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Original Article

Magnetic Nanoparticles In Targeted Cancer Therapy: A Comprehensive Review

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ABSTRACT

Cancer remains one of the leading causes of morbidity and mortality worldwide despite continuous advances in diagnosis and treatment. Conventional therapies such as chemotherapy, radiotherapy, and surgery are often limited by systemic toxicity, poor selectivity, multidrug resistance, recurrence, and damage to healthy tissues. In recent years, nanotechnology has emerged as a transformative strategy in oncology by enabling site-specific drug delivery and multifunctional therapeutic systems. Among different nanocarriers, magnetic nanoparticles (MNPs) have gained considerable attention because of their unique responsiveness to external magnetic fields, high surface area, tunable physicochemical properties, and theranostic potential. These nanoparticles can be magnetically guided toward tumor tissues, improving local drug concentration while minimizing off-target toxicity. In addition to targeted chemotherapy, magnetic nanoparticles are widely explored for magnetic hyperthermia, imaging enhancement, gene delivery, immunotherapy support, and combined diagnostic-therapeutic applications. Surface engineering with polymers, peptides, antibodies, and ligands further improves circulation time, biocompatibility, and receptor-specific uptake. Recent developments from 2023 to 2026 indicate increasing translational potential of multifunctional magnetic nanoplatforms for personalized cancer treatment. However, challenges such as toxicity, aggregation, immune recognition, scalable manufacturing, and regulatory approval remain significant barriers. This comprehensive review discusses recent progress in magnetic nanoparticles for targeted cancer therapy, including classification, synthesis methods, targeting mechanisms, therapeutic applications, safety concerns, and future perspectives.

Keywords: Magnetic nanoparticles, targeted cancer therapy, nanomedicine, hyperthermia, iron oxide nanoparticles, oncology.

INTRODUCTION

Cancer is a heterogeneous group of diseases characterized by uncontrolled cellular proliferation, tissue invasion, angiogenesis, and metastasis. It remains a major global health burden, with millions of new cases and deaths reported annually [1]. Despite progress in clinical management, many cancers continue to show poor prognosis because of late diagnosis, therapeutic resistance, and metastatic spread [2].

Conventional cancer treatments including chemotherapy, radiotherapy, and surgery remain essential clinical approaches. However, systemic chemotherapy is frequently associated with severe adverse effects due to non-specific biodistribution of cytotoxic drugs. Common toxicities include myelosuppression, nephrotoxicity, cardiotoxicity, gastrointestinal injury, and immune suppression [3]. Moreover, repeated treatment cycles often lead to multidrug resistance, reducing long-term efficacy [4].

Nanotechnology has introduced innovative strategies to overcome these limitations. Nanoscale drug delivery systems can enhance solubility of poorly water-soluble drugs, prolong circulation time, protect labile molecules, improve intracellular uptake, and promote preferential tumor accumulation through the enhanced permeability and retention (EPR) effect [5]. Several nanocarriers including liposomes, polymeric nanoparticles, dendrimers, lipid nanoparticles, and metallic nanoparticles have demonstrated value in oncology [6].

Among these systems, magnetic nanoparticles (MNPs) are especially attractive because of their unique ability to respond to externally applied magnetic fields. This property enables remote guidance and retention of drug-loaded particles at

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tumor sites, resulting in improved local drug exposure and reduced systemic toxicity [7]. In addition, magnetic nanoparticles can convert electromagnetic energy into heat under alternating magnetic fields, allowing selective tumor ablation through magnetic hyperthermia [8].

Iron oxide nanoparticles, particularly magnetite (Fe_3O_4) and maghemite (γ-Fe_2O_3), are the most widely studied magnetic nanomaterials because of their relatively favorable biocompatibility and biodegradability [9]. Their surfaces can be modified with polyethylene glycol, dextran, chitosan, silica, antibodies, peptides, folic acid, and aptamers to enhance stability, prolong circulation, and improve active targeting [10].

Recent studies published between 2023 and 2026 demonstrate rapid progress in multifunctional magnetic nanoplatforms integrating chemotherapy, imaging, immunotherapy, gene delivery, and photothermal therapy into single systems [11-13]. However, long-term toxicity, protein corona formation, large-scale reproducibility, and regulatory complexity remain major translational challenges [14].

This comprehensive review summarizes the recent advances in magnetic nanoparticles for targeted cancer therapy, with emphasis on classification, synthesis methods, targeting strategies, therapeutic applications, safety considerations, and future perspectives.

FUNDAMENTALS OF MAGNETIC NANOPARTICLES

Magnetic nanoparticles are particles typically ranging from 1 to 100 nm that exhibit magnetic behavior due to the presence of magnetic metals or metal oxides. Their nanoscale dimensions produce unique properties such as increased surface area, altered electronic behavior, improved tissue interaction, and tunable magnetic responses [15].

