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Magnetic nanoparticles (MNPs): Design, characterization, release mechanism and remote-controlled application for targeted therapeutics

Abhinav Babu[1], Aniket Bhardwaj[1], Saurabh Verma[1*]

[1]Centre for Industrial Pharmacy and Drugs Regulatory Affairs. Amity Institute of Pharmacy, Amity University, Noida, Uttar Pradesh, India, 201301

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Abstract

MNPs as novel drug delivery system (NDDS) approach possess several magnetic properties for targeted and controlled delivery in various biomedical application. Unlike normal nanoparticles, MNPs enable to respond to external magnetic fields, allowing for manipulation, guidance, and functionalisation within the body. This review encompasses a wide range of scientific and technological goals aimed in understanding their properties, synthesis methods, characterization techniques, surface functionalisation strategies and application. Drug delivery based on magnetic properties has advanced dramatically to enhance therapeutic bioavailability, stability, and targeted delivwery. Converting nanoparticles into MNPs involves introducing magnetic properties to the nanoparticles through core-shell structures, doping or coating with magnetic materials, physical or chemical reactions, or biological synthesis methods. However, this study demonstrates the versatility and potential of magnetic nanoparticles (MNPs) for various biomedical applications. Moreover, the *in vitro* and *in vivo* studies highlight MNPs' promising role in targeted drug delivery, imaging contrast enhancement, and magnetic hyperthermia for cancer therapy. Moving forward, further research is warranted to optimize MNPs' design, explore novel functionalization strategies, and address challenges related to biocompatibility, scalability, and regulatory approval. Therefore, MNPs reflects transformative impact across various fields, emphasizing their potential to drive advancements in healthcare, environmental protection, and technology. Continued research and innovation in this field are expected to unlock new opportunities and address global challenges, driving progress towards a healthier, cleaner, and more technologically advanced future.

∗Corresponding Author

Name: Dr. Saurabh Verma
Phone: +91 8400195418
Email: sverma6@amity.edu

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INTRODUCTION

On the verge of advancements in nanotechnology, nanoparticles have gained lots of importance in the field of drug delivery due to their size and specificity. Due to its wide range of emerging concepts, Magnetic nanoparticles (MNPs) having size range 1-100nm found its pace in terms of controlled delivery [21]. MNPs, do exhibit several magnetic properties that can function at molecular and cellular level, which are dependent on size to certain extent when it is dealt with nanotechnology. Due to its magnetic properties, they allow transportation of magnetic drug carriers to certain

location under the command of magnetic field that is produced by electromagnet and permanent magnet. This magnetic field controls the drugs movement which aids the magnetic carriers to reach any position of the body. The encapsulation of magnetic materials is difficult due to the internal and external barriers . This can be avoided by process called surface correction/functionalization that is more accurate and acceptable for the body. Metals such as iron, cobalt, nickel based or the metal oxide based MNPs do contribute to the efficient modern nano technology. The iron-oxide based MNPs such as Fe_2O_3 has garnered for having a unique carrier property to deliver chemical drugs due to various functionalization (modification in physical and chemical characteristics) that results in numerous morphologies such as nano tubes, nano wires, nano rods etc. The hollow form of MNPs also promises to incorporate numerous forms of drugs as it offers to exhibit high surface area, controlled pore volumes and thickness so as to deliver the drug in controlled manner.

The therapeutic potential of these delivery system involves 'intelligent particles' includes magnetic core (that attaches to the target), recognition layer (that identifies the receptor), therapeutic load (adsorbed inside the cavities of particles). The superparamagnetic core of the carrier enables the particle to be magnetically manipulated in the presence of an external magnetic field. The application determines the magnetic core's composition; for example, the only approved nontoxic magnetic minerals for medical use at the moment are magnetite (Fe_3O_4) and maghemite (γ-Fe_2O_3) with strong oxidative stability. Prominent medical application includes the use of MNP carriers in tumor therapy that is related to the sizes, shapes, and its surface coatings. By applying different surface coatings, it is possible to give these particles therapeutic qualities while avoiding the pharmacokinetic effects and toxicity of magnetic nanoparticles brought on by interactions with biological proteins or cells. It also encompasses applications in MRI-that has ability to track particles *in-vitro* and *in-vivo*. Cell purification, isolation and as a biosensor. Due to their high maximal magnetization, high permeability, and lack of preferred magnetization direction, iron oxide (Fe_3O_4 NPs) and cobalt ferrite ($CoFe_2O_4$) are potential nanomaterials for use as drug carriers in biocompatible iron-based magnetic nanoparticles. There are inherent toxicity cases hindered for cobalt ferrite along with insufficient tissue dispersion, insufficient bioavailability, insufficient biodegradation

Techniques For Synthesizing Magnetic Nanoparticles

Since, there are certain novel approaches underway and also various methods adopted for obtaining desired MNPs with certain size and morphologies. The significant methodologies for MNPs production are physical, chemical and biological or microbe method. The top-down approach underpins the physical approaches; that is synthesis begins with bulk material and depletes it to produce NPs. On the other hand, bottom-up approaches used in chemical and biological processes combine atoms and molecules to produce nano-particles of various sizes. The most popular techniques are ball milling, co-precipitation, thermal decomposition, microemulsion, hydrothermal and biological approaches [1].

Physical Method

Consists of top-down and bottom-up approaches; the top-down method is based on breaking down the bulk materials into nano sized by high intensity using ball milling. Obtaining nanoparticles via mechanical crushing in the right shape and size is challenging. On contrary, the bottom-up gives more finely nano scaled particles like laser evaporation etc. Other physical methods include electron beam lithography, gas phase and wire explosion method.

Ball/Mechanical milling

Top-down strategy of creating MNPs from the bulk material and a convenient way to o create metallic granular alloys and a variety of materials based on different starting materials. Many factors, such as the ball-to-powder weight ratio, milling time, milling speed, and container material, affect the manufacturing of MNPs via mechanical milling. Likewise, Fe_2O_3 and MgO were ground into powder using a ball mill to create nanocrystalline magnesium ferrite, which was subsequently reinforced at 700–900 °C. The working principle is based with the raw materials that are enclosed in a little cylindrical jar containing several steel balls as a grinding medium. As a result of repeated

collisions between steel balls and solid materials, the balls impart kinetic energy to the substance, resulting in nano- and micro-sized powder [20]

Laser evaporation

It is called laser ablation requires high energy laser which is bottom - up approach for production of MNPs via condensation of liquid or gaseous phase like iron oxide MNPs . In this, μm or mm-sized coarse-textured particles are used as the raw materials, and are evaporated through the laser beam focus. The material is targeted by the concentrated laser beam and placed at the bottom of a cell that is submerged in a liquid solution. A laser beam is used to irradiate the substance in a solution. When the material's vapors cool down in a gas phase, quick condensation and nucleation occur, which causes the production of nanoparticles.

Electron beam lithography:

It allows the creation of extremely high-resolution pattern that patterns colloidal NPs through electron beam which has shorter wavelength (0.2−0.5 Å). Higher doses are needed for patterning smaller features, possibly because they can effectively prevent blurring during exposure; the electron dosages utilized for patterning organic e-beam resists. It involves turning iron particles into iron oxides (Fe_3O_4) by using an electron beam. The process of producing nanoscale iron oxide nanoparticles (NPs) by precisely directing an e-beam across an iron particle-film-covered surface [19].

