Chapter 15
Role of Magnetic Nanomaterials in Biotechnological Applications

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Abstract The advent of nanoscience is considered bringing out the next breakthrough in medicine and biotechnology. For the past few decades, many research groups throughout the world are involved in synthesizing novel nanomaterial for several biotechnological applications. In the current chapter, the different types of magnetic nanoparticles along with their properties are discussed. Consequently, the different physical and chemical methods adopted for the synthesis of magnetic nanoparticles have been discussed. The applications of magnetic nanoparticles in biotechnology have been discussed in breadth. Firstly, the role of magnetic nanoparticles in magnetic resonance and sentinel lymph node imaging has been discussed. Thereafter, magnetically triggered drug release and utilization of magnetic nanoparticles in cryopreservation has been elaborated. Finally, the role of MNPs in bacterial sequestration and in cancer diagnosis and therapy has been outlined.

Keywords Magnetic nanoparticles · Biotechnology · Cancer · Imaging · Biosensing · Proteins · DNA

15.1 Introduction

Since the ninth century or a very long time ago, when Mesopotamian artisans used nanoparticles to create a dazzling effect on the surface of pots, there has been a strong scientific interest in the study of nanoparticles (NPs), which are currently the subject of much The Greek word from which "nano" is derived means "dwarf" [1]. Small particles with a magnetic and Ferromagnetic (FM) structure are referred to

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as Magnetic Nanoparticles (MNPs) in popular usage [2]. According to the International Organization for Standardization (ISO), a nanoparticle is a "nano-object with all three exterior dimensions in the nanoscale," where the nanoscale is defined as lengths between 1 and 100 nm [3]. Due to their particular qualities, such as their huge surface areas and quantum size effects, nanoparticles are thought of as a different form of matter. Additionally, it represents a fascinating compound that is present in a variety of living things and has a wide range of bio applications. These innovative, easily manufactured nanoparticles have various biomedical uses among all the many types of nanoparticles. Magnetic fields can control magnetic nanoparticles that contain magnetic elements including chromium, iron, cobalt, gadolinium, manganese, and nickel as well as their chemical components such oxides, ferrites, and alloys. Magnetic nanoparticles' physical and chemical properties are strongly influenced by their crystalline structures, sizes, shapes, and chemical composition. In addition to the features that all nanomaterials share, such as a low Curie temperature, a high magnetic susceptibility, and superparamagnetic, magnetic nanoparticles have special magnetic properties [4]. The highest priority for nanoparticles is in medicine, pharmaceuticals, or diagnostics for medication delivery. MNP research has gained a lot of attention in recent years, both technologically and from a fundamental science perspective. Researchers from the fields of chemistry, physics, and biology have all demonstrated a similar interest in synthesizing, understanding, and advancing a variety of applications in the field of MNPs. Over the past 10 years, a lot of research has been conducted in this field due to the potential biological applications of nanosized magnetic particles, such as enhancing magnetic resonance imaging (MRI) quality, hyperthermic cancer cell therapy, site-specific medication delivery, and modifying cell membranes [5]. The right processes, including precipitation, co-precipitation, thermal breakdown, hydrothermal synthesis, microemulsion synthesis, and plant-mediated synthesis, have been created to manage the size and shape of iron oxide magnetic nanoparticles, which influence their importance. The goal of this chapter is to summarize the extensive progress in various biotechnological fields that have been made by different parameters and we can use in different fields, also. so that the reader can use the chapter as a reference if necessary.

15.1.1 History of Magnetic NPs

MNPs have long been a topic of discussion. The Nobel Prize winner Louis Neel's 1949 work on geomagnetism is credited with providing the first insights into the unconventional magnetic behavior of very small magnetic particles. At the time, the nanoparticles were called "fine grains," which indicates magnetic information storage, or other modern applications of such nanoparticles and no one thought about the nanotechnology applications and also anticipated the biomedical. Neel discovered in 1947 that Fe grains with a diameter of < 32 nm are single domain particles. The coercivity of these grains was very high. In 1949, L. Neel proposed foundational research on the magnetism of single-domain grains 2 years later [6], which provides

a quantitative explanation for several geomagnetism experiments' results. In contrast to the thermal remanence that igneous rocks (solidified lava) can develop in the Earth's magnetic field at room temperature, some researchers found that igneous rocks possessed a thermal remanence that was substantially stronger. Furthermore, they learned that rocks heated by the Earth's magnetic field become magnetized in the direction of the field. By tracing the magnetization of rocks, it is possible to infer that the Earth's magnetic field had reversed direction numerous times in the past. The research was also used to date ceramics using pottery ("Terres cuites" in Neel's article). Therefore, the original driving forces behind the research of MNPs were geological and cultural heritage dating, very dissimilar from current topics of interest, which are primarily in biomedicine [7], Neel discovered that under a certain single-domain radius, RSD (he determines RSD16nm for Fe), the single-domain magnetic structure is no longer stable and the magnetization reverses spontaneously in a period known as "relaxation time," giving rise to the "superparamagnetic" behavior. This relaxation period's equation as a function of applied field and temperature was given by Brown [8] investigated this further, and as a result, the Neel–Brown legislation is currently employed in modern MNP applications [9].

15.1.2 Different Types of MNPs

One type of nanoparticle (NP) known as a Magnetic Nanoparticle (MNP) exhibits certain reactions when a magnetic field is applied. It has a large explicit surface area, small molecular size, magnetic responsiveness, and superparamagnetic [10]. In general, MNPs can be selectively connected to functional molecules and permit transportation to a particular location under an external magnetic field [11]. Magnetic nanoparticles are made up of chemically bound nano-forms of magnetic elements like iron, gadolinium, cobalt, nickel, manganese, and chromium. For its nanoscale size, it is superparamagnetic, offering significant potential for a variety of uses. A particularly specific interaction known as magnetism undergoes significant alterations at the nanoscale level [12]. There are several types of magnetic nanoparticles, however, the most significant ones are listed below:

i. Oxides: Ferrite

The magnetic nanoparticles that have been studied the most up to this point are ferrite nanoparticles. Because they are superparamagnetic when ferrite nanoparticles are smaller than 128 nm, they don't have the capacity for self-aggregated [13]. Only when an external magnetic field is present do they exhibit magnetic behavior. The remanence equals zero when the external magnetic field is removed once more. Similar to non-magnetic oxide nanoparticles, ferrite nanoparticles frequently have surfactants, silicones, or derivatives of phosphoric acid added to their surfaces to promote their stability in solutions.

ii. Metallic with a shell

By using surfactants, polymers, precious metals, and moderate oxidation, magnetic nanoparticles' metallic cores can become passive. These Co core, Co O shell, and gold outer shell nanoparticles have recently been studied for their production and exchange bias effects. When exposed to oxygen, Co nanoparticles develop an antiferromagnetic Co O layer on their surface. Recently, graphene was utilized to make nanoparticles with a magnetic core made of either elementary iron or cobalt and a nonreactive shell. The following advantages over ferrite or elemental nanoparticles: A greater level of organic solvents as well as stability in basic and acidic solutions.

15.2 Properties of Magnetic Nanoparticles

Magnetic nanoparticles' physical and chemical properties are significantly influenced by the synthesis method and chemical composition. The particles typically have a size between 1 and 100 nm and may exhibit super par magnetism.

15.2.1 Surface Properties and Charge

Veiseh et al. hypothesized that proteins will absorb charged MNPs, removing them from circulation [14]. Strong negative MNPs in particular cause an increase in liver uptake, while positive MNPs also bind to non-specific cells. The basic principles of electrophoresis—the movement of dispersed colloids with a fluid—are established when an external electric field is applied, since these produces an electric potential distribution. For the synthesis and utilization of nanoparticles, Duran et al. provide examples, such as coating and medication loading.

