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A REVIEW ON MAGNETIC NANOPARTICLES- SYNTHESIS, FUNCTIONALIZATION AND APPLICATIONS

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Abstract:

Magnetic nanoparticles are nanoparticles which exhibit superparamagnetic properties owing to their small size. They have wide range of applications which are mentioned else where in this review[1]. One of them is targeting of drugs to site of action, known by the terms site-specific drug delivery or drug targeting. In this method magnetic nanoparticles as drug carriers are administered in to the body and are manipulated by external magnetic fields to reach the target area. This method is highly valuable for treating cancers due to the advantages that normal cells are not exposed to the cytotoxic drugs. Further it resulted in improved efficacy, reduced drug dosage and side effects. Magnetic drug targeting requires two components, a nano sized carrier particle system and an external magnet system to guide the drug carriers to the target site. Till date there have been many efforts to design the magnet systems for targeted drug delivery. This review gives a detailed account on the preparation methods, applications along with recent progress that has taken place in this field

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INTRODUCTION

Magnetic nanoparticles are nanoparticles usually less than 100 nanometers in diameter, made of materials like metals or metal oxides. Such nanoparticles exhibit unique magnetic properties due to their small size, described as superparamagnetic [2]. When the size of the nanoparticles is reduced to the nanoscale, they can exhibit a phenomenon known as superparamagnetic, meaning which, the nanoparticles have no permanent magnetization but can become highly magnetic when exposed to an external magnetic field. The magnetic properties are typically described in terms of magnetization, susceptibility, and coercivity.

Magnetic nanoparticles can be prepared from most of metals, each with diffecrent magnetic properties and applications [3]. The choice of material depends on the desired properties and the intended application. Some common materials used to prepare magnetic nanoparticles and their specific applications are

Iron Oxides: Magnetite ($Fe3O4$): Magnetite is one of the most commonly used materials for magnetic nanoparticles. It exhibits strong magnetism and is used in various biomedical applications, including MRI contrast agents and targeted drug delivery systems.

Hematite (α-Fe2O3): Hematite nanoparticles are used in environmental applications, such as water purification and wastewater treatment.

Ferrites: Ferrite nanoparticles are made from various metal oxides, such as manganese ferrite (MnFe2O4), cobalt ferrite (CoFe2O4), and nickel ferrite (NiFe2O4). They are used in electronics, telecommunications, and microwave devices.

Cobalt Nanoparticles: Cobalt nanoparticles are used in high-performance permanent magnets and magnetic recording media.

Rare Earth Metals: Magnetic nanoparticles prepared from rare earth metals like neodymium (NdFeB) nanoparticles have extremely high magnetic strength and are used in advanced applications like high-performance permanent magnets and sensors.

Other Metals: Nnanoparticles prepared out of metals such as nickel (Ni) are used in applications like catalysis and sensors.

Metal Alloys: Various metal alloys can be prepared as nanoparticles with tailored magnetic properties. Examples include iron-platinum (FePt) nanoparticles which are used for data storage and magnetic sensors.

Core-Shell Structures: Magnetic nanoparticles can be prepared with a core-shell structure, where a magnetic core is coated with a non-magnetic shell, which allows for enhanced stability and surface functionalization for specific applications.

Composites: Magnetic nanoparticles can be incorporated into other materials to make them suitable for multiple functions. For example, they can be combined with polymers for flexible magnetic materials or with carbon nanotubes for enhanced electrical conductivity.

Methods of preparation:

Magnetic nanoparticles are generally prepared by using various synthetic methods and surface is modified using different functionalisation techniques for various applications. The synthesis of magnetic nanoparticles can be carried out using chemical methods, including co-precipitation, thermal decomposition, sol-gel processes, and hydrothermal synthesis. The choice of material and synthesis method depends on the desired size, shape, magnetic properties, and intended application of the magnetic nanoparticles. Surface modification and functionalization with various ligands or coatings are carried out to control stability, dispersibility, and interactions with biological or environmental systems, which is particularly important applications such as in medicine or environmental remediation.[4]

Co-Precipitation: This is one of the most simple and efficient technique for synthesizing magnetic nanoparticles, especially iron oxide nanoparticles. In this method, iron salts (e.g., iron chloride) are mixed with a base (e.g., sodium hydroxide) in a controlled environment. The reaction results in the formation of magnetic nanoparticles. The size and properties of the nanoparticles to be controlled carefuuly by adjusting the reaction conditions, otherwise the method give nanoparticles of large polydispersity index[5].

Thermal Decomposition: This method is often used to synthesize monodisperse (uniform in size) magnetic nanoparticles. It involves heating organometallic precursors (organic compounds containing metal atoms) to a high-temperature in a high boiling organic solvent in the presence of stabilizing surfactants. As the temperature increases, the precursors decompose and form magnetic nanoparticles. This method allows for precise control of particle size and shape. However, this method is that toxic chemicals, such as chloroform, hexane and iron pentacarbonyl are used in the synthesis.

