An overview of the applicability of magnetic nanoparticles in biomedical sciences

Maitreyee Khargharia, Kashif Raees

Department of chemistry, UIS, Chandigarh University, Mohali140413, India

Email:raeeskashif@gmail.com

ABSTRACT
Small objects with magnetic characteristics, usually less than 100 nanometers in size, are known as magnetic nanoparticles. Iron oxide, cobalt, nickel, and other magnetic materials are just a few examples of the materials that can be used to create these particles. Numerous possible uses for magnetic nanoparticles exist in industries like biomedicine, electronics, and environmental science. They can be utilized in bioengineering for magnetic hyperthermia, cancer therapy, targeted drug delivery, and magnetic resonance imaging. Various techniques, like chemical precipitation, heat breakdown, and solvothermal approaches, are frequently used to create magnetic nanoparticles. Magnetic nanoparticles can be covered with biocompatible substances for biological uses to increase their durability and lessen their toxicity. Magnetic hyperthermia, a cancer therapy that employs magnetic nanoparticles to produce heat in tumors, is another application for magnetic nanoparticles. Overall, MNPs have a diversity of potential applications and are still a hot topic for research and development. This review comprises of various magnetic nanoparticles like iron, cobalt and nickel, their synthesis and surface modification, along with their applications in biomedical sciences.

KEYWORDS
Magnetic Nanoparticles, Synthesis, Biomedical application, Nanomaterials, Iron oxide, Magnetic resonance imaging

1. INTRODUCTION

European Commission states that "the particle size of at least half of the particles in the number size distribution must measure 100 nm or below." Nanoparticles are materials that are extremely small in size. One of the factors contributing to nanoparticle success is their employment as nano catalysts, that has sped up reactions and increased the effectiveness of the end products. The surface generated in nanomaterials to perform homogeneous/heterogeneous reactions is the most crucial functional component of nanoparticles, and the whole reaction process is in the nanoparticle surface's advantage [1]. For a wide range of reasons, including the following generally, magnetic nanoparticles are employed in science: these nanoparticles are produced as a nucleus structure, with the core made of 2:3 iron oxides (Fe II/Fe III) and the shell created by silica coatings or the like. Magnetic nanomaterials are employed as nano catalysts in chemical and biological processes to boost up the reaction process and finally produce a new product as well as to enhance these reactions by modifying the potential environment [2]. The suitable qualities of magnetic nanoparticles are; simple production, low toxicity, extraction without loss of nanomaterials, avoidance of mixing with appropriate coatings, and lastly great efficiency of chemical and biological processes [3].

As nano evolved, many varieties of these were created as nano catalysts. The hollow, core/shell-shaped nanomaterials are organized in a tidy structure to create a tidy set. The following is how nanomaterials are categorized: Has open pores that can accommodate any type of linker, is branched to carry any type of useful molecule, could form gravitational bonds with both organic and inorganic poles, and is formed as a multilayer and polymorphic structure that can produce linear and annular chelates with the same molecules. Lastly, has an electric and magnetic field to travel in the field that is formed by electrons. Among these nanoparticles, magnetic nanoparticles are becoming increasingly popular and have found use in virtually every sector of science [4].

Due to their ability to be controlled by magnetic fields, magnetic nanoparticles (MNPs) are particularly useful for biomedical applications that place a focus on the creation of smart materials. Magnetic nanomaterials have been broadly utilized in hyperthermia, desired drug delivery systems, image analysis, the separation of biological molecules, leading to the hypothesis that they are also a key tool in the treatment of cancer [2]. Due to their ease of functionalization with polymers and other materials, iron oxide nanoparticles, has been used extensively at in vitro testing and even today for other purposes. The most prevalent infectious illness in the oral cavity is thought to be tooth decay, which causes permanent damage to the hard, outer layer of teeth. There are many cariogenic bacteria, including as Actinomyces species, Nocardia species, and Streptococcus species, which may create acid and, as a result, cause tooth caries [5]. Researchers Samira and Fereshteh (2022) investigated the biological activity of magnetic iron oxide nanomaterials, its bacterial production, as well as the effectiveness of Acid Red 88's biodegradation. A bacterial strain S2 that can produce iron oxide nanomaterials was identified from the sand of the Choghart iron mine. A 16S rDNA sequence comparison resolution was used in the phylogenetic analysis, which revealed that 99.68% of strain S2 was identical to Bacillus zhangzhouensis [6].