15.2.2 Size Dependent

Magnetic nanoparticles exhibit a wide range of distinctive magnetic phenomena, as opposed to their bulk counterparts. Their variations in size, shape, and composition have an impact on fundamental magnetic properties, such as coactivity (Hc) and susceptibility. Each nanoparticle transforms into a single magnetic domain when its size falls below a crucial value (Dc), and when the temperature rises over the blocking temperature, it exhibits super paramagnetic activity (Tb). These specific nanoparticles respond swiftly to applied magnetic fields and behave like enormous paramagnetic atoms with hardly any remanence (residual magnetism) and coactivity (the field required to bring the magnetization to zero). Due to their properties, superparamagnetic nanoparticles are extremely sought-after for MR contrast agents.

15.2.3 Composition, Shape, and Size

We have covered the compositional aspect of MNPs in this paragraph. The three most common types of magnetic Nanoparticles (NPs) at the moment are metal, metal alloy, and metal oxide. The most common NPs are iron, cobalt, nickel, silver, gold [15], and silver. Ferrites ($CoFe_2O_4$ and $Mn0.6Zn0.4Fe_2O_4$) and iron oxides ($–Fe_2O_3$ and Fe_3O_4) make up the majority of metal oxide NPs, while other metal alloy NPs include FeCo, FePt, and other elements. Similar to MNPs, there are numerous varieties accessible today. Although the most typical ones are Fe oxides and still Fe with a somewhat consistent composition, numerous others can be used for certain applications. Currently, ferrites with rare earth (RE) metals and additional elements like Zn, Ni, Co, etc. are intended for biomedical applications. Pure metal particles are receiving a lot of attention because of the huge magnetism that pure FeCo alloy particles and Fe can achieve. For use in permanent magnets or storage media technologies, some materials, such as FePt, aspire to have a very significant magnetic uniaxial anisotropy. Normally, RE alloys like Sm–Co or Nd–Fe–B are used to make permanent magnets, but recent efforts to make magnets without RE have prompted the development of MNPs made of Co carbides and Fe with incredibly low iron and extremely high anisotropy [16].

Size: The method used to determine the particle size affects the parameter, which is not a fixed value. The following diameters or similar radii are at least distinguishable.

- Visual radius: The radius of the physical particle can be seen via transmission electron microscopy (TEM) and atomic force microscopy.
- Diffraction radius: The coherent diffracting portion of the particle has a radius of this size. Single crystal particles may have a chaotic surface layer that is visible in TEM but does not affect diffraction.

Magnetic radius: The particle's sensitivity to magnetic fields is dependent on the effective radius of its magnetic core. Because the surface atoms have fewer neighbors and hence experience less exchange and anisotropy interactions, the magnetic behavior changes even in well-ordered particles. This is important in the context of the superparamagnetic.

15.2.4 Particle Shape

It is impossible to find real spherical particles since crystals are crystalline and have preferred crystallographic planes at their surfaces. The precursor type and concentration can be modified, as well as the inclusion of contaminants while synthesizing in an organic medium. The formation of the particle is kinetically controlled at high precursor concentrations, changing the particle's shape to cubic or tetrahedral. Nanocapsules and iron oxide nanorods/nanorices with rod-like structures have potential applications in the field of biomedicine. Original methods can also be used to create octopuses, flowers, and other strange things [17].

15.3 Different Synthesis Methods

There are two primary ways to create MNPs, and they are as follows: physical methods and chemical approaches. The most popular techniques include wire explosion, ball milling/mechanical process, laser evaporation, and EEW.

15.3.1 Physical Methods

The physical procedures are employed by both top-down and bottom-up approaches. The bottom-up strategy can result in evenly distributed, fine nanoscaled minuscule particles as opposed to the top-down strategy. The prime example of a bottom-up method is laser evaporation [18]. By using a top-down approach, high-intensity ball milling is used to break down bulk materials into nanoparticle sizes. The mechanical crushing of NPs to obtain the desired form and size is difficult [19]. MNPs are also produced physically utilizing a variety of methods, such as the inert-gas condensation method and the wire explosion method.

15.3.1.1 Ball Milling or Mechanical Method

A top-down method of creating MNPs from bulk material is through ball milling. The mechanical grinding of particles with a coarse texture into particles with a fine texture is an easy and practical technique [20, 21]. This technique was initially created in 1970 [22]. Steel balls continuously colliding with solid materials impart kinetic energy to the solids, resulting in a powder that is nano- or micron-sized. The key variables influencing the creation of nano/micro size crystals are the ball to powder ratio, ball size, vibration speed, and milling time. The primary drawback of this procedure is product contamination [23].

15.3.1.2 Laser Evaporation of MNPs

A bottom-up method called laser evaporation creates nanoparticles by condensation from a liquid or gaseous phase. A quick method for producing MNPs is laser evaporation, which is also known as laser ablation. This method can also be used to create iron oxide MNPs. Choosing coarse-textured raw materials (in the m or mm size ranges) and evaporating them through the focus of a laser beam are required steps in this process. The quick condensing and gas phase nucleation of the material's vapors after cooling results in the formation of nanoparticles. This procedure is less expensive and more efficient than wet chemistry methods, which create hazardous waste and need expensive chemicals [24].

15.3.1.3 Wire Explosion Technique

The wire explosion approach, a novel physiochemical technology, allows for the safe and clean synthesis of MNPs. There is no need for any extra procedures, such as by-product retreatment or NP separation from solution, in this very effective one-step approach. This technique was previously used to make iron oxide MNPs to remove arsenic from water [25]. To create fewer polluted nano powders, it is environmentally friendly and uses little energy [26]. It is not possible to manufacture monodispersed NPs using this approach [27].

15.3.1.4 Electrical Explosion of Wires Method (EEW)

Creating metal nanoparticles with this technique is unusual. It was created by Professor Yuri Kotov [28, 29] and is based on the metal wire evaporating when subjected to a strong electric current pulse. The wire, which has a diameter of 0.1–0.5 mm, overheats to 104 K in a matter of milliseconds when exposed to a 5 kV voltage. Before cooling and solidifying into spherical metal nanoparticles, the metal rapidly evaporates, and the vapors disperse in the inert gas. As with an electrical fuse, the fundamental operating principle is the same (Fig. 15.1).

The following are the key characteristics and technological benefits of the EEW.

The metal wire can only be used if it is initially pure. It serves as a limiting factor in the production of precise spherical metal particles with high purity. Crucible, milling, ball, or jar, contamination is not a possibility. It is possible to synthesize carbides, metal oxides, nitrides, etc. by changing the gas environment (O_2, N_2, etc.). The wire diameter and applied pulse energy, length, gas pressure, and flow rate are simple-to-tune variables that affect particle size. The average particle sizes are in the 10–100 nm range.

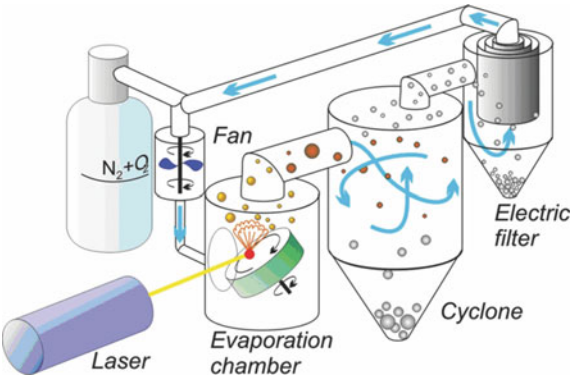

Fig. 15.1 Schematic representation fabrication of the iron oxide nanoparticles. Adapted with permission from AIP Publishing [30]

By synchronizing the supply and evaporation of the wire, a continuous pulsed system can be established in manufacturing. Because the high voltage is only applied briefly per microsecond, there is very little energy use. Since no waste is produced, the process is environmentally friendly.

