

NANOPARTICLES IN DRUG DELIVERY SYSTEMS: A COMPREHENSIVE REVIEW

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ABSTRACT

Nanoparticles have emerged as a revolutionary approach in modern drug delivery systems, transforming the way therapeutic agents are administered, distributed, and released in the body. Traditional drug delivery methods, such as oral and intravenous routes, often face multiple limitations including poor solubility of drugs, rapid degradation, systemic toxicity, and lack of site-specific targeting. These drawbacks lead to reduced therapeutic efficiency and increased side effects, making the search for novel delivery systems essential. Nanotechnology provides a powerful solution to these challenges, and nanoparticles, due to their nanoscale size (1–100 nm) and tunable physicochemical properties, have become one of the most widely studied platforms. Their high surface-area-to-volume ratio allows for enhanced drug loading, while their surface can be engineered with polymers, ligands, and antibodies to achieve targeted

delivery. Furthermore, nanoparticles are capable of controlled and sustained release, ensuring that the drug remains within the therapeutic window for an extended duration, thereby improving patient compliance. Different classes of nanoparticles, such as polymeric nanoparticles, lipid-based carriers, metallic nanoparticles, dendrimers, and carbon-based nanostructures, have shown significant promise in various therapeutic areas. For example, liposomes and lipid nanoparticles have been used in mRNA vaccines and antifungal therapy, polymeric nanoparticles in cancer treatment, and metallic nanoparticles in imaging and photothermal therapy. The ability of nanoparticles to cross biological barriers such as the blood–brain barrier has also opened new frontiers for treating neurological diseases that were

previously considered difficult to manage. However, despite their advantages, several challenges remain, including issues related to toxicity, large-scale production, regulatory approval, and long-term stability. Ongoing research is focusing on developing smart, stimuli-responsive, and hybrid nanoparticles to overcome these barriers. Overall, nanoparticles represent one of the most promising tools in pharmaceutical research and development, holding the potential to redefine the future of medicine by offering personalized, efficient, and safer drug delivery strategies.

KEYWORDS: Drug Delivery Systems, Targeted Therapy, Controlled Release, Liposomes, Polymeric Nanoparticles, Solid Lipid Nanoparticles (SLNs), Metallic Nanoparticles, Blood-Brain Barrier, Nanomedicine, Cancer Therapy.

INTRODUCTION

Drug delivery is a cornerstone of modern pharmacology and therapeutics, as the manner in which a drug is administered has a direct impact on its effectiveness, safety, and patient compliance. Conventional drug delivery systems, such as oral tablets, capsules, or injectable formulations, have served healthcare for decades but often fail to meet the complex demands of modern medicine. Problems such as poor aqueous solubility of many new drug molecules, limited bioavailability, short circulation half-life, systemic toxicity, and inability to selectively target diseased tissues reduce the therapeutic benefits of conventional approaches. For instance, anticancer drugs administered systemically not only damage tumor cells but also harm healthy tissues, leading to severe side effects like nausea, hair loss, and organ damage. Such drawbacks highlight the urgent need for advanced, efficient, and more patient-friendly drug delivery technologies. Nanotechnology, defined as the science and engineering of materials at the nanoscale (1–100 nm), has provided a promising avenue for overcoming these limitations. Nanoparticles, because of their extremely small size and unique surface properties, exhibit behaviors that are markedly different from bulk materials. At this scale, the increased surface area-to-volume ratio enhances reactivity, stability, and the ability to interact with biological systems at the cellular and molecular level. These characteristics make nanoparticles highly suitable for drug delivery applications, as they can encapsulate a wide range of therapeutic agents—both hydrophilic and hydrophobic—and protect them from premature degradation.

One of the most significant advantages of nanoparticles in drug delivery is their ability to achieve site-specific targeting. Nanoparticles can be engineered for passive targeting through

the Enhanced Permeability and Retention (EPR) effect, which allows them to accumulate preferentially in tumor tissues due to leaky vasculature. They can also be modified for active targeting by attaching ligands, antibodies, or peptides to their surface, enabling them to recognize and bind to receptors expressed on diseased cells. Beyond targeting, nanoparticles allow controlled and sustained drug release, ensuring prolonged therapeutic action while reducing dosing frequency.

The importance of nanoparticles is evident in their diverse applications across multiple medical fields. In oncology, nanoparticle-based drug delivery has revolutionized cancer therapy by minimizing side effects while improving drug concentration at the tumor site. In neurology, nanoparticles have been designed to cross the blood–brain barrier, a formidable obstacle in the treatment of diseases such as Alzheimer’s and Parkinson’s. In infectious diseases, lipid-based nanoparticles have improved the delivery of antifungal, antibacterial, and antiviral agents, and most notably, lipid nanoparticles were at the heart of the COVID-19 mRNA vaccine development, marking a milestone in pharmaceutical innovation.