Magnetic Iron Oxide Nanomaterials (MIONs) have drawn a lot of interest, particularly for usage in several medical fields such as MRI, stimuli responsive medication delivery, bio separation, and magnetic hyperthermia (MH) [3]. Iron-manganese oxide ($MnxFe_2$-xO_4) magnetic nanomaterials, incorporated in electro spun polyacrylonitrile (PAN), that gives durability and chemical tolerance, provide magnetic stimulation capacity for the catalytic activity. The magnetic nanomaterials (average size d = 40 7 nm) which have been initially made using quick as well as environmentally friendly sono-chemical method, and they were then incorporated into electro spun PAN nanofibers. A superhydrophobic surface with diameter of average 760 to 150 nm was provided by the final MNFs [7]. One of the most essential chemicals in the polyurethane industry, aniline is made when nitrobenzene is catalytically hydrogenated. Therefore, it is crucial to design new, multipurpose catalysts that are simple to recover from the reaction mixture. Sono chemical and combustion methods were used to produce transition metal-adorned palladium ferrites. In order to support palladium nanomaterials throughout the catalyst synthesis process, magnetic ferrites were first manufactured.

The ferrite particles were coated with "Pd" nanomaterials employing ultrahigh sonication during an alcoholic phase. Magnetic catalysts made of Pd/$NiFe_2O_4$, Pd/$ZnFe_2O_4$, and Pd/$NiZnFeO_4$ were all produced [8]. Huizhang et al, have created near-monodisperse $Ag_{@}Ni$ and $Ag_{@}Co$ nanoparticles with variable layer width using a versatile one-pot seed-growth technique. These NPs may be recycled magnetically and are superparamagnetic at room temperature. For the production of hydrogen gas from the hydrolysis of $NaBH_4$ in aqueous solution, excellent catalytic ability has been discovered [9]. Thermochemical inactivation of -amylase resulted in an increase in enthalpy (4.2-fold), a reduction in entropy (4.6-fold), and an increase in free energy (1.1-fold). Ch-MNP/PEI/GA/pH Enzyme's stability significantly increased, notably at alkaline pH levels. The enzyme Ch-MNP/GA/PEI Enzyme also maintained 83.2% of its starting activity after 15 consecutive cycles. The residual activity after 21 and 40 days of Ch-MNP /GA/PEI Enzyme storage at 4 C was 100% and 86% respectively. Finally, the immobilization method improved the catalytic durability as well as characteristics, increasing their usefulness for commercial operations that need less time and money [10]. Research on catalysis continues to focus on the creation of base metal catalysts for crucial industrial operations. Inside this study, the impacts of pyrolysis temperature on the morphological, architectural, surface, magnetic, catalytic characteristics of nickel nanoparticles (NiNPs) coated on silica were examined. The first successfully produced mono-dispersed Ni nanoparticles were encapsulated in graphitic shells, and they were categorized by high resolution transmission electron microscopy (HR-TEM), BET surface area measurement, X-ray photoelectron spectroscopy (XPS), CO-pulse chemisorption, XRD, superconducting quantum interference device (SQUID) measurement [11].

Due to their many distinctive characteristics, magnetic nanomaterials have a great deal of promise in environmental, biological, and therapeutic applications [12].

Strong reducing agents like iron enable the conversion of wide range of inorganic as well as organic pollutants, especially chlorinated solvents, found in polluted water sources to less dangerous ones. Numerous studies have shown that highly reactive nZVI may efficiently destroy various persistent pollutants, including pesticides and polycyclic aromatic hydrocarbons (PAHs) [13] [14][15]. Magnetic nanoparticles, particularly those made of nano zero-valent iron (nZVI), maghemite (g-Fe_2O_3), magnetite (Fe_3O_4), are among most extensively utilized nanoparticles and have inspired intense interest in engineering studies to clean up polluted water or environments beneath. One the most well-known instances is the subsurface insertion of nZVI to create responsive treatment areas. nZVI has the ability to immobilize or convert organic contaminants like chlorinated solvents and heavy metals like arsenic and chromium to less hazardous forms. Laboratory results are not the only indication of nZVI's efficacy. There are several businesses that have been developed to produce nZVI and use it to clean up the environment [16].

Due to the potential for employing magnetic fields to recover or purify nanomaterials, their magnetic characteristics are of interest in industrial applications [17]. Iron oxides Fe_2O_3/Fe_3O_4, genuine Fe and Co metals, and ferromagnets of the spinel type $MgFe_2O_4$, $MnFe_2O_4$, or $CoFe_2O_4$ may all be utilized as bases for the creation of nanoparticles [18]. The use of nanomaterials at petroleum as well as gas sector is a topic that major oil firms are studying in depth, as shown by the enormous sums of money spent in research and development related to nanotechnology. Recently, there has been a lot of research done on nanotechnology for various uses in oil and gas sector, including drilling fluids, better oil recovery, and other uses including cementing and well stimulation [19].