Depending on the type of metal and the desired attributes of the finished product. The production rate of a single EEW device is considerable (100–500 g/h). The EEW's simple method for surface modification of nanoparticles—either during manufacture, as in the case of I.V., or afterward, when the particles are dropped into a reactive liquid—is arguably its most intriguing aspect [30]. The MNPs in EEW can be modified in situ using both simple liquids and solutions, and the process is adaptable. The active metal surface becomes inert due to saturated hydrocarbons (hexane).

15.3.2 Chemical Method of MNPs

The various bottom-up strategies used in chemical synthesis are diverse. Below is a detailed explanation of some popular techniques for creating MNPs. There are as follows: Coprecipitation method, Thermal decomposition, Hydrothermal, Microemulsion, MNPs coating, and functionalization.

15.3.2.1 Thermal Decomposition

In this procedure, monodispersed NPs are produced at high temperatures using organometallic precursors. This approach results in MNPs with good crystallinity, regulated size, and clearly defined shape. To create MNPs with the necessary size and form, the organometallic precursors are degraded in the presence of organic surfactants [31]. In the process of creating MNPs, stabilizing agents such as hexadecyl amine, fatty acids, and oleic acid are used. The stabilizing agents used in the breakdown process have the power to delay NP nucleation, which controls MNPS growth and helps produce the ideal size of < 30 nm and a spherical shape. This process purportedly resulted in the production of magnetically active iron composites and Fe_3O_4 nanocrystals [32]. Metal nanoparticles (NPs) are made by thermally dissolving the zero-valent metal precursor $Fe(CO)_5$, while high-quality iron oxide MNPs can also be made via oxidation. However, if precursors degrade in the presence of cationic metal centers, metal oxide nanoparticles can be produced instantly [31, 33]. This method has been recommended as one of the finest ways to make MNPs that are uniform and shape on a large scale [34]. The biomedical industry forbids the use of this process due to the risk of creating hazardous organic-soluble solvents [35]. When producing magnetic particles of lower sizes, coprecipitation is less efficient than thermal composition.

15.3.2.2 Coprecipitation

The most popular technique for creating MNPs with regulated size and magnetic characteristics is coprecipitation (Fig. 15.2). It is frequently used in biomedical applications and involves the use of less toxic materials and techniques. When we require a lot of nanocrystals, the coprecipitation method of making MNPs is very practical and simple. This process is frequently used to create NPs with regulated sizes and desirable magnetic characteristics.

To create MNPs, various metal ions are dissolved in a solvent. By employing ferric chloride, manganese ferrite ($MnFe_2O_4$) NPs were created ($FeCl_3$). During the coprecipitation process, several factors, including metal ions, pH, their concentrations, reaction temperature, salt type, and particle size and shape, can have an impact on the composition of MNPs. A quick and easy way to make uniformly dispersed NPs of tiny size is through the coprecipitation of MNPs. It can occasionally be difficult to regulate the shape of MNPs via coprecipitation, even though this method is chosen for its simplicity of application combined with sodium hydroxide (NaOH) salts and manganese (II) chloride ($MnCl_2$) as well as the metal ions or the precipitant.

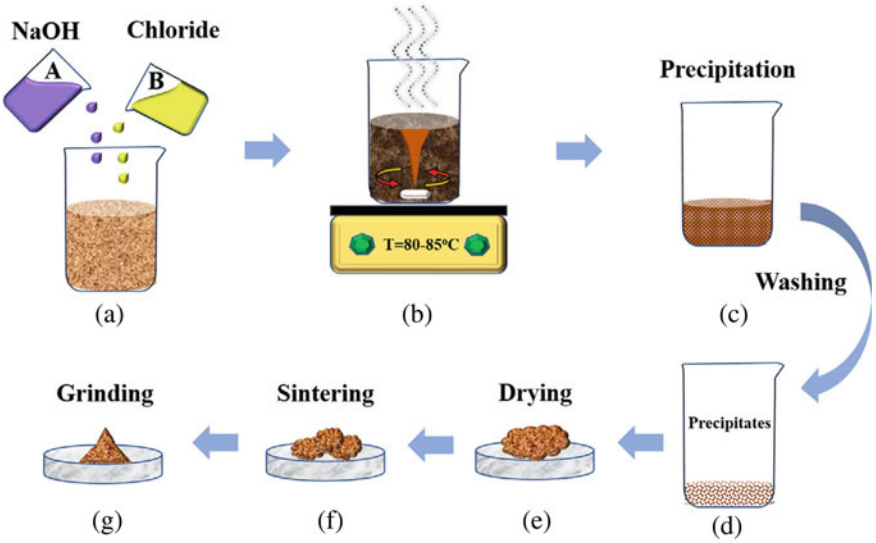

Fig. 15.2 Using the co-precipitation method, the above figure steps to synthesize ferrite nanoparticles: **a** solution of NaOH and chloride precursors, **b** stirring at 80–85 °C for 1 h, **c** precipitation, **d** precipitates after washing, **e** drying at 80 °C, **f** sintering at 1100 °C, and **g** ground final product. Adapted with permission from Wiley [36]

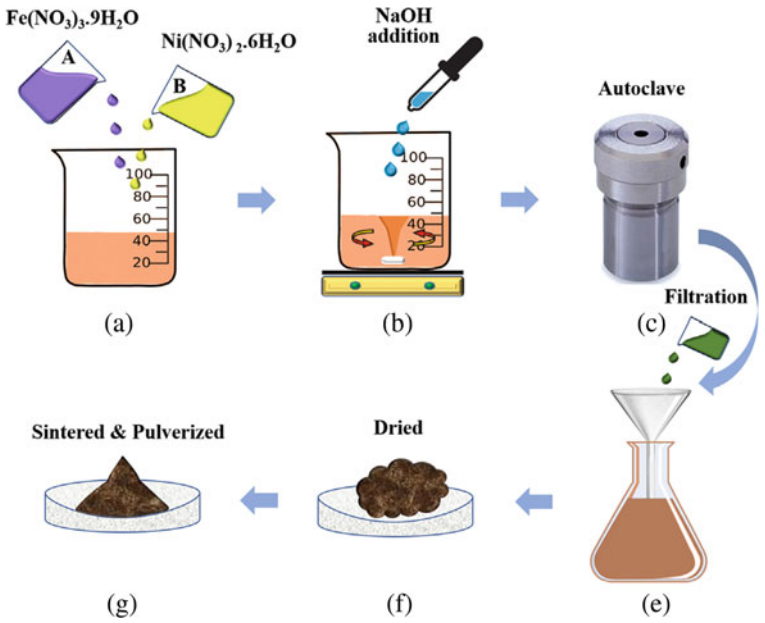

Fig. 15.3 Illustration of ($NiFe_2O_4/Fe_2O_3$) nanocomposite synthesis via hydrothermal method: **a** addition of $Fe(NO_3)_3{\cdot}9H_2O$ and $Ni(NO_3)_2{\cdot}6H_2O$ precursors, **b** magnetic stirring during the addition of NaOH(1 M) until to pH 12, **c** autoclave the mixture for 20 h at 180 °C, **d** filtration, **e** drying at 100 °C, and **f** annealed in the air for 2 h at 400–800 °C and pulverized to get the final product. Adapted with permission from Wiley [36]

15.3.2.3 Hydrothermal

Utilizing high pressure and temperature, this technique is utilized to create NPs in an aqueous solution (Fig. 15.3).

One of the successful solution reaction-based methods for producing MNPs at high pressure and temperature is hydrothermal synthesis, also known as solvothermal synthesis. MNPs are produced by the hydrothermal method via an oxidation and hydrolysis reaction [37]. You can make more NPs by contrasting this method with the microemulsion method. However, due to the high heat and pressure involved in this process, it must be carried out carefully and with specialized equipment. Comparatively, the hydrothermal process is preferred to others, such as sol–gel, since it results in NPs with the right size, shape, high crystallinity, and constant composition [38].

