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Therapeutic and Diagnostic Applications of Magnetic Nanoparticles in Cancer

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A B S T R A C T

Magnetic nanoparticles (MNPs) have emerged as a promising tool in cancer theranostics, which combines therapeutic and diagnostic strategies in a single platform. These nanoparticles, typically composed of iron oxide or other magnetic materials, offer unique advantages in cancer management, such as targeted drug delivery, imaging, and real-time monitoring of therapeutic efficacy. MNPs can be functionalized with targeting ligands such as antibodies, peptides, or small molecules to enhance their selectivity for cancer cells, thereby reducing off-target effects and minimizing toxicity. In addition to their therapeutic potential, MNPs enable advanced diagnostic techniques, particularly in magnetic resonance imaging (MRI) and hyperthermia-based treatments. As MRI contrast agents, MNPs enable high-resolution imaging for precise tumour localization and the monitoring of disease progression. Moreover, when subjected to an alternating magnetic field, MNPs can induce localized hyperthermia, effectively killing cancer cells through heat-induced cytotoxicity while sparing surrounding healthy tissue. The dual functionality of MNPs makes them ideal candidates for cancer theranostic applications, enabling the simultaneous diagnosis and treatment of tumours. Despite their potential, several challenges remain in the development of MNPs for clinical use, including issues related to biocompatibility, stability, scalability, and regulatory approval. Furthermore, the optimal size, surface modification, and drug release mechanisms of MNPs must be carefully designed to maximise therapeutic efficacy. Nevertheless, the integration of MNPs in cancer theranostics represents a promising area of research, with the potential to fundamentally change the personalized treatment of cancer by offering more effective, targeted, and non-invasive options.

Keywords: Magnetic nanoparticles, targeted therapy, cancer theranostics

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CONTENTS

1. Introduction

Theranostics refers to strategies that combine diagnosis and therapy into a unified system, allowing imaging, targeted delivery of therapeutics, and monitoring of response. In cancer treatment, theranostics can enhance specificity, reduce side effects, and allow more personalized therapy. Diagnostic modalities (e.g., MRI, fluorescence imaging) are paired with treatment (e.g., drug delivery, hyperthermia) within the same platform.

Magnetic nanoparticles (MNPs) represent a significant class of nanomaterials, typically synthesized from pure metals such as iron, cobalt, and nickel, or from combinations of metals and polymers [1]. Their applications in medicine have expanded rapidly, encompassing areas such as magnetic hyperthermia for cancer therapy [2], controlled drug delivery [3], magnetic resonance imaging (MRI) [4,5] and biosensing.

NPs of 10–100nm have significant attention in biomedical engineering due to their physical and chemical properties[6]. These NPs offer extremely high surface-area-to-volume ratios. NPs larger than 100 nm can be consumed by immune cells. Large NPs have reduced availability in blood flow and tissue[7]. In terms of therapeutics, there is a potential role for nanoparticles in tissue engineering[8,9]. Nanoparticles can also be engineered for selective drug and gene delivery to targeted organs or tissues, minimizing exposure of healthy tissue to drugs or genes[10,11].

Cancer, also known as a malignant tumor, is a major global health concern marked by uncontrolled cell growth, metastasis, and resistance to conventional treatments. Traditional therapies like chemotherapy and radiotherapy often cause severe side effects due to poor specificity. Nanotechnology offers promising solutions for targeted cancer management. Magnetic nanoparticles (MNPs), with their magnetic responsiveness and biocompatibility, enable precise tumor targeting and controlled drug delivery[3].

Furthermore, the potential of MNPs in cancer diagnosis, particularly through magnetic resonance imaging and biosensor applications, is explored. The discussion also addresses the current limitations of these approaches and identifies areas where MNPs, either in their current form or with enhanced designs, could improve cancer detection and treatment.

