

Entry

# Magnetite Nanoparticles for Biomedical Applications

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**Definition:** Magnetic nanoparticles (MNPs) have great potential in various areas such as medicine, cancer therapy and diagnostics, biosensing, and material science. In particular, magnetite ( $\text{Fe}_3\text{O}_4$ ) nanoparticles are extensively used for numerous bioapplications due to their biocompatibility, high saturation magnetization, chemical stability, large surface area, and easy functionalization. This paper describes magnetic nanoparticle physical and biological properties, emphasizing synthesis approaches, toxicity, and various biomedical applications, focusing on the most recent advancements in the areas of therapy, diagnostics, theranostics, magnetic separation, and biosensing.

**Keywords:** magnetic nanoparticles; iron oxide nanoparticles; biomedical application; diagnostics; therapy; drug delivery; theranostics; nanomedicine; magnetic resonance imaging; hyperthermia

## 1. Introduction

Nanotechnology combines various areas of science. The small sizes of nanomaterials possess unique chemical, physical, and biological properties. To date, many nanomaterial types have been described, and many more will be developed for various applications. Magnetic nanoparticles have great potential in biochemistry, nanomedicine, and bio-inspired material areas [1–8]. One of the most promising magnetic nanoparticles is iron oxide (II, III) due to their ferrimagnetism [1,9–11]. In particular,  $\text{Fe}_3\text{O}_4$  magnetite nanoparticles (MNPs) have demonstrated a promising effect in numerous applications [1–8].

MNPs have become a vital tool for material science, biochemistry, diagnostics, magnetic drug and gene delivery, hyperthermia, magnetic resonance imaging (MRI), and theranostics [1,3–5,7,9,12–30]. The manipulation of MNPs by an external magnetic field is essential for bioseparation and biosensing areas [1,6,17,30–33]. Moreover, magnetic transport of MNPs to the tissue allows targeted therapy and diagnostics (theranostics) applications [1–8,34]. A combination of possible local heating (hyperthermia), anticancer drug delivery, and monitoring by MRI or other imaging technology open the tremendous potential for cancer treatment [1–5,8,11,16,21,35].

Many papers about the synthesis, coating, and applications of MNPs have been reported [1–8,26,34,35]. The number of articles with the key term “magnetic nanoparticles” increases every year (Figure 1). The actual number of papers in the area is much higher, which can be calculated using other keywords. However, before 1996, less than 100 articles per year were published annually by the Scopus database. After the first successful clinical trial in 1996, the number of papers greatly increased. Since 2013, more than 5000 manuscripts have been published annually. Such results are associated with the increasing recognition of MNPs in achieving excellent results in various applications.

MNPs show high field irreversibility, high saturation field, and superparamagnetism, which are highly dependent on particle size and surface coating. The relationship between MNP size and magnetism (coercivity) has been extensively reported [36–40]. The coercivity gradually increases for bulk nanoparticles to a maximum value at a particular size. In this region, the magnetization is stable and nonuniform (Weiss domains, magnetic multi-domain state). The critical size of the magnetite nanoparticles, above which they become multi-domain, has been theoretically calculated and is 76 nm and 128 nm, respectively,

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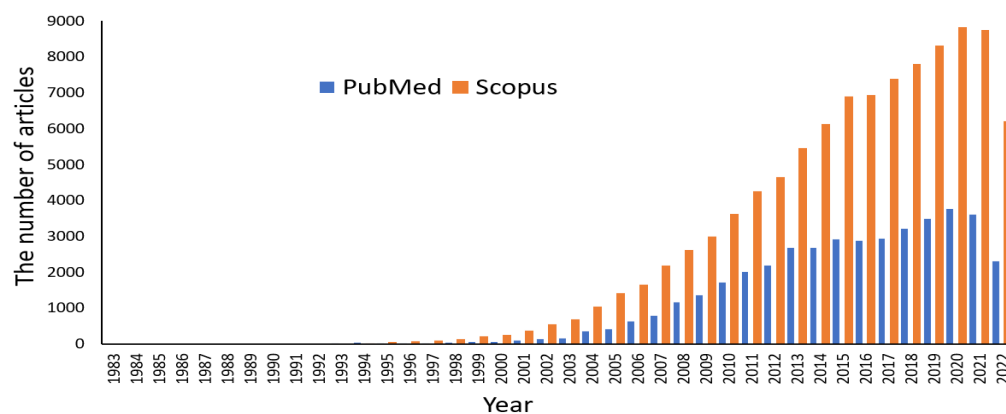
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for cubic and spherical nanoparticles [38]. However, the experimental data indicate that the critical size of transition between single- and multi-domain magnetic structure highly depends on the crystal structure and coating [37,38,41]. By reducing the size of the nanoparticles, the coercivity rapidly decreases to zero, reaching a superparamagnetic state [36,37]. Superparamagnetism is especially important in applications such as drug delivery and imaging. Particle sizes below 20 nm are required to achieve superparamagnetism for magnetite MNPs. Superparamagnetic MNPs provide a stronger response to external magnetic fields than simple MNPs. Frenkel J. and Doefman J. in 1930 predicted that, below a critical size, MNPs would consist of a single magnetic domain [42]. However, superparamagnetic MNP synthesis was achieved half a century later.



