamental scientific interest in their use and other technologies. These magnetic nanoparticles are utilized in a variety of biological applications, including biosensing, contrast agents, magnetic resonance imaging (MRI), and wound healing. The targeted drug delivery of the MNPs into controlled monodispersed size of the nanocrystals is one of the significant aspects of the nanocrystals. All of the superparamagnetic iron oxide nanoparticles that have been appropriately coated on their surfaces with polymer stabilizers are utilized in a variety of biomedical applications, including magnetic resonance imaging, contrast agents, targeted medication delivery, tissue engineering, cell separation, and others.

Due to the fact that nanomaterials can be manufactured with exceptional magnetic, electric, optical, mechanical, and catalytic capabilities that are significantly different from their bulk counterparts, it is necessary for all magnetic nanoparticles to have high magnetization values while also being smaller in size than 100 nanometres. In order to get the desired qualities of the nanomaterial, it is possible to precisely manage the size and form of the nanoparticles. The high potential that is used in the cold plasma process is responsible for the formation of nanoparticles, which are subsequently connected to the argon that serves as the carrier gas throughout the system. Within the framework of the plasma process, the creation of nanoparticles also involved the utilization of nitrogen gas and oxygen gas. The combination of nanoparticles is employed to create the microwave plasma, which is made up of the U-shaped glass. In addition to being washed five times, the particles that had been created were also subjected to an analysis of their surface topology, morphology, biocompatibility, and antibacterial activity.

2. Synthesis Methods of the Magnetic Nanoparticles

Bottom-up and top-down approaches are prepared by the synthesis procedures of MNPs. Bottom-up approaches are more common than top-down approaches. Ball milling, lithography, and bulk materials are examples of top-down approaches. The shattered micrometer and nanometer size is the result of these approaches. Atoms are the starting point for the bottom-up strategy, which is followed by the nucleation and growth process. The preparation of MNPs in GPC and wet chemical approach can be accomplished through a variety of different methods. As a supply of iron, a stock solution of 1.28M ferric chloride hexa hydrate ($FeCl_3 \cdot 6H_2O$), 0.6M ferrous chloride tetra hydrate ($FeCl2 \cdot 4H_2O$.), and 0.4M HCL was created by dissolving the corresponding compounds in milli-pore water while vigorously swirling the mixture. For the purpose of surface neutralization, a solution of 0.9-1.5M sodium hydroxide and 0.01M hydrochloric acid was made, and for coating, a solution of 1.5M sodium oleate (surfactant) with a pH of 9.4 was created. There was an addition of deoxygenated milli-Q water to wash the plasma-treated powder sample as well as the solution after the centrifuge had been decanted at 3500 revolutions per minute. In the bottom of the centrifuge tube, the samples were allowed to settle. The powder was washed five times, and then it was dried after the particles were gathered together [1].

2.1 Ball Milling Method

The procedure of ball milling, which was created by John Benjamin in 1970, is utilized for the preparation of powders that have a minimized size. The operating mechanism of the ball milling approach, which was proposed by fetch *et al.* [5, 6], is that there are three stages involved in the process of generating magnetic nanoparticles using the ball milling method. The first stage of the process involves the introduction of deformation and dislocations into bulk materials as a

result of the impact between the balls and the bulk materials involved. Because of the dislocation density, the ball milling time is maintained.