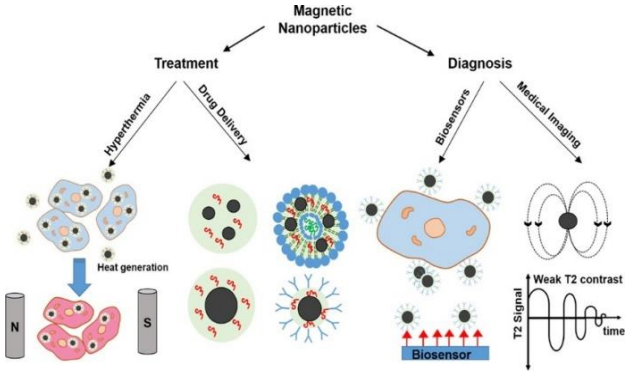

Fig.1: Different forms of the MNPs with considerable potential in hyperthermia, drug delivery, imaging, and biosensing for cancer treatment and diagnosis.

Magnetic nanoparticles (MNPs), composed of metals, alloys, or oxides, commonly iron, nickel, or cobalt, exhibit unique magnetic properties that make them highly valuable for biomedical applications [12]. Iron-based MNPs are particularly favoured due to their biocompatibility. These nanoparticles can be engineered to generate heat under alternating magnetic fields, enabling targeted damage to cancer cells [13].

MNPs improve the sensitivity and specificity of magnetic resonance imaging and have been developed as clinically approved contrast agents. The emergence of theranostics combines treatment, allowing disease targeting. Designing multifunctional MNP systems involves integrating controlled drug release, imaging enhancement, and other functionalities, underscoring their versatility in both diagnostics and targeted therapy, and highlighting their potential as a platform for personalised cancer management.

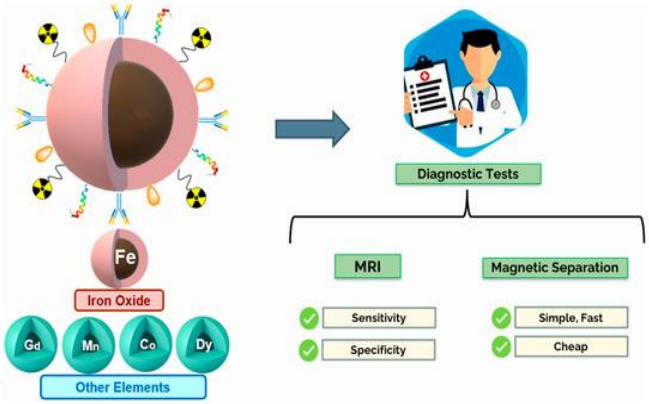

Fig.2: Magnetic nanoparticles serve as powerful tools for developing rapid, sensitive, and specific diagnostic tests across various imaging techniques.

2. Types of Magnetic Nanoparticles

2.1 Superparamagnetic Iron Oxide Nanoparticles (SPIONs): Superparamagnetic iron oxide nanoparticles (SPIONs) are MNPs with diameters smaller than 50 nm. MNPs possess large surface areas; can transport small molecules, proteins, and RNA; and exhibit an effect when exposed to high-frequency magnetic fields [14]. The shape of magnetic nanoparticles has not been extensively studied to extend their role in the biodistribution of SPIONs. However, a few researchers studying other nanoparticulate delivery systems have reported that rod-shaped and nonspherical nanoparticles show a longer blood circulation time compared with spherical particles [15].

Effectively engineered to reach their target tissue with minimal nonspecific cellular interactions. Targeting strategies can be classified into three groups, as illustrated in Fig. 3. Passive targeting leverages the inherent size of nanoparticles and the distinctive characteristics of the tumour microenvironment. Tumour tissues often exhibit leaky vasculature due to incomplete angiogenesis, allowing nanoparticles to accumulate selectively at the tumour site [16].