**Figure 1.** The number of articles published per year in PubMed (Medline) and Scopus databases under the search phrase “magnetic nanoparticle”. The lower number of papers in 2022 is because the literature search was conducted in September 2022. An upward trend is expected for 2022. PubMed comprises biomedical literature from the MEDLINE database and life science journals. Scopus database is the largest abstract and citation database, which covers much more than PubMed scientific journals, books, and conference proceedings.

Research on nano-emulsion began in 1943 (Figure 2, historical timeline) [43]. However, the nanotechnology concept was first proposed in 1959 by Richard Feynman in the lecture entitled “Plenty of Room at the Bottom”. This was a historical event in nanoscience. The first synthesis of iron nanoparticles by gas condensation was achieved in 1981. The concept of using magnetic forces for enhanced therapeutic and imaging performance has evolved over the years. Two of the milestones were the development of MNPs for imaging purposes in 1990 and silica-coated MNPs in 1995. Since 2000, numerous studies have investigated the potential applications of MNPs and nanocomposites with magnetic cores. Another essential development was the successful magnetic hyperthermia clinical trials in 2010. Magnetic hyperthermia utilizes MNPs that are exposed to an alternating magnetic field to generate heat in local regions [23,44]. Magnetic hyperthermia therapy was first proposed much earlier, in 1957. However, about fifty years were required to synthesize stable and non-toxic MNPs with optimal physical properties. Colloidal stability, biocompatibility, and toxicity studies are crucial for in vivo application. Recently, numerous MNP-based “Smart” nanocomposites with pH-stimuli-responsive drug release, theranostics, and multimodal constructions have been developed [5,8,13,24,25,45–49]. Numerous research papers have focused on the possible procedures for MNPs synthesis, coating, drug-loading, toxicity studies, and clinical trials [1,2,8,20,44,50–54].

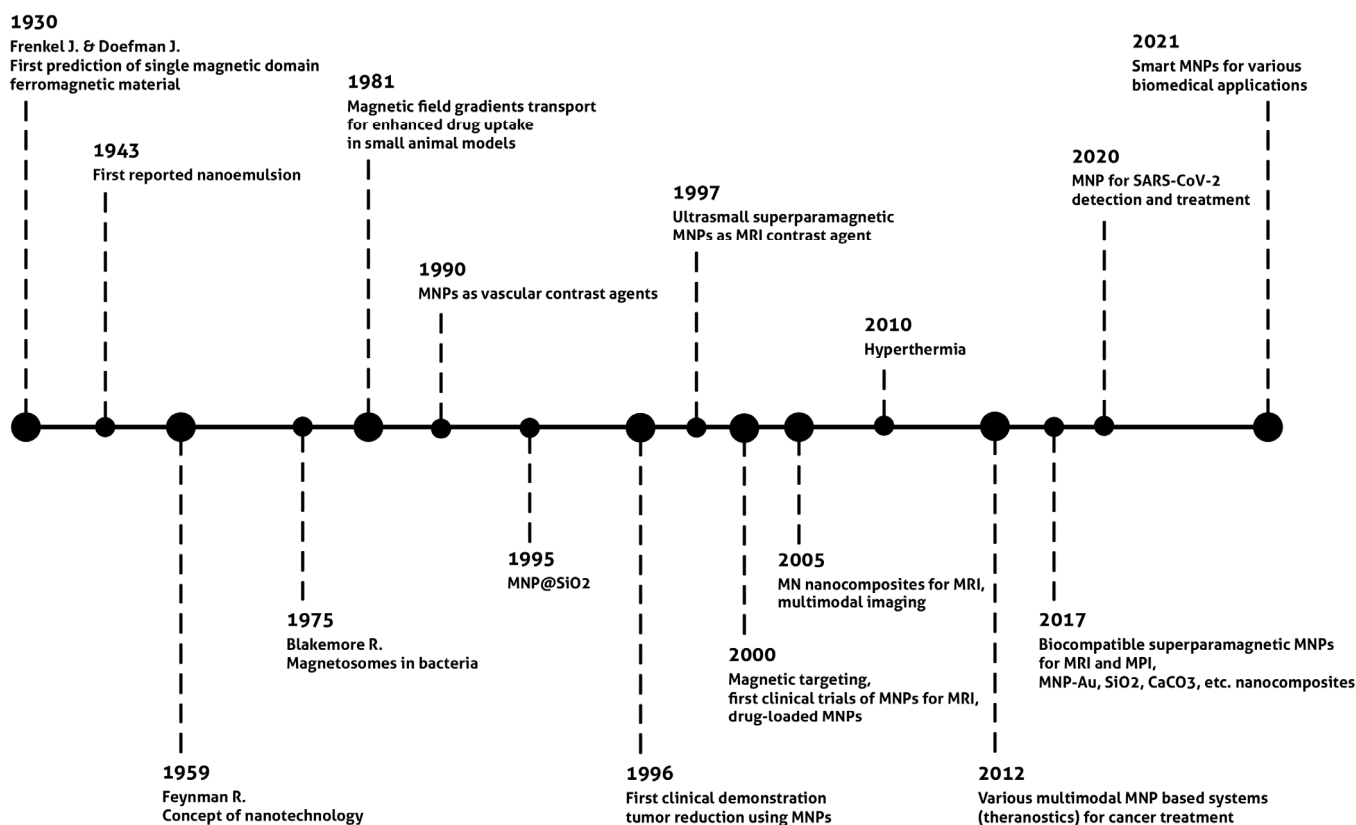


Figure 2. Historic timeline for development of MNPs.

