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DESIGN PREPARATION AND APPLICATIONS OF MAGNETIC NANOPARTICLES

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Abstract:

Magnetic nano particles are of great interest for researchers from a wide range of disciplines, including magnetic fluids in biotechnology/biomedicine, magnetic resonance imaging and environmental remediation. While a number of suitable methods have been developed for the synthesis of magnetic nano particles of various different compositions, successful application of such magnetic nano particles in the areas listed above is highly dependent on the stability of the particles under a range of different conditions. In the present review, first we have briefly discussed main synthetic methods of MNPs, followed by their characterizations and composition. Then we have discussed the potential applications of MNPs in different with representative examples. At the end, we gave an overview on the current challenges and future prospects of MNPs. We focus mainly on recent developments in the synthesis of magnetic nanoparticles, and various strategies for the protection of the particles against oxidation and acid erosion. Further functionalization and application of such magnetic nanoparticles in catalysis and bio separation will be discussed in brief. This comprehensive review not only provides the mechanistic insight into the synthesis, functionalization, and application of MNPs but also outlines the limits and potential prospects.

Key Words: *Magnetic nanoparticles, iron oxide ,magnetite , Hyperthermia*

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INTRODUCTION:

Magnetic nanoparticles (MNPs) are among the one form of NPs that shows certain reactions when the magnetic field is applied with little molecule size, huge explicit surface region, magnetic response, and superparamagnetism.[1] In such a manner, MNPs have different novel attractive properties like superparamagnetic, low Curie temperature, and huge magnetic susceptibility. MNPs might be amassed and situated beneath a steady magnetic field, and the warmth is spent by the electromagnetic wave in the alternating magnetic field. [2] The advancement of magnetic nanoparticles (MNPs) is promising for various applications. Magnetic nanoparticles find a unique place in the field of nanotechnology-based materials along with the effect in a study of, bio-sensing, nanomedicine, and analytical science. The above-mentioned utilization of magnetic nanoparticles and microparticles has helped a long way in discovering and treating microbial infections in the accompanying years. [3]

i). Drug delivery system conjugated with magnetic nanocarriers as like instance drug transporters.

(ii) Magnetic nanoparticles controlled by using the radio frequency waves gave another way to deal with disease treatment applications[4]

(iii) Magnetic detachment of natural entities added to the improvement of diagnostics for instance magneto acoustic tomography (MAT), computed tomography (CT), near-infrared (NIR) imaging, and magnetic resonance imaging (MRI).

The medications got from a common plant source called herbal medications are generally utilized as a medication due to their less toxicity. [5-6] In late many years the utilization of herbal medications has essentially expanded which is clear from the expanded worldwide market of natural medicines. A magnetic nanoparticle (MNPs) for herbal medicines incorporates focused on drug delivery, which lessens measurement recurrence, builds the solvency and absorption though diminishes disposal. Nanoparticles can be utilized to focus on the herbal medicines to singular organs which improve the focus on targeted drug delivery, adequacy, and wellbeing of the medication, diminish the rehashed administration to beat resistance, yet in addition, help to build the therapeutic worth by decreasing toxicity and expanding the bioavailability.

Advantages of Magnetic Nanoparticles:

MNPs, usually magnetite nanoparticles possess much more effective function like a transporter for a wide range of hydrophobic and hydrophilic pharmacological compounds and show the supplementing properties

(1) Biological compatibility
(2) Elevated chemical strength
(3) Held superparamagnetic properties
(4) Increased colloidal stability
(5) Reduces the drug wastage
(6) Decrease unfavourable responses of drug moieties
(7) Supported conveyance of moieties towards the chosen designated organ and
(8) Less expenditure in the production of MNPs identifies them as a most productive delivery system than different novel formulations.