Microemulsion: Microemulsion techniques use a system of dispersion of immiscible liquids typically oil and water stabilized by surfactants. surfactants, like dioctyl sodium dodecyl sulfate (DSS), cetyltrimethylammonium bromide (CTAB), sodium dodecyl sulfate (SDS) and polyethoxylated (e.g. Tween-20 and -80) are used for the formation of micellar microemulsion systems. The dispersed phase serves as a nano/micro-reactor, providing a confined environment for the nucleation and controlled growth of nano- and microparticles. The method offers good control over particle size and shape and is often used to prepare coated or functionalized nanoparticles. But unfavourable effects of residual surfactants on the properties of the iron oxide particles are disadvantage of the microemulsion method.[6]

Sol-Gel Synthesis: Sol-gel processes involve the formation of a colloidal suspension that undergoes a gelation process by hydrolysis and condensation of tetraethyl orthosilicate (TEOS) in ethanol and 30% aqueous H2O2 with Fe3+ solutions. The sol is then gelled by chemical reaction or solvent removal, to obtain a 3D iron oxide network. To get iron oxide nanoparticles, the formed gel is crushed after drying and solvent removal. Adding surfactant prior to gelation results in a decrease in the free energy of the system and consequently leads to the formation of nano-sized iron oxides without the formation of a 3D network.[7]

Metal reduction: Magnetic nanoparticles are also synthesized by the reduction of metal salts using reducing agents in the presence of surfactant molecules. Compared to the thermal decomposition approaches, where unstable non-metallic precursors are involved, metal reduction methods offer a larger variety of stable metal precursors, such as oxides, nitrates, chlorides, acetates, and acetylacetonates. Conventionally, hydride based reducing agents, such as sodium borohydride and lithium super hydride, are used for metal salt reduction. More recently, organic reducing agents such as polyols, hydrazine and dihydrogen gas have been employed for such reduction.[8]

Mechanical Milling: This method is suitable for preparing magnetic nanoparticles from materials like rare earth metals or alloys. It involves the grinding or milling of bulk magnetic materials into nanoscale particles. The size and properties of the nanoparticles can be controlled by adjusting the milling conditions.

Green Synthesis: In recent years, there has been growing interest in environmentally friendly or "green" methods for synthesizing magnetic nanoparticles. These methods often use natural extract like plant-based compounds, or biogenic processes to reduce and stabilize metal ions into nanoparticles. Biomolecules have the ability to aggregate inorganic metal ions in solutions and form nanosized aggregates. Size and shape of the resulting nanoparticles can be carefully tailored using suitable capping agents and right extent of agitation. Many reports on iron nanoparticles synthesized by green methods are available. [9,10,]

Functionalization:

The prepared nanoparticles are then functionalized with specific molecules or ligands on their surface to serve a variety of purposes. Some common reasons behind the surface modification and functionalisation are

- ✓ In this stage nanoparticles are enclosed in a layer that stabilizes the nanoparticles and prevents aggregation in biological fluids.
- ✓ The process of functionalisation renders the nanoparticles biocompatiblele, reducing potential toxicity and immune response.
- ✓ It provides targeting specificity by binding to receptors or molecules on the target cells or tissues owing to the specific ligands attached on to the surface.

Materials used to coat iron oxide nanoparticles are polymers, fatty acids like oleic acid, stearic acid, lauric acid and dodecylphosphonic acid amino acids like phenyl alanine, tyrosine, arginine, lysine and cysteine, metals like gold, gadolinium and silver and oxides like silica and TiO2.[11,12]

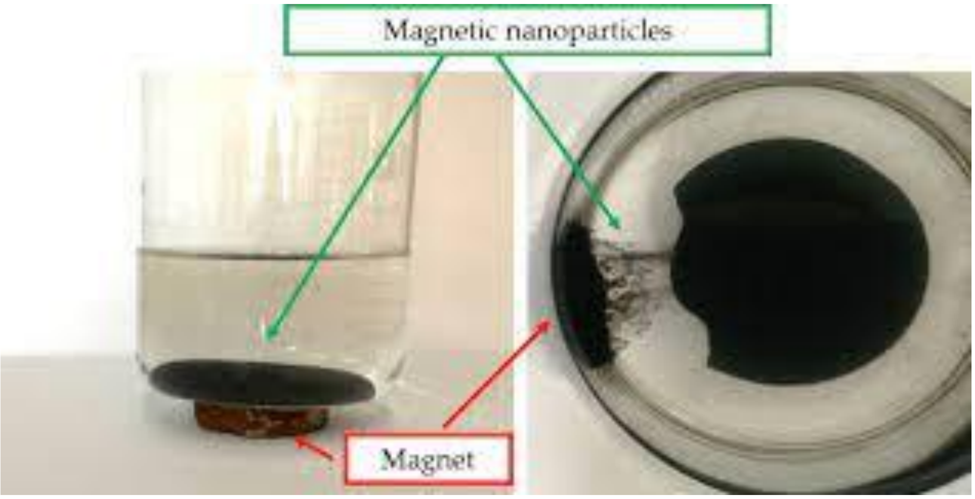
Conventional coatings with polymers such as dextran and PEG are most commonly used, not only because they are generally regarded as safe (GRAS), but also because they are not recognized by macrophages in liver and spleen when administered intravenously, therefore bypass the RES system and circulate for prolonged duration in the blood. Mmolecular weight and surface density of PEG coatings influence the stability, cytotoxicity, and circulation time of iron oxide nanoparticles. Dextran coating has no direct cytotoxic effects, the degradation of the dextran shell may influence certain cellular processes.

