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NANOPARTICLE MEDIATED DRUG DELIVERY SYSTEMS FOR CANCER TREATMENT

Chapter 9: Biomedical Applications of Nanoparticles in Cancer Therapy

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Abstract

Conventional therapeutic strategies are hindered by the limitations of the drugs, and cancer continues to be one of the most prevalent diseases causing morbidity and mortality worldwide, which have spurred the development of innovative drug-delivery technologies. Nanoparticles have proven to be versatile biomedical platforms that are useful in the delivery, stabilization, pharmacokinetics and biodistribution of anticancer agents. The small size and tunable physicochemical properties allow for the integration of small molecule drugs, proteins, nucleic acids, imaging agents and combinations of therapeutic payload. The applications of nanoparticles in biomedical field are explored in various areas of targeted drug delivery, chemotherapy, gene and RNA therapies, immunotherapy, photothermal therapy, photodynamic therapy, radiotherapy enhancement, magnetic hyperthermia, cancer diagnosis, molecular imaging, biosensing and theranostics. Liposomes, polymeric nanoparticles, polymeric micelles, dendrimers, solid lipid nanoparticles, nanostructured lipid carriers, metallic nanoparticles, magnetic nanoparticles, mesoporous silica nanoparticles, quantum dots, protein-based nanoparticles, and biomimetic nanocarriers are the major nanoparticle systems. While significant advances have been made, barriers to tumor heterogeneity, biological barriers, clearance of nanoparticles, toxicity, manufacture, scale-up, reproducibility, regulatory clearance, and translation to the clinic remain. In this chapter, the major biomedical





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applications of nanoparticles such as drug delivery in cancer therapeutics, advantages and disadvantages, clinical relevance, and future perspectives are discussed, focusing on the mechanism of action, advantages, limitations, and future perspectives. Nanotechnology can be coupled with precision oncology, artificial intelligence, personalized medicine and sophisticated molecular diagnostics to further help the development of safer and more effective cancer nanomedicines.

Keywords: Nanoparticles, Cancer therapy, Targeted drug delivery, Nanomedicine, Theranostics Gene delivery.

1. Introduction

Cancer is a complex group of diseases with abnormal cells that grow in an uncontrolled way, survive when they should not, invade tissues and spread to other parts of the body. Cancer develops and progresses via genetic and epigenetic changes, deregulated signalling pathways, interactions with the tumor microenvironment, immune evasion and angiogenesis. Although there have been significant advances in surgery, chemotherapy, radiotherapy, targeted therapy, hormonal therapy and immunotherapy, there are still difficulties in cancer treatment. These include the fact that tumors are heterogeneous, there is multidrug resistance, toxicity to other parts of the body, low drug solubility, inadequate drug penetration into tumors, and drug resistance at the time of disease recurrence [1, 2]. Modern chemotherapy is still a crucial aspect of cancer treatment. Many cytotoxic drugs, however, are not very selective for killing the malignant cells, and have a narrow therapeutic window. This can also lead to toxic concentrations in healthy tissues leading to myelosuppression, gastrointestinal toxicity, alopecia, cardio toxicity and immunosuppression. Moreover, certain anticancer agents are poorly soluble in water, metabolized quickly, have a short half-life and have poor biodistribution [1, 3]. A new way to overcome some of these challenges is through the use of nanotechnology. Nanoparticles are engineered structures at the nanoscale which can be used to carry therapeutic or diagnostic agents. The size, surface chemistry, morphology, charge, composition and functionality of these can be altered to affect their interaction with biological systems [3, 4]. Cancer nanomedicine or nanoparticle-based cancer therapy is a medical field that is comprised of nanotechnology and oncology, pharmaceutical sciences, molecular biology, materials science and biotechnology. The ability to enhance the solubility of the drug, to stabilize the labile therapeutic molecules, to modify the pharmacokinetics and to control the drug release, and even to enhance the delivery to the tumor tissue [3, 5] are some of the functions that the nanoparticles can fulfil. Drug delivery is not the only area of biomedical use of nanoparticles. They are the focus of growing research on cancer imaging, cancer diagnosis, bio sensing, gene therapy, immunologic therapy, Photothermal therapy, photodynamic therapy, magnetic hyperthermia, radiotherapy enhancement, and theranostic. One of the great benefits





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of nanotechnology is that a number of functions can be packaged in a single platform. A multifunctional nanoparticle might contain a chemotherapeutic agent, an imaging agent, and a targeting agent in addition to a diagnostic agent, a targeted delivery agent, and a therapeutic monitoring agent for example [4, 6]. But getting nanotechnology out of the research lab and into clinical practice is daunting. The behaviour of nanoparticles in the human body is influenced by a variety of factors including protein corona formation, immune recognition, biodistribution, tumour heterogeneity and biological barriers. Thus, it is necessary to understand all of the biological interactions of the nanoparticles for successful nanomedicine development [5,7].