1. Superparamagnetism

Many biomedical magnetic nanoparticles exhibit superparamagnetism, where particles become magnetized only in the presence of an external magnetic field and lose residual magnetization when the field is removed. This prevents irreversible aggregation and improves in vivo safety [16].

2. Properties Relevant to Cancer Therapy

- High drug loading capacity
- External magnetic targeting ability
- Controlled release potential[17].

3. Common Core Materials

Iron Oxide Nanoparticles

The most common biomedical magnetic nanoparticles due to favorable biosafety and biodegradability [18].

Ferrite Nanoparticles

Manganese ferrite, cobalt ferrite, and zinc ferrite exhibit stronger magnetic performance for hyperthermia applications [19].

Hybrid Magnetic Nanoparticles

Magnetic cores combined with gold, silica, lipids, or polymers improve multifunctionality and targeting efficiency [20].

SURFACE FUNCTIONALIZATION

Bare magnetic nanoparticles are inherently prone to oxidation, particle aggregation, and rapid recognition and clearance by the mononuclear phagocyte system, which significantly limits their circulation time and therapeutic efficiency in vivo. Therefore, appropriate surface coating is essential to improve their physicochemical stability, biocompatibility, and biomedical performance [21]. Various organic and inorganic materials have been widely employed as coating agents, including polyethylene glycol (PEG), dextran, chitosan, silica, gold shells, albumin, lipid layers, and stimuli-responsive polymers [22]. These coatings help prevent agglomeration, reduce nonspecific protein adsorption, enhance blood circulation time, and provide functional groups for further modification. In addition, targeting ligands such as folic acid, transferrin, monoclonal antibodies, peptides, and aptamers can be conjugated onto the nanoparticle surface to facilitate receptor-mediated endocytosis and selective uptake by cancer cells,

thereby improving tumor targeting and therapeutic outcomes [23].

SYNTHESIS METHODS

Common synthesis methods include co-precipitation, thermal decomposition, hydrothermal synthesis, sol-gel processing, microemulsion techniques, and green synthesis using plant-derived biomolecules. These methods significantly influence particle size, shape, crystallinity, and magnetic behavior [24].