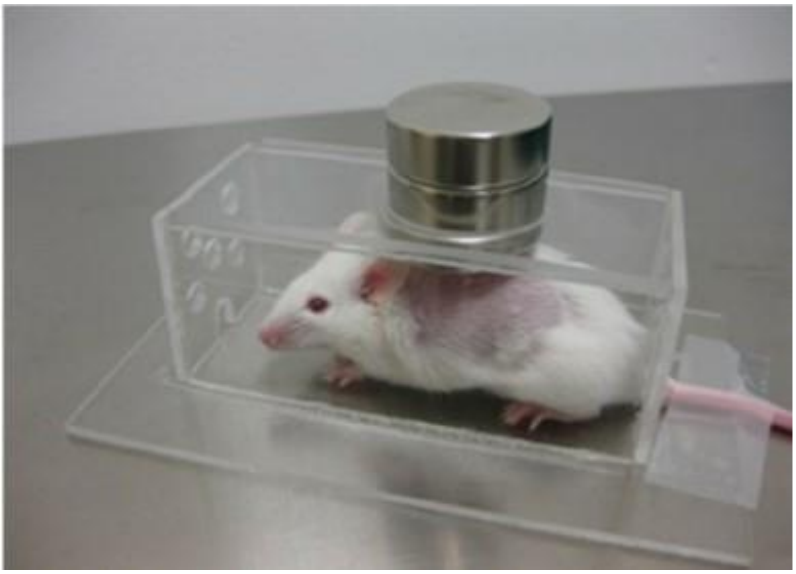
Iron oxide nanoparticles surface-functionalized with poly-N-vinylcaprolactam, poly-N,N-diethyacrylamide are sensitive to temperature changes, whereas polymers such as polyacrylic acid and poly-methacrylic acid are used to give pH - responsive polymeric coating. pH-sensitive drug carriers release the drug payload in response to the acidic environment of the target tissue (e.g., the tumor microenvironment). Thermosensitive carriers release the drug when exposed to elevated temperatures (e.g., using hyperthermia).

Targeting to specific site of action

The mechanism of drug targeting through magnetic nanoparticles involves a combination of physical forces, magnetic fields, and controlled drug release strategies.

External Magnetic Field Application: For the magnetic nanoparticles to reach the site of action an external magnetic field need to be applied externally to the patient's body using an electromagnet or a permanent magnet system. This magnetic field provides the driving force for the targeted delivery of magnetic nanoparticles. The nanoparticles respond to these forces and move in the direction of the field gradient, following the lines of magnetic force. The strength and orientation of the magnetic field is adjusted to control the movement of the nanoparticles. The behaviour of magnetic nanoparticles under the influence of external magnetic field is shown in the below picture[13]





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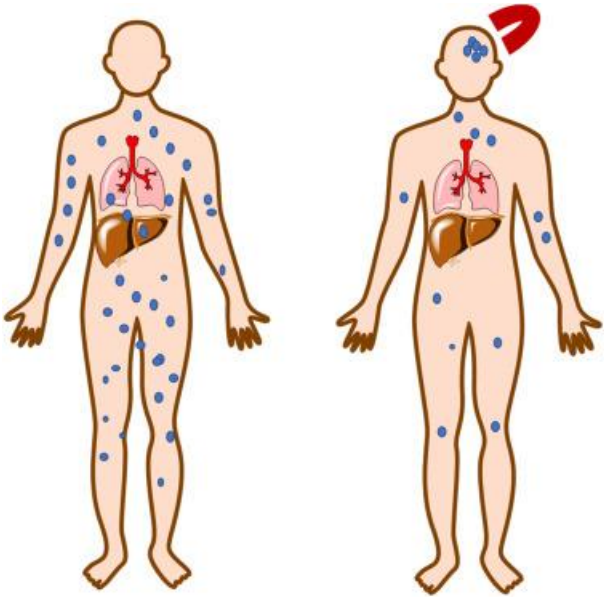
The following picture depicts the bio-distribution of magnetic nanoparticles after administration into the body. When administered intravenously the particles travel to the required site and concentrate at the site of action under the influence of the magnetic field provided by the external magnet assembly placed outside the body[14]