Despite these advances, the clinical translation of nanoparticle-based systems faces challenges. Issues related to biocompatibility, toxicity, large-scale manufacturing, and regulatory approval need to be addressed before nanoparticles can fully replace or complement conventional systems. Nevertheless, with ongoing advancements in material science, biotechnology, and pharmaceutical engineering, nanoparticles are poised to redefine the future of drug delivery.

Fundamentals of Nanoparticles

Definition

- Nanoparticles are drug carriers sized **1–100 nm** with unique properties for targeted therapy.

Key Characteristics of Nanoparticles

1. Size (1–100 nm)

- Cross biological barriers (e.g., BBB).
- Accumulate in tumors via **EPR effect**.

2. High Surface-to-Volume Ratio

- Large drug-loading capacity.

- Strong interaction with cells/tissues.
- 3. **Drug Loading & Encapsulation**
 - **Encapsulation:** Protects drug in core.
 - **Adsorption:** Drug sticks to surface.
 - **Conjugation:** Chemically linked drugs.
- 4. **Surface Modifiability (Functionalization)**
 - **PEGylation:** Longer circulation.
 - **Ligands/antibodies/peptides:** Active targeting.
 - **Polymers/biomolecules:** Improve solubility & safety.
- 5. **Biocompatibility & Biodegradability**
 - Safe materials (PLGA, chitosan, lipids).
 - Degrade into harmless byproducts.
- 6. **Stability in Biological Systems**
 - Resist premature release & degradation.

Mechanisms of Drug Delivery

1. **Passive Targeting (EPR effect)**
 - Accumulates in tumors via leaky vessels & poor drainage.
 - Simple but limited to certain tumors.
2. **Active Targeting (Receptor-based)**
 - Surface functionalization with ligands, antibodies, peptides.
 - Bind to receptors → endocytosis → drug release.
 - High specificity, reduced toxicity.
3. **Controlled / Stimuli-Responsive Release**
 - Release triggered by **pH, temperature, enzymes, light, magnetic field.**
 - Ensures localized & time-controlled drug delivery.

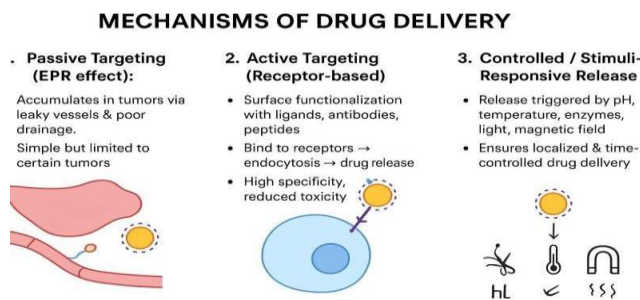


Fig: Mechanisms of Drug Delivery.

Types of Nanoparticles in Drug Delivery

1 Polymeric Nanoparticles

- **Definition:** Nanoparticles made from biodegradable and biocompatible polymers.
- **Materials:** PLGA (poly lactic-co-glycolic acid), PEG (polyethylene glycol), chitosan, etc.
- **Properties**
 - High stability in biological fluids.
 - Allow controlled and sustained drug release.
 - Can encapsulate both hydrophilic and hydrophobic drugs.
- **ADVANTAGES**
 - Biodegradable, safe for patients.
 - Can be surface-modified for targeted delivery.
- **Example:** Doxorubicin-loaded PLGA nanoparticles used in **cancer** therapy.

2 Lipid-Based Nanoparticles

• Types

1. Liposomes

- Phospholipid bilayer vesicles.
- Encapsulate hydrophilic drugs (inside aqueous core) and lipophilic drugs (inside lipid bilayer).
- Reduce toxicity of drugs.
- Example: *Liposomal amphotericin B* (antifungal drug).

2. Solid Lipid Nanoparticles (SLNs)

- Solid lipid core stabilized by surfactants.
- Provide controlled release and enhanced stability.
- Example: SLN formulations of anticancer drugs.

- **ADVANTAGES**

- Biocompatible.
- Improve solubility of poorly soluble drugs.
- Lower systemic toxicity.

3 Metallic Nanoparticles

- **Composition:** Gold, silver, platinum, iron oxide nanoparticles.

- **Applications**

- Drug delivery.
- Imaging and diagnostics (MRI, CT contrast).
- Photothermal therapy (heat-induced cancer therapy).

- **ADVANTAGES**

- High surface area for drug binding.
- Easily functionalized with ligands or antibodies.
- **Example:** Gold nanoparticles in targeted cancer therapy & diagnostics.

4 Dendrimers

- **Structure:** Highly branched, tree-like polymeric nanostructures with a central core.