2. SYNTHESIS

Iron oxide nanomaterials (-Fe_2O_3 and Fe_3O_4) [20][21][22], ferro magnet spinel-type $MgFe_2O_4$ [23], $MnFe_2O_4$ [24], and $CoFe_2O_4$ [25][26] are only a few examples of the many compounds and phases found in magnetic nanomaterials. In recent times, much research on the production of nanoparticles has been carried out. There have been several studies, particularly in the last few years, that detail high-efficiency techniques for synthesizing monodispersed magnetic nanoparticles with form control, excellent stability, and tiny sizes. To produce high quality magnetic nanoparticles, number of techniques have been extensively employed and contains thermal breakdown, co-precipitation, microwave assistance, biological way, microemulsion, hydrothermal approach [27]. According to Fig. 1, techniques for creating magnetic nanoparticles may generally be categorized.

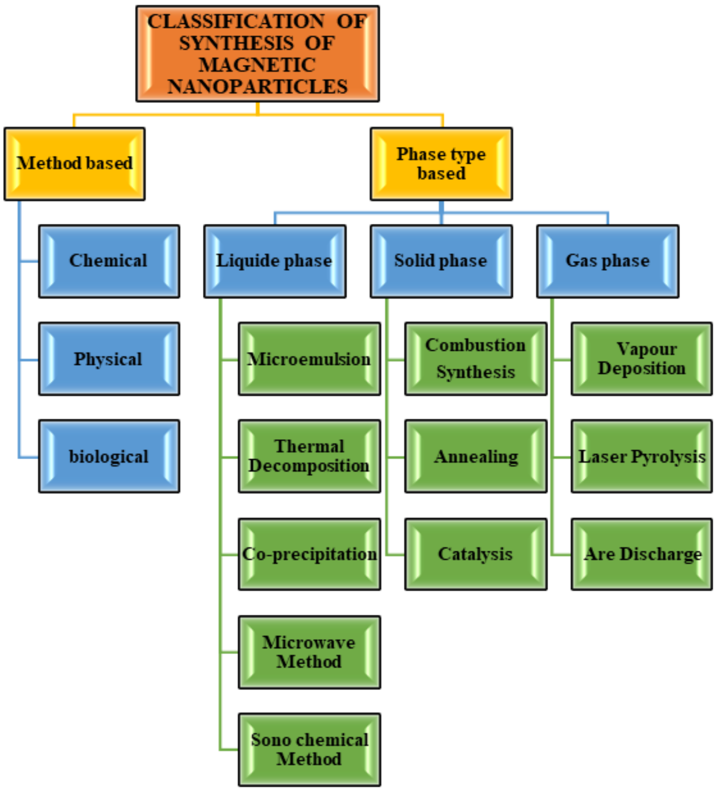

Fig. 1: Methods for the synthesis of Magnetic Nanoparticles

2.1 Precipitation of products from solutions

It is one of the earliest methods for making NPs. In precipitation reactions, a precipitating agent is added after the metal precursors have been dissolved in water like solvent, a solid that is insoluble when added. The primary benefit of precipitation processes is the production of enormous amounts of particles [28]. A homogeneous precipitation reaction is typically used to create uniform particles; this reaction involves the separation and development of the nuclei [29].

2.2 Coprecipitation

The most popular and effective approach for creating MNPs with regulated sizes and magnetic characteristics is co-precipitation [30]. Due to the simplicity of application and the lack of dangerous ingredients and procedures, it is widely employed in biomedical applications [29].

There are two steps to the co-precipitation process: first, a modest amount of nucleation takes place when the species concentration reaches a supersaturation threshold, and second the nuclei steadily expand (by dissolving the solvents on the particle surface). These two procedures must be separated in order to create monodispersed MNPs [31].

2.3 Hydrothermal Method

Several researchers have reported the successful synthesis of magnetic nanoparticles using the hydrothermal process, also known as solvothermal process. Beads of numerous materials have been produced successfully with this method. Typically, these reactions take place in aqueous medium at high pressures (4.3 MPa) in autoclaves or reactors and the temperature of 120 to 250 °C is maintained during the reaction. In these circumstances, water acts as a starting material and speeds up the rate of the reaction: the precursor's solubility rises and they become more mobile due to the water's reduced viscosity, resulting in a quicker Ostwald maturity and improved homogeneity and crystallization of MNPs [28][32].