CLASSIFICATION OF MAGNETIC NANOPARTICLES USED IN CANCER THERAPY

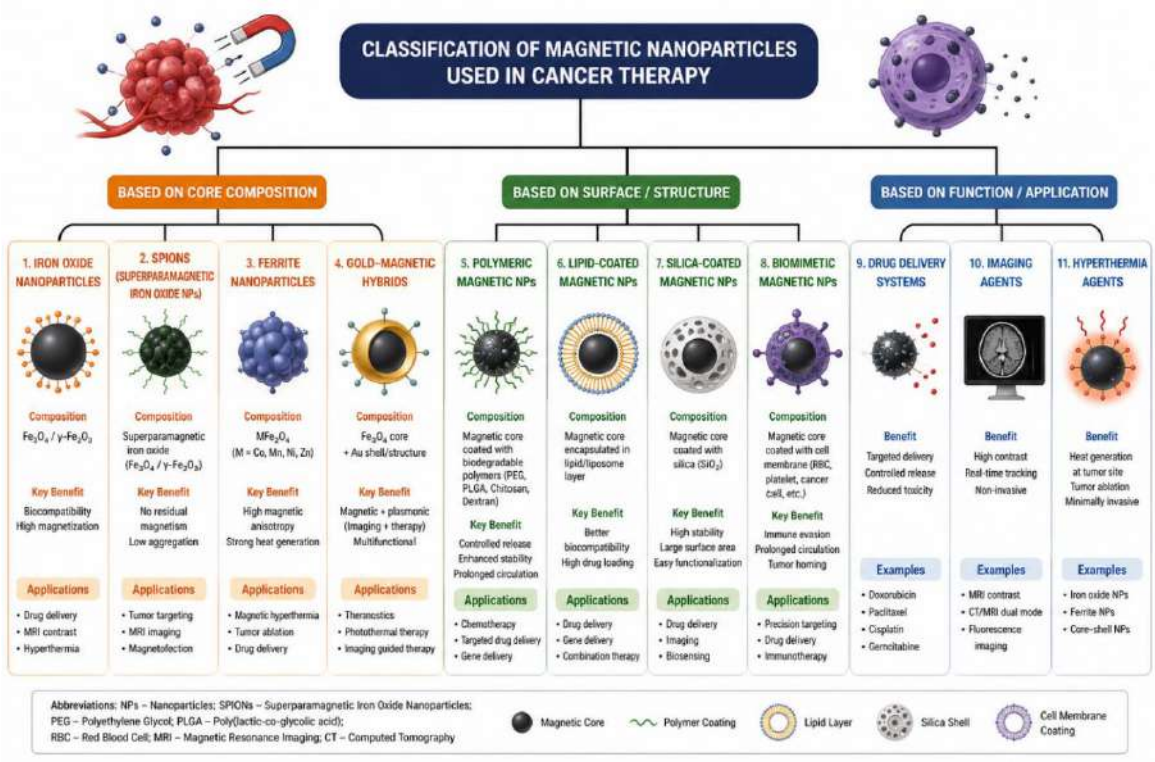

Figure 1: Classification of magnetic nanoparticles used in cancer therapy

TARGETING MECHANISMS OF MAGNETIC NANOPARTICLES IN CANCER THERAPY

Efficient tumor targeting is one of the principal advantages of magnetic nanoparticles (MNPs). These systems can improve local drug accumulation, reduce systemic toxicity, and enhance therapeutic efficacy through passive, active, and magnetic targeting mechanisms [25].

1. Passive Targeting

Passive targeting primarily depends on the enhanced permeability and retention (EPR) effect. Tumor vasculature is irregular, highly permeable, and poorly organized, allowing nanoparticles to extravasate into tumor tissues more easily than in normal tissues. In addition, impaired lymphatic drainage within tumors promotes nanoparticle retention [26].

Nanoparticles with optimized size (typically 10–200 nm), surface charge, and hydrophilic coatings demonstrate improved passive accumulation in tumor microenvironments [27]. However, EPR efficiency varies considerably depending on tumor type, vascular density, stromal barriers, and patient-specific factors [28].

2. Active Targeting

Active targeting involves surface modification of magnetic nanoparticles with ligands capable of recognizing overexpressed receptors on cancer cells. Following ligand-receptor interaction, nanoparticles undergo receptor-mediated endocytosis, improving intracellular drug delivery [29].

Common targeting ligands include:

- **Folic acid:** targets folate receptors overexpressed in ovarian, breast, and lung cancers
- **Transferrin:** targets transferrin receptors associated with rapidly dividing cells
- **HER2 antibodies:** used in HER2-positive breast cancer
- **RGD peptides:** target integrin receptors involved in angiogenesis
- **Aptamers:** nucleic acid ligands with high specificity [30]

Active targeting increases cellular uptake and may reduce non-specific biodistribution.

3. Magnetic Field-Guided Targeting

This is a unique feature of MNPs. An externally applied magnetic field near the tumor site can attract circulating magnetic nanoparticles and retain them locally, thereby increasing therapeutic concentration [31].

Magnetic targeting has shown promising results in superficial tumors, breast tumors, liver lesions, and localized solid tumors. Limitations include reduced magnetic penetration in deep tissues and the need for optimized field strength and particle magnetic moment [32].

4. Stimuli-Responsive Targeting

Modern magnetic nanoplatforms are often engineered to release drugs in response to tumor-specific stimuli such as acidic pH, elevated glutathione, enzymes, temperature, or alternating magnetic fields [33]. These systems improve selectivity and reduce premature drug leakage.