15.3.2.4 Microemulsion

To produce turbid systems of hydrophilic and lipophilic phases in surfactants, microemulsions and occasionally co-surfactants are utilized. This transparent,

isotropic system of water, oil, and amphiphile exists. This procedure involves mixing oil with a surfactant while stirring water magnetically at room temperature. Three types of emulsions exist microemulsions in which the ratios of the two components are roughly equal, oil in water (O/W), which is the aqueous phase with some oil droplets, water in oil (W/O), which is oil as the dominant phase with some water droplets. For instance, a surfactant coated with the droplets of water in an organic solvent in a microemulsion of the w/o type reduces the size of the MNPs [39, 40]. A w/o kind of microemulsion, which required using two microdroplets—one with a precipitating agent and another with a metal percussor which was used to make certain iron oxide MNPs [41]. MNPS was created using a silica coating and then changed with amino after this process, which was beneficial for separating tumor cells. By using microemulsion, small amounts of uniformly dispersed MNPs were produced.

15.3.2.5 MNPs Functionalization and Coating

MNPs are routinely coated with non-magnetic or magnetic materials to make them chemically stable and colloidal (ii) alter the magnetic properties of the MNPs; or (iii) give a different surface. One of the most popular types of coating materials is inorganic, such as silica (SiO_2), gold, or gadolinium. Another frequent option is non-polymer organic stabilizers such as oleic acid, stearic acid, phosphates, etc. Dextran, polyethylene glycol, polyvinyl alcohol, and others are common polymer stabilizers. In this case, the MNPs are fixed, which may not be appropriate for all applications. The MNPs are commonly covered in organic compounds during chemical synthesis. These organic coatings are very simple to create and may be applied on MNP surfaces physically or chemically to create a uniform single-particle covering with variable characteristics. Over the past few years, the surfaces of MNPs have been modified with biocompatible materials such as PEG, carbon, or gold for their prospective use in a range of applications, including the treatment of cancer [42]. It is quite simple to create these organic coatings, which can be applied physically or as already mentioned, by coating the MNPs with specific targeting ligands, therapeutic drugs, or contrast agents that can be employed to functionalize them. By doing so, it is possible to address some of the MNPs' most prevalent drawbacks, such as no specificity and a lack of biocompatibility, while simultaneously giving the MNPs new potential for multifunctional applications. In the context of biological applications, the functionalization of MNPs has drawn a lot of scientific attention. The functionalization of MNPs in biological applications has received a lot of scientific attention. For instance, chemotherapy drug molecules (such as doxorubicin) can be attached to the surface of MNPs, revolving them into magnetic drug carriers that can deliver a large dose of the drug to the tumor area and release the drug in a localized manner, reducing the toxicity of the drug to the rest of the body [43].

15.4 Characterization Methods of MNPS

To evaluate their physicochemical and magnetic properties, the MNPs are described using a variety of tools. Different physicochemical and magnetic properties can be demonstrated by varying the size of NPs. The following tools are used for characterization: Scanning Electron Microscopy (SEM), UV Spectrophotometer, Transmission Electron Microscopy (TEM), Mossbauer Spectroscopy (MS), Energy Dispersive X-ray Diffraction (EDXD), Atomic Force Microscopy (AFM), Fourier Transform Infrared (FT-IR) Spectroscopy [44]. We can utilize more and more of the instruments listed above to study the structure and magnetic characteristics of magnetic nanoparticles.

15.4.1 Surface and Size Morphology

Depending on modifications in size and form, MNPs' physicochemical properties can change. Surface area, size, and particle dispersion are calculated using the Brunauer–Emmet–Teller (BET) and Dynamic Light Scattering (DLS) methods. While it is possible to analyze the surface morphology of MNPs using techniques like SEM/FESEM, TEM/HRTEM, and AFM. We can quantify their diameter by using these tools to get pictures of them that give us a basic idea of their size and shape. Step height, surface roughness, and particle distribution location are used by the AFM technique. Using TEM, it is possible to learn about the size, composition, and morphology of NPs. SEM, on the other hand, offers details regarding the composition and surface topography of the materials. Size estimation is possible using field-emission SEM (FESEM), high-resolution TEM (HRTEM), and XRD methods. Using TEM, it is possible to identify NP aggregation state, crystallinity, lattice spacing, and electron phase shift [45, 46]. Use XRD to determine the crystallinity of NPs. The distribution and average size of the particles can be determined using methods including Mossbauer spectroscopy, DLS, and photon correlation spectroscopy.

15.4.2 Characterization of the Magnetic Properties

MNPs can be measured for magnetization and susceptibility. Magnetometers that use vibrating samples are ideal for this. SQUID magnetometry is needed when the sample quantity is extremely small. Hysteresis loops and other DC magnetization experiments provide values for spontaneous magnetization, remanence, and coercivity. The size distributions of the particles in SPM particles can be described by fits to the lognormal distribution of the Langevin function distributions [47]. The irreversibility temperatures and Zero-field Cooling-Field Cooling (ZFC–FC) curves of M(T) display blocking which offers additional insights into particle distribution

and interactions. The AC susceptibility, which scans the field's frequency and can track the blocking temperatures as a function of frequency throughout a broad range, is another characteristic of the Neel and Brown relaxation processes. 1 Hz to 1 MHz can be easily covered by common equipment.

Sometimes, it's challenging to distinguish between distinct magnetic phases with conventional techniques, and Mossbauer spectroscopy is a crucial tool for separating them. The method can also provide light on the superparamagnetic behavior since the collapse of the hyperfine field affects the blocking temperature. The interaction between absorber nuclei and gamma rays which is the origin of the Mossbauer effect has a comparable frequency of about 60 MHz, which is significantly faster than the much slower direct magnetization or susceptibility measurements described above. The heating efficiency of the MNPs is assessed using a physical metric called the Specific Absorption Rate (SAR). Thermal energy is shown as a unit. The MNPs release mass and time as magnetization switching processes take place in alternating magnetic fields. Serving as the SAR unit is W/g.

In the field of hyperthermia, the SAR parameter has been widely used to assess magnetic particle heating potential and to determine the upper and lower exposure limits for the frequency and field strength of the applied magnetic fields. The most important benefit of laboratory-made equipment is that it is designed and constructed with consideration of the requirements of the various experiments required by the research. Some equipment uses one of two measuring techniques: In some circumstances, a nonmagnetic, nonconducting thermometer records the temperature increase that occurs when the alternating field is applied. Other technologies get the SAR from the loop area via the high-frequency recording of the full hysteresis loop (100 kHz to 1 MHz).

15.5 Applications in Biotechnology

15.5.1 Magnetic Resonance Imaging

Over the past few decades, research in the fields of medicine and biology has been significantly influenced by nanoscience and nanotechnology. Nanoparticles have some unique qualities, such as a high surface-to-volume ratio, quantum properties, and the capability to transport other substances because of their small size. For many medical applications, these qualities make them appealing [48].