2. Fundamentals of Nanoparticles in Cancer Nanomedicine

The nanoparticles are typically defined by their nanoscale size and by the presence of peculiar physicochemical properties. They have a large surface area to volume ratio and can be surface-functionalized, making them good candidates for biomedical applications.

The major characteristics relevant to cancer nanomedicine include:

- Particle size
- Surface charge
- Surface chemistry
- Shape and morphology
- Hydrophobicity/Hydrophilicity
- Drug-loading capacity
- Encapsulation efficiency
- Biodegradability
- Colloidal stability
- Surface functionalization

These properties influence the biological fate of nanoparticles, including circulation, biodistribution, tumor accumulation, cellular uptake, intracellular trafficking, and clearance [3, 5].

2.1 Particle Size

The size of the particle has a significant impact on circulation, penetration of tissues, uptake by the cells and elimination. Smaller nanoparticles may have enhanced tissue penetration while larger nanoparticles may have enhanced uptake by the mononuclear phagocyte system. Thus, the proper sized particle size for an application is to be determined.





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2.2 Surface Charge

The surface charge affects the interactions of nanoparticles with plasma proteins and cell membranes. The cellular uptake of positively charged nanoparticles is potentially increased and the nonspecific interactions and toxicity are also potentially increased. Particles that are neutral or slightly charged might have better circulation properties [5].

2.3 Surface Modification

Nanoparticle surfaces may be modified using polyethylene glycol (PEG), antibodies, peptides, aptamers, carbohydrates, or other ligands.

Surface modification can:

- Improve colloidal stability
- Reduce nonspecific protein adsorption
- Prolong circulation
- Facilitate active targeting
- Enhance cellular uptake

2.4 Drug Loading and Encapsulation

Nanoparticles can incorporate various therapeutic agents, including:

- Small-molecule drugs
- Proteins
- Peptides
- DNA
- RNA
- siRNA
- mRNA
- CRISPR-related components

The drug may be encapsulated, adsorbed, or chemically conjugated to the carrier.

3. Major Types of Nanoparticles Used in Cancer Therapy

Several nanoparticle platforms have been investigated for cancer applications.





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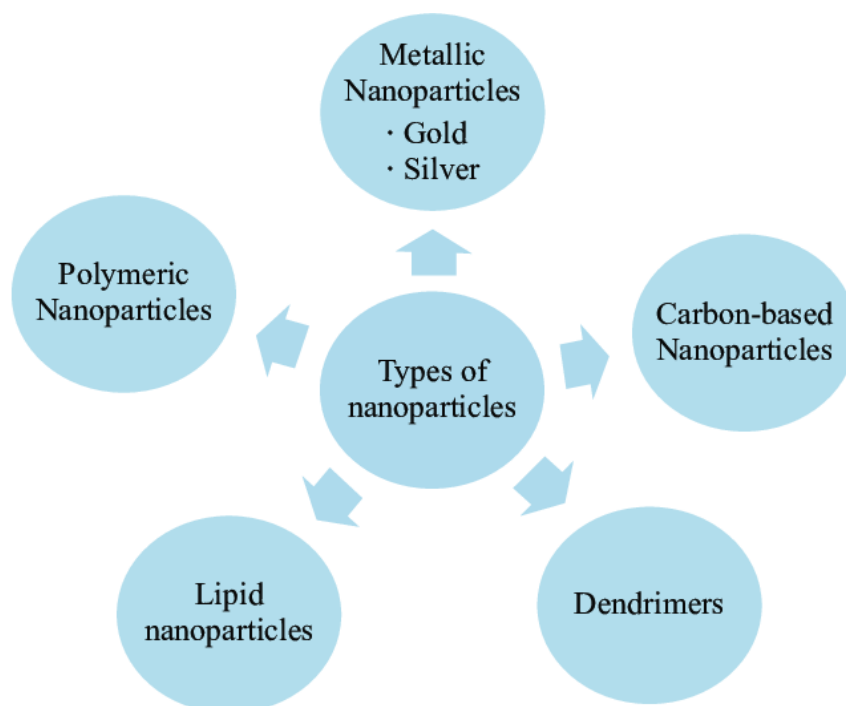


Fig.1 Types of nanoparticles

3.1 Liposomes

Liposomes are made up of phospholipid bilayers which enclose an aqueous core. They are able to transport hydrophilic and hydrophobic drugs. There is extensive clinical evidence of the potential of liposomes, especially in enhancing the delivery of anticancer drugs [1, 3].

3.2 Polymeric Nanoparticles

The polymers, which are used to prepare polymeric nanoparticles, include PLGA, PLA, chitosan and other biodegradable polymers. These can offer prolonged drug-release and can be functionalized at the surface [3, 8].

3.3 Polymeric Micelles

Polymeric micelles have a hydrophobic core and hydrophilic shell. They can be used as a tool to increase the aq. solubility of poorly water-soluble drugs in particular.

3.4 Metallic Nanoparticles

Gold, silver, iron oxide, and other metallic nanoparticles have been investigated for imaging, drug delivery, photothermal therapy, and magnetic hyperthermia [9, 10].