Gas-phase deposition method/vapour phase:

Consists of both chemical and physical vapour deposition (CVD and PVD). When iron and other metals are used as raw materials, the results and output from these two approaches will differ. PVD allows for the formation of both thin films and composite nanoparticles. Finer iron oxide nanoparticles in this instance, as well as fine particulate powder and nanocomposite/thin films, would be produced by the procedure. The successful and economical application of gas-phase synthesis for MNPs by numerous researchers .

EXPLODING WIRE METHOD

Physiochemical approach which is a safe and clean process for synthesizing MNPs. This approach eliminates the need for further processes like NP separation from solution and byproduct retreatment, making it a highly productive one-step process. It involves a metal wire evaporating while being subjected to a strong electric current. The resulting metal particles are completely spherical in shape and extremely pure, limited to the original purity of metal wire. The resulting metal particles are completely spherical in shape and extremely pure, limited to the original purity of metal wire. Since there is no waste produced, this process is considered environmentally friendly[10].

Chemical method:

The chemical synthesis techniques include many bottom-up strategies comprises either quick injection of chemicals into hot surfactant solution followed by high temperature, or the mixing of reagents at a low temperature and slow heating under regulated circumstances. Co-precipitation is common chemical approaches followed by sol-gel method, thermal decomposition, and hydrothermal methods, each with its own advantages and considerations.

Co-precipitation method:

One of the most prevalent methods that is extensively and commonly used to create iron oxide nanoparticles This process uses a weak reducing agent, such as sodium hydroxide or ammonia etc.

To convert iron precursors into iron oxides. It is the most precise and efficient method for producing 50 nm-diameter superparamagnetic iron oxide nanoparticles, or SPIONs. Fe_3O_4NPs are produced by coprecipitating Fe^{2+} and Fe^{3+} ions. It covers chemical processes taking place in a monophasic liquid media[5]. The reaction involves:

$$Fe^{2+} + 2\ Fe^{3+} + 8\ OH \rightarrow Fe_3O_4 + 4H_2$$

The process by which iron oxide nanoparticles are formed from precursor molecules by unplanned nucleation and growth has a highly variable reaction pathway that is reliant upon the reducing agents, pH strength, the concentration of precursors, and the rate at which they are added. In addition, temperature, pH, and ionic strength can regulate and alter the particle size.

Thermal decomposition:

It is a process that involves heating the material. The thermal decomposition temperature is the point at which a chemical begins to break down.

Since heat is required to break the bonds between the chemicals, this process is endothermic. For example: High quality iron oxide NPs of 15nm can be produced. This technique uses severe temperatures to create monodispersed NPs using organometallic precursors. The MNPs generated by this approach exhibit great crystallinity, regulated size and well-defined form. To create MNPs with the appropriate size and form, the breakdown of organometallic precursors is done in the presence of organic surfactants. Stabilizers employed in the breakdown process have the ability to reduce NP nucleation, which in turn regulates MNP growth and aids in the production of a spherical shape and the desired size of less than 30 nm. This method was claimed to produce magnetically active iron composites and Fe_3O_4 nanocrystals [14].

Micro emulsions:

They are stable isotropic mixtures produced by mixing the components (oil+water+surfactant) and do not require high shear conditions. For instance, in a microemulsion of the w/o type, surfactant was used to coat water droplets in an organic solvent, thereby decreasing the size of MNPs. Reverse microemulsions (water in oil), bi-continuous, and direct emulsions (oil in water) are the three main types of microemulsions. Metal nanoparticles have been successfully synthesized using a reverse microemulsion method that uses surfactants to produce uniform and small-sized nanoparticles. A few iron-oxide MNPs (as shown in **Figure 1**) were made using the w/o kind of microemulsion, which involved using two microdroplets—one with a precipitating chemical and the other with a metal percussion device. This procedure was used to create MNPS coated in silica, which were then modified with amino to help to separate tumorous cells.

Hydrothermal method- Iron oxide nanoparticles are created using this synthesis process by crystal growth at high pressure and temperature conditions (usually below 300 °C). Higher-crystallinity is produced at the same time that the reaction rate is increased. Using an organic solvent and iron precursor solution, highly crystalline iron oxide nanoparticles with a size range of 14 to 25 nm have been created. Synthesized MNPs' shape and crystallinity are dependent on temperature, time, pressure, and solvent mixing conditions. Using this procedure instead of the microemulsion method can result in a higher yield of NPs.

Figure 1 Microemulsion technique for obtaining Iron based MNPs.

Sol-gel method-

Involves the hydrolysis and polycondensation processes of metal alkoxides to create gel at ambient temperature. To create a sol or colloidal solution, metallic salts are dissolved in water or other solvents and uniformly distributed. Stirring and raising the temperature causes the van der Waals forces between the particles to arise, increasing their contact. Gel is eventually formed by heating the combination until the solvent is eliminated and drying the solution. This process useful for making silica-coated and iron oxide MNPs.

Biological/microbial method:

Biological entities like bacteria, fungi, plant extracts, and protein-mediated synthesis can be used to create iron oxide nanoparticles. Since, the particles produced may be less stable, non-uniform, with less homogeneity and more agglomeration due to which there have been comparatively fewer reports on biological agent-mediated synthesis of iron oxide nanoparticles. As shown in **Figure 2,** bacteria that are known to extracellular synthesis of iron-based magnetic nanoparticles, including greigite (Iron thio-spinel), when supplemented with an iron supply were used to create iron oxide nanoparticles. Potential pathways for metal nanoparticle myco-synthesis. Three mechanisms are involved: 1) nitrate reductase activity; 2) quinones shuttle electrons; and 3) a mixed mechanism. Microbes typically create inorganic compounds (intra- or extracellularly), many of which have distinct morphological properties and are nanoscale in size.

Process known as "biologically induced biomineralization" is the extracellular creation of

iron oxide nanoparticles or crystals in the culture medium. When synthesis takes place inside the internal environment of sulphur-reducing or magneto-tactic bacteria, it is known as biologically regulated biomineralization (BCM), and it results in the production of well-ordered crystalline particles. Using a bottom-up method, plant extracts can also be utilized to create iron oxide nanoparticles or metal nanoparticles in general instead of only microorganisms. An iron oxide nanoparticle with a rod-like shape was created employing a leaf extract from Moringa oleifera. These nanorods exhibits super para-magnetism and had an average particle size of 15 nm. Rod-shaped iron oxide nanoparticles were reported to have good antibacterial activity, much like spherical iron oxide nanoparticles. Additionally, neem extracts have been employed as a mediator in the iron oxide nanoparticle production process.