One of the most effective process for making crystals of various things is the hydrothermal method [33]. As a contrast, the hydrothermal approach uses a variety of wet-chemical techniques to crystallize substances from aqueous solutions at temperature130 to 250 °C and having high pressures [34].

2.4 Thermal Decomposition Method

Thermal decomposition is now a most dependable processes for generating good MNPs for a variety of purposes. The initial results of thermal breakdown to produce superior semiconductor crystals, and this process has now been expanded to include the creation of magnetic nanoparticles [35].

Three steps make up the thermal decomposition process for the creation of magnetic nanoparticle. These are nucleation, formation of small nanocrystals and particle growth. Small nanocrystals start to form when the solution is warmed once more to solvent's boiling point. Finally, the solution is cooled at room temperature after being refluxed at higher temperature for a while to form nanocrystal. Each stage is carried out in a sealed environment with an inert atmosphere [31]. Particle size is a crucial factor in biomedical applications like MRI, hence MNP synthesized with this technology may be useful in these fields [36][37]. The exact regulation of size and morphology may also depend on the reaction's temperature, duration, and ageing period [18].

2.5 Microemulsion

A thorough examination is required to determine the impact of process parameters on the characteristics of nanoparticles, however the microemulsion is a technology that shows promise since it allows for greater control of nanoparticle's form and size [38].

Recently, the microemulsion technique has been extensively investigated for synthesizing the nanoparticles [39]. Microemulsions are thermodynamically stable colloidal suspensions in which surfactants enable the coexistence of two originally impermeable fluids in a single phase. Inouye et al., the first team to synthesize magnetic nanomaterials inside the microemulsion by oxidizing iron salts, even though Schulman et al. were the ones to coin the term microemulsion [18]. Since then, it has been shown that making microemulsions is an easy, convenient way to make MNPs [32].

In the presence of surfactant, the dispersion of water and oil forms a thermodynamically stable microemulsion. At the water and oil interface, surfactant molecules may form a single layer, with the hydrophilic head groups in the aqueous phase and hydrophobic tails dispersed in oily phase [34][40]. This process has various advantages over other ones, such as the usage of simple tools, the capacity to synthesize a wide variety of materials with exact control over particle composition and size the creation of nanomaterials with crystalline composition and large specific surface area, the use of simple synthesis conditions, and close to atmospheric temperature and pressure [41]. With a higher saturation magnetization, microemulsion process produces smaller particles [34].

2.6 Sol-gel Method

K. Chandramauli et al(2023), Sol-gel auto-combustion is used to create Cr substituted Cu-Co ferrite Cu0.7Co0.3Fe_2xCrxO_4 series (with = 0.00 to 0.25 in increments of 0.05) nanoparticles. Scherrer equation has been utilize to find the crystallite sizes of the prepared samples, which range between 19 to 44 nm. For concentrations up to x = 0.1, the lattice constant is shown to decrease; higher concentrations of chromium, however, have seen a little increase in the lattice constant. Sol-gel auto combustion has been used to create complex ferrite nanomaterials [42]. Additionally, crystallite size of the sample, as determined by XRD data, fell between 19.28 to 32.92 nm. The computed lattice constants range from 8.4099 to 8.4441. The FTIR data showed that after the doping of Cr ions, the spinel structure remained unaltered. The materials show as polygonal-shaped grains in FESEM pictures, while sometimes irregularly shaped gains with mild aggregation emerge [43]. First, sol-gel chemical synthesis was used to create MgxCa (0.90-x) Zn0.10Fe_2O_4 nanomaterials. Sol-gel process was also used to create materials that are almost identical and have good adjustable electromagnetic characteristics. All raw materials are purchased from SIGMA-ALDRICH, USA in hydrate form, including Mg nitrate, Ca nitrate, Zn nitrate, Fe nitrate, and others [44]. A new two-step surfactant sol-gel method is used to create Fe_3C/few-layered graphene core/shell nanomaterials submerged in a carbon matrix, with the hydrolysis, polycondensation, and drying processes all occurring in the same pot. The current method is relied on how oleic acid and oleyl amine interact, acting on the precursor micelles when a densification temperature given in a reducing environment [42] on the microwave-sintered $NiTiO_3$ nanomaterial sol-gel synthesis. Crystal structure was established using X-ray diffraction and the activation energy was found to be 0.04 eV. The M-H curve showed superparamagnetic behavior at ambient temperature [45].