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3.5 Dendrimers

Dendrimers are highly branched macromolecules with multiple functional groups that can be used for drug and gene delivery.

3.6 Solid Lipid Nanoparticles

Solid lipid nanoparticles contain a solid lipid matrix and may improve drug stability and controlled release.

3.7 Nanostructured Lipid Carriers

NLCs contain a mixture of solid and liquid lipids and may provide improved drug-loading capacity compared with some solid lipid systems.

3.8 Mesoporous Silica Nanoparticles

Mesoporous silica nanoparticles have a porous structure with a high surface area, making them suitable for drug loading and controlled release.

3.9 Quantum Dots

Quantum dots are semiconductor Nanocrystals with unique optical properties and are mainly investigated for imaging and diagnostic applications.

3.10 Biomimetic and Biological Nanocarriers

Emerging systems include:

- Exosome
- Extracellular vesicles
- Cell membrane-coated nanoparticles
- Protein nanoparticles
- Virus-like particles
- Hybrid nanoparticles

These systems attempt to exploit biological mechanisms for improved delivery and immune evasion [4, 6].

Table 1 Major Nanoparticle Platforms and Their Biomedical Applications

Nanoparticle	Major Characteristics	Biomedical Applications
Liposomes	Phospholipid bilayer	Drug delivery, imaging, theranostics
Polymeric nanoparticles	Biodegradable polymeric matrix	Controlled drug and gene delivery





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Polymeric micelles	Hydrophobic core and hydrophilic shell	Delivery of poorly soluble drugs
Gold nanoparticles	Optical and photothermal properties	Imaging, photothermal therapy
Magnetic nanoparticles	Magnetic responsiveness	MRI, magnetic hyperthermia
Dendrimers	Highly branched structure	Drug and gene delivery
SLNs	Solid lipid matrix	Controlled drug delivery
NLCs	Solid and liquid lipid mixture	Drug delivery
Mesoporous silica	High surface area and porous structure	Drug loading and controlled release
Quantum dots	Tunable fluorescence	Molecular imaging
Exosomes	Biological membrane	RNA and drug delivery
Hybrid nanoparticles	Combination of materials	Multifunctional therapy

4. Nanoparticles in Targeted Cancer Drug Delivery

Targeted drug delivery is one of the most extensively investigated applications of nanoparticles. The objective is to increase drug exposure at the tumor site while reducing systemic exposure to healthy tissues.

Nanoparticle targeting can be divided into:

1. Passive targeting
2. Active targeting
3. Antibody-mediated targeting
4. Stimuli-responsive targeting

4.1 Passive Targeting

The EPR effect is often considered a hallmark of “passive targeting.” There may be abnormal permeability of the tumour vessels and impaired lymphatic drainage. Some solid tumors might be suited for accumulation of nanoscale material as a result of these properties [11, 12]. The EPR effect, however, is very variable and patient-dependent and can differ from one tumor type





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to another. Thus, EPR is not sufficient to account for all types of nanogold uptake into human tumors and clinical translation has proven to be less successful than the initial preclinical studies suggested [12, 13].

4.2 Active Targeting

Active targeting involves the attachment of specific ligands to nanoparticle surfaces.

Examples include:

- Antibodies
- Peptides
- Aptamers
- Folic acid
- Hyaluronic acid
- Transferrin

These ligands can recognize receptors or antigens expressed by cancer cells.

4.3 Antibody-Mediated Targeting

Antibodies provide molecular recognition and may facilitate receptor-mediated internalization. Nanoparticles functionalized with antibodies have been investigated for targeted delivery of chemotherapeutic drugs, nucleic acids, and imaging agents [3, 5].

4.4 Stimuli-Responsive Targeting

Smart nanoparticles can release drugs in response to specific stimuli.

Internal stimuli

- pH
- Enzymes
- Redox conditions
- Reactive oxygen species
- Hypoxia

External stimuli

- Light
- Ultrasound
- Magnetic fields
- Temperature

These approaches may improve spatial and temporal control over drug release [14].





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Table 2 Targeting Strategies in Cancer Nanomedicine

Targeting strategy	Mechanism	Advantages	Limitations
Passive targeting	Tumor accumulation through biological transport mechanisms	Simple design	Variable tumor accumulation
Active targeting	Ligand-receptor interaction	Enhanced cellular uptake	Receptor heterogeneity
Antibody targeting	Antibody–antigen recognition	High specificity	Cost and immunogenicity
pH-responsive	Acid-triggered drug release	Controlled release	Variable tumor pH
Enzyme-responsive	Enzyme-mediated release	Tumor-specific activation	Variable enzyme expression
Light-responsive	Light-triggered release	Temporal control	Limited tissue penetration
Magnetic-responsive	Magnetic field activation	Remote control	Requires specialized equipment

5. Nanoparticles for Chemotherapy

Chemotherapy remains a major component of cancer treatment. However, conventional chemotherapy is associated with systemic toxicity and pharmacokinetic limitations.