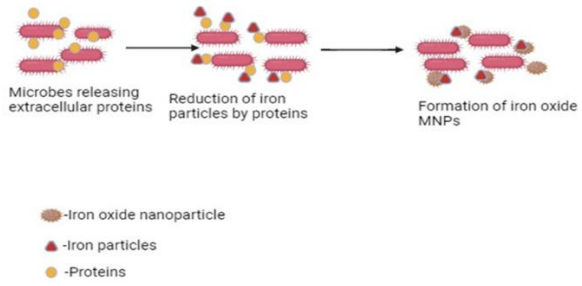

Figure 2 Synthesis of iron-based magnetic nanoparticles by microbial method

Techniques Adopted for the Characterization of MNPs

For determining the accuracy of MNPs, the scrutiny of its characterization has gained importance onto its field. Its characterization involves surface morphology (size and shape), its external magnetic field etc. Different characterization techniques are categorized based on the materials they are intended for, the information they may supply, or the concept/group of the approach used. For instance, the coherence between the spins produces exceptional magnetic characteristics if a magnetic nanoparticle decreases to the point where it can no longer support a domain wall (a separated uniformed region of magnetization). The size, shape, and crystal structure of the nanomaterials can be determined using microscopy-based techniques such as TEM, etc. Certain techniques, like the magnetic approaches, cater to specific families of materials. More-over information about the structure, elemental composition, optical characteristics, and other general and more specialized physical properties of the nanoparticle samples can be obtained using a variety of different techniques. These methods include scattering, spectroscopy, and X-ray methods [13].

Techniques to determine shape and size of MNPs

Because of the significant advancements made in the chemical synthesis of nanostructures, nanotechnologists are now able to manufacture MNPs with precisely controlled composition and form. Research on the heat emitted by anisometric nanoparticles—such as nano-cubes, nano-octopods, nanoflowers, elongated nanoparticles, and nano-disks—as well as, in certain situations, the related heat release mechanisms has been intense in recent years The physicochemical properties of MNPs can be altered by modifications to their size and shape. The measurements of surface area, size, and particle dispersion are made using nanoparticle tracking analyzer (NTA) Dynamic Light Scattering (DLS) methods. While methods such as TEM can be used to assess MNPs' surface morphology.

X-ray diffraction method

It provides comprehensive details about the phases, crystalline structures, lattice characteristics, and crystalline grain size. By comparing the position and intensity of the X-ray peaks with the reference database that is accessible, one can ascertain the composition, crystal structures, and phase characteristics. The broadening of the peaks can be used to establish the crystalline grain size. The size of the crystalline particles and lattice stresses are the primary causes of the X-ray peaks' widening. To evaluate the surface binding energy and density of states, for instance, X-ray absorption comprises both extended absorption fine structure and X-ray absorption near edge structure. Another example is the extensive application of X-ray photoelectron spectroscopy in surface chemical analysis, electronic structures, elemental composition, and element oxidation state[16].

TEM (Transmission Electron Microscope)

It offers direct images of the nanoparticles which is widely used method for determining the size, shape, and homogeneity of nanoparticles. While SEM provides information about the samples' composition and surface topography. The size, shape, and elemental makeup of the nanoparticles affect how much of the electron flux interacts with them, with some of it being transmitted through them. TEM makes it easier to image in real time how nanoparticles dynamically change over time. This method of measuring the size and form of magnetic nanoparticles in suspensions is particularly demanding because of the substantial absorption of electron energy with liquid molecules. This also allows for the measurement of interparticle distances in a solution, which has been demonstrated to be a crucial factor in the magnetic response of the magnetic nanoparticles.

Dynamic light scattering (DLS)

It is 1a method that is frequently employed to determine the size of particles suspended in colloid solutions. The impact of surface coating, concentration, size, and shape of the nanoparticles on the colloidal stability of the magnetic nanoparticles has been demonstrated through the application of the DLS approach. DLS method yields precise size results for middle-sized magnetic nanoparticles that are consistent with those obtained from TEM and SEM pictures. If the heterogeneity and poly-disparities of the magnetic nanoparticles are substantial, the DLS approach is not an appropriate one to use for analysis. This is due to the fact that the larger nanoparticles scatter a significantly greater amount of light, making it harder to detect the light than that of the smaller nanoparticles do scatter.

Nano particle Tracking Analyzer (NTA)

As opposed to the DLS method, it determines the size distribution at a lower concentration limit. A microscope concentrates the dispersed light onto a camera to capture the movement of the particles (as shown in **Figure 3)** [4]. The primary benefit of the NTA over the DLS is that the aggregation of bigger nanoparticles. Research indicates that NTA outperforms DLS in terms of accuracy for both monodisperse and polydisperse samples. The primary distinction between DLS and NTA is that DLS examines a collection of nanoparticles while NTA follows individual nanoparticles. The NTA has a more complicated operating method than DLS due to its different operation mode.

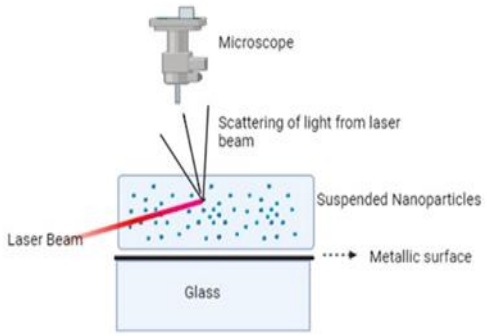

Figure 3 Nanoparticle size determination by scattering of light

Fourier transform infrared spectroscopy (FTIR): It is an approach emphasizing the assessment of electromagnetic radiation absorption at mid-infrared (4000–400 cm−1) wavelengths. A molecule's dipole moment changes in some way as it absorbs infrared radiation, making it IR active. The vibration and rotation of molecules influenced by infrared radiation at a particular wavelength is measured using FTIR. The monodentate or bidentate bonding on the Fe-Pt magnetic nanoparticles can be identified using FTIR. There have been multiple attempts to push the limits of this approach to study magnetic nanoparticles as small as a few nm due to its relatively inexpensive cost.

Techniques To Determine Magnetic Characteristics

The production of MNPs via various synthetic techniques determines their magnetic properties. The size range of MNPs exhibits superparamagnetic properties, ranging from nanoscale to microscale. These NPs exhibit magnetic sensitivity and can interact with external magnetic fields when they are subjected to them. However, there is no evidence of magnetism when there is no external magnetic field. Because of this characteristic, MNPs can be extremely useful in regulated therapy and controlled drug administration. To measure important characteristics of iron oxide nanoparticles and other MNPs, magnetization experiments in both constant and time-varying magnetic fields are frequently performed. The net magnetization is measured using methods such as SQUID

(superconducting quantum interference device) magnetometry and VSM (vibrating sample magnetometer) .

Mossbauer spectroscopy

an analytical approach to assess the spin states, oxidation states, and spin ordering of Mossbauer-active elements (like Fe) in order to identify magnetic phases. If the measurements are made as a function of temperature, Mossbauer spectroscopy may throw light on the quantification of the magnetic anisotropy energy and thermal blocking/unblocking (superparamagnetic response). For example, Mossbauer spectra as a tool for studying the local state of electrons on the Fe-Co nanoparticle surface quantitatively. Since the Mossbauer isomer shift merely identifies the charge state on the nucleus, it is not strictly a probe for figuring out the oxidation number of the dopant atoms.