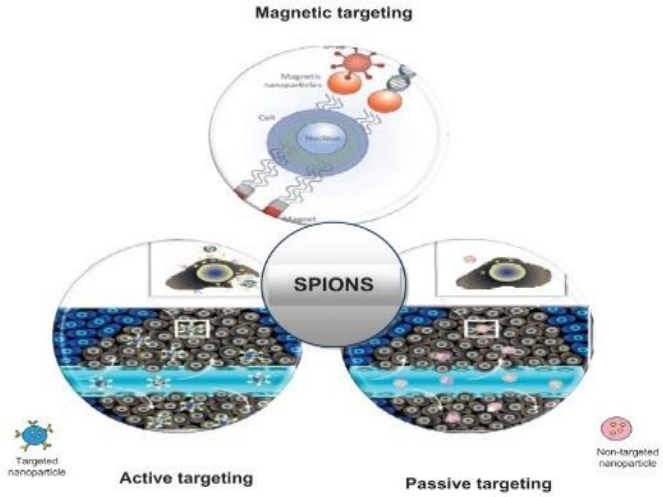

Fig.3: Superparamagnetic iron oxide nanoparticle targeting approaches.

Chemotherapeutic agents with poor solubility and limited bioavailability can be attached to or encapsulated within these nanostructures. The efficiency of these nanoparticles in delivering drugs, however, is influenced by their size, shape, and various chemical and physical properties. At room temperature, SPIONs display superparamagnetic behaviour when their size is below 30nm.

2.2 Ferrite Nanoparticles:

Ferrite magnetic nanoparticles are utilized in cancer theranostics for both diagnosis and treatment, leveraging their magnetic properties and tumour-targeting capabilities. They serve as contrast agents in magnetic resonance imaging, induce localised heat to kill cancer cells through magnetic hyperthermia, and act as carriers for precise drug or gene delivery. Additionally, ferrite MNPs can improve chemotherapy effectiveness by generating reactive oxygen species (ROS) in the acidic tumour microenvironment, which can directly destroy tumour cells [17].

The technique merges the distinct attributes of divalent metal ions (Co, Ni, or Ca) with the native properties of iron oxide nanoparticles o enhance their functionality. These ferrites exhibit strong magnetic behaviour, a high surface area, small particle size, and the biocompatibility necessary for biomedical applications. [17].

2.3 Metallic Magnetic Nanoparticles:

Metal-based nanoparticles for cancer theranostics incorporate one or more metallic elements, each offering distinct properties suitable for specific imaging or therapeutic applications. Common examples include nanoparticles composed of gold, silver, copper, platinum, iron, lanthanides, and quantum dots (QDs). Existing chemotherapeutic agents often cause significant side effects, display uneven distribution across tissues and organs, and have low targeting specificity [18,19]. Nanotechnology applied to human health provides novel approaches for treating many human diseases, including cancer [20]. Metallic nanoparticles are used in the biomedical realm. Metallic NPs based cancer therapy and diagnosis are listed in Table 1.

Fig.4. Metallic nanoparticles application

Table 1: Metallic nanoscale materials have desirable applications in cancer theranostics

S.No	Nanoparticle	Application of theranostics
1	Gold (Au)	Drug delivery system, Anticancer effect, Fluorescence probe
2	Silver (Ag)	Anticancer, Fluorescence probes, Photodynamic therapy
3	Iron (Fe)	Magnetic resonance imaging (MRI) contrast agent, anticancer agent, paramagnetic probe
4	Titanium (Ti)	Drug delivery system, anticancer, photodynamic therapy,
5	Platinum (Pt)	Photothermal therapy, anticancer effect
6	Manganese (Mn)	Magnetic resonance imaging (MRI) contrast agent, anticancer agent
7	Aluminum (Al)	Drug delivery system, anticancer effects
8	Zinc (Zn)	Fluorescence probes, Drug delivery system, anticancer effects
9	Copper (Cu)	Photothermal therapy, anticancer effects, Drug delivery system, Bioimaging, Biosensors

Table 2: Synthesis methods for magnetic nanoparticles

Method	Temperature (°C)	Solvent	Advantages	Disadvantages
Co-precipitation	25–85	Water	Safe, cost-effective, and requires low synthesis temperature.	Surface oxidation, poor size distribution
Thermal decomposition	100–320	Organic compounds	High-quality particles, small size.	Complicated, time-consuming, low production rate.
Hydrothermal	220	Water–ethanol	Simple, eco-friendly, cost-effective.	High pressure and temperature increase the synthesis time.