Nanoparticles can improve chemotherapy by:

1. Increasing drug solubility
2. Protecting drugs from degradation
3. Modifying pharmacokinetics
4. Improving tumor exposure
5. Providing controlled release
6. Facilitating combination therapy





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5.1 Liposomal Chemotherapy

Liposomes are the most clinically promising nanocarriers. Liposomal formulations may alter the distribution of anticancer drugs and may help to decrease some toxicities. A well-known example is the liposomal doxorubicin. The behavior of the doxorubicin in terms of its pharmacokinetics has been altered by the process of encapsulation and this has been exploited in several cancer indications [1, 15].

5.2 Albumin-Bound Nanoparticles

Albumin-bound paclitaxel represents another clinically important nanoparticle formulation. It was developed to avoid the need for certain solvent systems used in conventional paclitaxel formulations and to modify drug delivery characteristics [16].

5.3 Combination Chemotherapy

Nanoparticles can potentially co-deliver multiple drugs. This approach may help achieve coordinated drug exposure and overcome resistance mechanisms.

Examples of potential combinations include:

- Chemotherapy + gene therapy
- Chemotherapy + immunotherapy
- Chemotherapy + Photothermal therapy
- Chemotherapy + photodynamic therapy

Table 3 Nanoparticle Applications in Chemotherapy

Application	Example	Potential Benefit
Liposomal drug delivery	Liposomal doxorubicin	Modified pharmacokinetics
Albumin-based delivery	Albumin-bound paclitaxel	Solvent-free formulation
Polymeric delivery	PLGA-based systems	Controlled release
Micellar delivery	Polymeric micelles	Improved solubility
Combination delivery	Multiple drugs	Synergistic treatment
Targeted delivery	Ligand-functionalized systems	Improved cellular uptake





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6. Nanoparticles in Gene and RNA Therapy

Gene therapy aims to modify cellular genetic material to treat disease. In cancer, therapeutic strategies may involve replacing defective genes, silencing oncogenes, activating tumor suppressor pathways, or modifying immune responses.

Nanoparticles can protect nucleic acids from enzymatic degradation and facilitate cellular delivery.

6.1 siRNA Delivery

Small interfering RNA (siRNA) can silence specific genes involved in cancer progression. However, naked siRNA is unstable and poorly enters cells.

Nanoparticles can:

- Protect siRNA
- Improve cellular uptake
- Facilitate endosomes escape
- Promote intracellular gene silencing

6.2 mRNA Delivery

mRNA-based approaches can transiently express therapeutic proteins or stimulate immune responses. Lipid nanoparticles have become particularly important for nucleic acid delivery and represent a major technological platform in modern medicine [17].

6.3 microRNA Delivery

MicroRNAs regulate gene expression and may function as oncogenes or tumor suppressors. Nanoparticles can potentially deliver therapeutic microRNAs or inhibitors of oncogenic microRNAs.

6.4 CRISPR/Cas-Based Delivery

Nanoparticles are being investigated for the delivery of CRISPR-associated components for genome editing. Potential applications include modification of oncogenic pathways and enhancement of immune-cell function.

However, challenges include:

- Off-target effects
- Efficient intracellular delivery
- Immunogenicity
- Long-term safety





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Precise genome editing

Table 4 Nanoparticle-Based Nucleic Acid Delivery

Therapeutic	Mechanism	Potential Cancer Application
siRNA	Gene silencing	Suppression of oncogenes
miRNA	Gene regulation	Restoration of tumor suppressor pathways
mRNA	Protein expression	Cancer vaccines and immunotherapy
DNA	Gene expression	Gene replacement
CRISPR components	Genome editing	Modification of cancer-related genes

7. Nanoparticles in Cancer Immunotherapy

Cancer immunotherapy has transformed oncology by activating or restoring immune responses against malignant cells.

Nanoparticles can improve immunotherapy by delivering:

- Antigens
- Adjuvants
- Cytokines
- Immune checkpoint modulators
- mRNA
- siRNA
- Immunostimulatory molecules

7.1 Nanoparticle-Based Cancer Vaccines

Nanoparticles can function as carriers for tumor antigens and adjuvants. They may improve antigen stability and facilitate uptake by antigen-presenting cells.

7.2 Immune Checkpoint Modulation

Nanoparticles can deliver agents targeting immune checkpoint pathways, potentially improving localized immune activation.





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7.3 Dendritic Cell Activation

Nanoparticles can promote antigen delivery to dendritic cells and enhance antigen presentation.

7.4 Combination Immunotherapy

Nanoparticles may combine immunotherapy with:

- Chemotherapy
- Photothermal therapy
- Radiotherapy
- Photodynamic therapy

Such combinations may increase tumor antigen release and enhance immune recognition [18].

8. Photothermal Therapy

Photothermal therapy (PTT) uses materials capable of converting light energy into heat. Nanoparticles can accumulate in tumors and convert externally applied light into localized thermal energy.