Measurement of hysteresis loop

The magnetic materials show significantly different magnetic properties from their bulk form as they get closer to the nanoscale. As temperature fluctuations surpass the energy barrier, MNPs exhibit superparamagnetic behaviour, otherwise they act like single domain nanoparticles. Surface anisotropy and other extra anisotropies are caused by the dominance of unpaired electrons at nanoscale sizes. Vibrating sample magnetometry (VSM) or a superconducting quantum interface device (SQUID) can be used to measure the hysteresis loops; SQUID offers a much greater resolution in this case. When examining samples in various forms, such as thin films, crystals, powders, liquids, and gases, the SQUID is helpful. Both VSM and SQUID are extremely sensitive instruments; for example, the sensitivity of the VSM is 10−6 emu, but the sensitivity of the SQUID is up to 10−10 emu. If an external magnetic field is continuously supplied, the SQUID and VSM can also detect residual magnetization and magnetic saturation. Measurements of minor hysteresis loops are carried out at fields lower than the magnetic nanoparticles' saturation field. When a cyclic magnetic field is applied, such as in research involving hyperthermia, these observations are highly helpful in describing the magnetization response of the magnetic nanoparticles that do not reach complete saturation. For instance, tiny hysteresis loop tests to show the magnetic nanowires' heating efficiency for nano-warming applications [17].

AC field technique

detects the high frequency hysteresis loops of magnetic nanoparticles. In order to properly develop magnetic recording media, it is essential to determine the effects of applied field rate on coercivity, which is why the AC field technique was initially proposed. Because superparamagnetic nanoparticles exhibit zero coercivity at static fields and rise with applied field frequency, this technique has become a crucial tool for evaluating the heating efficiency of magnetic nanoparticles. For biomedical uses like hyperthermia, the frequency dependence of the coercivity of the superparamagnetic nanoparticles was discovered to be a remarkable source of heat generation.

Electron holography

A holographic imaging method that uses electron waves. This method obtains holographic pictures by means of an electron beam with great spatial and temporal coherence. The primary benefit of electron holography is that, as opposed to relying just on surface magnetization states or stray fields, this method directly offers information about internal magnetic structures. The off-axis and in-line holography configurations are the most widely utilized methods for imaging nanoparticles among the several configurations available. One method for observing the magnetization distribution and determining the saturation magnetization of multi-segmented Fe-Ga/Cu nanowires is to use off-axis electron holography under Lorentz microscopy. In comparison to other magnetic imaging methods like magnetic force microscopy, electron holography was also demonstrated to be helpful for high resolution visualization of the magnetic domain walls and/or domain wall pinning in magnetic nanoparticles.

Magnetic force microscopy (MFM)

It is a type of imaging-based scanning probe microscopy that gauges the magnetic forces acting on the probe. To capture the magnetic stray fields of the magnetic nanoparticles in the MFM, a nanoscale probe is covered with a few tens of nano-meters of magnetic material. The MFM's primary benefit is its ability to photograph the magnetic domains that show the direction of magnetization. It is frequently used to show the

fields of interaction between magnetic nanoparticles. This method's great sensitivity has also been used to measure the number of magnetic nanoparticles incorporated into cells in situations where optical imaging methods, including fluorescence imaging, are difficult.

Magnetic Properties for Controlled Release

Since therapeutic compounds can be remotely controlled to move particles to the target region, MNPs play a critical role in this process which possess the name "magnetic targeted carriers." Because of their inherent magnetic qualities, magnetic nanoparticles have super-magnetic, super-saturation, and magnetic susceptibility qualities that present a special chance to be utilized. Although MNPs' size, content, and synthesis process vary depending on the application, super-paramagnetic, ferro, and free particles can all be employed for a range of focused drug delivery applications. Because of the network unit's magnetic moment and the characteristics of the fields, MNPs are greatly affected by the external magnetic field; as a result, they behave like an inert particle when the external magnetic field vanishes. NPs may differ from bulk materials in a number of magnetic parameters, including magnetic anisotropy, magnetic moment per atom, Curie temperature, and coercivity field. The magnetic characteristics of nanoparticles are determined by five primary components. The following are the ones that are related to nanoparticles: (a) their geometrical characteristics; (b) intra-particle and inter-particle magnetic interactions; (c) particle-particle and inter-particle magnetic interactions; (d) interactions between the nanoparticles and the matrix material; and (e) interactions between the particles and the magnetic field applied to them. The two primary characteristics that determine the magnetic properties of nanoparticles (NPs) are A) finite-size effects (single-domain, multi-domain structures, and quantum confinement). B) surface effects (resulting from oxidation, dangling bonds, surface staining, and other processes that break the symmetry of the crystal structure at the particle's surface). Because there are more surface atoms relative to core atoms, surface effects become more relevant as particle size decreases.

Single Domain Particles

A single-domain particle has a homogeneous magnetization and all of its spins oriented in the same direction. Rather than through domain wall motion, spin rotation will reverse the magnetization as there are no domain walls to move so as a result, the nanoparticles exhibit high coercivity. Due to the decrease in magnetic fields and consequently the appearance of superparamagnetic characteristics, MNPs offers a promising future.

Super Paramagnetic

The magnetic anisotropy of the NPs directly affects their super paramagnetic properties, and the amount of magnetic anisotropic energy (EA) is at its lowest when the NPs' magnetic moment points in the direction of the easy crystal axis. The anisotropy of the magnetic crystal in spherical magnetic nanoparticles is equal to the overall magnetic anisotropy. In general, MNP behaviour is comparable to that of superparamagnetic atoms. Each nanoparticle behaves like a paramagnetic atom but has a huge magnetic moment, even though they still have low magnetic characteristics. It is known as superparamagnetic behaviour. The NPs' magnetic direction rapidly shifts in super-paramagnetic material instead of going in a single direction. However, the magnetism of superparamagnetic nanoparticles (temporary magnets) may be adjusted externally and therefore, they are a better fit for biomedical applications than their ferromagnetic counterparts (permanent magnets). It is intended for the majority of biomedical applications for the particles to be primarily non-magnetic and to only become magnetic during imaging and/or therapy within a designated spatio-temporal window. Furthermore, superparamagnetic nanoparticles have superior pharmacodynamics, biodistribution, and excretion pathways than ferromagnetic ones since they are often smaller. When an external magnetic field is present, the particles display superparamagnetic characteristics such as high magnetic moments, quick reaction, and minimal residual magnetization and coercivity. The moment the magnetic field is removed, the superparamagnetic substance becomes non-magnetic. Due to the absence of any chance of the nanoparticles aggregating unintentionally, this guarantees a safe elimination from the body. For biomedical applications, these nano-systems' size, surface charge, intrinsic magnetic characteristics, stability in an aqueous media, and toxicity must all be taken into account. The fate of the particles in vivo is

ultimately determined by their physicochemical characteristics. Smaller nanoparticles—typically less than 20 nm—are preferred in most cases. Ferri- and ferromagnetic nanoparticles achieve a single magnetic domain with a single high magnetic moment value at such small scales[12].