Polyol	25 up to boiling point	Ethylene	Precise control over size and shape, cost-effective, and low-cost industrial method.	Difficult to synthesize small particles.
Sol–gel	10–30	Water	High purity, homogeneity	Impurities are hard to remove.
Microemulsion	20–50	Organic	High magnetisation value.	Complicated, slow reaction kinetics.

3. Synthesis of magnetic nanoparticles

The synthesis of magnetic nanoparticles (MNPs) requires careful control of colloidal behaviour and a multi-step procedure, as experimental conditions significantly influence particle size, shape, and surface properties. Ideally, methods should produce reproducible results without simple purification, such as magnetic separation. Common chemical approaches—co-precipitation, thermal decomposition, and microemulsion—are cost-effective and allow precise control over size, morphology, and composition (Fig.5). Physical methods, such as gas-phase decomposition and electron beam lithography, often yield less uniform nanoparticles. the goal is to produce highly crystalline MNPs with narrow size distributions and strong saturation magnetisation for optimal biomedical performance.

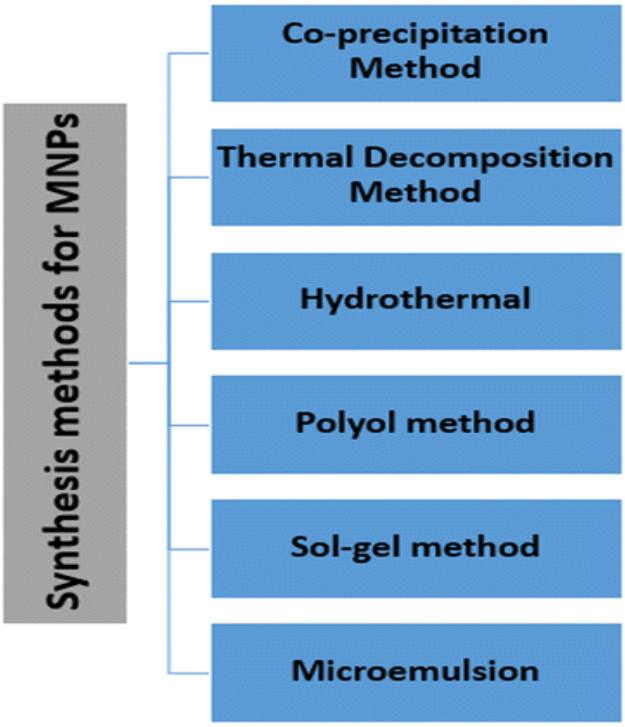

Fig.5: Synthesis methods for magnetic nanoparticles

3.1 Co-precipitation method:

The co-precipitation method is widely used for synthesizing magnetic nanoparticles (MNPs) for biomedical applications due to its simplicity, safety, and cost-effectiveness. It involves reacting ferrous (Fe^{2+}) and ferric (Fe^{3+}) salts in a 2:1 ratio under alkaline conditions to produce magnetite (Fe_3O_4) nanoparticles [21]. Synthesis can occur at room temperature or 80–85 °C, with particle recovery via centrifugation or magnetic separation. Maintaining pH (7.5–14) and inert or alkaline conditions is crucial to prevent oxidation to $Fe(OH)_3$, which alters properties. Surface coatings, proteins, or starch improve stability and biocompatibility. Co-precipitation MNPs are widely applied in cancer theranostics as MRI contrast agents, hyperthermia mediators, and drug carriers [22].