Gold nanoparticles are widely investigated because of their favorable optical properties.

The mechanism includes:

Light absorption → Photothermal conversion → Local temperature increase → Protein denaturation → Membrane damage → Cancer-cell death

PTT can be combined with chemotherapy or immunotherapy.

Advantages

- Minimally invasive
- Spatially controlled
- Potential for combination therapy
- Reduced systemic drug exposure

Limitations

- Limited light penetration
- Dependence on tumor accessibility
- Potential damage to surrounding tissues
- Need for specialized equipment

Near-infrared wavelengths are particularly attractive because of improved tissue penetration compared with visible light [9, 10].

9. Photodynamic Therapy

Photodynamic therapy (PDT) involves three major components:

1. Photosensitizer





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2. Light
3. Molecular oxygen

Upon activation by appropriate light, the photosensitizer generates reactive oxygen species (ROS), which cause oxidative damage to cancer cells.

Nanoparticles can improve PDT by:

- Improving photosensitizer solubility
- Increasing tumor accumulation
- Protecting photosensitizers
- Enhancing cellular uptake
- Co-delivering photosensitizers and drugs

PDT can also induce vascular damage and stimulate antitumor immune responses.

10. Nanoparticles in Radiotherapy

Radiotherapy uses ionizing radiation to damage cancer-cell DNA. Nanoparticles can potentially enhance radiation effects.

High-atomic-number materials such as gold nanoparticles have been investigated as radio sensitizers.

Potential mechanisms include:

- Increased local energy deposition
- Generation of reactive oxygen species
- Enhanced DNA damage

Nanoparticles may therefore increase tumor sensitivity to radiation while potentially allowing dose optimization.

However, careful evaluation is required to determine the biodistribution and safety of radio sensitizing nanoparticles [9].

11. Magnetic Nanoparticles and Hyperthermia

Magnetic nanoparticles, particularly iron oxide nanoparticles, have been investigated for magnetic hyperthermia.

The general mechanism involves:

Magnetic nanoparticle accumulation → Alternating magnetic field → Heat generation → Increased tumor temperature → Cancer-cell damage

Hyperthermia can cause:

- Protein denaturation
- Membrane disruption
- Increased oxidative stress





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- Enhanced sensitivity to chemotherapy and radiotherapy
- Magnetic nanoparticles may also be used for MRI and potentially for combined diagnostic and therapeutic applications.

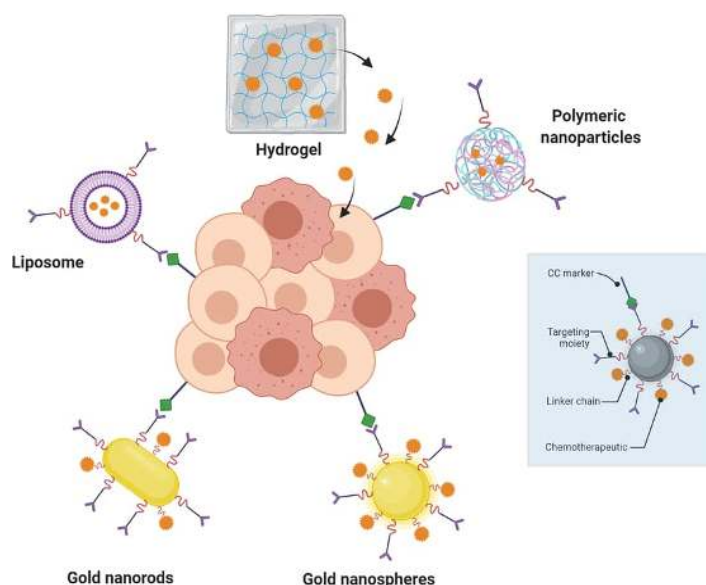


Fig.2 Mechanism of nanoparticle-mediated cancer drug delivery

Table 5 Nanoparticle-Based Physical Therapies

Therapy	Nanoparticle	Mechanism
Photothermal therapy	Gold nanoparticles	Light-to-heat conversion
Photodynamic therapy	Photosensitizer-loaded nanoparticles	ROS generation
Magnetic hyperthermia	Iron oxide nanoparticles	Magnetic-to-heat conversion
Radiotherapy enhancement	Gold and other high-Z nanoparticles	Increased radiation effects
Ultrasound-responsive therapy	Specialized nanocarriers	Acoustic activation





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12. Nanoparticles in Cancer Diagnosis and Imaging

Early and accurate cancer diagnosis is critical for improving treatment outcomes. Nanoparticles have been investigated as imaging probes and diagnostic platforms.

12.1 Magnetic Resonance Imaging

Super paramagnetic iron oxide nanoparticles can influence MRI contrast and have been investigated for tumor imaging.

12.2 Optical Imaging

Quantum dots and fluorescent nanoparticles can provide strong and tunable optical signals.