Materials that exhibit super-paramagnetic behaviour have characteristics including a large, continuous magnetic moment that functions like a huge paramagnetic atom, as well as negligible anti-residual force, residual magnetism, and a quick response to applied magnetic fields. Distinction between super paramagnetic and ferromagnetic are illustrated in **Table 1**

Other characteristics of MNPs to impart medical application, where it must have a single domain and a crystalline structure; provided to have the same size distribution and the narrowest feasible size distribution. Every nanoparticle in a given sample needs to be the identical form as they attracted a great deal of interest from a variety of scientific domains because of their distinctive surface chemistry, nontoxicity, biocompatibility, and—most importantly—their inducible magnetic moment. Methods for enhancing certain attributes such as poor biodegradability, chemical instability, and biocompatibility in a physiological setting depend on surface modification of MNPS and superparamagnetic iron oxide nanoparticles

Surface Functionalization & its Importance in controlled delivery

Transforming a material or device's surface characteristics to accomplish certain objectives, such eliciting a desirable bio-response or preventing a potentially harmful reaction, may be done effectively and frequently more simply through surface functionalization. Magnetic nanoparticles (MNPs) with strategically functionalized surfaces have transformed drug delivery, allowing for targeted and effective

Table 1 Characteristic differences between Super-Paramagnetism and ferromagnetism

Properties/characteristics	Super-Paramagnetism	Ferromagnetism
Structure	Single domain	Multiple domain
Remaining(remanent) magnetization	Magnetization returns to zero when the external field is removed	Magnetization persists after field removal.
Size Dependence	More prevalent in nanoscale materials such as nanoparticles or small clusters.	Majorly observed in bulk materials.
Magnetic Moment Alignment	Moments can randomly align in the absence of an external field.	Moments align in the same direction.
Application	Application in biotechnology, magnetic imaging, drug delivery, and high-density storage	Used in permanent magnets, data storage, transformers, electronic components. .

employ spherical nanoparticles mostly. Naturally, they also make use of more intricate structures like nanotubes and nanowires. With respect to its stability and biocompatibility by using core-shell structures, that incorporates a metal or metal oxide core in a covering of polymer or inorganic materials that has been discovered to attach to biomolecules. Regarding Hydrodynamic size and small size, less than 50 nm in size is another characteristic of this field. Due to the fact that it promotes diffusion and shields particles from the body's reticuloendothelial system's removal (RES). Magnetic materials' morphological structures have therapeutic treatments. The primary problem with MNPs in terms of size scales is long-term intrinsic instability, which can happen in two ways: (1) dispersibility loss, where bare MNPs tend to clump together as a result of Van der Waals forces, defeating the strong magnetic attraction and high surface energy between particles; and (2) magnetism loss, where MNPs oxidize. To improve MNPs' hydrophilicity and biocompatibility, a functionalized surface can be created around their surface. By decreasing the surface area generated and, thus, indirectly lowering the surface energy required for agglomeration to occur, MNP

encapsulation prevents agglomeration. For instance, encasing iron nanoparticles in shells resembling graphene was a widely recognized technique for boosting their durability and maintaining certain magnetic characteristics. Because the carbon coating is light and completely encases the magnetic core in nanoparticles, it is also regarded as the ideal encapsulating material. MNPs with surface functionalization provide unmatched aiming accuracy. In order to minimize off-target effects, MNPs are guided to certain cell receptors or tissues by the conjugation of targeting ligands (antibodies, peptides). Targeted delivery effectiveness is confirmed by in vivo biodistribution research and in vitro cell binding tests. The technique of surface functionalization of nanoparticles (NPs) seeks to enhance and/or add features that will be beneficial for their application in medicine. The integration of various organic and inorganic molecules at the nanoscale by the utilization of covalent and non-covalent bonds, such as hydrogen bonds, electrostatic force, and van der Waals interactions, is known as surface functionalization of nanoparticles. For ligands and NP surfaces to create covalent connections, many linker molecules are usually utilized. The use of homo- or hetero-bifunctional cross linkers is often the initial step in surface modification, with the aim of adding an organic functional group (R–NH2, RCOOH, and many more) for the binding of biological molecules. The most popular techniques for functionalizing MNPs, taking into account the kind of coating (organic or inorganic), the materials and precursors that are utilized, and the appropriate characterization techniques. Using MNPs (magnetite Fe_3O_4) coated with polymers and biopolymers, biomolecules, or macromolecules for responsive and targeted medication delivery. For coating inorganic NPs (such a Pt shell), and MNPs specifically, a variety of polymers have been used, including hydrophilic polymers (like functional poly-aspartamide) that aid in the particles water solubility. Inorganic shells, for example, may be made to have different compositions and thicknesses to give adjustable qualities and improved stability. However, compared to other methodologies, their synthesis might be more difficult, requiring careful control over reaction conditions and multi-step procedures. Moreover, there is a chance of core-shell mismatch, which can complicate smooth integration. Because there is a large selection of ligands available, the ligand exchange variation is highly versatile and may be performed in moderate settings, reducing the risk of damaging the magnetic core. However, because ligands may separate over time, the stability may be restricted, making it difficult to precisely manage the thickness of the shell [3]. The type of the surface and the adsorbing material both influence the driving force behind substance adsorption. Through surface functionalization, both organic and inorganic chemicals play a major role in stabilizing freshly produced nanoparticles and other techniques as discussed in **Table 2** With organic molecules, MNPs with tiny molecular coatings have the primary benefit of being able to address large hydrodynamic diameters (>50 nm. Citrates, phosphates, amines, thiols, and a variety of polymers (chitosan, dextran, PEG, polyvinyl alcohol (PVA), poly (lactic-co-glycolic acid) (PLGA), alginate, poly-acrylic acid, etc.) have recently been incorporated in the organic materials. Polymer-coated iron oxide nanoparticles (IONPs) have drawn a lot of interest in recent years due to their wide range of applications in several scientific domains, including nanomedicine.

Mechanism of MNP for Its Controlled Release

Nanoparticles created for imaging; drug-carrying nanoparticles need to be precisely physico-chemically designed in order to be targeted. Various loaded medications, which of course required careful design on nanoparticles to amass distinct therapeutic agents, to circumvent cellular drug resistance. So, to achieve the intended therapeutic impact, the therapeutic agent's secretion and the loaded agent's retention rate need to be adjusted. Drug release often starts when the cell cycle is at its most favorable, and after intracellular harvesting has occurred, the concentration and length of drug release may be ascertained. Now the drug can be directed and concentrated at the tumor site or other target tissues if an external magnetic field made of permanent magnets and a gradient above the field are used. In some cases, external magnetic fields are applied to guide and concentrate the functionalized MNPs to the target site. By manipulating the magnetic field gradients, MNPs can be directed to specific regions within the body, enabling enhanced targeting efficiency and spatial control. These particles are not selectively targeted, and this is frequently achieved by non-specific techniques such tissue-specific pore size or

Table 2 Techniques and observation for functionalization strategies

Functionalization Techniques	Precursor	Observations
Inorganic coatings	Inorganic substances such as metal oxides, silica, and gold encase MNPs. For example, silylation/polymerization has been used to produce core–shell Fe3O4/Pt MNPs	Silica coated offers controlled release.
Organic encapsulation	PEG, polymers, or citrate are examples of organic ligands that are transferred onto the surfaces of MNPs via covalent or non-covalent interactions.	This modifies surface charge and adds biocompatibility and colloidal stability. MNPs' improved dispersibility in biological medium makes it easier to use them for targeted imaging and medication administration.
Ligand exchange	Precise control of MNP characteristics is made possible by substituting functional molecules (amines, thiols) for native surface ligands.	Targeted drug delivery is made possible by this approach by attaching therapeutic payloads or conjugating targeting ligands.
Bioconjugation	Through affinity interactions, MNPs are coupled with biomolecules (peptides, antibodies) to produce targeted capabilities.	For imaging and medication administration, antibody-conjugated MNPs provide excellent cellular or molecular targeting.
Responsive polymers	Applying stimuli-responsive polymers (temperature, pH) onto MNP surfaces allows for the regulated release of drugs in certain microenvironments.	Appropriate for controlled medication release.

increased permeability and retention effect (EPR) in tumor tissues. The targeting ligands on the surface of the MNPs are designed to recognize and bind selectively to biomarkers or receptors that are overexpressed or unique to the target cells or tissues. This binding interaction is often mediated by specific molecular recognition events, such as antigen-antibody interactions or receptor-ligand binding [8].The mechanism is also governed by the magnetic targeting and various approaches like active and passive targeting.