2.7Sonochemical Method
Iron oxide magnetic nanoparticles (NPs) were synthesized on a wide scale utilizing a straightforward sonochemical method employing cheap and non-toxic metal salts as starting materials. By using XRD, TEM, EDS, and VSM, the magnetic iron oxide NPs as-prepared have been characterized. Fe_3O_4 NPs were effectively synthesized via a sonochemical method, as shown by X-ray diffraction and EDS analyses [46]. MNPs were created in this work using the sonochemical coprecipitation approach. Analysis using XRD and FTIR supported the creation of the spinel structure. The superparamagnetic behavior of these MNPs was validated by the study of the magnetic behavior of the MNPs utilizing VSM [47].

3. TYPES OF MAGNETIC NANOPARTICLES

3.1 Iron oxide-based nanoparticles
Super-paramagnetic iron oxide nanomaterials (SPOINs) have unequalled magnetic capabilities, are nontoxic, very affordable, biocompatible, and can be recycled or reused using basic magnets [48].

Due to its deep tissue penetration, magnetic hyperthermia relied on nanomaterials has garnered significant interest and is thought to be a viable technique for treating cancer. Specific absorption rate (SAR), which measures the effectiveness of magnetothermal conversion, is a crucial factor that profoundly affects the outcomes of therapy. Magnetic hyperthermia is indicated by high SAR effects might be obtained without using an excessive number of nanoparticles, lowering the possibility of negative side effects issues. Iron oxide nanomaterials with high SAR are thus widely desired. Two heat generating processes for iron-oxide NPs, namely hysteresis loss and relaxation loss, have been studied extensively [49].

By employing citric acid as that of the fuel and iron nitrate as that of the oxidizer in a solution combustion synthesis, magnetic iron oxide nanomaterials were created. It was examined how the features of nanomaterials were affected by the combustion reaction ignition process, microwave heating, conventional heating. The SEM and TEM, thermogravimetric and DSC, X-ray powder diffraction, magnetic measurements, adsorption-desorption isotherms, specific surface area were used to categorize the produced nanomaterials [50].

As bearers for aimed drug delivery, magnetic separation and cellular selection, tissue repair, MRI, magnetofection, and other applications, magnetic nanomaterials—such as magnetite (Fe_3O_4) and maghemite (-Fe_2O_3)—have a number of exceptional properties [51][52][53][54][55][56][57][58]. Magnetic nanoparticles must have a variety of characteristics, to be used in biomedical applications. Furthermore, a protective coating that is non-toxic and biocompatible must be coated to the MNPs. In addition to providing the necessary surface qualities, the biocompatible layering of the surface must prevent the aggregation, sedimentation, microbial degradation of nanomaterials. It must also provide good colloidal stability in an aqueous carrier [50].

Cell separation, immunoassay, hyperthermia, drug administration, tissue regeneration, tumor targeting are just a few of the uses for inorganic magnetic iron oxide nanomaterials, which have the chemical formula Fe_3O_4 [59].

3.2 Nickel based nanoparticles

The magnetic material known as nickel ferrite spinel was created for a variety of engineering purposes, including the development of magnetic devices, switching devices, permanent magnets, anti-cancer medications, color imaging, drug delivery, microwave absorbers and catalysis etc. [60][61][62] By using the sol-gel process, Ti-doped Ni ferrite and Copper-doped Ni ferrite nanomaterials were created. Utilizing XRD, SEM, and UV, the produced nanoparticles were analyzed to determine their structure, shape, and optical properties [63][64] demonstrated repeatedly over nickel (Ni) micro pads included in a microfluidic system, core-shell magnetic nano-particles could be effectively aggregated and limited. This technique improved the 4-mercaptobenzoic acid SERS signal's constancy and potency (4-MBA). The electrochemical reduction of Ni ions by autocatalytic plating, such as using $NaPO_2H_2$ in either basic or acidic conditions, provides the basis for the simple and speedy chemical process of electroless coating of Ni-P [65].

3.3 Cobalt based nanoparticles

Cobalt (Co) and Cobalt oxide nanoparticles, which may unintentionally develop in working environments, can be employed in catalysts, pigments, magnetic fluids and gas sensors, and in other energy storehouse applications [66]. Under ideal circumstances, 1, 2-dichloroethane was utilized as a solvent and t-BuOOH was used as an oxidizing agent, and cobalt ferrite magnetic nanomaterials with mean diameters 25 nm was employed as an effective catalyst. With aid of an outer magnet, it was simple to detach the catalyst from the reaction medium, and the catalyst may be recycled several times without losing its effectiveness [67]. Metal oxide NPs have been shown to preferentially used against tumor cells and being non-toxic to healthy cells. Most common cancer in children and in adults is leukemia. Among the known methods for synthesizing nanoparticles, the use of nanoparticles has recently emerged as a straightforward, efficient, affordable and environmentally responsible method [68]. Epoxy resin has been mixed with various cobalt ferrite nanoparticle concentrations. Through the use of XRD, FTIR, and FESEM, the synthesized compositions have been studied. The morphological characteristics show that Co ferrite has been arranged as agglomerated grains with sizes between 0.31 and 0.72 micrometers. The goal of this study is to draw attention to how crucial nanofillers are to the mechanical characteristics of epoxy resin [69].