Preparation of Magnetic Nanoparticles

MNPs are normally present in the superparamagnetic state and the widely utilized nanomaterial is the iron oxide nanoparticle, including magnetite (γ-Fe_2O_3) and magnetite (Fe_3O_4). Notably, MNPs have a significant part in disease finding, drug conveyance, and treatment. The critical parts of Magnetic nanoparticles are the magnetic core, surface covering, functionalized external covering, and the hydrodynamic layer. The middle part displays superparamagnetism, which can be worked by an outside magnetic field. Iron, Cobalt, Nickel is a portion of the attractive material utilized for showing superparamagnetism. Among these nanoparticles with iron oxide is more profitable as it biodegrades effectively, simple to plan, ties to ligands, infiltrates effectively through cells. Because of attractive powers, the conglomeration after some time can be seen if the attractive centre isn't covered by a non-attractive grid[7].

Precipitation from Solution:

As per the hypothesis proposed by Lamer, improvement of homogenous nanoparticles is in the increase, and seeding measures are isolated specifically in three particular stages. Stage 1, of the framework, gains its efficiency, and hence the single unit of polymer namely monomer fixation increments occur. When the hyper saturated fixation is accomplished, adequate energy occurs in the framework causing the explosion of the nucleus, which concludes with the formation of uniform scattered colloids possessing restricted area dissemination. The seeds like crystallites present in media that triggers heterogeneous nucleation increase the range of nanoparticle width.

Precipitation:

It is a helpful and simple strategy for producing MNPs of ferrites and metal oxides using solid solutions. The addition of alkali takes place in a passive atmosphere at indoor temperature or at higher. The chemical reaction takes place in an aqueous media. Under non-oxidizing conditions, pH

levels for total precipitation should be in the midst of 8 and 14, with a stoichiometric proportion of (Fe3+/M2+) 2:1. The mean area of the MNPs can be restrained to a substantial dimension from 15 to 2 nm by controlling the ionic strength and pH of the media in which precipitation occurs. Fe_3O_4nanoparticles size decrease as pH and ionic strength increase. P^H and ionic strength can affect the electrostatic surface charge of particles. Under the aforementioned conditions, the collection of the essential particles brings about magnetite particles that are delivered inside $Fe(OH)_2$ gel. This set up affidavit shapes the globular glasslike particles. To obtain more modest particles, polyvinyl liquor (PVA) is added to iron salts. The parts, size, and shape of the formulated MNPs rely upon various sorts of salts used such as chlorides, nitrates, and sulphates. The arrangement of Fe_3O_4 nanoparticles is made by the hydrolysis in fluid arrangements, for example, ferrous and ferric salt at various percentages used along with the alkali 1, 6-hexane diamine. The molar proportion ratio change between ferrous to ferric particles can result in the production of controlled attractive characteristics of Fe_3O_4 nanoparticles. In this arrangement, soluble base substance, a measure of emulsifier, and response temperature are the basic factors that predominantly affected the eventual outcome. In this technique, the significant deterrent for the arrangement of MNPs is particle agglomeration because of its nano-size range which prompts improve surface energy and enormous explicit surface territory. [9]

Micro-emulsion:

The microemulsion is a thermodynamically steady combination. The water in oil emulsion is the most commonly used microemulsion identified in the formulation of homogenous MNPs. W/O emulsion is the Emulsion frameworks are made of three constituents: water, oil, and a surfactant, which is an amphiphilic molecule that diminishes the interfacial tension. Reagents containing water nano droplets fill in go through quick combination and the blend for precipitation response measure utilized for MNPs production. Surfactants such as nanodroplet dividers encircle the circular outline of the water pool. This nanodroplet divider gives the confines to particle development which brings about the decrease in the particle mean size throughout the gathering and interaction of impacting. In this way, the water pool size is a boundary to control the size of the round nanoparticles (water to surfactant molar proportion, W_0 esteem). For the most part, the bigger the molecule size, the higher the worth of W_0. At the point when two comparative w/o microemulsions are blended, comprising of the favored reactant, will bring about a consistent crash between microdroplets which mix and then break, and eventually structure the aggregation of molecules in colloidal solution and get accelerated. The basic principle behind this technique being the estimation of surfactant, that relies upon various Physico-chemical qualities related to the framework including the antagonistic impact on properties of particles because of outstanding measure of surfactants.[10]