Passive Targeting

This process makes it easier for macromolecules and nanoparticles to escape from the arteries and accumulate in the tissue due to increased leakage. The improved penetration and retention effect (EPR) is the primary tenet of passive targeting. The inactivation accumulation and targeting takes place between 1 and 10 nm for nanoparticles. An additional passive targeting source comes from the innate removal of cells from the reticulo-endothelial system (RES), including tissue macrophages, blood monocytes, and bone marrow cells.

Active Targeting

Strong affinity ligands are employed at the particle surface to specifically target molecules at the patient's cell surface in order to deliver the particles into the target tissue. Specific binding can help ligand-induced endocytosis, which is a route for cellular internalization. Particles that have accumulated due to EPR antigen-antibody or receptor-ligand interactions are present in malignant organs like cancers.When it comes to distribution and highly specific molecular detection of the desired structure, monoclonal antibodies are employed as targeted agents. Conversely, tiny molecules and several layers produce stronger bonds.Therefore, a variety of ligands, including small molecules, peptides, proteins, and antibodies, are used to create super paramagnetic iron nanoparticles.

Factors that Influence the Design for Active Targeting

Density of target molecules

Because of the multivalent phenomena, the density and arrangement of bound ligands have a substantial impact on how well nanoparticles attach to their target tissue. In several systems of nanoparticles, to increase the likelihood of binding to biological targets. Using varying concentrations of RGD peptides in iron oxide with varying crosslinks, it was found that while ligands can attach simultaneously at larger concentrations of RGD, multivalent interactions are prevented by ester repulsion if the ligand density is greater than one.

Particle size

Particle size also has an impact on multivalent binding; the study discovered that particles ranging in size from 2 to 100 nm. It is not possible for anything smaller than 25 nm to attach to many ligands on the same cell. However, bigger nanoparticles are more difficult for cells to endocytosis; in general, particles between 25 and 50 nm are appropriate for both multivalent binding and endocytosis.

Particle shape

In comparison to spherical nanoparticles, oblique nanoparticles have a tendency to bond more and stronger, while nano-shaped worm formations have an improved capacity to bond.

Magnetic Targeting

There has been a lot of interest in using magnetic nanoparticles in conjunction with applied magnetic fields to selectively control the accumulation and release of drug in target tissues while minimizing the impact on surrounding tissue because biological tissues respond very little to magnetic fields. Magnetic field parameters, such as field strength, direction, and duration of exposure, can be adjusted to optimize the targeting efficiency and spatial distribution of MNPs within the target tissue or organ. Fine-tuning of magnetic field parameters may be necessary to achieve optimal therapeutic or diagnostic outcomes while minimizing adverse effects. Specifically, time-variant magnetic fields have been utilized to induce drug release from thermally sensitive nanocarriers, whereas spatially variant magnetic fields have been employed to promote aggregation of drug-loaded magnetic nanoparticles at target regions. Concentrating strong force fields, high gradients, or the impact created by the earth magnet at the target area, this method creates a high concentration of sensitive MNPs at the desired spot. In order to be investigated for targeted medication delivery, magnetic nanoparticles have to satisfy a number of strict requirements. Particle circulation time, drug dispersion, drug release, accumulation, and, if necessary, cellular uptake must all be balanced by their size and surface treatments. Due to the high magnetic attraction between particles, magnetosomes can aggregate and precipitate in water and biological fluid environments, which might impair their ability to target magnetically. MNPs produced by thermal breakdown have a lower particle size than natural magnetosomes but the same crystal shape and magnetism (high saturation magnetization and low coercivity)[11]. Superparamagnetic nanoparticles (MNPs), as one of the most promising nanoscale drug carriers, have been employed to accumulate drugs specifically to a diseased site under the control of an external magnetic field, minimizing the undesirable side effects. One of the most promising nanoscale drug transporters, superparamagnetic nanoparticles (MNPs), have been used to minimize unwanted side effects by selectively accumulating medicines to a sick region while being controlled by an external magnetic field.

Metabolic Fate of Magnetic Nanoparticles

MNPs like iron oxide nanoparticles involves having several essential functions and that living things possess systems for transferring and storing iron in non-toxic forms. Several evidence suggests that iron oxide nanoparticles cause cells to activate iron-coping systems and that these materials breakdown products find their way into regular iron metabolic pathways. Evaluations of the toxicity of iron oxide nanoparticles with varying sizes and surface functionalization at the cellular level were also conducted. Systematic administration of IONPs in the blood stream faces the initial uptake by the liver and spleen. IONPs uptake is mediated by the mononuclear phagocytic system via endocytosis in kupffer cells of the liver and macrophages of spleen. IONPs are degraded in the lysosomes of kupffer cells and macrophages, thereby releasing the free iron from IONPs, which affect the iron homeostasis. Any surface alterations affect the MNPs' biodistribution and interaction, as well as their internalization process, metabolism, and potential toxicity within cells and organs. The

MNPs' biodistribution patterns and duration of circulation throughout the body are influenced by both their surface chemistry and mode of administration. 10–100 nm is considered the ideal range for delivery for certain purposes since MNPs larger than 200 nm are known to be eliminated via renal clearance, whereas MNPs smaller than 10 nm are known to be taken up by the spleen by mechanical filtration. It has been determined particles bio-distribute 80–90% in the liver, 5–8% in the spleen, and 1-2 % in the bone marrow.

Toxicity of MNPs

Because of their toxicity, MNPs may have a reduced ability to have therapeutic effects. Moreover, they may migrate and accumulate within organs, which may trigger immunological or inflammatory reactions. If these MNPs manage to get into the cell, their toxicity may interfere with nuclear functions or result in membrane leakage or obstruction, which may have a negative impact on cell survival, proliferation, and metabolic activity. The possible toxicity effects of MNPs have been divided into several categories, including DNA genotoxicity etc. as shown in **Figure 4**. In most IONP-based nanotoxicity investigations, the generation of reactive oxygen species (ROS) has been identified as a primary cause of cell death. The production of ROS can be caused by a number of stressors, including temperature, interactions with pathogens, and external objects. Anions, hydroxyl radicals, and hydrogen peroxide are examples of ROS that are produced as a result of mitochondrial oxidative metabolism.