4. Surface Modification

To enhance the ION’s properties, such as reducing self-aggregation and boosting stability, materials such as polymers, surfactants, inorganics like silica, organics like oleic acid are sometimes coated on them. The intricate interactions between polymers and surfactants have the power to change a solution's wettability, foaming behavior, viscosity and detergency [70].

Recently, it has been investigated to modify the characteristics of MNPs by surface modification or coating utilizing biocompatible compounds like polyvinylpyrrolidone (PVP), polyethylene glycol (PEG), polyvinyl alcohol (PVA), dextran. Iron oxide nanoparticles must have a polymer coating that is non-antigenic, protein-resistant, and increases blood spin time. Effects of coating agent adsorption on the behavior of magnetic iron oxide have been the subject of many investigations. The synthetic polymer polyvinyl alcohol is one of them. Its flexibility and low toxicity enable it to adhere to magnetic iron oxide nanoparticles, preventing their attraction to one another or agglomeration. Co-precipitation is one of the techniques that have been discovered to create polymeric magnetic nanoparticles [71][59].

Polymeric biomaterial: Because of their elasticity, variety, and high density of energy, polymeric substances are impressively exploited for layering and surface functionalization [72]. According to the classifications made [73][74][75][76], they may be either conducting, non-conducting, charged, or neutral, homopolymer or copolymer hydrophilic or amphiphilic, manufactured or natural.

Non-polymeric substances: The stability of NPs through creation of micelle and liposomes, small organic compounds often utilized include surfactants, carboxylates, and molecules of organophosphorus [73]. To boost the hydrophilicity of the MNPs, many chemical compounds have been utilized, including vitamins, dopamine, amino acids, cyclodextrin, dimercaprol succinic acid. Carbon: To improve the biocompatibility, dispersity, and stability of MNPs, inorganic materials based on carbon such as carbon dots, carbon NPs, carbon nanotubes, as well as graphene are also utilized as surface coatings. To maintain the unique properties of MNPs, a biocompatible, hydrophilic coating material called silica is utilized [76]. The positively charged core substance of magnetic nanoparticles are insulated from electrostatic and steric charges by the polymeric silica layer thanks to their bond. This material is often used in diagnostic and therapeutic purposes because of its excellent water solubility, heat resistance, wide surface area, superior mechanical toughness, and subsequent functionalization.

Metals: Because of its durability and compatibility, silver and gold like metals are often utilized for surface coating. These metals are typically expressed as core-shell, satellite, dumbbell -like structures.

Due to their distinctive characteristics, gold-coated MNPs are widely employed in applications such as enzyme immobilization, immunoassays, bio separation and purification, and diagnostics. MNPs with silver coatings have better biocompatibility and magnetic and optical characteristics [77]. There have been reports of peroxidase and antibacterial activity in silver-decorated MNPs. Such magnetic nanoparticles have also found use in in vitro diagnostics, nucleic acid biosensing, and other fields [76].

5. BIOMEDICAL APPLICATIONS OF MNPs

5.1MRI

Of all the applications for aimed iron oxide nanomaterials, molecular imaging is definitely the most promising. In vitro and animal research have looked at specific applications for iron oxide nanomaterials [78].

The primary use of MRI is as a diagnostic technique which enables non-invasive viewing of internal organs and also other bodily components. Two physicists, independently noticed in 1946 that materials like water or paraffin will absorb and release energy when subjected to magnetic oscillations at radio frequencies under a high magnetic field. The immediate chemical environment around the nucleus considerably affects these relaxation durations, which is why changes in tissue provide somewhat varying contrast. By reducing relaxation durations and enhancing tissue contrast, contrast agents are used in MRI to enhance the visibility of aberrant disease [73]. Due to the high amounts of carbohydrates and water in our bodily tissue, the standard hydrogen MRI may detect background noise signals (1H-MRI). Other naturally occurring hetero nuclear based MRI contrast agents have been created to address the issue, including C, P, F, O, and N. Particularly, the use of fluorinated perfluorocarbons as contrast agents for many numbers of medical applications, including lung imaging, cell tracking, and tumor identification, has drawn significant interest. However, a crucial factor in their use as MRI contrasts is efficient renal clearance and successful target imaging. Novel dual (T1 and T2) MRI contrast agents based on manganese (Mn) were developed. Using Mn and nano texaphyrin-phospholipid blocks, this comparison was established (Mn-nano texaphyrin). Excellent stability and flexibility to release manganese were shown by this nano contrast [79][80][81]. In addition, MRI contrast agents alter the surrounding tissues' MRI-detected relaxation times. Different contrasting chemicals are used in the MRI method [55].