3.2 Thermal decomposition method:

Highly crystalline, homogeneous, and monodisperse magnetic nanoparticles (MNPs) are frequently synthesized using the thermal breakdown process and pyrolysis[23]. Organometallic precursors are heated in high-boiling organic solvents, such as oleic acid or oleyl amine, typically between 100 and 350 350°C. For MRI applications where particle size is crucial, this technique is valuable because it offers precise size control (4–30 nm). Compared to co-precipitation, the resultant MNPs exhibit superior crystallinity, dispersibility, and repeatability. Before being used in biomedical applications, they must undergo thorough purification, which is both costly and time-consuming[24].

3.3 Hydrothermal method:

The hydrothermal method produces magnetic nanoparticles (MNPs) in sealed autoclaves under controlled temperature and pressure. It is eco-friendly, cost-effective, and solvent-free, with some post-treatment steps[25]. This method allows good control over particle size, shape, and magnetic properties, making it useful in biomedical therapy. However, producing ultra-small particles (<10 nm) remains challenging, and the reaction often proceeds slowly at elevated temperatures[26].

3.4 Polyol method:

The polyol method utilises polyols as solvents, reducing agents, and stabilizers to produce nanoparticles with precise control over their size and morphology [25,27]. Different shapes, such as spheres, rods, or flower-like structures, can be achieved by varying the precursor concentration and reaction temperature[28]. This method is environmentally friendly, economical, and straightforward, as it eliminates the need for additional calcination steps.

3.5 Sol–gel method:

The sol–gel method synthesizes magnetic nanoparticles through hydrolysis and condensation of metal alkoxides or precursors. The process involves forming a sol, then drying it into a gel, and removing the solvent to obtain nanoparticles[29]. It yields high-purity, homogeneous, and size-controlled particles suitable for biomedical use. However, impurities may form during synthesis, which are difficult to remove[30]. Overall, it offers excellent control over particle size and composition.

3.6 Microemulsion method: The microemulsion method produces magnetic nanoparticles (MNPs) using stable mixtures of oil, water, and surfactant[31]. Nanoparticles are formed inside microdroplets, which allows the control of

size, shape, and composition. The process typically gives particles with high magnetisation values. However, the method requires high temperatures and shows slow reaction kinetics. MNPs obtained are usually larger in size compared to the methods[32].

4. Diagnostic Applications

4.1 Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging (MRI) produces high-resolution, three-dimensional images for disease diagnosis and monitoring by stimulating water protons in tissues and detecting their relaxation signals. MRI images are classified as T1 (longitudinal) or T2 (transverse) weighted, depending on the type of signal measured. Paramagnetic compounds, such as gadolinium (Gd^{3+}) [33] complexes, are commonly used to enhance T1 (positive) contrast, while magnetic nanoparticles (MNPs), particularly iron oxide nanoparticles, are widely applied as T2 (negative) contrast agents due to their strong magnetisation and ability to influence nearby water protons[34,35]. Theranostic nanoplatforms combining iron oxide NPs with polymeric shells or complexes like Fe^{3+} -terpyridine have demonstrated improved contrast efficiency by increasing water proton interaction, enabling more precise cancer detection and monitoring[35].

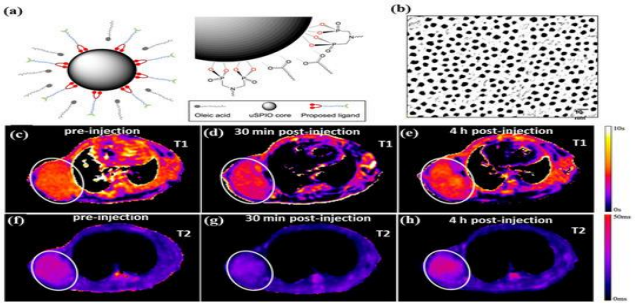

Fig.6. Ligand exchange process of uSPIOs, (b) TEM image, and (c–h) T1/T2 mapping of uSPIOs in mice at different time intervals.