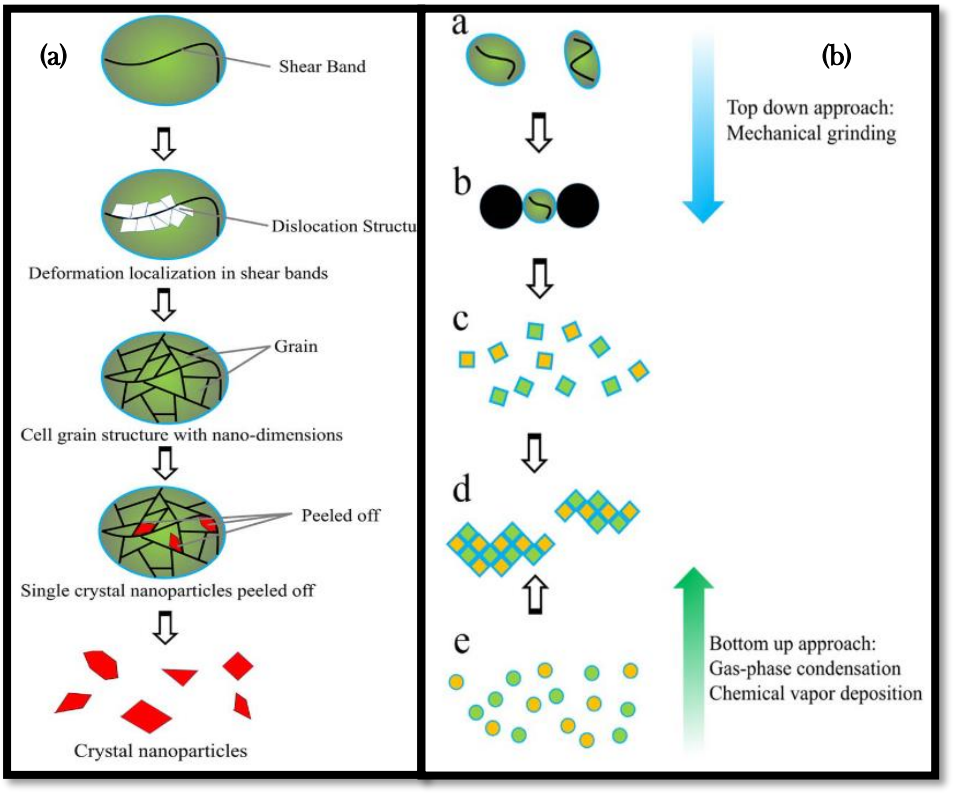

Figure 1. a) Schematic representation of ball milling mechanism for the formation of crystalline MNPs. b) schematic drawing of typical Top Down and Bottom-Up approach for MNPs ((a) Bulkmaterial. (b) Grinding ball. (c) Nanoparticles. (d) Clusters. (e) Atomic level.)

There is either buildup or rearrangement in the second stage. The third stage will involve the randomization of the grain size of the substance. Dry milling and wet milling are two distinct approaches to ball milling that were developed in order to manufacture magnetic nanoparticles by ball milling. During the ball milling process, there are no solutions or surfactants added, and the dry milling method does not involve any of these additions. The sole components of the ball milling jars are the raw ingredients and the ball. Through the use of this technique, the size of the MNPs is increased, and the resulting effect is referred to as the cold welding effect. Additionally, Jian-Ping Wang et al. pointed out the below image shows the MNPs synthesis of bottom up and Top Down approach in the [4-7].

2.2 GPC Method

Atoms are nucleated and grown during the GPC process, which is a bottom-up approach. This results in the formation of MNPs.

When contrasted with the ball milling method, this technique allows for greater control over the crystallinity and size of the particles contained inside the material. Nine to nine. Additionally, Yama-muro *et al.* pointed out that the most important component in obtaining monodispersed MNPs is the nucleation and growth process of nanoparticles that are separated into various space regions. According to Wang et al.'s findings from 2006, the field-controlled plasma heating effect has the potential to assist in controlling the phase and crystallinity of MNP formulations. In addition, this approach is capable of producing tetragonal, body-centered, and Meta stable phase Fe nanoparticles with great success [11-14]. The GPC system makes use of a sputtering source; however, the process that is responsible for the production of nanoparticles is completely distinct from the method that is used to prepare thin films via sputtering. By using this technique, atoms are generated atomic vapour close to the surface of the target after being kicked from a target. For the formation of magnetic nanoparticles, rather than thin films, a high sputtering pressure is utilized. This results in a reduced mean free path for the atoms' movement. In order to determine the size of the nanoparticles, the sputtering current, the magnetic field intensity at the surface that is being targeted, the sputtering pressure, and the gas flow rate are all taken into consideration. It has been demonstrated that the various magnetron sputtering sources of many nanoparticles may be successfully synthesized as high magnetic moment MNPs [15-17].