MRI or Magnetic Resonance Imaging is a technique that is frequently used for the diagnosis of cancer [49, 50]. Magnetic resonance imaging (MRI) creates images of tissues using the magnetic properties of protons rather than ionizing radiation [51]. This is a noninvasive imaging technique and this creates three-dimensional anatomical images which are useful for the early detection, diagnosis, and follow-up of diseases. Proton dipoles, typically derived from water molecules, are normally positioned within tissue and exhibit a magnetic response in MRIs at the moment

of investigation. There are some examples of Paramagnetic and super-paramagnetic materials like europium (Eu), gadolinium (Gd), manganese, and neodymium (Nd) as examples of paramagnetic materials and those containing iron oxide in the shape of magnetite (Fe_3O_4) and/or g-Fe_2O_3 are examples of super-paramagnetic materials. Iron oxide-based MNPs were used for molecular imaging as they induce a more effective contrast. A powerful and persistent external magnetic field aligns the magnetization of the protons and results in equilibrium magnetization along the z-axis (Mz). The injection of such an exogenous radio frequency (RF) pulse disrupts the equilibrium magnetization. This pulse provides energy to protons by spinning their magnetic moments off the *z*-axis, in phase, and at the flip angle. While emitting RF energy, the protons undergo various relaxation processes to return to their resting alignment. The distribution of signal intensity levels is represented by grayscale images created using the Fourier transform of the measured RF signals after a predetermined amount of time. Protons randomly orient themselves under normal circumstances, producing no overall magnetic moment. After the MRI machine creates the magnetic field, the protons position themselves either parallel or antiparallel to the primary magnetic field. This process, known as longitudinal magnetizable, produces a total magnetic vector (M) which reflects in the direction of the main magnetic field. Gradient coils inserted into the main magnets change the direction of the magnetic field, allowing MRI to image along the *x*, *z*, or *y* axes. Protons revolve around the primary magnetic field's long axis in-phase and out-of-phase at a pace that is directly proportional to the magnetic field's strength [52]. The net magnetizable vector then rotates 90° in the direction of the transverse plane as a result of radio frequency pulses used by doctors to excite protons into an energetic, in-phase condition. Protons finally return to their initial state of longitudinal out of phase and loosen up to their normal state via spin–lattice (T1) and spin–spin (T2) relaxation, respectively [53, 54]. Because of magnetic field inhomogeneities, protons de-phase significantly faster than T2, owing to T2 relaxation and these inhomogeneities [55]. Protons relax across the transverse plane to the longitudinal plane, causing changes in the net magnetic vector that are subsequently utilized to scan tissues.

To improve the accuracy of MRIs, contrast agents are used. Based on their capacity to influence T1 images and also known as T2/T2* relaxation times [56, 57]. T1 contrast agents change the water proton's longitudinal (T1) relaxation times to produce a strong signal and increase the clarity of cells and image intensity. Agents with T2/T2* affect the transverse (T2/T2*) relaxation times. Dark negative signal intensities are produced by water protons in images. Although SPN-based contrast agents are also known to impact T1, their main outcome on T2* relaxation allows for the finding of hypo-intense regions on the acquired image [58]. Because their ability to change T2 and T2* settling time is proportional to their ability to alter the local magnetic field, SPN-based contrast agents with high magnetic vulnerability and relaxivity are preferred.

SPNs have been used to identify and monitor individual cells, as well as to scan tissues and cell clusters [59]. A variety of non-specific SPN-based contrast agents are available for the application of general imaging [60]. These non-specific SPNs, however, are unable to aggregate successfully in limited microniches, including

tumor regions. Tumor-specific delivery of SPNs can boost their accumulation in cancer locations and improve MRI resolution by connecting tumor-specific targeting molecules to the SPN outer shell. Conjugating anti-fetoprotein and anti-glypican antibodies to the SPN shell, for example, can be utilized to target hepatocellular cancer precisely [62]. Future research into specialized contrast agents will improve the availability of MRI as a non-invasive and effective technology for imaging certain disorders. Non-specific SPN-based contrast agents, on the other hand, have unquestionably revolutionized tissue imaging and diagnosis.

15.5.2 Sentinel Lymph Node Imaging

Sentinel node imaging using lymphoscintigraphy reveals the lymph flow path from the cancer location as well as the lymph nodes that are most near the tumor. The term "sentinel lymph nodes" refers to these lymph nodes. The body's lymphatic system can better be visualized with the use of this nuclear medicine scan. In many ways, lymphatics are a complex network of tiny blood vessel-like structures, but instead of carrying blood, they carry a clear fluid called lymph. Numerous locations throughout the lymphatic pathways are home to lymph nodes. Lymphoscintigraphy depicts the lymphatics in numerous body regions and not only reveals their anatomical location and network structure but also their functionality.

Lymph nodes (glands) are small bean-shaped structures that function as nodes to filter lymphatic fluid, removing waste items such as viruses, germs, and cancer cells. The humoral immune system's antigen presentation and crucial processes in cell-to-cell contact also take place in lymph nodes. The first lymph node to collect drainage from particular tumor tissue is referred to as an SLN. There could be more than one SLN for a specific tumor in some circumstances. Since they are the location where the initial tumor has the most chance of spreading, SLNs are essential. Therefore, the malignancy seen in neighboring lymph nodes or SLNs (local lymph nodes) and/or additional accompanying organs determines the stage and degree of spread for oncologists. The spread of cancer informs the creation of a suitable course of treatment. No cancerous cells present SLNs show no evidence of spread; however, it could also imply that cancer has a minimal capacity to spread through a patient. Staging cancer and estimating the extent of In a patient, metastasis are crucial since they are significant. determinants of survival and recurrence. As a result, the presence of cancer in SLNs or surrounding lymph nodes (regional lymph nodes) and/or additionally linked organs aids oncologists in determining the stage and amount of cancer spread (metastasis) and informing the formulation of an effective treatment strategy. The absence of cancer cells in SLNs implies that no dissemination has occurred and may also indicate that cancer in the patient has a poor metastatic ability. The draining Lymph Node (dLN) nearest to the cancer is identified, followed by lymphadenectomy for biopsy to check for the presence of cancer cells. Torchia and colleagues achieved detection of SLNs in sedated pigs using interstitial and intradermal injections of ultra-tiny superparamagnetic iron oxide (USPIO) (0.25 mg

of ferumoxtran-10) in 2001 (Fig. 15.4). The ferumoxtran-10 (Combidex, Advanced Magnetics Incorporated, Cambridge, MA) first-generation USPIO nano-particle has a core diameter of 46 nm and hydrodynamic diameter of 20–40 nm, with only an iron oxide core coated with a layer of dextran. These particles have considerable T1 relaxation effects. Due to the dextran coating, ferumoxtran has a plasma half-life of even more than 24 h in humans. Ferumoxtran was discovered to elude the body's reticuloendothelial system due to its lengthy blood half-life. This makes it ideal for sentinel node mapping. In the study, MRI images were utilized to identify SLNs from 15 min to 48 h after injection. Hiraiwa et al. used a subcutaneous injection of commonly available thermoresponsive MNPs into the thoracic wall of rats to test them as MRI contrast agents. This study shed light on the viability of using commercially available MNPs for SLN mapping. The thermoresponsive polymer loadings of poly N-isopropyl acrylamide in the MNPs studied varied. Pouw et al. [62] used magnetic SLN mapping in ex vivo colorectal cancer tissue (12 patients) to demonstrate the feasibility of using a portable magnetic probe based on a vibrating samples magnetometer (Sentimag, Endomagnetics LTD., London, UK) to estimate the quantity of SPIONs in lymph nodes. With growing interest in noninvasive SLN imaging modalities, MNP-based systems are an appealing and practical option that has the potential to become the diagnostic tool of choice. Higher sensitivity for tracers, pictures with higher resolution, and no tissue penetration depth constraints provide clear advantages over traditional diagnostic procedures.