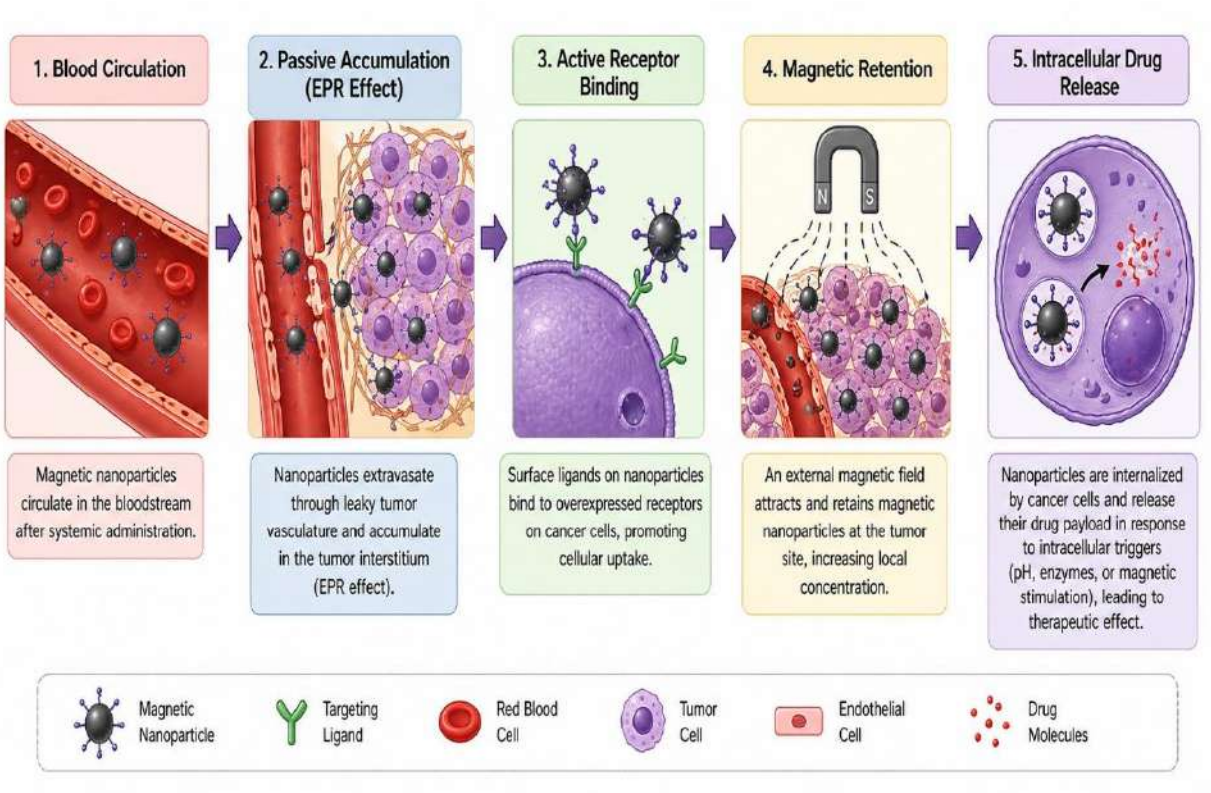

Figure 2: Tumor Targeting Strategies of Magnetic Nanoparticles

DRUG DELIVERY APPLICATIONS IN CANCER THERAPY

Magnetic nanoparticles are widely investigated as carriers for chemotherapeutic drugs, nucleic acids, proteins, and combination therapeutics. Their ability to deliver payloads directly to tumors can improve efficacy while reducing systemic adverse effects [34].

1. Delivery of Chemotherapeutic Drugs

Several anticancer drugs have been successfully incorporated into magnetic nanoparticle-based

delivery systems, including doxorubicin, paclitaxel, cisplatin, methotrexate, gemcitabine, and docetaxel, demonstrating the broad applicability of these nanocarriers in cancer therapy [35]. Drug loading onto magnetic nanoparticles can be achieved through multiple strategies such as surface adsorption, covalent conjugation, encapsulation within carrier matrices, or polymer entrapment, depending on the physicochemical properties of the drug and desired release profile. These approaches enable efficient drug protection, enhanced bioavailability, and site-specific delivery. Furthermore, controlled drug release from magnetic nanoparticles can be stimulated by environmental or external triggers such as acidic pH, enzymatic activity, or magnetic hyperthermia-induced heating, thereby improving precision therapy and minimizing systemic toxicity [36]. Recent investigations have reported that doxorubicin-loaded PEGylated iron oxide nanoparticles exhibited significantly superior tumor suppression compared with free doxorubicin, while simultaneously reducing dose-related cardiotoxicity, highlighting their promise as safer and more effective chemotherapeutic platforms [37].

2. Gene Delivery

Magnetic nanoparticles can deliver siRNA, miRNA, plasmid DNA, and CRISPR components to tumor cells. Magnetically enhanced transfection, known as magnetofection, improves nucleic acid uptake and gene silencing efficiency [38].

This approach is being explored to suppress oncogenes, reverse drug resistance, and activate tumor suppressor pathways.

3. Protein and Peptide Delivery

Therapeutic peptides, antibodies, and cytokines may be delivered using magnetic carriers to improve stability and tumor localization [39].

4. Combination Therapy

Magnetic nanoparticles enable simultaneous delivery of multiple therapeutic agents, such as chemotherapy plus immunomodulators or chemotherapy plus photothermal agents [40].

Table 1: Major Drugs Delivered Using Magnetic Nanoparticles

Drug	Cancer Type	Benefit of Magnetic Carrier
Doxorubicin	Breast, liver	Reduced cardiotoxicity
Paclitaxel	Ovarian, lung	Improved solubility
Cisplatin	Solid tumors	Reduced nephrotoxicity
Methotrexate	Leukemia	Sustained release
Gemcitabine	Pancreatic	Enhanced tumor uptake

MAGNETIC HYPERTHERMIA

Magnetic hyperthermia is a minimally invasive therapeutic approach in which magnetic nanoparticles generate localized heat (typically 42–46°C) under an alternating magnetic field, causing selective cancer cell death [41].