2.3 Sol-Gel Method

There is just one type of wet chemical process that is extensively utilized to generate thin films and nanoparticles, and that is the sol-gel method [18-20]. A number of benefits are associated with this approach, including a high degree of stoichiometric control, a restricted size distribution, and a low processing temperature. The sol-gel method may be broken down into two distinct approaches: the first is the aqueous sol-gel approach, in which water is used as the reaction medium, and the second is the non-aqueous sol-gel approach, in which an organic solvent is employed when the reaction medium. It was reported by Niederberger *et al.* [20] that the aqueous sol-gel method is better appropriate for the preparation of bulk oxides as opposed to nanoparticles. Within the context of the non-aqueous sol-gel method, the organic medium not only contributes oxygen to the formation of a metal oxide, but it also assists in the modification of the properties of nanoparticles, including their size, shape, and structure. When it comes to preparing magnetic nanoparticles, there are a few different procedures that can be utilized in addition to the ball milling, GPC, and thermal breakdown techniques. The creation of MNPs can also be accomplished using different methods, such as co-precipitation, microemulsion, solvothermal, sonochemical microwave assisted, chemical vapor deposition, carbon arc, and laser pyrolysis. Ball milling, GPC, and sol-gel techniques are some of the methods that are

discussed in this chapter for the preparation of MNPs. Both positive and negative aspects are associated with any strategy. A significant quantity of nanoparticles can be obtained at a very low cost by the use of the ball milling process. By using the GPC approach, it is possible to generate nanoparticles that have a core shell structure, a well-defined crystallinity, and relatively small size.

2.4 Precipitation and Co Precipitation

The preparation of magnetic nanoparticles began with the precipitation process, which is also the oldest method. Adjusting the pH of a solution containing iron salt results in the formation of a fine suspension of iron oxide with particles as small as 5 nanometers. The production of magnetic nanoparticles can be accomplished using this technology, which does not call for any specialist facilities [28].In the process of creating nanoparticles (NPs), there are two distinct categories that may be distinguished: the physical and the chemical procedures. There are a substantial variety of synthesis methods, ranging from the precipitation method to sophisticated methods and complex procedures, which is the reason why this is utilized so extensively. Microemulsion, hydrothermal reactions, sonolysis, thermolysis, electrospray, flow injection, reduction, electrochemistry, thermal decomposition, and the GPC method are the synthetic methods that are utilized the most frequently. These are the procedures that are carried out under specific conditions that alter the physiochemical characteristics of the magnetic characteristics of the MNPs while simultaneously causing a change in those properties. For the purpose of obtaining magnetic nanoparticles with a diverse composition, including Fe, Co, and Ni, the precipitation and co-precipitation procedures are utilized extensively. This approach is widely utilized in the synthesis of magnetic nanoparticles (MNPs) containing magnetic metal oxide nuclei from the appropriate salts in a basic medium, in an environment that is inert, and at room temperature or above. The method is very reproducible in the reaction conditions that are adjusted. The synthesis of this particular form of MNPs is mostly dependent on the sources of metal ions as well as components of the reaction medium that include temperature, pH, and the ionic strength of the medium. The magnetic nanoparticles exhibited a low level of stability when exposed to the conditions of the environment, oxidizing or disintegrating when exposed to an acidic medium [18]. Currently, the nanoparticle synthesis process involves the use of numerous additives in the precipitation and co-precipitation procedures. The primary goal of these methods is to stabilize the nanoparticles, and addition can operate as a reducing agent that promotes nucleation. The polyvinyl alcohol (PVA), oleic acid, and derivatives of polyethylene glycol (PEG), as well as liposomes, are examples of substances that are utilized for the purpose of stabilizing or reducing agents.