12.3 Computed Tomography

High-density nanoparticles, particularly gold nanoparticles, have been investigated as contrast agents.

12.4 Molecular Imaging

Nanoparticles can be functionalized with ligands that recognize specific cancer biomarkers. Potential targets include:

- HER2
- EGFR
- VEGF
- Integrin's
- PSMA

12.5 Bio sensing

Nanoparticle-based biosensors can detect:

- Cancer proteins
- Circulating tumor DNA
- microRNAs
- Exosomes
- Tumor-associated biomarkers

Table 6 Nanoparticles in Cancer Imaging

Nanoparticle	Imaging modality	Application
Iron oxide	MRI	Tumor imaging





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Gold	CT and optical imaging	Tumor detection
Quantum dots	Fluorescence	Cellular imaging
Silica nanoparticles	Optical imaging	Molecular imaging
Up conversion nanoparticles	NIR imaging	Deep-tissue imaging

13. Nanoparticles in Cancer Theranostics

Theranostics combines diagnosis and therapy in a single integrated platform.

A theranostic nanoparticle may contain:

- Therapeutic drug
- Imaging agent
- Targeting ligand
- Stimuli-responsive component

The concept allows simultaneous or sequential:

Diagnosis → targeting → Therapy → imaging → Treatment monitoring

Theranostic nanoparticles have been investigated in:

- Molecular imaging
- Drug delivery
- Photothermal therapy
- Photodynamic therapy
- Image-guided surgery
- Monitoring therapeutic response

Theranostics may contribute to personalized medicine by helping clinicians identify suitable patients and monitor treatment response.

However, the development of complex multifunctional systems presents additional challenges related to manufacturing, characterization, safety, and regulatory approval [6, 19].





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14. Nanoparticles for Overcoming Multidrug Resistance

Multidrug resistance (MDR) is a major cause of cancer treatment failure. Cancer cells may develop resistance through:

- Increased drug efflux
- Altered drug targets
- Enhanced DNA repair
- Reduced apoptosis
- Changes in cellular metabolism

Nanoparticles may help address MDR through several mechanisms.

14.1 Co-Delivery

Nanoparticles can co-deliver chemotherapeutic drugs with MDR inhibitors.

14.2 Gene Silencing

siRNA can potentially suppress genes responsible for drug resistance.

14.3 Improved Cellular Uptake

Nanoparticles may enter cells through endocytosis and potentially bypass certain drug-efflux mechanisms.

14.4 Controlled Release

Intracellular release may increase drug concentrations within cancer cells.

Combination strategies involving chemotherapy and gene therapy are particularly promising for overcoming resistance.

15. Nanoparticles in Combination Cancer Therapy

Cancer is a complex disease, and combination therapy is often necessary.

Nanoparticles can potentially co-deliver two or more therapeutic agents.

Potential combinations include:

- Chemotherapy + gene therapy
- Chemotherapy + immunotherapy
- Chemotherapy + PTT
- Chemotherapy + PDT
- Radiotherapy + immunotherapy
- PTT + PDT





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16. Nanoparticles and the Tumor Microenvironment

The tumor microenvironment (TME) consists of:

- Cancer cells
- Fibroblasts
- Immune cells
- Blood vessels
- Extracellular matrix
- Cytokines
- Growth factors

The TME can promote tumor progression and therapeutic resistance.

Nanoparticles are being developed to modify or exploit the TME.

Potential strategies include:

- Targeting tumor-associated macrophages
- Modifying tumor-associated fibroblasts
- Degrading extracellular matrix
- Modulating tumor hypoxia
- Altering tumor acidity
- Promoting immune activation

Nanoparticles may also deliver drugs that modify the TME and improve penetration of therapeutic agents.

17. Nanoparticles in Precision and Personalized Cancer Medicine

Precision oncology is an approach based on the sequence and biology of the individual tumour to determine the treatment. Nanoparticles could be used as a tool in precision medicine to help with:

- Biomarker-specific targeting
- Patient-specific drug delivery
- Molecular imaging
- Theranostics

At the genetic and molecular level. Targeting at the level of the genome and the transcriptome. In the case of the application of ligand-targeted nanoparticles, for instance, patients might be chosen for the treatment according to the expression of a receptor.

Nanoparticles and molecular diagnostics can thus be integrated to improve the treatment of cancer in a more personalized manner.





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18. Safety, Toxicity, and Biocompatibility

Nanoparticles have possible therapeutic applications, but may have unexpected biological effects. Considerations for safety are:

- Cytotoxicity
- Immunotoxicity
- Oxidative stress
- Inflammation
- Genotoxicity
- Complement activation
- Organ accumulation
- Long-term persistence

The toxicity of nanoparticles is related to:

- Size
- Shape
- Surface charge
- Composition
- Dose
- Route of administration
- Exposure duration

The advantages of the biodegradable nanoparticles in degradation and safety have been suggested but degradation products need to be evaluated as well.

19. Clinical Translation and Regulatory Challenges

Although numerous nanoparticle systems have been investigated in preclinical research, relatively few have achieved clinical translation.