## 2. Synthesis of Magnetic Nanoparticles

Many research articles have focused on the synthesis and coating procedures of MNPs to obtain desired morphology, particle size, physico-chemical properties, and biocompatibility [1,7,9–11,28,50,51,55]. The basic techniques involved in MNP synthesis are physical, chemical, and biological in nature (Figure 3, classification of synthetic approaches). Each route produces MNPs with various properties, which highly depend on the synthesis conditions [1,8,35,56–58]. This section presents the most common syntheses, their advantages, and their effects over different properties of MNPs.

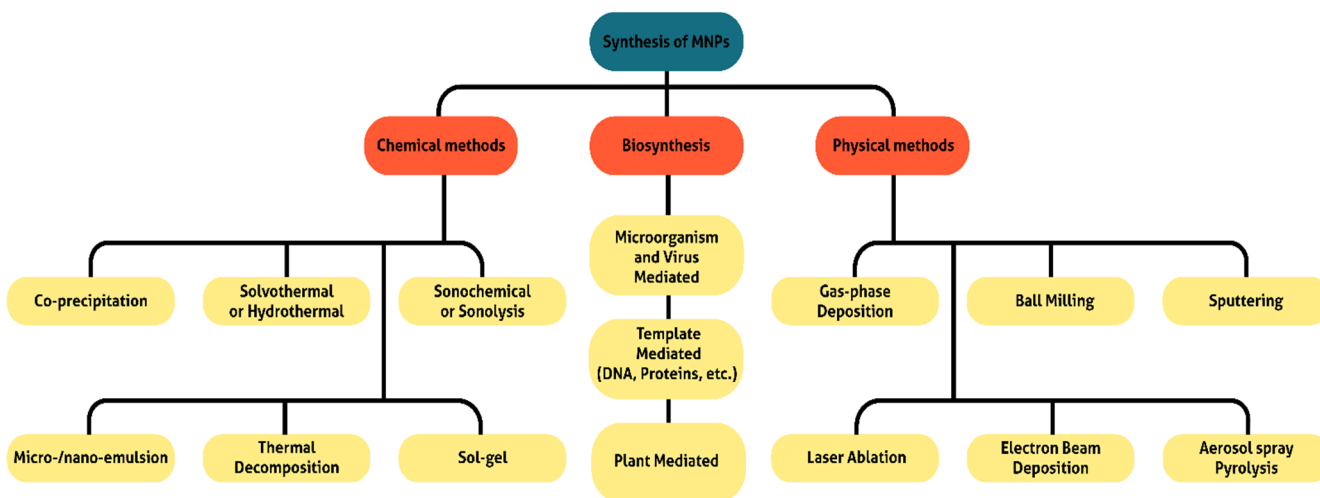


Figure 3. Primary MNP synthesis methods.

Co-precipitation is a widely used, simple, and cost-effective chemical synthesis, which proceeds in an aqueous solution with a high yield and purity (Table 1). However, the procedure often requires surfactant and clear reaction parameters (concentration, temperature, tube size, mixing speed, etc.) [1,56]. The method is conducted in a mixture of Fe (II) and Fe (III) salts with base (NH<sub>3</sub> or NaOH solution) at ambient temperature or slight heating. To prevent Fe (II) oxidation in base conditions, the presence of inert gas flow is recommended. The changes of such simple reaction conditions result in not having the same size and shape of nanoparticles, such that reproduction of the synthesis method usually fails to produce MNPs with the same physico-chemical and biological properties. Moreover, “in one person’s hands”, the MNPs size usually varies from one synthesis to another. The only possibility is to thoroughly record all actions, equipment, and chemical manufacturers during synthesis.