In-vitro toxicity:

MNPs toxicity have been associated with characteristics such as dose-dependency, duration, surface modification, concentration, size, and shape. The likelihood of harmful consequences increases with the quantity of nanoparticles. Optical, electron, and atomic force microscopy are some of the methods most frequently used in in vitro assays to analyse cell viability, proliferation, and differentiation. These methods are based on image observations of nanoparticles internalizing in the cells at very small scales range of nanometers, and they can be further used to analyse data through analytical software. An analytical tool for examining the impact of eryptosis indices on red blood cells' (RBCs) cellular membrane architecture and function is in-vitro testing. Altogether, significant alterations in Fe_3O_4 MNPs were able to modify the mechanical characteristics of erythrocytes; pathogenic modifications in cell membranes, aberrant calcium levels in the cytosol, and oxidative stress also induced programmed cell death in vitro and in vivo.

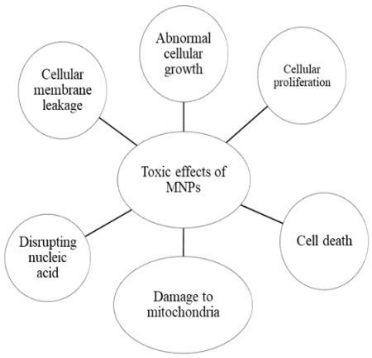

Figure 4 Potential toxicity effects of MNPs observed with in-vitro and in-vivo models

In-vivo toxicity

MNPs in the range of 10–100 nm is the most favoured size to be employed within the body because smaller particles (less than 10 nm) are eliminated via renal extravasation, while larger particles (more than 200 nm) are caught by the spleen. Designing nanoparticles with selectivity towards cells and tissues, their metabolism, and clearance requirements to comprehend the potential toxicity requires an understanding of pharmacokinetic elements such as absorption, distribution, metabolism, and excretion in an organism's system. Through interactions with cells and other biological elements, MNPs can be absorbed into the body. Once inside, they can be transported throughout the organs and undergo further metabolization.

Toxicity in Invertebrates:

Because toxicity studies are crucial to preserving the equilibrium between the surrounding environment and the ecological chain, they are significant in tiny invertebrate model studies. Accordingly, a study was examined on how iron oxide MNPs harmed the mutual relationship between plants and the fungus Arbuscular mycorrhizal. Fe_3O_4 MNPs were found to be toxic to fungi at high concentrations of 10.0 mg/kg, having a detrimental effect on the mutual relationship between fungi and plants that included a decrease

in the amount of photosynthetic carbon left for fungi as well as a negative influence on soil carbon accumulation and phosphorus cycling. Because of these elements that contradict soil fertility and crop production, a more thorough assessment of agricultural yields and ecological balance is required[2]. In a study on water fleas (Daphnia magna), IONPs of the same size (5–6 nm) were coated with four distinct substances: ascorbate (ASC-IONP), citrate (CIT-IONP), dextran (DEX-IONP), and polyvinyl-pyrrolidone (PVP-IONP). Each IONP was shown to have distinct effects, however PVP-IONP showed the least acute toxicity when compared to other IONPs, with the lowest rate of adsorption and accumulation and the maximum colloidal stability. The paper's findings also revealed that the production of ROS, ion leakage from the core material, and a decline in colloidal stability might all lead to toxicity.

Toxicity in Vertebrates

Owing to the benefits of low inter-species variation caused by the enormous biological sample size generated from a single parent, simple MNP administration by aquatic exposure, and a significant reduction in the sacrifice of higher vertebrates to comply with the 3R principle. In one study, iron oxide nanoparticles and iron salts were tested for toxicity in blackfish (Capoeta fusca). The authors examined iron absorption over a 28-day period following a variety of toxicity experiments, chronic exposure to a sub-lethal concentration of Fe_3O_4 NPs, and iron salts. The toxicity and metabolization of single core and multicore MNPs coated with DMSA, citric acid, and PEG were examined for their toxicological characteristics in the subsequent investigation. Human hepatocellular carcinoma (Hep G2), human colorectal adenocarcinoma (Caco-2), and an amphibian model (Xenopus laevis) during its embryonic development were employed for in vitro investigation. Vertebrate models, such as Xenopus laevis, should be taken into account as they can provide rapid, low-cost, and large-scale alternatives before the toxicity of nanotherapeutics is assessed in rodent models. In a different experiment, the toxicity of magnetic iron oxide (MION) nanoparticles prepared in conjunction with carob leaf extract was assessed by incorporating them into specific Wistar rat brain regions. Thirty rats were split into two main groups at random: the control group and the MIONs-treated group (15 rats in each group); six rats in each group were used to measure the iron content of the samples using inductively coupled plasma-optical emission spectrometry (ICP-OES), and nine rats in each group were used to examine the histology and perform biochemical analyses; the magnetic iron oxide nanoparticles triggered neuronal degeneration in the hippocampus and striatum regions of the brain, despite the fact that no significant changes in body weight were noticed. Furthermore, the magnetic iron oxide nanoparticles disrupted the homeostasis of iron in striatum [6].

Biomedical Application of MNPs

Magnetic nanoparticles (MNPs) have been considered as a crucial instrument in the treatment of cancer because of their distinct dynamic magnetizations under alternating magnetic fields. One such use is magnetic hyperthermia therapy [15]. The review of MNPs' biomedical applications was divided into seven sections: magnetic resonance imaging (MRI), cancer therapy, drug and gene delivery, tissue engineering, biosensors, and other areas. The studies suggests that MNPs' special properties make them highly promising for a wide range of biomedical applications. The development of more appropriate methods for testing MNPs in vivo and in vitro to determine their cytotoxicity and biocompatibility is another area of interesting study. MNPs are widely used in a variety of applications, such as hypothermic cell death of malignant cells and magnetic bio-separation for DNA extraction. In addition to its applications in magnetic bio-separation and magnetic hyperthermia, MNPs can be utilized as drug delivery systems (DDSs)**Error! Reference source not found.**. The main imaging techniques that make use of the magnetic characteristics of the particles are positron emission tomography (PET), computed tomography (CT), magnetic resonance imaging (MRI), and magnetic particle imaging (MPI). The *in-vivo* application includes:

Magnetic hyperthermia (MHT) in cancer therapy

One of the most potential biological uses of MNPs in cancer treatment is hyperthermia. It is a medical method in which tumour are killed by applying heat. The mechanism of magnetic hyperthermia is based on raising the tumour microenvironment's temperature to 41–47°C, which can either cause

apoptosis or necrosis through a sequence of metabolic processes that ultimately result in cell death[9]. A number of factors, including size, saturation magnetization levels, magnetic field parameters, anisotropy (magneto-crystalline or form), and magnetically induced hyperthermia, affect how much heat dissipation MNPs provide. The three forms of hyperthermia treatment are whole-body, regional, and localized. While whole-body hyperthermia therapy is typically used to treat metastatic cancer that has spread throughout the body, local hyperthermia therapy concentrates on a single targeted site within the body part, regional hyperthermia therapy typically targets larger tissue areas (such as limbs and organs). Local hyperthermia treatment is the most widely used approach in contemporary MHT among them.