5.2Cancer Therapy

Furthermore, just 35,000 of the approximately one lakh distinct types of chemicals in our environment have been researched, and only around 300 of them have been shown to cause cancer. Remaining sixty-five thousand substances in nature have not yet undergone testing. Uncontrolled cell division, which results from environmental influences and genetic problems, is the cause of cancer [82].MNPs have a significant deal of potential for producing heat in applied magnetic field and raising the malignant tumor's temperature to 42–45 °C [83]. Radioimmunotherapy (RI) is a kind of cancer treatment that combines radionuclides and antibodies [12]. Radioisotopes that are often employed for therapeutic purposes generate ,particles, or Auger electrons, damage DNA via a variety of processes, including the formation of ROS, and impair DNA repair [84]. The hypoxic condition of the tumor cells, which allows for decreased ROS generation, poses challenges for RI, such as poor permeability and radiosensitivity [85]. Biocompatibility, simplicity of surface functionalization, high surface volume ratio of SPIONs make them popular in RI [84].

5.3Drug Delivery

It is a process which disperses bioactive substances or components at a certain location. A recent situation shows that in order to take advantage of different therapeutic treatments by offering a safe delivery method, it is necessary to innovate focused medication delivery. In the realm of nanomedicine, IONPs are among the most widely used theragnostic tools for precise and regulated drug administration [55]. Drug delivery (targeted) and therapy aim to bring a medicine directly to the root of the illness and treat it deliberately without having any harmful effects on the body in a range of situations [86]. In drug delivery, there are 3 fundamental purposes: directing the medication to the intended place, lowering the drug's adverse outcome on the organs or tissues nearby, and managing the drug's release to prevent the traditional overdosing/underdosing cycle. MNPs provide a strategy for achieving these objectives. As a result, the layer on the surface of MNPs has been tuned to regulate drug delivery, drug release, and drug load in the required field. The aim of surface coating is to provide MNPs functional groups so they are more suited for drug combination, in addition to lowering toxicity and improving biocompatibility. MNPs have a broad range of uses in targeted drug administration due to their special characteristics, including magnetism and simplicity of manipulation using an (EMF), which directs drug-carrying MNPs to the desired location [87]. Nanotechnology-based drug delivery systems have greatly enhanced drug delivery since the medication's pharmacokinetics have changed, extending its time in the circulation, lowering its toxicity, and lengthening its half-life. Use of MNPs as drug delivery vehicles is now becoming prevalent owing to their special features in addition to those found in other nanomaterials [88]. The limited effectiveness, poor absorption, and low selectivity of traditional drug delivery methods make them unsuitable for treating a wide range of medical conditions. These factors make it tough to deliver therapeutic doses of drugs to the appropriate targets at the appropriate times and in the appropriate quantities. Use of MNPs for regulated medication delivery may eliminate these drawbacks and issues. By precisely targeting the intended tissue or organ, magnetically controlled drug delivery achieves two drug delivery milestones: decreasing the side effects of the treatment and allowing the drug to be released in a regulated manner without the usual underdosing cycle/overdosing issues. It serves as most effective and widely applied method for getting the drug to the intended location [89]. Passive or active targeting of IONs might cause tumor sites to accumulate. Nanoparticles may erupt from the circulation and penetrate tumor cells via the increased permeability and retention (EPR) effect, known as passive targeting. Responsiveness of magnetic nanoparticles to a magnetic field is used, however, in active targeting with an applied magnetic field. Additionally, IONs may be functionalized with targeting ligands, dipped with natural and synthetic polymers, surfactants, fatty acids, which enables the use of these nanomaterials as drug delivery systems with better pharmacokinetics and selectivity [90].

5.4Hyperthermia

Hyperthermia, a method where cancer cells are heated to temperatures between 41 to 47 C, may destroy cancer cells. Iron oxide nanoparticles, which exhibit minimal toxicity, simple production, and favorable physicochemical features, are the most popular nanomaterials employed for applications of hyperthermia. To maximize the therapeutic impact and decrease the required dose and side effects, this therapy may be coupled with the precise delivery of 11 of 25 therapeutic medicines into the tumors cells [90].