**Table 1.** MNP synthesis comparison.

	Methods	Procedure	Conditions	Temperature, Time	MNPs Size and Yield *
Chemical	Co-precipitation	Very simple	Ambient	20–150 °C, min	Relatively narrow, High
	Hydro/Solvothermal	Simple	High pressure	150–250 °C, h/day	Very narrow, High
	Sonochemical	Very simple	Ambient	20–50 °C, min	Narrow, Medium
	Emulsion	Complicated	Ambient	20–80 °C, h	Narrow, Low
	Thermal decomposition	Very simple	High temperature	250–400 °C, h	Very narrow, High
	Sol-hel	Simple	High temperature	300–500 °C, 3–4 h	Very narrow, High
	Wet Reduction	Very simple	Ambient	20–150 °C, min	Relatively narrow, High
	Electrochemical	Complicated	Ambient	25 °C, min/h	Narrow, High
Physical	Polyol Synthesis	Simple	High temperature	200–350 °C, 7–10 h	Relatively narrow, High
	Gas-phase deposition	Simple	High temperature	150–250 °C, h	Narrow, Medium
	Ball milling	Very simple	Power ball/ Ambient	25 °C, h/day	Highly broad, Medium
	Spattering	Very simple	Ambient	25 °C, min/h	Broad, High
	Laser ablation	Simple	Ambient	25 °C, min/h	Broad, High
	Electron beam deposition	Simple	Ambient	25 °C, min/h	Broad, Medium
Biological	Aerosol spray pyrolysis	Simple	High temperature	300–500 °C, h	Broad, Medium
	Microorganism and virus mediated	Complicated	Ambient	25 °C, h/day	Broad, Medium
	Template-mediated	Simple	Ambient	25 °C, min/h	Relatively narrow, High
	Plant-mediated	Complicated	Ambient	25 °C, h/day	Broad, Low

\* Yield: High = > 90%, Medium = 60–90%, Low lower = 60%.

A hydrothermal or solvothermal method is used to prepare MNPs under high pressure and temperature, generally carried out in an autoclave [1,8,35]. This method yields excellent shape-controlled, monodisperse ultrafine magnetite nanopowders. This route is chosen over other approaches to grow high-crystalline MNPs. However, the synthesis procedures usually require a large reaction time.

In the sonochemical or sonolysis method, acoustic cavitation produces bubbles via ultrasound [1]. The shape and size of MNPs can be easily controlled through the intensity of irradiation, irradiation time, and reaction time. Despite the synthesis requiring high-intensity ultrasound, the reaction occurs quickly in mild conditions.

Micro- or nano-emulsion method include a stable liquid mixture (usually water and ‘fatty’ solvent) and amphiphilic surfactant. The properties of MNPs are highly dependent on surfactant type. The method has a narrow working window to obtain stable emulsion, high solvent consumption, and low MNP yield [57]. These shortcomings make the emulsion method unprofitable.

Recently, some modern biosynthesis approaches and green technologies for MNP synthesis have been reported [1,56,58]. Of course, the first, and best, ‘researcher’ of this technology is the magnetostatic bacterium. Using intracellular biomineralization processes, magnetostatic bacteria can synthesize specific organelle magnetosomes [58]. At the moment, many researchers use plant extracts, DNA, and proteins as templates, microorganisms, viruses, and fungi for MNPs green/biosynthesis [1,56,58] (Table 1).

In addition to these synthetic routes, gas-phase deposition, ball milling, spattering, laser ablation, electron beam deposition, aerosol spray pyrolysis, electrochemical synthesis, and

wet reduction microbial synthesis, among others, have been reported [1,8,35,56–58]. Table 1 summarizes some primary synthetic methods along with their conditions and characteristics.

### 3. Toxicity of Magnetic Nanoparticles

The toxicity of MNPs is an important factor for future healthcare applications [50]. The synthetic procedures of MNPs may look easy. However, MNPs toxicity depends on size, coating, surface modification, etc. MNPs with a size higher than 200 nm will be filtrated by the spleen. The nanoparticles less than 10 nm can be quickly removed through renal clearance. The surface chemistry of MNPs is also important. Having the wrong coating for MNPs leads to magnetic core oxidation, aggregation, instability in physiological liquids, and high reactive oxygen species (ROS) formation [3,13,50,51,54,59–61]. Various organic molecules (tannic, polyacrylic, lauric, myristic, hyaluronic, and oleic acids), inorganic coating (gold, silica, calcium carbonate), artificial (tween or polysorbate, polyethylene glycol, polyethylene imine, etc.), and natural polymers (e.g., dextran, chitosan, proteins such as albumin, casein, etc.) are used to improve MNP properties [3,7,11,22,24,62–87]. However, no universal recipe exists. For example, PEG-coating enhances the colloidal stability of MNPs and decreases protein adsorption [24,79,88]. Oleic acid is the primary surfactant for improving magnetic properties and stabilize the MNPs [84,85]. Protein-coating provides greater biocompatibility and biodegradability and less immunogenicity than MNPs [7,62,89–91]. For the major human plasma protein, human serum albumin (HSA) [92–94], adsorption on the MNPs surface prevents nucleation and aggregation and increases colloidal stability in aqueous solution in a wide pH range [62,72,95–103]. Albumin coating prevents non-specific interactions with blood components and immune response [62,95,97,101,102,104]. HSA enhances biocompatibility, prolongs blood circulation of MNPs, and provides targeted delivery to tumors [7].