Thermal Decomposition:

The presence of iron precursors deterioration and hot natural surfactants results in an improved model with slender mass appropriation, great mass control, and unrivalled crystallinity of dispersible and single magnetic NPs. The existence of premium semiconductor nanocrystals and oxides in fluid-less environments enables the production of nanoparticles via thermal degradation. Thermal decomposition of raised bubbling natural solvents of an organometallic compound with settling surfactant can produce a monodisperse magnetic nanocrystal. In warm deterioration, the metal is zero valent precursors of the organometallic compound with the arrangement Iron Pentacarbonyl which prompts the planning of metal nanoparticles yet there is oxidation which may prompt the taking to the soaring value. The ratio of underlying materials such as surfactants, solvents, and organometallic compounds will play a significant boundary in determining the size and morphology of the MNPs.[11]

Solvo-thermal Routes:

Aqueous, otherwise known by the term hydrothermal approach, is the technique employed in the production of MNPs as ultrafine powder. The above process was carried out using the fluid media in reactors or autoclaves, under the pressure increased up to 2000 psi and temperature increased up to 200°C. Crystals of many unusual substances are delivered by the interaction with water. This technique is found to be additionally utilized in shaping dislodging free specific crystal particles, and the molecules created using this strategy may possess a higher degree of structural order contrasted with different strategies [12.] Wang et al. used aqueous strategies to make Fe_3O_4 powder. They arranged the nano-sized Fe_3O_4 powder (40 nm) at a temperature of 140°C maintained for 6h making a scattering charge of energy 85.8 emu g-1.

Gas-Phase Synthesis:

Spray pyrolysis, laser pyrolysis, arc discharge and sonochemical are the demonstrated methods that are identified as promising methodologies for the continuous and direct synthesis of distinct MNPs

while keeping all experimental variables under exhaustive control.

Spray Pyrolysis: Spray pyrolysis technique, involves the sprinkling of a homogeneous mixture of solute and solvent passes into the solid in the reactor sequence, solvent evaporation occurs through reactants series, solute condensation as droplets, preceded by chemical decomposition using heat, followed finally by drying up of the particles that precipitate at higher temperatures. By and large pyrolysis-related cycles are utilized in the creation of the attractive nanoparticles which initiates in the presence of Fe3+ ions followed by the portion of the natural segments which go about as reducing agents. Ferric salt is partially decreased by the natural compound in this process, for example, a combination of the Fe+3 and Fe+2, in this way the advancement of the magnetite, which finally oxidized to the maghemite. Without the diminishing agents, hematite is created as an option of the maghemite. Nature of iron antecedent salts in liquor solutions, uniform Fe3 O4 components can be accomplished with the molecule sizes ranging from 5 to 60 nm and morphology. Subunits are principally made of denser components of the round shape, with a normal distance between 6 and 60 nm, which have been generated using ferric nitrate and ferric chloride solutions, individually.[13]

Laser Pyrolysis: When compared to gas heating in a furnace, this method provides for extremely limited warming and rapid cooling. Laser light warms iron precursor in the vaporous blend and the combination of gas streams and makes the small, non-totalled, and slight estimated nanoparticles. The pyrolysis is maintained at optimum experimental conditions, and the size of crystal magnetite nanoparticles changes with tight size circulation ranges of 2-7 nm. This strategy incorporates the progression of gases, which warmed with the normal influx of CO_2 laser, to support the substance response. Using Fe_2O_3 NPs, a biocompatible magnetic scattering was produced by conventional laser pyrolysis of $Fe(CO)_5$ fumes. This strategy utilized a beat CO_2 laser; thusly limiting the time allows the creation of yet more modest particles [14].