Heat generation occurs through Néel and Brownian relaxation mechanisms. Cancer cells are more heat-sensitive than normal tissues because of poor vascular cooling capacity and altered stress responses [42].

Benefits of Magnetic Hyperthermia

- Localized tumor destruction
- Sensitization to chemotherapy
- Sensitization to radiotherapy
- Reduced damage to healthy tissue

- Potential immunogenic cell death induction [43]

Recent clinical studies continue to evaluate iron oxide nanoparticle hyperthermia in glioblastoma, prostate cancer, and recurrent solid tumors [44].

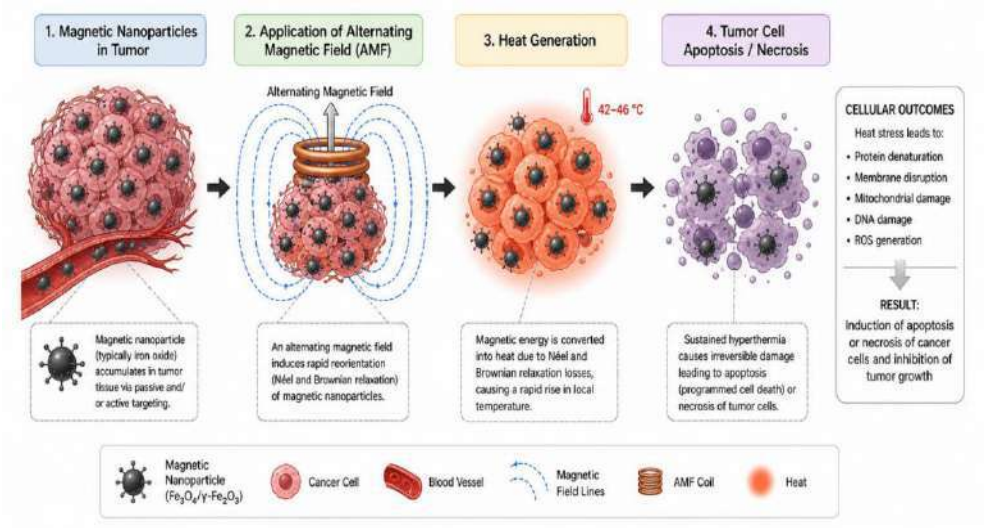

Figure 3: Mechanism of Magnetic Hyperthermia

IMAGING AND THERANOSTIC APPLICATIONS

Magnetic nanoparticles serve as excellent contrast agents in magnetic resonance imaging (MRI), enabling visualization of tumor localization, biodistribution, and treatment response [45].

Theranostics refers to combined therapy and diagnostics in a single platform. Examples include:

- MRI-guided chemotherapy delivery
- Hyperthermia + imaging
- Drug release monitoring
- Multimodal imaging (MRI + CT + fluorescence) [46]

Recent multifunctional nanoplatforms integrate gold shells, fluorescent dyes, or radionuclides with magnetic cores for real-time precision oncology [47].

IMMUNOTHERAPY AND GENE-ASSISTED APPLICATIONS OF MAGNETIC NANOPARTICLES

Cancer immunotherapy has transformed oncology by enabling the immune system to recognize and destroy malignant cells. However, many immunotherapeutic agents suffer from poor tumor penetration, systemic immune-related adverse effects, and limited response rates. Magnetic nanoparticles (MNPs) are increasingly investigated as delivery systems to improve localization and controlled release of immunomodulatory agents [48].

1. Immune Checkpoint Delivery

Checkpoint inhibitors targeting programmed cell death protein-1 (PD-1), programmed death ligand-1 (PD-L1), and cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) have shown major clinical benefits. Magnetic nanocarriers can enhance local delivery of these biologics or related nucleic acids to tumors, potentially reducing systemic toxicity [49].

2. Cancer Vaccines and Antigen Delivery

MNPs can transport tumor antigens, adjuvants, or mRNA payloads to dendritic cells and lymphoid tissues, improving antigen presentation and T-cell activation [50].

3. Gene Editing and RNA Therapy

Magnetic nanoparticles are being used to deliver:

- siRNA for oncogene silencing
- miRNA mimics or inhibitors
- CRISPR/Cas systems
- mRNA-based therapeutic constructs [51]

Magnetically assisted uptake may increase intracellular delivery efficiency.

TOXICITY AND SAFETY CONSIDERATIONS

Although magnetic nanoparticles offer substantial therapeutic promise, safety remains a critical factor for clinical translation. Toxicological responses depend on particle size, surface charge, coating material, dose, administration route, biodegradability, and duration of exposure [52].