The cytotoxic effect of MNPs lies in Fe ion release, dysregulation of ion channels and gene expression, immune response, inflammation, ulceration, metabolic disorders, decrease in growth rate or changes of alterations, etc. [5,50,54]. The literature on the topic usually presents the simplest cytotoxicity assay (MTT test) on cancer cell lines [105,106]. The MTT assay usually shows only ‘acute toxic effects’. It does not provide interaction with blood proteins and cells, tissue-specific toxicity, chronic toxicity, etc. Moreover, cancer cells have activated “survival systems”. Recent research has moved significantly forward with *in vivo* toxicological assays [54]. The MNP dose, initial concentration, biodistribution, and circulation time greatly influence the trials. MNP accumulation in tissues may interfere with physiological Fe metabolism and activate inflammatory or immune responses [50,54,60]. MNP degradation in the cells may lead to ROS formation with cell or mitochondrial membrane damage, adverse cell proliferation, DNA oxidation with subsequent point mutation formation, and cell death. Extended toxicity experiments are hard-going work for the many researchers involved, which greatly slows down the progress in this area [54]. Despite the widespread introduction of MNPs, new and easier toxicity tests are required. Integration of nanotoxicology and nanomedicine into one element has proven to be a significant step toward the sustainable development of nanotechnology for biomedical applications [107,108].

### 4. Biomedical Applications of Magnetic Nanoparticles

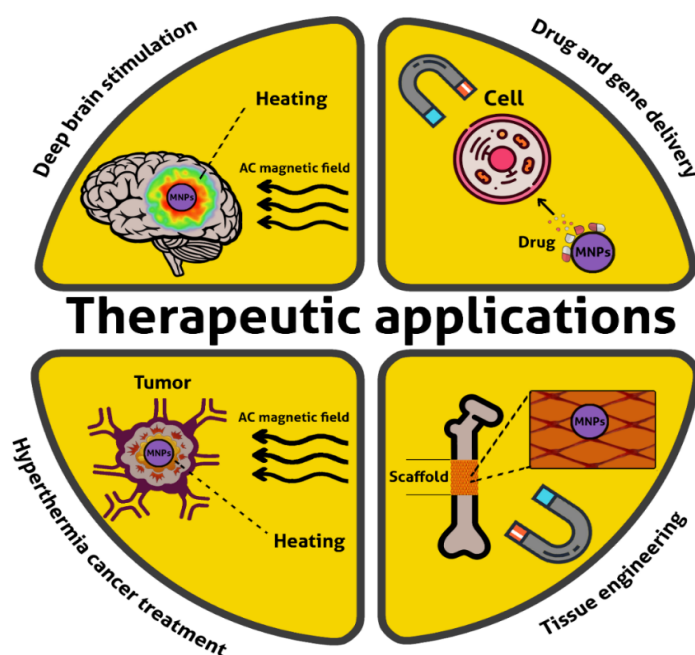
MNPs have great potential in the nanomedicine field. Magnetic nanoparticles have been widely used for analytical purposes for biomolecule detection, disease diagnosis, and treatment. This section focuses on the therapeutic, diagnostic, theranostic, magnetic separation, and biosensing applications of MNPs.

#### 4.1. Therapy

Nanoparticles have become extremely popular for cancer treatment. Their ability to pass cell membranes is a potential method to solve the problem of drug resistance [109]. MNPs may act as a carrier providing magnetically guided drug delivery (Figure 4, top



right). Moving the MNPs by the influence of an external magnetic field is currently used for modern chemotherapy in several diseases, including cancers [109,110]. Solid tumors usually have an immature, highly permeable vasculature. For better growth, tumors produce a nutritional gap in which nanoconstructions accumulate. This effect is known as the enhanced permeation and retention effect (EPR effect). For cancer treatment, MNPs can act as nanocarriers for chemotherapeutic drugs. The whole nanoconstruction must be stable in blood and not prematurely release the drug. In the tumor media, the drug release should be effective. Controlled drug release is a stumbling stone for drug-loaded MNPs. A combination of siRNA and antisense oligonucleotides may be used instead of a chemotherapeutic drug [111–114]. Such cocktails can drastically influence the targeted gene activity, resulting in a therapeutic effect [115]. This technology is called magnetofection and is defined as the delivery of nucleic acids using MNPs. Magnetofection has been introduced as a powerful tool for nucleic acid delivery into cells [114]. The method shows good results in vitro and in vivo [113,114,116–125].



**Figure 4.** Therapeutic applications of MNPs. MNPs could be applied in various fields of therapy, such as drug/gene delivery, hyperthermia cancer treatment, deep-brain stimulation (DBS), and tissue engineering for regenerative medicine.

Several strategies could be used for such an approach. One is covalent drug conjugation, which possesses hard-synthesized smart construction [8,35,109]. A physiologically cleavable linker for drug binding may be used in this case. However, much work is also conducted on noncovalent drug-loading procedures on the MNP surface. For example, doxorubicin (DOX) is a primary chemotherapeutic drug for drug-loaded MNP synthesis. DOX has been FDA-approved for more than 50 years. However, multidrug resistance and many side effects are also associated with DOX [126,127]. DOX-loaded MNPs are much more popular [128–138]. Researchers have tried to obtain good drug capacity per MNP and high stability at plasma pH~7.4. At the same time, effective drug release is required in the tumor environment and endosomal compartment with pH~4–5. However, for such promising constructions, simple MNPs may not be used. The magnetic core may be protected by noble metals (e.g., gold [139]), calcium carbonate [65,140], various polymers, and proteins [7,8,35,125,141]. For example, albumin protein MNP bio-inspired coating results in low ROS production, excellent biocompatibility, and moderate particle uptake, which is shown in in vitro and in vivo experiments [7]. Moreover, albumin coating could be chemically modified by address groups for cancer-tissue-targeted delivery [142–144], magnetic