2.5 Thermal decomposition Method

For the preparation of magnetic nanoparticles, the thermal breakdown process is the straightforward approach that is utilized most frequently. For the purpose of producing

nanoparticles, this technique involves the breakdown of organometallic compounds in organic solvents through the application of heat, while also requiring the presence of stabilizing chemicals [27, 28]. One of the benefits of metal nanoparticles is their high saturation magnetization, which is particularly appealing to the medical profession. However, the technological sector and data storage devices are not the only areas that are interested in these nanoparticles.

The water-soluble magnetite nanoparticles were manufactured by employing the straightforward method, and the size of the nanoparticles was controlled by the iron supply during the reaction period. Following the reaction time, the morphology of the nanoparticles undergoes a change, transitioning from a spherical shape to a cubic shape over the course of a considerable amount of time. With the addition of the dicarboxylic-terminating PEG as a surface protective agent, the same group was able to establish a one-step synthesis of water-soluble MNPs. This was accomplished by using the same reaction conditions.

This thermal breakdown process is the most common way for synthesizing metal oxide nanoparticles. It is also possible to create metal nanoparticles by making use of the appropriate metal carbonyl sources. The incorporation of nanoparticles into the air atmosphere led to a significant oxidation, which was then followed by a treatment that inhibited the oxidation process. These treatments included coatings with polymers, which ultimately resulted in MNPs that were stable in the air atmosphere. It has been found that oxide nanoparticles are more stable in air than their metallic counterparts. Within the framework of the thermal decomposition technique, there are two distinct approaches to the manufacture of oxide nanoparticles: the precursor with zero solvent metal oxide nanoparticles, which are produced by the addition of the oxidant at a high temperature.

3. Biocompatibility of magnetic nanoparticle

One of the most significant concerns in regenerative medicine is toxicity, which also plays a vital role in the field. Over an extended length of time, the particles, which are poisonous in nature, have the potential to dramatically reduce the therapeutic efficacy of the treatments that are based on cells. In the event that magnetic nanoparticles are incorporated into the treatment and implanted within the body, there is a persistent concern that the MNPs will migrate through the organism, penetrate the organs, and accumulate there.

4. Surface Coating Strategies

The conjugating chemical substances, including as polyethylene glycol (PEG), Chiston, Lipids, and Proteins, have the potential to improve the biocompatibility and chemical stability of MNPs [27]. Examples of these chemicals include Chiston. The magnetic nanoparticles should be effectively managed in the various settings of both vitro and vivo in order to ensure the most

biological application stability and chemical stability possible. In the field of nanomedicine, there are two types of coating tactics: organic and inorganic.

These coating strategies are used in diverse areas by magnetic nanoparticles. In addition, the shape and size of the magnetic nanoparticles can have an effect on the magnetic saturation, coercivity, field, and anisotropy of the material.