Applications of Magnetic nanoparticles:

Drug delivery:

Magnetic nanoparticles using an external magnetic field, can be guided deep inside the tissue, which increases the bioavailability of the drug and magnetic field control enables the precise targeting of the drug .The main target of magnetically guided drug delivery is to the drug directly to the diseased tissue without having an impact on the rest of the body. Several marketed preparations containing magnetic nanoparticles were in use for various applications, primarily in the field of medicine and diagnostics.

Marketed preparations containing magnetic nanoparticles

Name of the Product	Used in	Type of nanoparticles
Feraheme® (Ferumoxytol):	iron deficiency anemia with chronic kidney disease	iron oxide nanoparticles coated with a carbohydrate shell
Resovist® (Ferucarbotran)	magnetic resonance imaging (MRI) for liver imaging	iron oxide microparticles coated with carboxydextran
Combidex®	lymph node imaging in prostate cancer	Contrasting agent containing iron oxide nanoparticles
Magtrace® and Sentimag®	help surgeons locate and remove sentinel lymph nodes accurately during surgery	iron oxide nanoparticles
Endomag®-Magseed	used to mark tumors for precise surgical removal	Stainless steel rod with low nickel content coupled with iron oxide nanoparticle sening system
Endomag®-Magtrace	sentinel lymph node detection	iron oxide and a sugar coating (carboxydextran) held in salt water
NanoTherm®	Treatment of cancer, particularly brain tumors	aminosilane-coated iron oxide nanoparticles and the application of an alternating magnetic field

Diagnosis of diseases:

Magnetic nanoparticles interact with external magnetic field and alter the magnetic fields in their vicinity, due to which they are used to elevate magnetic resonance imaging (MRI). MRI doesn't require the use of ionization radiation to imaged tissue like other imaging techniques, but the magnetic character of protons is utilized for image creation.[15,18]

Cancer theranostics:

Magnetic nnanoparticles are used to construct nanoscale imaging probes for early detection and visualization of cancer development [18,21]. Magnetic nanoparticles offer unique physicochemical properties & Super magnetic characteristics, which make them ideal candidates for hypothermia therapy cancer [17]. Magnetic nanoparticles-based hyperthermia therapy is its deep tissue penetration & magnetism-assisted specific killing of cancer cells without damaging healthy tissue.

Bacterial theranostics:

Recently, Magnetic nanoparticles-based strategies have been developed to treat infections caused by multi-drug resistant bacteria as well as bacteria-related biofilm [20,21,22].

The mechanisms by which Magnetic nanoparticles Kill microbes are through disrupting Plasma membrane, releasing toxic metals, ROS generation that interfere the synthesis of major bacteria components [21].

Biosensing:

The Magnetic nanoparticles -based sensors have shown remarkable application in different fields including food technology, lab-testing, clinical diagnosis, and environmental monitoring [23,24]. Because of the high signal-to-background ratio Magnetic nanoparticles can be used as magnetic probes to detect the analytes in biological Samples.

Environment:

The purification of water has been reported by applying Magnetic nanoparticles especially targeting bacteria, dye degradation, removal of organic species. One of the best examples is Fe3O4 amino acid for the magnetic separation of contaminants from waste water [27].

Previously, different studies reported chemical pollutants like pesticides and antibiotics are degraded by using Magnetic nanoparticles with catalytic and photocatalytic properties through oxidation and reduction processes (28).

Agriculture:

Magnetic nanoparticles are helpful in plant protection, seed germination and improving soil quality [29,30] for example, iron oxide Magnetic nanoparticles can be used as soil nutrition to increase production with minimum negative impacts.

Catalysis:

The limitation of heterogenous catalysis has been reduced and minimized using catalysts that are supported by. Magnetic nanoparticles. The Magnetic nanoparticles have the ability that they provide a high surface area to Support active sites for reactants to be converted into products easily[31].

Magnetofection:

Nanoparticle-mediated Magnetofection is a transfection method used for delivering nucleic acid under the influence of an external magnetic field (24).This techniques increases the efficiency of delivering genetic material into cells [32,33,34,35]

CONCLUSION:

Metallic substances when reduced to nanoscale size exhibit superparamagnetic property which has very useful applications. Magnetic nanoparticles are an effective tool for targeted drug therapy and have important applications in material science and environmental remediation. Diagnostic imaging of human body for any type of deformations and Tumors was made much easier through the magnetic nano systems. There is scope for vast research to device magnetic nanoparticle systems for more drugs, which may help decreasing unwanted effects of many drugs giving an effective therapy.

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