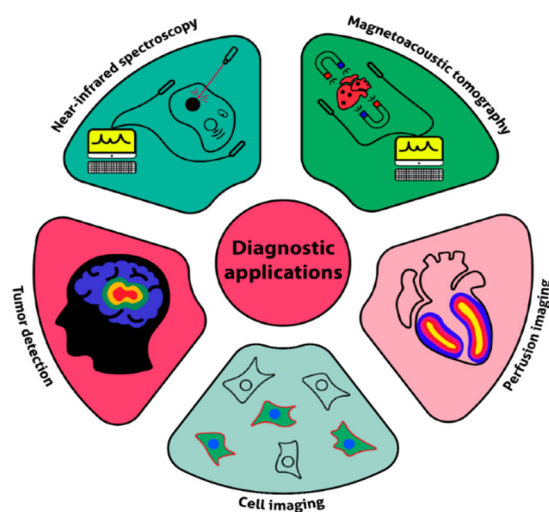
resonance imaging, or fluorescence reporter groups [145–148]. The protein–nanoparticle corona is an important tool to prevent MNPs' toxic side effects and enhance stability and biocompatibility.

Hyperthermia is a well-established method for cancer treatment [23]. MNP in an alternating magnetic field generates heat (Figure 4, bottom left). The high temperature in local regions damages tumor cells. However, the results of the heat release are highly dependent on the MNPs' size, shape, geometry, and coating [23,149]. The recent progress in the chemical synthesis of MNPs with well-controlled composition and morphology has allowed us to go forward with hyperthermia in medicine. The other limitation is that MNPs should be successfully delivered to the desired tissue. Combined cancer therapy may be obtained for drug-loaded MNPs. A smart drug-loaded construction can use the hyperthermia effect to disrupt the tumor tissue. In this way, a cumulative effect in the cells can occur [150,151]. Hyperthermia temperature rise may be easily controlled, which could be exploited in multiple therapeutic approaches. For example, deep-brain stimulation (DBS) could be obtained by a magnetic hyperthermia procedure (Figure 4, top left). Under low heating, temperature-sensitive ion channels cause an influx of  $\text{Ca}^{2+}$ -sensitive promoter and activation of individual neurons [152,153]. Moreover, shot MNP heating by an external radio-frequency magnetic field provides the local pH changes, which regulate the complex formation and cell processes [154].

MNPs can magnetically stimulate stem cells, which influences protein synthesis and gene expression. This effect may be used for damaged tissues or organ repair and regeneration (tissue engineering, Figure 4) [155]. MNPs have been used for bone, tendon, cartilage regeneration, and neuroregeneration [156–173].

#### 4.2. Diagnostics and Theranostics

Over the past few decades, MNPs have become essential for various imaging techniques [1,20,28,97,174–176]. MNPs play an important role in magnetic resonance imaging (MRI) and magnetic particle imaging (MPI). MRI is a primary medical method that provides high resolution and excellent contrast capabilities without the use of damaging ionizing radiation [28]. It is often used for disease detection, diagnosis, and treatment monitoring. MRI is based on the nuclear magnetic resonance (NMR) effect of water protons, which depends on the concentration, relaxation times ( $T_1$  and  $T_2$ ), and mobility of the water molecules in tissues. Using MNPs, it is possible to change the signal from the water protons and see the localization of the paramagnetic tracer. MNP-based contrast agents are helpful for malignant tumor detection. Since 1990, numerous papers have been published on MNP applications for MRI [20,28,174–176] (Figure 5, application examples).