1. Oxidative Stress

Iron-containing nanoparticles may catalyze reactive oxygen species (ROS) generation, leading to oxidative stress, mitochondrial dysfunction, inflammation, and DNA damage when improperly designed [53].

2. Organ Accumulation

After systemic administration, nanoparticles may accumulate in the liver, spleen, lungs, kidneys, or bone marrow because of uptake by the mononuclear phagocyte system [54]. Long-term retention may raise safety concerns.

3. Immunogenicity

Certain surface chemistries may trigger complement activation, cytokine release, or hypersensitivity reactions. Surface PEGylation and biomimetic coatings can reduce immune recognition [55].

4. Hemocompatibility

Nanoparticles intended for intravenous administration must be evaluated for hemolysis, platelet aggregation, coagulation disturbances, and endothelial toxicity [56].

5. Strategies to Improve Safety

- Use biodegradable iron oxide cores
- Apply biocompatible polymer coatings
- Optimize particle size and dose
- Reduce aggregation tendency
- Employ targeted delivery to lower systemic exposure
- Conduct long-term biodistribution studies [57]

CLINICAL PROGRESS AND TRANSLATIONAL STATUS

Several magnetic nanoparticle systems have advanced from laboratory research into clinical or near-clinical development. The most mature applications are imaging contrast enhancement, iron replacement therapy, and magnetic hyperthermia [58].

1. Hyperthermia in Glioblastoma

Iron oxide nanoparticle-mediated hyperthermia has been clinically investigated in recurrent glioblastoma and other aggressive tumors as an adjunct to radiotherapy [59].

2. Imaging and Diagnostics

Magnetic nanoparticles have a long history as MRI contrast materials, although newer formulations continue to be optimized for oncology imaging and lymph node mapping [60].

3. Drug Delivery Translation

While targeted magnetic drug delivery remains highly promising, challenges such as scale-up manufacturing, regulatory characterization, and consistent in vivo targeting still limit commercialization [61].

4. Personalized Oncology

Recent trends from 2025–2026 emphasize patient-specific nanomedicine platforms guided by imaging, biomarkers, and AI-supported treatment planning [62].

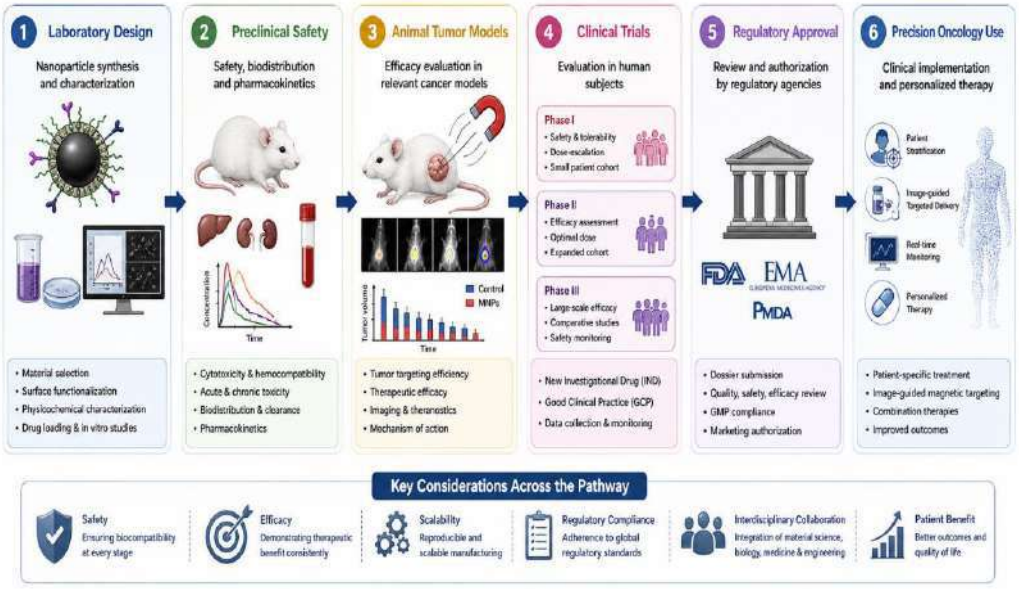

Figure 4: Translational Pathway of Magnetic Nanoparticles

MANUFACTURING AND REGULATORY CHALLENGES

For successful commercialization, magnetic nanoparticle-based systems must demonstrate consistent product quality, proven safety, therapeutic efficacy, and the ability to be manufactured at industrial scale. However, several technical and regulatory challenges remain before widespread clinical translation can be achieved. Major concerns include maintaining batch-to-batch reproducibility, achieving narrow particle size distribution and uniformity, ensuring sterility assurance, controlling endotoxin contamination, preserving surface ligand consistency, maintaining physicochemical stability during storage, and establishing cost-effective large-scale manufacturing processes [63]. In addition to these manufacturing requirements, regulatory authorities demand comprehensive characterization of nanoparticle formulations, including their physicochemical properties, pharmacokinetic behavior, biodistribution, toxicity profile, immunogenic potential, and long-term safety outcomes before approval for human use [64]. These stringent requirements are essential to ensure reliable performance and patient safety in commercial biomedical applications.