4.2 Magnetic Particle Imaging (MPI):

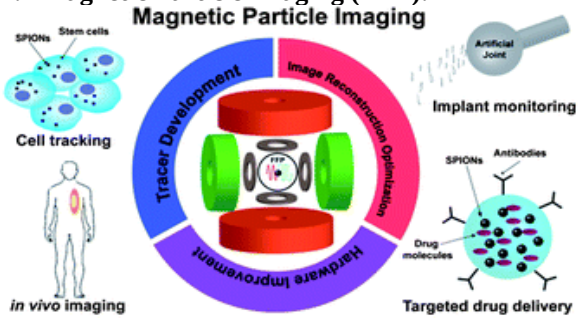

Fig.7. magnetic particle imaging (MPI)

A comparatively recent imaging method is based on a direct quantification of the spatial distribution of iron oxide Nanoparticles in a tissue as a magnetisation response to a magnetic field. It provides a higher contrast than that of the MRI polymer-NP system, promising MPI contrast properties [36]. Magnetic particle imaging (MPI) is an emerging technique that directly maps the distribution of superparamagnetic iron oxide nanoparticles. With high sensitivity and rapid image acquisition, MPI produces tomographic images with excellent temporal and spatial resolution, offering contrast and sensitivity comparable to established imaging methods, such as **MRI** – Magnetic Resonance Imaging, **CT**–Computed Tomography (also called CAT scan: Computed Axial Tomography), **PET** – Positron Emission Tomography, **SPECT** – Single Photon Emission Computed Tomography, **X-ray** and **Ultrasound** – Ultrasonography (uses high-frequency sound waves for imaging).

4.3 Fluorescence Imaging:

Typically, a fluorescently labelled polymer is used to perform fluorescence imaging in conjunction with MRI[37]. Iron oxide nanoparticles functionalized with a two-photon fluorescent polymer enabled the detection of pancreatic beta cell mass, an early biomarker of type 2 diabetes[38]. Dye release was triggered by the acidic environment of pancreatic Beta cells, enabling the fluorescent detection of these cells using both confocal one-photon and two-photon microscopy. In addition, the nanoprobe effectively inhibited the harmful aggregation of human islet amyloid polypeptide, which is implicated in beta-cell degeneration associated with type 2 diabetes. The magneto-fluorescent nanogels described in the section on polymer nanoprecipitation exhibited dual emission (red and green) in cells under different excitation wavelengths, demonstrating their potential for fluorescence-based imaging of cancer cells[39].

5. Therapeutic Applications

5.1 Magnetic Hyperthermia:

Hyperthermia and thermal therapy treat cancer by elevating tumour temperatures above normal body levels, damaging cancer cells and enhancing immune responses [40,41]. Immune suppression mechanisms also help prevent the proliferation of damaged cells. Magnetic nanoparticles (MNPs) can be directly injected into tumours and heated via external magnetic fields, enabling localised treatment [41]. Experimental results revealed that oleic acid–stabilized iron oxide nanoparticles significantly inhibited Walker 256 carcinoma growth, leading to improved survival rates in treated animals compared to controls[42]. Similarly, in prostate cancer, MNP-mediated hyperthermia under alternating magnetic fields enhanced the destruction of cancer cells[43,44]. These results suggest MNPs are promising for targeted hyperthermia therapy, offering precise tumour eradication with limited side effects. Nonetheless, further research is needed to optimize efficacy and confirm clinical safety.

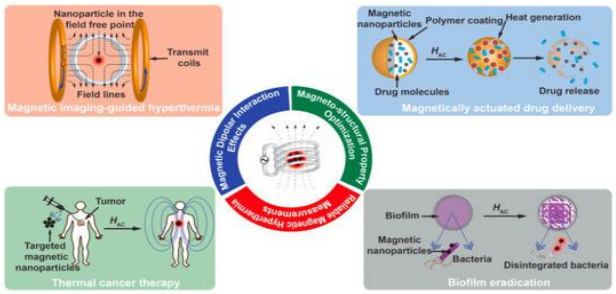

Fig.8. Schematic illustration of magnetic nanoparticle-mediated hyperthermia for cancer therapy.