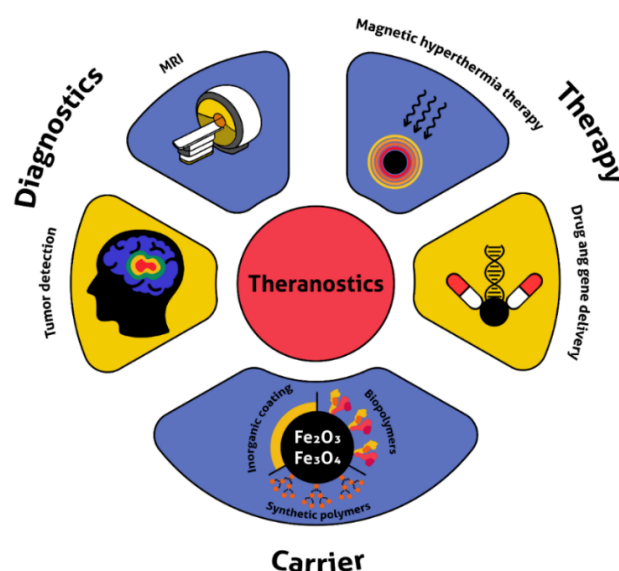


**Figure 5.** Diagnostics applications of MNPs via MRI and MPI techniques.

Using  $T_1$  contrast agents, the MRI image becomes brighter and  $T_2$  darker. MNPs are often known to shorten the  $T_2$  time, which leads to a dark zone on the MRI image. The MNP coating influences the relaxation time due to changes in water molecule availability near the magnetic core [28]. However, the universal recipe that obtains the best MRI agent is unknown [28]. In 1996, the FDA approved the Feridex<sup>®</sup>  $T_2$ -contrast agent for liver lesion detection. Feridex is a dextran-coated aqueous colloid of superparamagnetic MNPs. In the same period, several dextran-coated MNPs (e.g., Endorem, Resovist) were also approved for clinics. However, Feridex and some other contrast agents were withdrawn in 2009 due to side effects and major safety concerns (see Section 3, possible toxicity effects) [20]. Notably, the novel biocompatible MNP-based MRI contrast agents are still receiving attention for clinical use. There are a number of successful cell experiments, extensive safety experiments, and undergoing pre-clinical animal studies [20]. However, clinical trials for use in humans are not successful or in the early stages of investigations [20].

MPI is a relatively novel non-invasive technique [5]. MPI was first conceived in 2001 and reported in 2005. It uses changing magnetic fields to generate a signal from superparamagnetic MNP tracers. The signal can be observed without background, providing information about the probe location with a high signal-to-noise ratio. Among the applications of MPI are cell tracking, tumor detection, and blood-pool, vascular, and perfusion imaging (Figure 5) [5]. The high sensitivity of MPI is suitable for cancer detection in the early stage.

Recently, various MNP-based constructions for multimodal imaging have been developed [20]. These include systems for simultaneous MRI and MPI detection and combinations with computed tomography (CT), single-photon emission computed tomography (SPECT), positron emission tomography (PET), optical and ultrasound imaging, and magneto-acoustic tomography [8,20,177,178]. Combining MNP-based imaging and therapeutic approaches provides possible theranostic construction production (Figure 6) [5,8,20]. Theranostic MNPs offer considerable potential for drug-resistant cancer treatment. The primary theranostic system combines MRI and chemotherapeutic drugs or hyperthermia treatment (Figure 6). The progress in this area is limited, but has increased over the last several years [5,7,8,20].



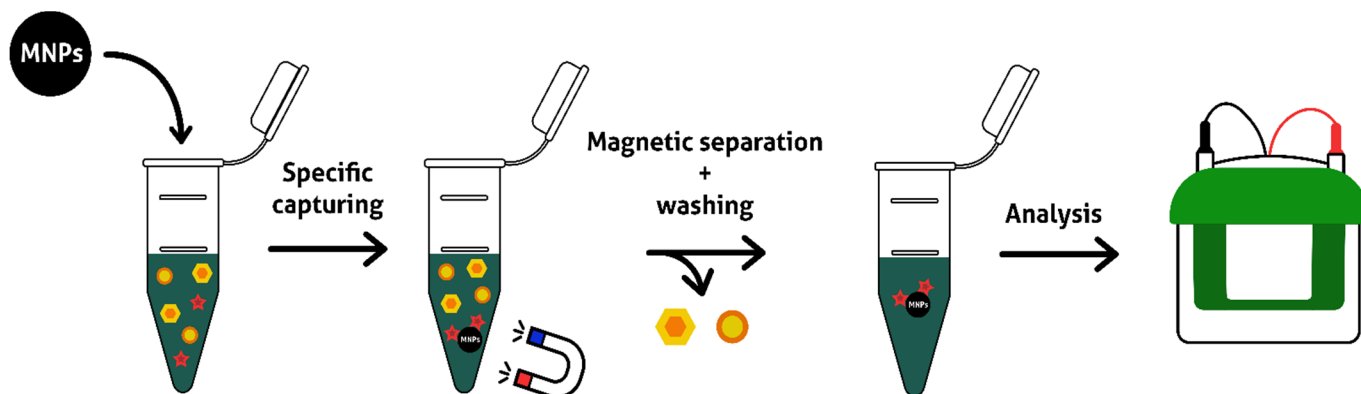
**Figure 6.** Therapy and diagnostics application combination (theranostics).

#### 4.3. Magnetic Separation, MNP-Based Biosensors, and Magnetic Microreactors

The purity of materials plays a crucial role in further analysis, which is why fast and low-cost separation approaches have to be designed. Magnetic separation is the process by which various compound separations use a magnet to attract magnetic substances (e.g., MNPs).



The process is an important method for the bioseparation and quantification of peptides, proteins, nucleic acids, and metabolites [6,22,32,33,179–192]. Moreover, magnetic separation may be used for more than simple biomolecule capture. Recently, magnetic cell separation has become a vital method for a wide range of applications [6]. Magnetic separation using MNPs is more efficient than traditional approaches, which require several stages, organic solvents, and chromatography systems [2,32,182,184,193–196]. The procedure of magnetic separation is presented in Figure 7.