FUTURE PERSPECTIVES

The future of magnetic nanoparticles in cancer therapy is highly promising, with ongoing research focused on developing more intelligent, precise, and multifunctional treatment platforms. Key anticipated advancements include artificial intelligence (AI)-guided nanoparticle design for optimizing particle characteristics and therapeutic performance, personalized tumor-targeted systems tailored to individual patient biomarkers, and smart stimuli-responsive release platforms capable of delivering drugs in response to internal or external triggers. Emerging strategies also involve combined immunotherapy and magnetic hyperthermia systems to enhance anticancer immune responses, magnetically guided gene-editing approaches for precise genetic interventions, and real-time image-guided therapy for simultaneous diagnosis and treatment monitoring. In addition, biodegradable next-generation nanomaterials are expected to improve long-term safety and reduce accumulation-related toxicity [65]. The integration of diagnostics, therapy, and continuous monitoring into a single magnetic nanoparticle platform has the potential to significantly transform precision oncology and improve clinical outcomes.

COMPARATIVE ADVANTAGES AND CURRENT LIMITATIONS

Magnetic nanoparticles (MNPs) offer several advantages over conventional and non-magnetic nanocarriers in targeted cancer therapy. Their external controllability, multifunctionality, and compatibility with imaging technologies distinguish them from many other delivery systems [66].

1. Major Advantages

- Precise Tumor Localization

Unlike passive nanocarriers that depend mainly on the enhanced permeability and retention effect, MNPs can be actively concentrated at tumor sites using external magnetic fields, improving local therapeutic exposure [67].

- Reduced Systemic Toxicity

By limiting exposure of healthy tissues to cytotoxic drugs, magnetic targeting may reduce adverse effects commonly observed with standard chemotherapy [68].

- Multifunctional Capability

Magnetic nanoparticles possess remarkable multifunctional capability, allowing a single nanoplatform to integrate several therapeutic and diagnostic functions within one system. Such platforms may simultaneously serve as carriers for targeted drug delivery, contrast agents for magnetic resonance imaging (MRI), mediators for magnetic hyperthermia treatment, and vectors for gene delivery. In addition, they can be engineered for biosensing applications to detect disease biomarkers and enable real-time treatment monitoring during therapy [69]. This multimodal functionality supports the development of theranostic systems that combine diagnosis, treatment, and response evaluation, offering a highly efficient and personalized approach to modern cancer management.

- Controlled and Triggered Release

Drug release can be designed to respond to pH, enzymes, temperature, redox environment, or magnetic stimulation [70].

- Personalized Therapy Potential

Magnetic systems may be customized according to tumor type, receptor profile, and imaging findings, supporting precision oncology [71].

2. Current Limitations

Despite strong promise, several limitations remain.

Limited Deep Tissue Magnetic Penetration

External magnetic fields lose strength with distance, making treatment of deep-seated tumors more challenging [72].

Heterogeneous Tumor Uptake

Dense extracellular matrix, poor perfusion, and irregular vasculature can reduce nanoparticle penetration [73].

Long-Term Safety Uncertainty

Repeated dosing and chronic nanoparticle retention require further long-term human safety evaluation [74].

Manufacturing Complexity

Clinical translation requires scalable, sterile, reproducible, and cost-effective manufacturing processes [75].

Regulatory Uncertainty

Multifunctional systems combining device-like and drug-like features may face complex regulatory pathways [76].

EMERGING INNOVATIONS (2025–2026)

Recent years have shown rapid innovation in magnetic nanomedicine. Several advanced directions are expected to shape next-generation cancer therapy.

1. Biomimetic Magnetic Nanoparticles

Nanoparticles coated with cancer cell membranes, platelet membranes, red blood cell membranes, or exosomes may evade immune clearance and improve tumor homing [77].

2. AI-Assisted Nanoparticle Design

Artificial intelligence and machine learning are being used to optimize particle size, ligand density, release kinetics, and patient selection [78].

3. Magnetic Microrobots

Micro/nanorobotic systems containing magnetic materials may navigate through body fluids under magnetic control for ultra-precise drug delivery [79].