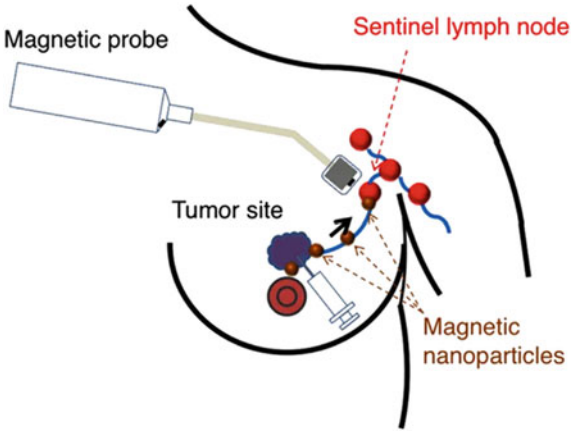

Fig. 15.4 Schematic depiction demonstrating the idea of magnetic detection of sentinel lymph nodes (SLNs) in breast cancer patients using a handheld magnetic probe and magnetic nanoparticles (MNPs). MNPs are injected into the body and collected in the SLNs via the axillary lymphatic system, where they are detected by a magnetometer. Adapted with permission from Elsevier [61]

15.5.3 Magnetic Fluid Hyperthermia

Magnetic hyperthermia is the phenomenon of MNPs creating heat in response to an external magnetic field that alternates. Thermal energy is lost to the environment during magnetizable cycles due to frictional losses caused by the dynamics of viscous suspensions, hysteresis losses in multi-domain MNPs, and Néel or Brown relaxation. The hysteresis loop shows that the temperature increase in multi-domain ferromagnetic or ferrimagnetic substances is primarily due to hysteresis losses. The amount of thermal energy lost to the environment is calculated by combining the hysteresis loop area [63]. Hysteresis losses are heavily influenced by the magnetic field's intensity when it is applied. The type and size of an MNP domain structure have a large influence on the hysteresis of the MNPs and, as a result, their hyperthermia properties [64]. Despite the lack of hysteresis (under normal conditions), superparamagnetic materials lead to magnetic hyperthermia via Néel and Brownian relaxation. In this case, the magnetization of SPNs could be slower than just the magnetization of the applied magnetic field, generating a hysteresis loop that confers hyperthermia features on superparamagnetic materials [65]. SPN magnetizable lags behind the real magnetizable of the applied magnetic field due to the instability and gradual decay of nanoparticle magnetizable in a fluid. Initially the nanoparticles align against or with the applied magnetic field when the same is applied. As previously mentioned, Brownian relaxation refers to the interval that exists between the reversal of the magnetic field and the magnetizable state. When applied to this situation, Brownian relaxation produces heat as a result of friction between MNPs and the medium around them, such as blood. Brownian relaxation is thought to be size and viscosity dependent because it takes longer for Brownian relaxation to occur as MNPs grow in size and the carrier fluid's viscosity rises [66]. The heating effect depends on the amount of energy delivered per second, so the Néel and Brownian relaxation times have a significant impact. Only after MNPs have relaxed and become susceptible to magnetization once more can clinicians re-magnetize them. Consequently, the frequency of the alternating magnetic field should correspond to the estimated relaxation times for an efficient to create an efficient heating effect. Magnesium hyperthermia is one of the many potentials uses for MNPs in the management of infectious and cancerous diseases [51]. Additionally, by employing a heat-labile coating and magnetic hyperthermia, cytotoxic chemicals may be released into cancer cells in a controlled manner (Fig. 15.5).

Using an external magnetic field, Hu et al. recently demonstrated the regulated two medications release (Paclitaxel and Dox) from heat-sensitive polyvinyl alcohol (PVA) coated SPIONs. Furthermore, because of the antibody's anticancer action and the cancer cells' selectivity, antibody conjugation with MNPs increased hyperthermia efficacy. Examples include MNPs with anti-FGFR1 aptamer tags for improved MNPs and magnetic hyperthermia coupled with antibodies for improved anti-cancer effects of cryptotanshinone [67].

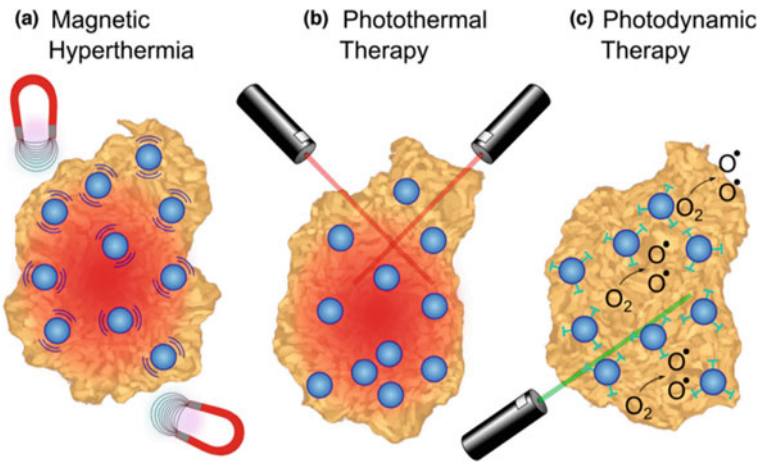

Fig. 15.5 Tumor ablation therapy using MNPs is gaining popularity, including **a** Photothermal treatment (cancer cell death by the heat generated from MNPs upon light), **b** hyperthermia is caused by magnets (necrotic tumor destruction by heat generated from MNPs upon alternating external magnetic field), and **c** photodynamic treatment (death of cancer cell using cytotoxic singlet oxygen species generated from MNPs conjugated with a photosensitizing agent. Adapted with permission from MDPI [67]

15.5.4 Magnetic Particle Imaging

Magnetic particle imaging (MPI) is a new biomedical imaging technology that enables the direct quantitative mapping of superparamagnetic iron oxide nanoparticle spatial distribution. Tomographic images with great temporal and spatial resolution can be created thanks to MPI's enhanced sensitivity and short picture capture times. MPI is projected to outperform currently available medical imaging modalities such as X-ray scans, Magnetic Resonance Imaging (MRI), Computed Tomography (CT), ultrasound, Positron Emission Tomography (PET), and Single Photon Emission Computed Tomography (SPECT).

Magnetic Particle Imaging (MPI) is a novel noninvasive tomographic method that directly detects superparamagnetic nanoparticle tracers. The approach has the potential to be applied to material science and diagnostic imaging. In medical research, it is now used to detect the three-dimensional placement and number of nanoparticles. Imaging uses zero ionizing radiation and can produce a signal at any depth inside the body. Scientists at the Royal Philips Research lab in Hamburg developed MPI in 2001. The first system was created and reported on in 2005. Since then, academics at other universities around the world have refined the technique. MPI hardware differs significantly from MRI hardware. By varying magnetic fields, MPI devices generate a signal from Superparamagnetic Iron Oxide (SPIO) nanoparticles. These fields are specifically designed to produce a single magnetic field-free zone. A signal is only created in this location. When this region is moved across a sample, an image

is produced. Because tissue has no natural SPIO, a signal has only been observed whenever the tracer is administered. This produces photos with no background. MPI is typically used in tandem with anatomical imaging modalities (such as CT or MRI) to provide information on the site of the tracer.

Magnetic particle imaging differs from magnetic resonance imaging (MRI) in the following ways: Even though the technology and imaging techniques appear to be comparable, the physics of magnetic particle imaging (MPI) differs from that of MRI. This can lead to some confusion, therefore it's critical to point out the distinctions. Magnetic field gradients, transmit and receiver coils, pulse sequences, relaxation effects, and the reciprocity concept will be familiar to MRI users. In contrast, MRI produces a signal from tissue, whereas MPI produces a signal only from Magnetic Nanoparticle (MNP) tracers. There is no background signal from anatomy in MPI. MPI is thus classified as a "molecular imaging" technique.

MPI has been proposed as a suitable platform for functioning brain imaging, which needs both extremely sensitive imaging and shorter scan times for appropriate temporal resolution. MPI is used to detect increases in Cerebral Blood Volume (CBV) produced by neuro activation. MPI-based functional neuroimaging has been demonstrated in rodents and offers a promising sensitivity advantage over other imaging techniques. In the long term, this could allow researchers to assess functional neuro activation on a single patient basis, integrating functional neuroimaging into clinical diagnostics.