4.1 Coating techniques

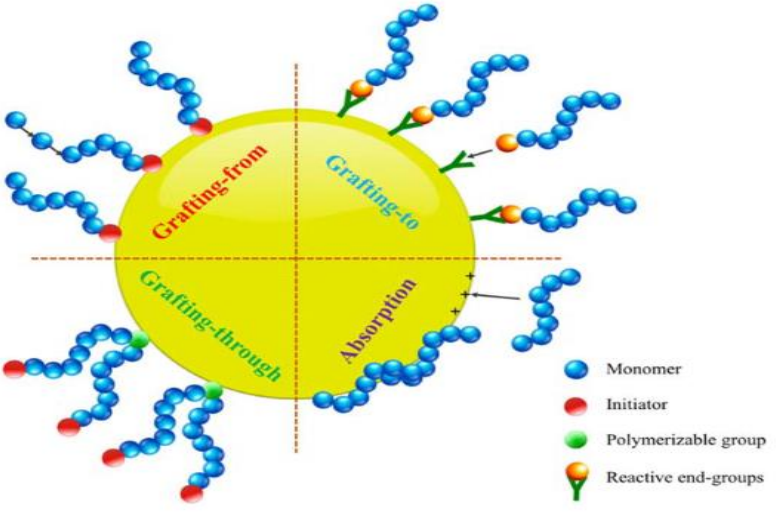

Figure 2. Schematic representation of different coating techniques for MNPs

4.2 Types of Coating Techniques

1) Organic coatings
2) In organic coatings
3) Biocompatibility and toxicity

4.2.1 Organic coating

The magnetic nanoparticles that are produced through the use of organic solutions are single-crystalline and monodispersed, and they have relatively high magnetic moments [20]. It was frequently discovered that the particle was hydrophobic, which necessitated several additional surface modification processes. This allows the hydrophobic surfactants that are present on the nanoparticle to be replaced with hydrophilic ligands through the process of reacting with the hydrophilic molecules. For this type of ligand exchange method, polyethylene glycol (PEG) is the polymer that is utilized the most because of its biocompatibility and its capacity to limit the amount of nonspecific response that occurs between MNPs and proteins. In

spite of the fact that PEG is normally utilized to reduce the amount of nonspecific protein absorption. There is a significant disadvantage associated with it, and that is the tendency for oxidative destruction [21]. To find a solution to this issue, polyzwitterions were developed. These polyzwitterions are constructed from zwitterionic repeat units that do not possess a net charge. Not only did the MNPs exhibit a better level of stability and a minimal level of agglomeration in aqueous and physiological environments, but they were also undetectable by the immune system of the body, which made them interesting candidates for drug delivery applications.

In the process of ligand exchange, polyethylene glycol (PEG) and many other polymers, including dendrimers [22], polyethylene oxides [23], and dextran's [24], are also utilized. Shell encapsulation is another method that may be utilized to enhance the biocompatibility and hydrophilicity of MNPs. Surface coating is another method that can be utilized. Through the manipulation of the concentration of the solvent type polymer, it was possible to tailor the size of the MNPs that were embedded in a copolymer matrix (poly D-L-Lactide co-glycolide) block of polyethylene glycol as well. In addition to the coating of polymers, MNPs that have been coated with biomimetic cell membranes have also been investigated in order to simplify the application of MNPs in the treatment of cancer due to their improved biocompatibility and active ability [26, 27]. The functionalization of PEG chains, on the other hand, can make it possible to bioconjugate with a variety of ligands or therapeutic agents, hence broadening the range of applications that can be found in the biomedical field [28-30]. It is possible for coatings to modify the final diameter of the MNPs as well as their thickness, which can have a major impact on the relaxation and distribution capacity in vivo [25, 31]. This is one of the difficulties associated with coatings. Magnetic nanoparticles are driven primarily by the magnetic characteristics of the magnetic nanoparticles (MNPs), which are inextricably tied to their morphological structure, which includes crystal regularity, as well as the orientation of the MNPs, which is determined by their conjugation with biologic molecules. The size distribution is another component that should be taken into consideration. It is better to have a size that is less than 100 nm and allows for a reduction in phagocytosis [31, 32].

4.2.2 In Organic Coating

A silica coating is one of the inorganic coating materials that is used the most frequently. Vinayls, acrylics, alkyd (oil base), modified alkyd silicon, phenolic alkyd, and epoxy ester are all examples of organic coating materials; however, silica is the only one that is biocompatible and has the ability to generate non-aggregated and stable suspensions [26]. The subsequent functionalization of alkoxysilanes is made possible by the addition of silica to the outer shell. Research was conducted to investigate the influence of the silica coating on the saturation magnetization and the curie temperature of the MNPs. The goal of this research was to achieve a more effective control of the magnetic properties of the MNPs that were coated with silica, particularly in order to meet the temperature requirement for the hyperthermia therapy. When