4. Combination with Immunotherapy

Magnetic hyperthermia plus immune checkpoint blockade is a highly promising strategy because local heating may enhance tumor antigen release and immune activation [80].

5. Real-Time Smart Monitoring

Future systems may integrate biosensors capable of measuring pH, oxygen, glucose, or tumor biomarkers during therapy [81].

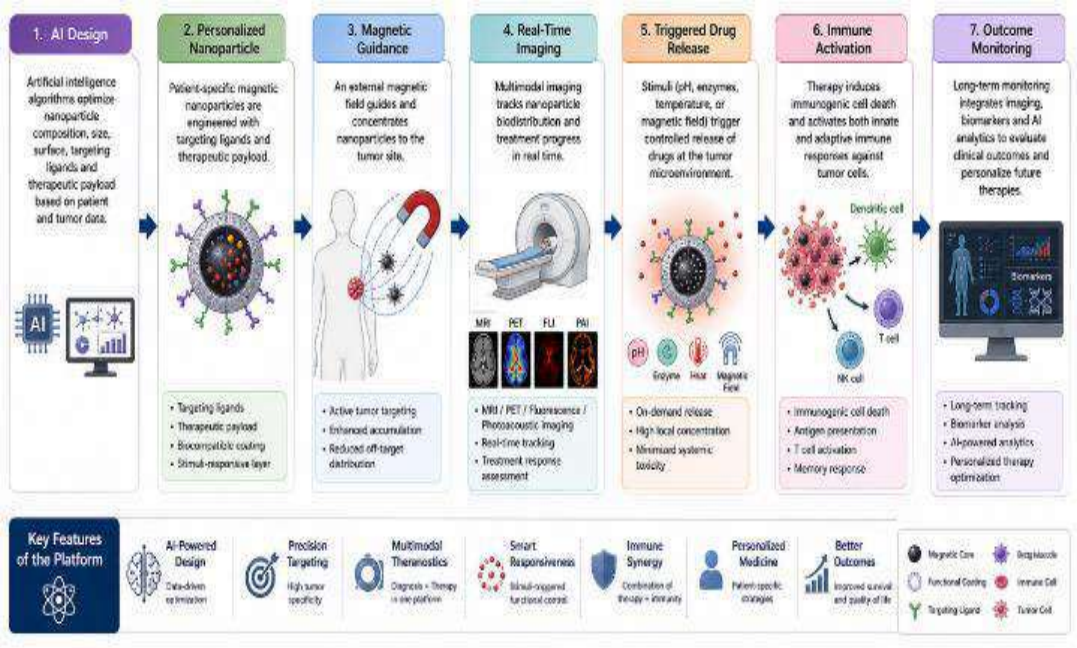

Figure 5: Future Smart Magnetic Nanomedicine Platform

RESEARCH GAPS AND OPPORTUNITIES

Although progress is substantial, several research questions remain:

- What is the safest repeat-dose schedule in humans?
- How can deep tumors be efficiently magnetically targeted?
- Which coatings best avoid immune clearance?
- How can animal results better predict human outcomes?
- What manufacturing methods reduce cost while preserving quality?
- Which patient populations benefit most from magnetic nanotherapy? [82]

Collaborative work between pharmaceutical scientists, oncologists, engineers, toxicologists, and regulatory experts is essential.

CONCLUSION

Magnetic nanoparticles represent one of the most promising nanotechnological strategies for targeted cancer therapy. Their unique magnetic responsiveness enables externally guided tumor localization, while their adaptable surface chemistry allows efficient loading of anticancer drugs, genes, proteins, and imaging agents. In addition to targeted chemotherapy, magnetic nanoparticles support magnetic hyperthermia, theranostics, immunotherapy enhancement, and personalized treatment planning.

Recent advances from 2023 to 2026 demonstrate clear movement toward multifunctional and clinically translatable magnetic nanoplatforms. Surface-engineered iron oxide systems, hybrid magnetic composites, and stimuli-responsive carriers have shown improved tumor selectivity, controlled release, and therapeutic efficacy in preclinical studies. Emerging integration with artificial intelligence, biomimetic coatings, and combination immunotherapy may further accelerate progress.

However, important challenges remain, including long-term toxicity evaluation, deep tissue targeting efficiency, batch reproducibility, regulatory complexity, and large-scale manufacturing. Addressing these barriers will determine the speed of clinical adoption.

Overall, magnetic nanoparticles have the potential to transform cancer treatment from generalized systemic therapy toward image-guided, localized, and personalized precision oncology. With continued interdisciplinary research and carefully designed clinical trials, magnetic nanomedicine may become a key component of future cancer care.

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