Major challenges include:

Manufacturing

Production of complex nanoparticles may be challenging at larger scales, and it may be difficult to replicate the production at a large scale.

Batch-to-Batch Variability

The particle size, drug loading and biological activity are all affected by small formulation changes.

Stability

Nanoparticles may undergo:

- Aggregation





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- Drug leakage
- Oxidation
- Hydrolysis

Regulatory Complexity

Comprehensive assessment of:

- Quality
- Safety
- Efficacy
- Pharmacokinetics
- Toxicity
- Manufacturing consistency

Clinical Heterogeneity

This is because the amount of nanoparticles in the tumor and the response to treatment may vary between patients and between different tumors.

20. Clinically Relevant Nanoparticle-Based Cancer Medicines

There are a few products already in clinical use, based on nanoparticles. They are clinically effective and thus demonstrate that the nanotechnology can change the property and activity of already used anticancer drugs, which is why they are promising. But clinical application of next generation of multifunctional nanoparticles is still difficult [1, 3, 15, 16].

21. Future Perspectives

The future of cancer nanomedicine is expected to focus on the development of smart, personalized, multifunctional, and targeted nanocarriers. Smart nanoparticles can respond to tumour-specific stimuli such as pH, enzymes, temperature, light, or magnetic fields, enabling controlled drug release at the tumour site. Biomimetic nanoparticles incorporating cell membranes, proteins, or other biological components may improve circulation, biocompatibility, immune evasion, and tumour targeting. Artificial intelligence and machine learning can assist in optimizing nanoparticle size, surface chemistry, drug loading, biodistribution, and toxicity, thereby accelerating formulation development. Personalized nanomedicine may allow nanoparticle selection according to individual tumour characteristics and patient-specific molecular profiles. Emerging nanorobotic systems may eventually enable highly localized delivery of therapeutic agents, although they remain largely experimental. Multifunctional theranostic nanoparticles may integrate imaging, targeting, drug delivery, controlled release, and therapeutic monitoring within a single platform. In addition, advances in lipid and polymeric nanoparticles are expected to support RNA nanomedicine, including the delivery of mRNA, siRNA, miRNA, and gene-editing therapies. Overall, these emerging technologies have the potential to make cancer treatment more precise, effective, and safer,





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although challenges related to toxicity, manufacturing, stability, cost, and regulatory approval must still be overcome.

22. Conclusion

Nanoparticle-based platforms have proven to be an important platform for the research and therapy of modern cancer. They are able to deliver therapeutic molecules and alter the distribution of drugs, thus providing possibilities for enhancing the therapeutic index of anticancer drugs. Various nanocarriers such as liposomes, polymeric nanoparticles, micelles, dendrimers, metallic nanoparticles, magnetic nanoparticles, solid lipid nanoparticles, Mesoporous silica nanoparticles and biological nanocarriers are reported to be useful for cancer application. Nanoparticles are not just applied to typical chemotherapy. They encompass targeted drug delivery, gene and RNA therapy, immunotherapy, Photothermal therapy, photodynamic therapy, radiotherapy enhancement, magnetic hyperthermia, cancer diagnosis, molecular imaging, bio sensing and theranostics. These possibilities entail the integration of diagnosis and therapy by combining several functions in a single nanoparticle. However, there are a number of issues that need to be addressed. Tumor heterogeneity, uptake variability of nanoparticles, biological barriers, protein corona, clearance by the immune system, toxicity, manufacturing complexity and scale-up, as well as regulatory issues, continue to hinder clinical translation. Although conceptually relevant the EPR effect is quite variable among humans and should not be taken as a standard mechanism for the successful targeting of tumor cells. The future of cancer nanomedicine will be moving towards the precision, personalized, multifunctional and biologically informed nanocarriers. The integration of nanotechnology and artificial intelligence, molecular diagnostics, genomics, immunotherapy, RNA therapeutics, and personalized medicine might provide new opportunities for cancer management. Finally, a balance of technological sophistication, clinical effectiveness, safety, reproducibility, manufacturability and cost-effectiveness will be necessary for a successful translation.

References

1. Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: progress, challenges and opportunities. *Nat Rev Cancer*. 2017;17(1):20-37.
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209-249.