Sonochemical Method:
Sonochemical strategy is an option cutthroat technique to extra tedious manufacture strategies and makes new materials for certain momentous properties. The acoustic cavitation brings about the ultrasonic physicochemical impacts, which prompts the readiness of huge and implosive imploding of the fluid air pockets. These give the nearby area of interest a stunning wave or adiabatic pressure in deep of the gas portion of folding eddy. Rules are being portrayed tentatively in remembrance of the above areas of interest, keeping the pace of reducing the temperature past 1010 Ks-1, transitory temperatures of 5000 K, and a pressing factor of 1800 atmosphere. These limit conditions were useful in the development of the new stage and seem to possess a cluster shearing force impingement considerable in the development of the large mono dispersive nanoparticles.[15]

Arc Discharge:
A large number of carbon-covered MNPs are found to be delivered through the circular segment release strategy, in which precursors of the metal are regularly filled inside a cave drill into the graphite anode followed by the curve vaporization. This method can be used to coat magnetic metal carbides. The item is by and large made out of the mixes of divergent carbon; including carbon exemplified metal particles, pieces of graphite, and carbon nanotubes. During aggregation, the metal particles have expansive size circulation [16].

Solid Phase Synthesis:
Carbon typified Magnetic Nanoparticles are created by using strong stage strategies. Occasions mainly depend upon raised temperature strengthening of substances like Cobalt nanoparticles, Fe_2O_3, polymers, Fe, and carbon powders [17]. Though the size of the formed nanoparticles and the properties related to the magnetic strength of a definitive detailing can't be managed, and even the superparamagnetic particles cannot be accomplished since the basic molecule dimensions were normally greater than 10 nm.

Combustion Synthesis:
An ignition reaction is found to be much useful for the manufacture of carbon-exemplified MNPs. Martirosyan et al. shaped, $CoFe_2O_4$, cobalt ferrite, translucent nanoparticles (50-100 nm) through the carbon ignition. In their ignition creation technique, the exothermic oxidation of carbon delivers a warm response wave to multiply all through the strong reactant combination of Cobalt Oxide and Fe2 O3 converting it into the cobalt ferrite. With growing burning temperatures, the normal molecule dimensions of the magnetic nanoparticles were found to be expanded [18].

Hydrogels:
A colloidal gel is usually a gel that will grow incredibly inside the watery arrangement. The gels are normally made out of a hydropic natural

elastomer segment which is interlinked through either non-covalent or covalent bonds. A two-step emulsifier-free emulsion polymerization was used to produce colloidal gels merged with attractive nanoparticles. For example, the thermal delicate magnetic immune spheres were formed by covalently joining bovine serum albumin (BSA), which is of immense value in the immune propensity cleaning against BSA antibodies from antiserum [19].

Evaluation of Magnetic nanoparticles [20]:

Characterization parameters	**Analytical methods/Instrumentation**
Particle size	photon correlation spectroscopy (PCS), transmission electron microscopy (TEM), scanning electron microscopy (SEM)
Surface electrical potential	Zeta potential measurement
Molecular weight	Gel permeation chromatography
Density	Gas pycnometer
Drug Release	In vitro diffusion cell,dialysis bag

CONCLUSION:

Though progress in clinical applications of magnetically targeted carriers has been slow since first introduced in the 1970s, the potential for this technique remains great. Rapid developments in particle synthesis have enabled the use of new materials for more efficient capture and targeting and novel strategies are being developed for applying magnetic fields which could lead to treatments for diseases such as cystic fibrosis and localized cancerous tumors. Though clinical trials are few, the results have been promising. While magnetic targeting is not likely to be effective in all situations, with further development it should provide another tool for the effective treatment of a variety of diseases.