5.2 Targeted Drug Delivery

5.2.1 Passive targeting:

Passive targeting enhances MRI detection and cancer diagnosis by exploiting the natural accumulation of magnetic nanoparticles (MNPs) in tumours through leaky vasculature caused by cancer-induced angiogenesis [45]. However, nanoparticle delivery efficiency depends on physicochemical properties such as size, surface charge, and hydrophobicity [46]. Hydrophobic and positively charged nanoparticles exhibit shorter circulation times, whereas hydrophilic and negatively charged ones circulate longer [47]. Although leaky tumour vessels facilitate nanoparticle accumulation, passive targeting alone often results in insufficient nanoparticle delivery for effective molecular MRI or therapeutic outcomes, highlighting the need for improved targeting strategies.

5.2.2 Active targeting:

Active targeting enhances cancer-specific delivery by using magnetic drug treatment or ligand-mediated interactions with antibodies, folate, lectins, and peptides [48]. In magnetic drug delivery, therapeutic agents are attached to or encapsulated within nanoparticles such as liposomes, micelles, or dendrimers. This approach has been explored for treating tumours and other diseases. External magnetic fields can direct magnetically targeted aerosols to specific lung regions, improving drug localisation. Inhaled magnetic aerosols show promise for treating lung cancer, chronic obstructive pulmonary disease (COPD), cystic fibrosis, and respiratory infections, offering a controlled and effective method for localised therapy [49].

5.3 Gene Delivery:

There is growing interest in using gene silencing and RNA interference for cancer therapy. However, siRNA is quickly degraded by endonucleases before entering cells. To address this, iron oxide nanoparticles were functionalized with chitosan and siRNA for MRI imaging and RNA interference[50]**.** Coating the nanoparticles with PEG and poly-L-arginine improved biocompatibility and siRNA delivery. Chitosan enabled siRNA to escape endosomes[51] , allowing pH-triggered release into the cytoplasm via polymer-coated magnetic nanoparticles for gene silencing.

6. Future Perspectives

The rise of treatment-resistant cancers and limitations of gadolinium-based contrast agents (GBCAs) highlight the need for safer alternatives. While GBCAs enhance MRI imaging, they pose serious risks, especially for patients with kidney issues, potentially causing Nephrogenic Systemic Fibrosis (NSF) [52,53]. Environmental concerns also arise from acid in water. Iron oxide nanoparticles (IONPs) are a biocompatible, biodegradable alternative for cancer theranostics. Iron oxide nanoparticles serve as versatile platforms for MRI contrast enhancement, targeted drug delivery, magnetic hyperthermia, and gene delivery, offering integrated solutions to current limitations in cancer diagnosis and therapy[54].

7. Conclusion

Magnetic nanoparticles (MNPs) are emerging as a highly versatile tool in cancer theranostics due to their multifunctional capabilities, including enhanced imaging, targeted drug delivery, and magnetic hyperthermia. Their small size, tunable properties, responsiveness to magnetic fields, and versatile surface functionalization allow precise tumour targeting and real-time monitoring. Despite these advantages, several challenges remain in translating MNPs to clinical use, such as maintaining in vivo stability, achieving controlled drug release, ensuring reproducible large-scale production, and confirming long-term biocompatibility. Regulatory guidance from agencies such as the European Medicines Agency (EMA), emphasising safety, efficacy, and quality control, along with growing international collaborations and investments, is facilitating the clinical translation of MNPs. With ongoing innovations in design, functionalization, and multimodal strategies, MNPs have the potential to transform personalised cancer therapy by effectively integrating diagnosis and treatment, ultimately improving patient outcomes.

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