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3. Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. *Nat Rev Drug Discov.* 2021;20(2):101-124.
4. Deore AD, Ahire MS, Mahajan KS. Herbal Medicine Meets Nanotechnology: A Transformative Approach. *Asian Journal of Pharmaceutical Research.* 2025;15(3):302-8.
5. Blanco E, Shen H, Ferrari M. Principles of nanoparticle design for overcoming biological barriers to drug delivery. *Nat Biotechnol.* 2015;33(9):941-951.
6. Mura S, Couvreur P. Nanotheranostics for personalized medicine. *Adv Drug Deliv Rev.* 2012;64:139-161.
7. Jadhav SP, Ahire SM, Pawar PS, Mahajan SK, Sonawane DD. Exploring Natural Oils: Role in Antimicrobial Activity and Preservation. *Asian Journal of Research in Pharmaceutical Sciences.* 2026 Jan 5;16(1):59-64.
8. Makadia HK, Siegel SJ. Poly lactic-co-glycolic acid (PLGA) as biodegradable controlled drug delivery carrier. *Polymers (Basel).* 2011;3(3):1377-1397.
9. Dreaden EC, Alkilany AM, Huang X, Murphy CJ, El-Sayed MA. The golden age: gold nanoparticles for biomedicine. *Chem Soc Rev.* 2012;41(7):2740-2779.
10. Pissuwan D, Valenzuela SM, Cortie MB. Therapeutic possibilities of plasmonically heated gold nanoparticles. *Trends Biotechnol.* 2006;24(2):62-67.
11. Danhier F. To exploit the tumor microenvironment: passive and active tumor targeting of nanocarriers for anti-cancer drug delivery. *J Control Release.* 2016;244(Pt A):108-121.
12. Ahire SM, Pawar PS, Shewale VV, Jadhav SP, Mahajan SK. Magnetic Particles for Targeted Drug Delivery and Biomedical Applications.
13. Sindhvani S, Syed AM, Ngai J, Kingston BR, Maiorino L, Rothschild J, et al. The entry of nanoparticles into solid tumours. *Nat Mater.* 2020;19(5):566-575.
14. Torchilin VP. Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. *Nat Rev Drug Discov.* 2014;13(11):813-827.





WISELEAF SCIENTIFIC VENTURES

15. Barenholz Y. Doxil®—the first FDA-approved nano-drug: lessons learned. *J Control Release*. 2012;160(2):117-134.
16. Desai N, Trieu V, Yao Z, Louie L, Ci S, Yang A, et al. Increased antitumor activity, intratumor paclitaxel concentrations, and endothelial cell transport of Cremophor-free, albumin-bound paclitaxel, ABI-007, compared with cremophor-based paclitaxel. *Clin Cancer Res*. 2006;12(4):1317-1324.
17. Bahiram U, Ahire M, Ahire S, Mahajan S. Biomedical Applications of Nanoparticles Derived from Curcumin & Resveratrol. *International Journal of Pharmacognosy*. 2024;6(2):53-9.
18. Riley RS, June CH, Langer R, Mitchell MJ. Delivery technologies for cancer immunotherapy. *Nat Rev Drug Discov*. 2019;18(3):175-196.
19. Kelkar SS, Reineke TM. Theranostics: combining imaging and therapy. *Bioconjug Chem*. 2011;22(10):1879-1903.
20. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an emerging platform for cancer therapy. *Nat Nanotechnol*. 2007;2(12):751-760.
21. Pawar PS, Ahire SM, Jadhav SP, Patil CD, Mahajan SK. Ginkgo biloba and Gastrodia elata: Bridging Traditional Wisdom and Modern Therapy in Parkinson's Disease. From ancient roots to nano routes: targeted delivery of Ginkgo and Gastrodia for Parkinson's disease (PD) treatment. 2025;4:56.
22. Shi J, Votruba AR, Farokhzad OC, Langer R. Nanotechnology in drug delivery and tissue engineering: from discovery to applications. *Nano Lett*. 2010;10(9):3223-3230.
23. Caminade AM, Turrin CO. Dendrimers for drug delivery. *J Mater Chem B*. 2014;2:4055-4066.
24. Müller RH, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery: a review of the state of the art. *Eur J Pharm Biopharm*. 2000;50(1):161-177.
25. Medintz IL, Uyeda HT, Goldman ER, Mattoussi H. Quantum dot bioconjugates for imaging, labelling and sensing. *Nat Mater*. 2005;4(6):435-446.





WISELEAF SCIENTIFIC VENTURES

26. Peer D, Park EJ, Morishita Y, Carman CV, Shimaoka M. Systemic leukocyte-directed siRNA delivery revealing cyclin D1 as an anti-inflammatory target. *Science*. 2008;319(5863):627-630.
27. Ahire SM, Pawar PS, Sonawane VN, Jadhav SP. Personalized Medicine and Pharmacogenomics: Impact of Genetic variation on Drug Response and Individualized Therapy-A Review. *Asian Journal of Pharmacy and Technology*. 2026 Jan 27;16(1):91-8.
28. Blanco E, Hsiao A, Mann AP, Landry MG, Meric-Bernstam F, Ferrari M. Nanomedicine in cancer therapy: innovative trends and future directions. *Nat Rev Cancer*. 2024.
29. Lammers T, Kiessling F, Hennink WE, Storm G. Drug targeting to tumors: principles, pitfalls and pre-clinical progress. *J Control Release*. 2012;161(2):175-187.
30. Wicki A, Witzigmann D, Balasubramanian V, Huwyler J. Nanomedicine in cancer therapy: challenges, opportunities, and clinical applications. *J Control Release*. 2015;200:138-157.