S. No	Nanoparticles	Therapy	Application	Reference
1.	Iron oxide nanoparticles with dextrancoating	Herpes simplex virus vector	Intra-arterial	Rainov et al. 1995 [21]
2.	Iron oxide nanoparticles	L6 IgG monoclonal antibody	Intravenou intraarterial, intratumoral	Remsen et al. 1996 [22]
3.	Iron oxide nanoparticles with starch coating	*In vivo* application of magnetic nanoparticles in cancer therapy. Mitoxantrone	Intra-arterial	Alexiou et al. 2000 [23]
4.	Iron oxide nanoparticles (Fe_3O_4)	Hyperthermia	Intratumoral	Hilger et al. 2002 [24]
5.	Iron oxide nanoparticles (Fe_3O_4)	Iron oxide nanoparticles (Fe_3O_4) within liposomes	Intratumoral	Tanaka et al. 2005 [25]
6.	Iron oxide nanoparticles (Fe_3O_4) with dextran coating	Anti-VEGF monoclonal antibody	Intratumoral	Chen et al. 2006 [26]
7.	Ironoxide nanoparticles (Fe_3O_4)coated with poly lacticacid	Arsenic trioxide	Intravenous	Li et al. 2007 [27]
8.	Iron oxide nanoparticles (Fe_3O_4) with aminosilane coating	Hyperthermia	Intratumoral	Johannsen et al. 2007 [28]
9.	Iron oxide nanoparticles with dextran coating and ^{111}In-marked L6monoclonal antibody	Hyperthermia	Intratumoral	DeNardo et al. 2007 [29]
10.	Iron oxide nanoparticles with polylysine coating	NM23-H1 gene (an anti-metastatic gene)	Intravenous	Li et al. 2009 [30]
11.	Iron oxide nanoparticles (Fe_3O_4)	Hyperthermia (alternating magnetic field)	Intravenous/intratumoral	Balivada et al. 2010 [31]
12.	Iron oxide nanoparticles (Fe_2O_3,Fe_3O_4)	Hyperthermia (alternating magnetic field)	Intratumoral	Bruners et al. 2010 [32]
13.	Iron oxide nanoparticles with PEG coating	Arginine-glycine-aspartic acid or chlorotoxin	Intravenous	Fang et al. 2010 [33]
14.	Iron oxide nanoparticles with dextran coating and binding for tumor-specific antigenuMUC-1	siRNA against BIRC5	Intravenous	Kumar et al. 2010 [34]
15.	Iron oxide nanoparticles with dextrancoating	Human adenovirus type 5 early region 1A (E1A)	Intratumoral	Shen et al. 2010 [35]
16.	Iron oxide nanoparticles (Fe_3O_4)	Adenoviruses	Intratumoral	Tresilwised et al. 2010 [36]

17.	Iron oxide nanoparticles (Fe_3O_4) with aminosilane coating	Hyperthermia	Intratumoral	Maier-Hauff et al. 2011 [37]
18.	Iron oxide nanoparticles with PEG coating	Apoptosis inducing peptide	Intravenous	Agemy et al. 2011[38]
19.	Iron oxide nanoparticles with dextran coating	Hyperthermia	Intratumoral	Dutz et al. 2011 [39]
20.	Iron oxide nanoparticles with polyethylene coating	Plasmid DNA comprising a cytokine gene	Intratumoral	Plank et al. 2011 [40]
21.	$Mn_xZn_{1-x}Fe_2O_4$ coated with humanalbumin and folate	Radionuclide ^{188}Rhenium cisplatin	Intratumoral	Tang et al. 2011 [41]
22.	Iron oxide nanoparticles	Hyperthermia	Intratumoral	Wang et al. 2012 [42]
23.	Iron oxide nanoparticles coated with starch and dextran	Hyperthermia	Intraperitoneal	Toraya-Brown et al. 2013 [43]
24	Superparamagnetic iron oxide (SPIO) nanoparticles	Hyperthermia	Sub cutaneous	Russell, B. *et al.* 2021[44]
25	PEGylated Starch-Coated Iron Oxide Nanoparticles	Photothermal therapy	Intravenous	Amatya, R. *et al.2021* [45]

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