compared to organic and inorganic coatings, the frequency with which hyperthermia therapy is utilized is significantly higher. Metals are materials that carry electricity, and metallic coatings make it possible for inductive heating to occur when an AC magnetic field is present. As a result of its ability to conjugate with a wide variety of biomolecules, including DNA and proteins, gold has emerged as the most effective metallic coating for MNPs. In addition, the molecular coating of magnetic nanoparticles, which consists of a combination of inorganic magnetic cores, primarily oxides, and organic shells, plays a very significant role in the field of biomedicine for the purpose of diagnosing and treating tumor cells.

This coating not only controls the anisotropy and increases the saturation magnetization, which makes the nanoparticles more effective, but it also makes them magnetically driven and improves their bio cytocompatibility [27].

4.2.3 Biocompatibility and Toxicity

The surface structure of organic molecules can be altered by ligands, which can replace missing bonds, hence lowering spin disorder and causing a shift in surface anisotropy [34]. By doing so, organic molecules can adjust the surface structure [30-33]. An iron oxide nanoparticle-coated citric acid set was synthesized using a coprecipitation approach in a microwave reactor. The nanoparticles were coated with citric acid. In the solution, two nanoparticle assemblies were produced by adding 1 mmol of CA-iOA and 2 mmol of CA-iOH. The results showed that the lower ILP values (1.8 nHm2 Kg-1) and the higher ILP values (4.1 nHm2 Kg-1) were obtained. The results indicate that the demagnetizing contacts are controlled by the concentration of citric acid and that they lessen the heating properties [27]. If the sample is synthesized under conditions of a lower concentration of citric acid and longer reaction durations (CA-iOA), the interparticle core interactions are stronger. While the inorganic nanoparticle-based cancer treatment or therapy has brought various benefits for the treatment of cancer, there are still many challenges to overcome. Before these findings can be successfully transferred into therapeutic applications, there are still a few problems and challenges that need to be addressed. It is still not clear how these nanoparticles are able to penetrate the tissue of the tumor once they have been deposited. Following that, it is a significant obstacle to overcome the physiological barriers that exist in vivo, such as the lungs, liver, spleen, and kidneys, in order to build nanoparticles that have a high selectivity to the areas that are wanted in vivo [23].

4.3 Coating Materials

There is a requirement for corrosion protection for the nanoparticles that make up the magnetic core. While in vivo applications are being carried out, this coating also inhibits the leakage of potentially hazardous components into the body.

Here listed the types of coating materials like

1) Natural polymers

2) Synthetic organic polymers

3) Silica

4) Gold

4.3.1 Synthetic Organic Polymers

Some natural polymers, such as cellulose, are too rigid to be manipulated in order to coat nanoparticles, while others, such as many others, lack the mechanical strength necessary to do so. There is a possibility that synthetic polymers could offer a solution to this issue [NR59]. Magnetic nanoparticles can be made from a variety of synthetic polymers, including polyethylene glycol (PEG), polyvinyl alcohol (PVA), and poly L-lactic acid (PLA), as described by Nithin et al. (2004) and Qiu and Winnik (2000). When it comes to coatings, the choice of synthetic polymers is determined by the surface qualities that are required for the applications [29].