Controlled and targeted delivery

One of the most advanced technologies in cancer treatment nowadays is Targeted drug delivery (TDD). It lessens adverse effects, concentrates the loaded medications on the cancer site, and regulates the quantity of drug flow towards the targeted tissues. Over time, there has been a significant growth in the use of MNPs in TDD. Gold or polymers, which are biocompatible materials, are typically used to functionalize MNPs. To make sure the anticancer medication may either be conjugated on the surface of MNPs or loaded within them, functionalization is done. An external magnetic field is used to direct the drug-laden MNP to the intended cancer spot once the medication has been loaded.

MRI imaging-The most widely used biomedical imaging method in diagnostic medicine is magnetic resonance imaging (MRI). Its main use is to produce high-resolution pictures of human tissues in two and three dimensions. The basis of magnetic resonance imaging (MRI) is nuclear magnetic resonance. They track the movement of the cells and offer molecular details on their viability and efficiency. When the cells are loaded with highly adequate numbers of MNPs, MRI delivers resolution as small as the cell's size. RNA-loaded magnetic liposomes are utilized to detect dendritic cell movement through the usage of magnetic particles in cell tracking and proliferation. Brain stem cell tracking using magnetic resonance imaging (MRI) is possible with iron-doped calcium phosphate nanoparticles.

The in-vitro application of MNPs involves:

Bioseparation

Under the influence of an external static magnetic field, magnetic bioseparation uses the special magnetic characteristics of magnetic particles to separate different biological molecules. Purification of DNA, proteins, antigens, and antibodies from their libraries is necessary before to their use in any biological application. To assess particular gene expression, for example, DNA detection and separation are essential steps prior to the polymerase chain reaction (PCR) stage. MNPs are mostly preferred due to their superparamagnetic property. Moreover, due to their strong magnetic force, biomolecules could be transported easily towards targeted sites within the human body. Purification and isolation of different biomolecules, such as antibodies, DNAs, proteins, antigens, and nucleic acids could be performed at a highly purified percentage due to the strong magnetic force of MNPs.

Biosensors

With a high sensitivity for early illness diagnosis, biosensing is an effective platform for the detection of bacteria, biomolecules, cells, DNA, sugars, and viruses. Analytical tools used in the biomedical industry are called biosensors. Their primary job is to translate chemical, biological, or biochemical reactions into electrical impulses **Error! Reference source not found.**.

Lab on chip system

Lab-on-a-chip (LOC) systems, also known as total micro analysis systems, are designed to fit all necessary functionalities onto a single, small-sized chip. These chips can be used for localized medication delivery, disease indicators, or to identify toxins; for instance, hollow Fe/Ga based MNPs. In microfluidic devices, it is possible to regulate the MNP synthesis's nucleation, growth conditions, and reaction parameters. The ability to control microfluidic MNPs even in nano-litre quantities, made possible by recent technology advancements, enables the isolation and detection of circulating tumour cells (CTCs). By margination, microfluidic layouts made it possible to distinguish between healthy red blood cells (hRBCs) and infected red blood cells (iRBCs). In addition to viruses such as norovirus, MNPs microfluidic technology has also accomplished HIV detection

platform. Additionally, automated MNP-based microfluidic μ-hall platform bacteria detection has been carried out that has ability to measure a single magnetically tagged bacterium at a cheap cost and with little sample preparation and test time; simple glucose sensor was created using a microfluidic system in which MNPs were filled with microreactors for enzymes.

Current and Future Challenges of MNPs

One of the main obstacles impeding the clinical application of IONPs is their safety for human use. Despite the fact that IONPs were licensed and used in clinics, for example, as contrast media and iron substitutes, a number of research have revealed that factors like composition, size, surface, characteristics, dosage, and delivery method can affect how safe are these medications. According to several researchers, the majority of IONPs were not eliminated from the body and instead collected in key organs including the liver and spleen, which can be hazardous. Moreover, the overabundance of free Fe released by Fe_3O_4 NPs might help cells produce reactive oxygen species (ROS), which can cause oxidative stress and impair the mitochondrial activity of the liver [7]. Additionally, MNPs with various coatings are hazardous to brain tissue and have been linked to neurodegenerative illnesses including Parkinson's and Alzheimer's. Therefore, before SMNPs are fully used in clinical settings, more research on the toxicity of SMNPs over the long term in the human body must be done. The lack of an efficient MF gradient in SMNPs makes it difficult for external magnets to target deep organs within the body, which presents another issue when employing them as DDS. Making MNPs with high magnetic moments or using superconducting magnets which may provide strong magnetic gradients, are the two ways to resolve. The diseased conditions that occur in people cannot be adequately reflected in an animal model, such as a mouse, because the type of malignancy varies from person to person. Moreover, the last obstacle to the commercialization of smart nano-carriers is the absence of clear regulatory requirements. In realm of the magnetic nanoparticles (MNPs), future challenges loom large, each presenting unique hurdles and opportunities for researchers and industries alike. One of the foremost concerns is the biocompatibility and toxicity of MNPs, particularly in biomedical applications, where their interaction with biological systems must be thoroughly understood and mitigated. Moreover, improving the targeting efficiency of MNPs is paramount for their efficacy in targeted drug delivery and imaging applications. However, the journey towards clinical translation of MNPs is fraught with regulatory challenges, necessitating meticulous attention to safety, efficacy, and manufacturing standards.

Conclusion

Magnetic nanoparticles, with their unique properties and wide-ranging applications, are at the forefront of scientific and technological advancements. In the field of medicine, these nanoparticles have revolutionized targeted drug delivery systems by allowing precise localization and controlled release of therapeutic agents, minimizing side effects and improving treatment outcomes. Moreover, their utility in medical imaging, such as magnetic resonance imaging (MRI), offers clinicians valuable insights into disease diagnosis and progression. In cancer therapy, magnetic nanoparticles have emerged as promising tools for hyperthermia treatment, where they generate heat when exposed to alternating magnetic fields, effectively destroying cancer cells while sparing healthy tissue. Beyond medicine, magnetic nanoparticles play a vital role in environmental remediation efforts. Their ability to selectively adsorb and remove heavy metals and organic pollutants from water sources and contaminated soil makes them indispensable in cleaning up environmental hazards and restoring ecosystems. In sensor technology, magnetic nanoparticles enable the development of highly sensitive and selective sensors for detecting a wide range of analytes, including biological molecules, gases, and environmental pollutants. Their ability to amplify signals and provide rapid detection makes them invaluable for applications in healthcare diagnostics, environmental monitoring, and industrial process control. In the realm of technology, magnetic nanoparticles hold immense potential for advancing data storage capabilities. Research is underway to harness their magnetic properties for developing next-generation magnetic storage devices with higher storage densities and faster data access speeds, addressing the ever-growing demand for data storage in the digital age. In conclusion, magnetic nanoparticles represent a versatile and promising class of

materials with multifaceted applications spanning medicine, environmental remediation, technology, and catalysis. Continued research and innovation in this field are expected to unlock new opportunities and address global challenges, driving progress towards a healthier, cleaner, and more technologically advanced future.

Future Perspectives

This review focused on Magnetic particle applications that has been made possible by advances in methods for synthesis and surface modification. Therefore, further research is needed to achieve continuous procedures for the synthesis of particles with the necessary sizes, properties and surface functional groups for novel applications. As research continues to advance, we can expect further innovations and applications of MNPs in diverse areas, ranging from biotechnology to materials science, contributing to significant advancements in various fields

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Ethical Approval

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Conflict of Interest

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