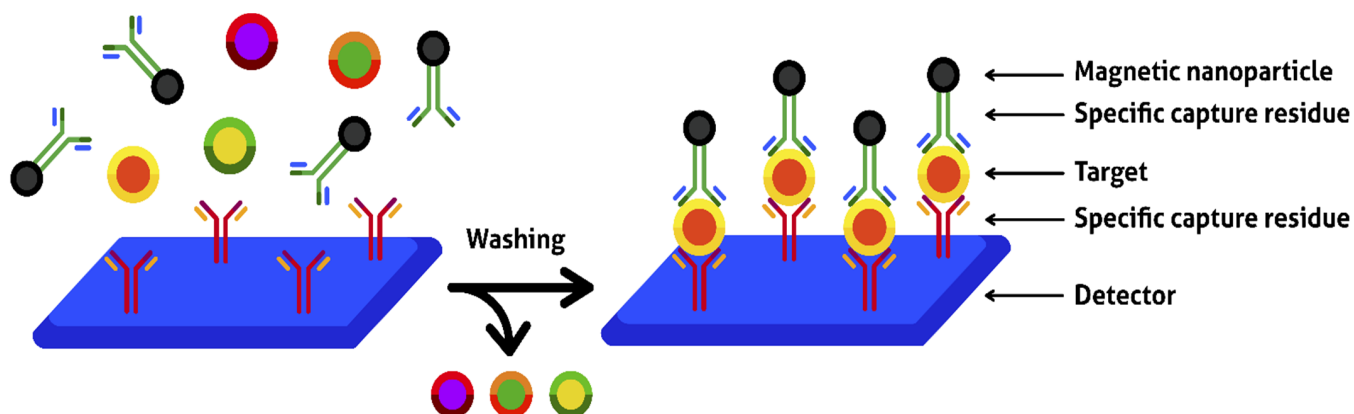
**Figure 7.** Basic principles of magnetic separation. Magnetically separated targets may be released and analyzed by various physical and biochemical methods. Hexagon, circle, and star are analytes in the solution. The star is a specific analyte, which can be bound for the MNP's surface.

Of course, these are not simple MNPs used for organic molecule and biopolymer separation. The surface of the MNPs could be modified by ligands, which can specifically bind the target molecule. Antibodies, aptamers, DNA/RNA, or proteins are used for such modification [6,16,32,180,191]. For example, avidin-coated MNPs and biotinylated oligonucleotides are utilized for specific nucleic acid separation. The biotinylated oligonucleotide forms a duplex with a targeted nucleic acid. Afterward, MNPs are added, and biotin residue interacts with avidin, forming a high-affinity complex. Such avidin-coated MNPs are commercially available elsewhere.

MNP-based biosensors could be widely used in the detection of antibiotics, toxins, antigens, proteins, nucleic acids, disease biomarkers, pathogenic bacteria, and viruses [17]. One of the MNP-based sensing strategies is presented in Figure 8. MNP may be used for target magnetic separation into the detector zone or magnetoresistive sensors [17,197–199]. The first approach enhances detection sensitivity, decreases analysis time, and provides a high signal-to-noise ratio and complex sample analysis [199]. Without a magnet, the MNP moves along with the sample in the solution, but when using a magnet, the MNP-target complex is focused on the signal generation zone. The detection of the target may be achieved with a wide range of methods: electrochemical (e.g., voltammetry, amperometry, potentiometry, electrochemiluminescence, and impedance), optical (e.g., surface plasmon resonance, and fluorescence spectroscopy), and piezoelectric [199,200]. Magnetoresistive sensors are based on the binding of MNPs to a sensor surface, which results in electrical current changes. These sensors demonstrate extremely high sensitivity. However, it is not possible to detect multiple analytes in the solution since the change in the magnetic field is restricted to only one parameter [199].

Magnetic microreactors have attracted wide attention in nanobiotechnology [201–208]. Enzyme immobilization on the MNPs with reliable magnetic properties facilitates solid-phase biocatalysis. This strategy offers high stability in enzymes during biomass processing and their easy separation by an external magnetic field. The process of enzyme recovery becomes an easy procedure for the protection of enzymes from inhibition, pH, and thermal denaturation in the continuous-mode microreactor. The MNP–enzyme system has major advantages in homo- and heterogeneous catalysis in high mass-transfer rates, selectivity, high yield, easy recovery, recyclability, and high activity [208]. Future research should be

oriented toward magnetic enzyme microreactor configurations, optimization, and application extensions. As it stands, this technology may already represent a significant step in biotechnology.



**Figure 8.** Schematic representation of the MNP sensing approach. MNPs form a stable complex with target and detector surfaces. The sorption on the surface is caused by a specific capture residue or a magnetic field. The red and yellow circle is the specific analyte.

## 5. Conclusions

MNPs are a promising platform for creating novel therapy, diagnostics, theranostics, and sensor constructions. Such systems may occupy a niche in the development of next-generation drugs for disease detection and treatment. Moreover, multifunctional MNPs with bio-inspired coatings could be a breakthrough in nanomedicine. Even after many years of research, there are still many challenges that must be taken into account for translating MNPs into clinics. Understanding the physical, chemical, and biological problems and principles of property manipulation for MNP may lead to a new era in nanomedicine.

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