4.3.2 Silica

The amorphous material that possesses a high mechanical strength is this one. Because of the presence of silanol groups (Si-OH) on the surface, it carries negative charges at pH levels below 3. The techniques for functionalizing silica surface for use in biomedical applications are extensively available in the literature [11]. In clinical applications of magnetically focused carriers, the progress has been gradual since it was originally developed in the 1970s; yet, the potentials for this approach continue to be quite high. Because there are so many different variables that need to be managed, designing a multifunctional magnetic nanoparticle that is efficient is a challenge. In addition, organic and inorganic coatings play an active role in the magnetic hyperthermia performance of small magnetic nanoparticles (about 10 nm), which is a significant characteristic to take into consideration during the design phase of biocompatible applications [20]. The purpose of this work was to identify an adequate mix of magnetic nanoparticles that would create suitable targeted hyperthermia and perhaps appropriate circumstances for being loaded with a positively charged medication at a neutral PH while simultaneously releasing it into the acidic environment of the tumor. Having a blocking temperature lower than 300k, it has been demonstrated that both inorganic MNPs and biomimetic (Mam C mediated BMNPs) nanoparticles are superparamagnetic. This means that they behave as paramagnetic at this temperature, but they exhibit a relatively high saturation magnetization when they are in the presence of an external magnetic field. Furthermore, they are able to be magnetically guided to a specific target size [21]. The current investigation presents a composition of nanoparticles, specifically 25% BMNPs and 75% MNPs, which, despite having the highest hyperthermia response, enhanced the stability of the sample. Additionally, the drug nanocarrier that was created to release the medication in response to changes in PH was also developed at this time.

When inorganic and biomimetic nanoparticles are mixed, there is the possibility that combined targeted chemotherapy and targeted hyperthermia could be achieved. Recent advancements in the creation of contrast agents for imaging and touch that are based on inorganic nanoparticles have been made in the area of contrast enhancement surface modification tissue targeting clearance and toxicity. In the near future, it is anticipated that contrast agents that are based on inorganic nanoparticles will enter clinical applications.

These contrast agents are predicted to be extremely sensitive, target specific, and safer to use. As contrast agents, small compounds including organic dyes and radio isotopes that have been coupled to targeted ligands have been utilized extensively in a variety of settings, including clinical hospitals and research laboratories. The inorganic nanoparticles are gaining more and more attention as potential contrast agents in the future because to the extraordinary features that they possess [22-25]. The use of nanoparticles composed of organic components, such as liposomes, micelles, and polymeric particles, as contrast agents for molecular imaging has also been investigated [19, 20]. Superparamagnetic nanoparticles are distinguished from other types of particles by the fact that they do not possess permanent magnetic moments when they are not subjected to an external magnetic field, but they are able to rapidly react when subjected to such a field [18]. As contrast agents for magnetic resonance imaging (MR Imaging), more than ten different types of superparamagnetic nanoparticles are now available for commercial use. The superparamagnetic nanoparticles that are utilized the most are those that are employed on iron oxides and are typically smaller than 20-30 nm in magnitude. Nanoparticles made of iron oxide have the ability to function as MR contrast agents for clinical diagnostics [29, 37]. They also have the ability to improve the proton relaxation of particular tissues. For almost twenty years, both (α-Fe_2O_3) maghemite and Fe_3O_4 magnetite nanoparticles have been investigated for their potential use as magnetic resonance (MR) contrast agents. In Europe, both of these materials have previously been approved for clinical usage [34, 36].

5. Conclusion

Over the course of the last few decades, magnetic nanoparticles (MNPs) that possess physical properties have been synthesized for the purpose of application in biological and biomedical applications. Furthermore, a significant number of the synthesis procedures have been put into commercial production. In order to successfully manufacture MNPs, a number of different techniques have been utilized, including thermal decomposition, ball milling, GPC, the sol-gel method, and co-precipitation. In addition, surface functionalization of polymer, biomolecule, and ligand surface coatings is required in order to alter the biological and contact capabilities of the coatings. The two types of coatings that are inorganic and organic are distinct from one another, with organic coatings having a greater number of uses notably for magnetic hyperthermia. In addition, the review contains a study that focuses on magnetic nanoparticles. The purpose of this article was to discuss a variety of methods for producing magnetic