For the applications of magnetic hyperthermia, iron oxide nanomaterials with excellent magnetic heating effectiveness are particularly sought. High SAR reduces the danger of side effects and administration issues by allowing magnetic hyperthermia effects to be accomplished without using large amounts of nanoparticles. Iron oxide nanoparticles with high SAR are thus widely desired [49]. The IONPs are susceptible to hyperthermia, which may be influenced by the use of an A [6]. When a tissue's temperature rises over what is deemed medically appropriate, hyperthermia occurs in living tissues. Cancer treatment uses hyperthermia to destroy cancer cells. Additionally, it is used to induce local drug release from thermosensitive vehicles [2, 3]. To successfully treat cancer cells using hyperthermia, the temperature of the cancer cells has to be raised to between 43C and 45 C. As a result, a raise in temperature of 6–8 C is needed. Fast hyperthermia-based therapy is made possible by iron oxide nanoparticles' ability to give strong heating performance at a low dosage [51].

5.5Bio-separation

A technology called biosensing turns certain bio-recognition activities into quantifiable signals. The analytical tools that do biosensing are under the category of biosensors. Recently, the terms "nano biosensor" and "nanotechnology" have been combined. By identifying particular pathogens in the provided sample, nano biosensors aid in the diagnosis of illness. To guarantee early illness diagnosis, it is crucial to create accurate, quick, and sensitive pathogen detection methods. Therefore, there is a significant need for quick, affordable, and accurate biosensing techniques. It has previously been shown that magnetic IONPs can find a variety of diseases. Therefore, magnetic IONP-based nano biosensors have applications for both pathogen detection and biosensing, resulting in a multifunctional approach to disease diagnostics [55][91]. For many years, magnetic bio separation has been a crucial step in many bioscience disciplines. Different separation techniques are being explored. There are many ways to create and modify magnetic nanoparticles, and interactions that take place when biomolecules bind to magnetic nanoparticles are also reported. To demonstrate the effectiveness of the magnetic bio separation technology, certain real-world instances of magnetic bio separation procedures are also described [92].

5.6 Cell labelling

A controlled cell labelling technique using ultra-small, superparamagnetic iron oxide nanomaterials is described in the lesson. This process could make almost all cell types sufficiently magnetic so that they can be detected by high-resolution MRI and perhaps subjected to magnetic manipulation. Here, we outline the key criteria that must be met throughout the labelling process in order to effectively utilize labelled cells, measure the magnetic load, and distribute or follow-up magnetic cells. Additionally, we provide some suggestions for MRI-based cell identification and quantification, as well as specific magnetic guidance on a few real-world in vitro and in vivo case studies [93]. Chemical coatings which have a efficiency of high cell labelling without having any toxicity effects can be very beneficial for cellular imaging because they give more control without the use of transfection agents, which can be more expensive, have potential toxicological repercussions, and need to have their own clinical approval [94].

5.7 Gene delivery

Magnetic nanomaterials are been used in medicine as a gene delivery, mainly as contrast-enhancers for MRIs. However, magnetic particles must first have their surfaces altered to allow the attachment of the target molecules, as was mentioned above, in order for them to function as efficient carriers for Deoxyribonucleic acid or medicinal drugs. As an alternative, targeted molecules might be included in a shell that degrades over time, releasing the molecule as it does [95]. The vast ability of gene therapy to heal deadly, incurable illnesses has not yet been fully appreciated. Strong research efforts are now being made in this area to develop less hazardous and more effective methods. The use of nanoparticle technology to fundamental biological and clinical research has advanced quickly. Another crucial factor is nanoparticle size, however there aren't many studies on it. MNP size has considerable effects on transfection efficiency because cells endocytose MNPs. Magneto plex is created by PEI-MNPs, increasing its impact on the magnetic force [96].

6. CONCLUSION

Magnetic nanoparticles have shown a high possibility for implementation in a variety of study and commercial areas, including physics, chemistry, electronics, environment, and healthcare due to their distinctive characteristics. Magnetic nanomaterials have some drawbacks, including decomposition, clustering, loss of magnetic characteristic, and bad store durability. These restrictions can be removed by stabilizing nanomaterials using appropriate covering materials like plastics, metal, metal compounds, silica, and other artificial and organic safe materials. In this review article, magnetic nanoparticle's synthesis, their surface modification, types of magnetic nanoparticles like iron, nickel and cobalt have been successfully discussed. Biomedical applications of magnetic nanoparticles like magnetic hyperthermia, MRI, cancer therapy, drug delivery, bio separation, cell labelling, gene delivery has also been reviewed.

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