15.5.5 Magnetically Triggered Drug Release

In recent years, a significant amount of research has concentrated on developing new ways of producing drug nanocarriers, such as dendrimers [68] nanoparticles [69–71], and nanogels [72]. Although the small size of these nanocarriers improves drug permeability and retention [73], these delivery systems are not selective and cannot control drug release correctly. Magnetic Nanoparticles (MNPs), also known as Superparamagnetic Iron Oxide Nanoparticles (SPIONs), have a unique advantage for hyperthermia and targeting when compared to other potential nanocarriers due to their intrinsic magnetic feature. When nanoparticles are subjected to a high-frequency magnetic field, they generate heat, which can be used for localized hyperthermia cancer therapy [74]. Drugs mixed with magnetic nanoparticles can be given to specific areas while avoiding adverse effects when modulated by an external magnetic field. These characteristics bode well for magnetic nanoparticle applications in biomedicine. As a result, considerable effort has been expended on the creation of controlled targeted delivery and release by hyperthermia in a local high-frequency alternating magnetic field (HAMF) [75–77].

Since nanoparticles aggregate in organs and tissues other than the designated target location, there is a great deal of interest in developing nanoparticle drug carriers that release their therapeutic payload in response to external stimuli [78]. Magnetism is one among many techniques for producing "triggered" releases; other famous

examples include light, ultrasound, and temperature. Magnetism can be beneficial since triggered pharmaceutical release can be combined with imaging techniques such as MRI or MPI, as well as other therapies such as MFH. Furthermore, tissue penetration depth does not limit magnetic triggering, and MNPs can be modified and functionalized in a variety of ways [79]. Because of their biocompatibility, liposomes have been a favored alternative for drug administration in general. Doxil, a liposomal version of the chemotherapy medication doxorubicin, is currently in clinical usage and decreases doxorubicin's cardiotoxicity. Several different liposomal nanomedicines have been explored in clinical trials; however, they do not improve overall survival when compared to delivering free medication. As a result, ways of triggering drug release in liposomes, such as the construction of magneto-liposomes, which may release medicine in response to an AMF, have been examined. The heat emitted by the MNPs in an AMF elevates the heat of the liposomal membrane above the transition point, allowing the drug to leak out of the liposome.

The magnetically driven release has also been achieved with polymeric nanoparticles and hydrogels. The mechanism of release is comparable to that of liposomes. MNPs in an AMF generate heat that is used to activate a polymer or hydrogel transition, allowing for higher drug release. Drug cargo may also be loaded onto the particle via thermally labile bonds that dissolve when an AMF is present. The fundamental challenge in using these carriers is minimizing passive, diffusion-driven release at body temperature to near zero while maintaining sufficient release in the AMF [80]. In this strategy, patients would be given nanoparticle drug carriers, which would subsequently be scanned using MPI to detect particle location and heated using an AMF to achieve localized drug release. Particles may be photographed without significant heating because the AMF strengths used for imaging with MPI are significantly lower than those required to activate heat and medication release. The future of magnetically triggered drug release is promising, given the multiple potential platforms for magnetically triggered release and the advancing MPI technology.

15.5.6 Nano Warming of Cryopreserved Tissue and Organs

A key obstacle in meeting the needs of transplant patients is the lack of methods for preserving vascularized organs and tissues. The window between organ/tissue procurement and transplantation could be extended beyond the current preservation time limit (3–24 h depending on the organ/tissue), allowing for thorough testing, careful matching of donors and recipients, and treatment preparation [82]. Cryopreservation through vitrification has the potential for a significant increase in tissue shelf-life. Using highly concentrated concentrations of cryoprotective chemicals, this method permits biologics to be stored at cryogenic temperatures (CPAs) [81]. CPAs enable the liquid to cool to a glassy state, which suppresses crystallization and counteracts the damaging effects of ice formation within the tissue.

Although vitrifying small tissues has been successful, it has been difficult to maintain the structural stability and functioning physiology of large multicellular tissues

and organs. The primary problem is connected with existing rewarming technologies, which include immersing complete organs in a temperature-controlled bath, resulting in thermomechanical strains generated by temperature gradients. One method to overcome this challenge is nano-rewarming, which uses CPA solutions containing SPIONs (magnetic CPA or mCPA), which release heat in reaction to an applied AMF. The study of nano-rewarming is extremely new. Etheridge et al. [82] suggested the fundamental idea of warming a vitrified solution with an AMF. Theoretical research on thermomechanical stresses during magnetic particle imaging-guided drug delivery followed this (MPI). The use of selection field gradients with superposed alternating magnetic fields (AMFs) can be used to photograph and/or heat magnetic nanoparticles (MNPs). By using this technique, doctors may be able to see where the MNP and medicine are located and then only activate the release of heat and the drug where they want it.

Wang et al. [83] used nano-rewarming to cryopreserve human umbilical cord mesenchymal stem cells. The scientists showed that mCPA improved vitrified cells' viability upon AMF rewarming. The particles used in the assays were made using the co-precipitation technique. Particle coating and particle persistence in the CPA solution are not mentioned by the authors. Without any coating, particles produced by the coprecipitation technique are very likely to aggregate and precipitate in fluids other than water. Highly negative particles cause quick nonspecific internalization, as shown in their uptake tests. While being in its early stages, nano-rewarming appears to hold great promise for organ banking. Nanoparticles produced by the coprecipitation method have been used in investigations thus far. The simplicity with which enormous amounts of nanoparticles can be created is a benefit of this type of synthesis. However, polydispersity and low repeatability of warming rates are the key drawbacks. Prior studies' physicochemical and magnetic characterization of mCPAs is restricted, making a rigorous evaluation of formulation improvements unfeasible [84].

15.5.7 Proteins and DNA Separation

Extraction, purification, and selective manipulation of peptides and proteins is a critical necessity in biotechnology and life sciences. Electrophoresis, ultrafiltration, precipitation, and chromatography are examples of traditional methods [85]. In terms of effectiveness and selectivity, affinity chromatography is frequently regarded as the method of choice among those available. However, liquid chromatography can only be used on pre-treated solutions. In homogenous matter, such as protein synthesis mixes, the particulate-free circumstances required for proper commercial column use are incompatible. Because it uses affordable materials and does not require laborious sample preparation, magnetic separation utilizing MNPs is an interesting alternative technique for the selective and trustworthy capture of certain proteins, DNA, and entire cells [86]. Magnetic separation works on a fairly simple premise. MNPs with an immobilized affinity tag, ion-exchange groups, or hydrophobic ligands are mixed

in with the required compounds. Any biological fluid or fermentation broth, including whole blood, plasma, urine, or crude cell lysates, may be utilized as samples. After a suitable incubation period during which the affinity species are permitted to tightly bind to the ligands attached to the MNPs, the complexes are isolated by magnetic decantation, and the impurities are removed. Finally, using the proper elution procedures, the target molecules are purified and removed from the MNPs. MNPs functionalized with ligands containing Ni^{2+}-chelating species, such as nitrilotriacetic acid (NTA), are currently used in the most extensively researched affinity tag-based method for magnetic separation of proteins. This method enables the preferential sequestration of (6 His)-tagged proteins with highly conserved folding down to picomolar concentrations.

New developments in the isolation of biomolecules using MNPs imply that this technique has the potential to be generic and adaptable. Similarly, if appropriate anchors and ligands are applied, various affinity tags that selectively engage with distinct biological targets might be anticipated. To create a tight and reversible capture ideal for Ab sorting, for instance, MNPs functionalized with specific peptides, such as protein A or G, with significant affinities for the Fc region of human IgG Abs can be utilized. For many reasons, MNP protein separation is superior to conventional affinity chromatography. The purification process is easy, rapid, affordable, and scalable [87]. Nano-sized sequestrants have a high surface-to-volume ratio; therefore, little material is needed for the separation procedure. Additionally, no specific tools like centrifuges, filters, or liquid chromatography systems are required for magnetic separation, and there is no need for sample concentration after elution. It is important to note that there are currently automated methods for protein separation or nucleic acids. To separate and concentrate DNA or RNA, selective oligonucleotides grafted onto MNPs can be utilized. These allow the capture of complementary strands [88].