nanoparticles by utilizing high-tech instruments. These procedures made it easy to manufacture magnetic nanoparticles that exhibited the magnetic behaviors that were described in the previous sentence. As potential cancer treatments, this article discusses targeted drug delivery, hyperthermia, radiation therapy, wound-healing treatment, and targeted drug delivery as a better substitute for cancer treatment. These are all examples of treatments that are currently being used and will be used in the future. The utilization of superparamagnetic nanoparticles in magnetic resonance imaging (MRI) has been a significant advancement in the assortment of techniques that are accessible to doctors. Because of the effectiveness of the agents, they have been suggested for use in imaging the gastrointestinal system and the liver. There appears to be a great deal of optimism regarding the potential for increased utilization in lymph node and functional imaging. The majority of the recent research has focused on cellular imaging of in vivo macrophage activity. Other areas of investigation include stem cell migration and immune cell trafficking, as well as targeted iron oxide nanoparticles for molecular imaging studies. These studies are now in the proof of concept stage, primarily in animal models.

Particularly over the course of the last ten years, significant advancements have been made in the realm of magnetic nanoparticle production, which encompasses a wide variety of compositions and sizes that can be adjusted. It is necessary to have a reproducible and industrial approach that does not involve any lengthy purification phase in order to ensure that the synthetic procedures are cost effective. This is because the large-scale synthesis of iron oxide crystalline nanoparticles, which are characterized by a high degree of crystallinity and subsequently high magnetization at saturation, necessitates such a technique. In a more fundamental sense, it is necessary to investigate the mechanism of surface anchoring the poly or monomeric coating by utilizing the new surface binding. Additionally, it is necessary to investigate the influence of the coating layer on the structural and magnetic properties of the iron oxides. Surface effects can result in a decrease in the magnetization of small nanoparticles, such as oxide nanoparticles, in comparison to the bulk value. When it comes to predicting the stability of the coating to forward agglomeration in various mediums (aqueous, saline, cell culture, biological), having an understanding of the surface anchoring of the coating will be very helpful. This can be accomplished through electrostatic steric repulsion or electrostatic steric attachment. In order to improve the logical design of new stable coatings, it will be of great assistance to construct a surface model of the interaction between the coating and the surface of the iron oxide. For the objective of enhancing the ability to define the fundamental properties of the superparamagnetic particle surface, the novel cold atmospheric pressure plasma method is being developed. These qualities include the particle's size, surface composition, surface charge, hydrophilicity, and hydrophobicity.

Probably one of the most important aspects of research on superparamagnetic materials is the establishment of reliable structure-pharmacokinetic correlations. Additionally, the nature of the structural surface coating on the iron oxide surface will not only influence the size and colloid, but it will also play a significant role in the clearances of pharmacokinetic, metabolic, and

vascular tissues. Furthermore, the biodistribution properties will modulate the diffusion of tissue in tumor tissues. One of the many obstacles that needed to be conquered in order to develop a new iron oxide that is both effective and selective for cellular and molecular imaging. Regarding the targeted iron oxides that incorporate bio vectors that are able to recognize a biological target, as well as the surface modification techniques that are used to graft bio vectors, it is necessary for these procedures to be reproducible and to enable the precise introduction of a well-defined number of bio vectors.

It is necessary to develop new analytical instruments that are accurate in determining the quantity and number of bio vectors that are present on the surface of nanoparticles. The nanoparticles' interaction with the immune system, as well as the optimization of the molecular interaction between the particle attached receptors or ligands, are both being investigated. Live in the animal. The purpose of future research should be to overcome the various problems that are encountered in the implementation of nanomedicine. To substantiate confirmation of the concept employing the various controls, particularly in MRI molecular imaging, more preclinical investigations should be carried out in animal models and disease states that are relevant to the study. The investigations on biocompatibility and safety has to be carried out for the purpose. The proof-of-concept experiments conducted in human bodies are not sufficient. For the purpose of synthesis and improvement of magnetic nanoparticle size, biocompatibility, and surface coating with magnetic materials, the Cold Atmospheric Pressure Plasma technique is being utilized in the field of biomedical applications.

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