15.5.8 Biosensing with Magnetic Nano Switches

A nano biosensor detects biological agents like antibodies, nucleic acids, infections, and metabolites. The basic idea is to attach bio-analytes of interest to bioreceptors, which then modify the physiochemical signal associated with the binding. Highly sensitive NP-based biosensors have been created as a result of the special electrical, magnetic, and optical properties of specific metal and metal oxide nanoparticles functionalized with affinity ligands, as well as agglomerative phenomena brought on by particular interactions at their surface. For the colorimetric and fluorescence-based detection of oligonucleotides, proteases, Abs, and other molecular species, gold nanoparticles and semiconductor nanoparticles (so-called quantum dots) have been utilized extensively [89]. The main disadvantage of optical biosensing assays is the requirement to reduce sample turbidity or background signals from biological extracts. By utilizing the unusual magnetic properties of MNPs, a new class of nanosensors has been produced. The Weissleder group made the initial suggestion for magnetic relaxation nano switches in a series of influential papers that showed

the effectiveness of this new nano biosensor for the precise and sensitive detection of a wide range of biological species, including DNA, and proteins, pathogens, and processes like enzymatic function. These magnetic relaxation switches were made up of 3–5 nm iron oxide MNPs coated with a 10 nm thick dextran layer that was crosslinked and functionalized with amino groups to covalently anchor the affinity ligands. In the presence of a specific molecule that is specifically recognized by the affinity ligands anchored on the MNPs, such nano switches can undergo reversible assembly, resulting in a change in transverse magnetic relativity ($R2 = 1/T2$) of water protons near the floating nano dipole.

The outer-sphere diffusion theory states that when MNP clusters are sufficiently small, such as within a few hundred nanometers, the assembly has the effect of lowering the average $T2$ value. $T2$ is increased relative to individual MNPs dispersed in the same fluid or matrix when big agglomerates (with sizes ranging from a few micrometers) develop. With magnetic relaxation nano-sensor assays designed to produce reversible nano assemblies upon MNP interaction with specific analytes in solution in either a forward (clustering) or reverse (de-clustering) configuration, both approaches are advantageous depending on the experimental requirements.

Recently, a multiplexed, quantitative, and quick analysis of unprocessed biological material using a chip-based diagnostic magnetic resonance (DMR) device was established. Assemblies of MNPs with higher magnetization promote molecular interaction amplification, which produces the signal. The device's potential has been demonstrated by simultaneously measuring the quantity and presence of proteins, recognizing bacteria, and researching them at the molecular level with extraordinary sensitivity [88].

15.5.9 Bacteria Detection and Sequestration with MNPs

Bacteria are one of the most common living organisms on the planet, having adapted to all available biological niches. As symbionts and parasites, bacteria have a biodiverse impact on the ecological system. They benefit their hosts and are economically significant in the food, agricultural, pharmaceutical, and petroleum industries, among others. They do, however, exhibit pathogenicity to humans and other living things. The presence of unwanted microbes in natural resources makes them difficult to utilize [90].

In complex biological mixtures, bacteria at low concentrations are typically challenging to identify using conventional analytical techniques. However, it is anticipated that nanotechnology would improve environmental monitoring and clinical diagnostics by enhancing sensitivity, selectivity, and analytical time-efficiency. To capture and identify ultralow-level bacteria, Gu et al. developed the MNP system. The D-Ala-D-Ala dipeptide, a crucial component of the microbial capsule, is strongly bound by polyvalent vancomycin, enabling the magnetic capture and enrichment of bacteria. The reported detection limit of this approach, which is comparable to the best polymerase chain reaction assays, was four colony-forming units (cfu) per mL.

Gram-negative bacteria like *E. coli* were also isolated and detected using FePt@Van MNPs. Bacteria might be found in blood samples thanks to the FePt@Van and fluorescent dye combo. By utilizing the interactions between bacteria and the carbohydrates on mammalian cell surfaces, El-Boubbou et al. developed silica-coated magnetic glyco-NPs that could identify *E. coli* strains in 5 min while also eliminating up to 88% of the bacteria from the sample. *Staphylococcus aureus* cells in a mixed cell population could be targeted and trapped with exceptional efficiency and selectivity by MNPs functionalized with a single-domain Ab [91]. The authors employed MNPs with high inherent susceptibility to selectively target infections. The detecting signal was amplified and measured using a miniaturized NMR device after the specimen was concentrated in a microfluidic chamber.

15.5.9.1 MNPs in Cancer Diagnosis

Recently, the development of more effective and economical nanosized contrast agents for CT and MRI for cancer than those already on the market has attracted a lot of attention. Superparamagnetic iron oxide particles (50–100 nm in size) are considered potential MR contrast agents by certain researchers because of their significantly higher magnetic susceptibility than traditional MR contrasts like gadolinium. Many of the commercially available contrast agents for MRI today are composed of superparamagnetic iron oxide (SPIO) nanoparticles covered with carboxydextrane. By synthesizing SPIO nanoparticles with the ability to disperse in chitosan, scientists have generated ferrofluid, which is used to improve MRI contrast agents. In the aforementioned experiment, such MRI image contrast values were comparable to Resovists'. Additionally, there have been advancements made in the diagnosis of colorectal cancer; iron-oxide or iron-cored nanoshells can now be utilized as contrast agents for MRI imaging, which, in addition to being non-invasive, could lead to the development of powerful and practical diagnostic tools.. Recently, magnetic micro/nanoparticles have been employed extensively as signal reporters to find malignant cells and identify other biomolecules. Due to their unique magnetic properties, nanoparticles play two key functions in bioassays: acting as a probe and carrying surface markers for a variety of covalent and non-covalent reactions with antibodies, nucleic acids, and other recognition molecules.

15.5.9.2 MNPs in Cancer Therapy

In recent years, the use of magnetic nanoparticles in cancer treatment has grown significantly. The best therapeutic potential, according to some authors, is found in applications that have three parts: a therapeutic load, a magnetic core, and a recognition layer. Now, a variety of techniques can be used to conjugate these particle suspensions with antibodies while still maintaining the colloidal stability and integrity of the particles. Many types of nanoparticles combined with the anti-Human Epidermal

Growth Factor Receptor 2 (HER2) monoclonal antibody have been created and investigated due to promising results in biological and preclinical applications for the treatment of breast cancer. Another possible method for treating breast cancer is hormone-conjugated nanoparticle therapy. For instance, some publications assert that LHRH- superparamagnetic iron oxide nanoparticles (SPIONs) can be used to target cancer cells in both primary breast tumors and lung metastases by assessing the sub-cellular distribution of SPIONs in tumors and organs using transmission electron microscopy. Overall, there are still a lot of difficulties to be solved before iron-based nanoparticles that target tumors may be successfully deployed in vivo. Functional group modifications of the drugs during conjugation with a nanoparticle, low drug loading efficiency, nanomaterials' failure to reach tumor tissue from the blood, drugs being transported to cancer cells' endosomes or lysosomes instead of their cytoplasm, and a decrease in targeting ability due to weak connections with a nanoparticle are a few examples. Given that many medical professionals think cancer treatment should be based on the quality of life both during and after treatment as well as prognostic factors and chemotherapy, tolerability, compliance, and quality of life may therefore become the most important factors in cancer therapy in the future. According to our analysis, magnetic nanoparticles provide a significant future potential for efficient cancer treatment. Thus, regional health agencies must support laboratories engaged in the development and production of nanoparticles with adequate financing and other resources. Chemotherapy and radiotherapy will undoubtedly continue to be indispensable tools in the fight against cancer, but as nanotechnology develops, it will open up new applications for these tried-and-true treatments.

15.6 Conclusions

Biotechnological and biological applications of MNPs span a wide spectrum of applications magnetic resonance imaging (MRI) to therapeutic agents in cancer treatment. The use of the MNPs for a particular application requires a specific method for synthesis, which results in synthesis of the MNPs having special properties. In addition, the development of an efficient MNPs system for delivering genes into targeted cells, which is a main strategy for understanding gene/protein functions and to improve therapeutics are the field which have a lot of scope to be explored.

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