- **Properties**

- Multiple functional end groups → allow high drug loading capacity.
- Monodispersed (uniform in size).

- **ADVANTAGES**

- Can carry both drugs and genetic material (DNA, siRNA).
- Controlled release via surface modification.
- **Example:** PAMAM (polyamidoamine) dendrimers used for anticancer drug delivery.

5 Carbon-Based Nanoparticles

- **Types**

- **Carbon Nanotubes (CNTs):** Cylindrical nanostructures with excellent drug-loading capacity.
- **Graphene Oxide (GO):** Sheet-like structure for loading drugs and genes.

- **Applications**

- Cancer therapy.
- Gene delivery (DNA, RNA).
- Biosensing and imaging.

- **ADVANTAGES**
 - High surface area.
 - Strong drug binding via π - π interactions.
- **Example:** Carbon nanotubes used for delivery of anticancer drugs & genes.

Advantages of Nanoparticle Drug Delivery

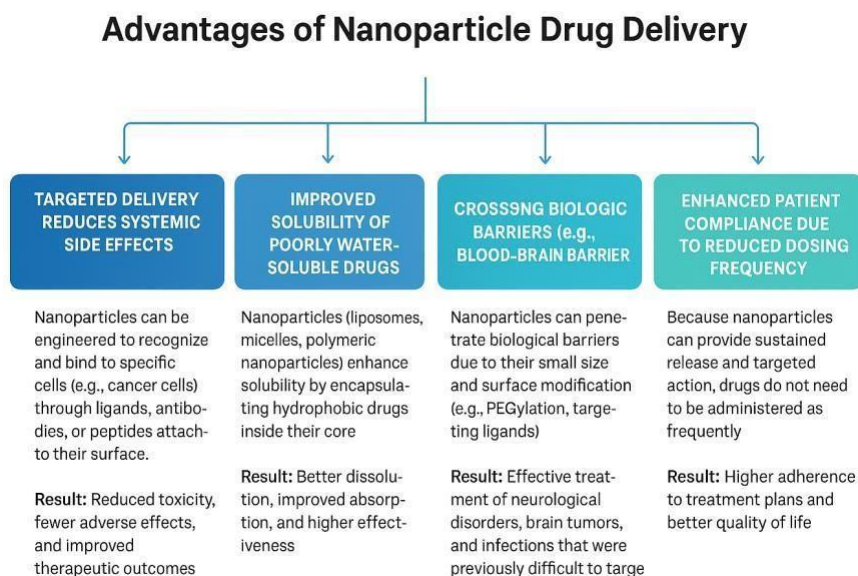


Fig: Advantages of nanoparticle in drug delivery.

1. Targeted Delivery Reduces Systemic Side Effects

- Nanoparticles can be engineered to recognize and bind to specific cells (e.g., cancer cells) through ligands, antibodies, or peptides attached to their surface.
- This targeted approach ensures that the drug accumulates primarily at the diseased site, minimizing exposure to healthy tissues.
- **Result:** Reduced toxicity, fewer adverse effects, and improved therapeutic outcomes.

2. Improved Solubility of Poorly Water-Soluble Drugs

- Many modern drugs are poorly soluble in water, leading to low absorption and poor bioavailability.
- Nanoparticles (liposomes, micelles, polymeric nanoparticles) enhance solubility by encapsulating hydrophobic drugs inside their core.
- **Result:** Better dissolution, improved absorption, and higher effectiveness.

3. Controlled Release Ensures Steady Drug Levels

- Nanoparticles can be designed to release drugs gradually over time (sustained release) or in response to specific stimuli (pH, temperature, enzymes).

- This helps in maintaining consistent drug levels in the blood, avoiding peaks and troughs.
 - Result: Increased efficacy, reduced frequency of dosing, and better patient outcomes.
4. **Crossing Biological Barriers (e.g., Blood-Brain Barrier)**
- One of the biggest challenges in drug delivery is transporting drugs to protected organs like the brain.
 - Nanoparticles can penetrate biological barriers due to their small size and surface modifications (e.g., PEGylation, targeting ligands).
 - Result: Effective treatment of neurological disorders, brain tumors, and infections that were previously difficult to target.
5. **Enhanced Patient Compliance Due to Reduced Dosing Frequency**
- Because nanoparticles can provide sustained release and targeted action, drugs do not need to be administered as frequently.
 - This reduces the burden on patients (especially those with chronic illnesses requiring lifelong medication).
 - Result: Higher adherence to treatment plans and better quality of life.

Challenges and Limitations of Nanoparticle Drug Delivery

CHALLENGES AND LIMITATIONS



Toxicity and biocompatibility concerns due to long-term accumulation



High production costs and complex manufacturing processes



Regulatory challenges for approval and standardization



Stability issues during storage and transport

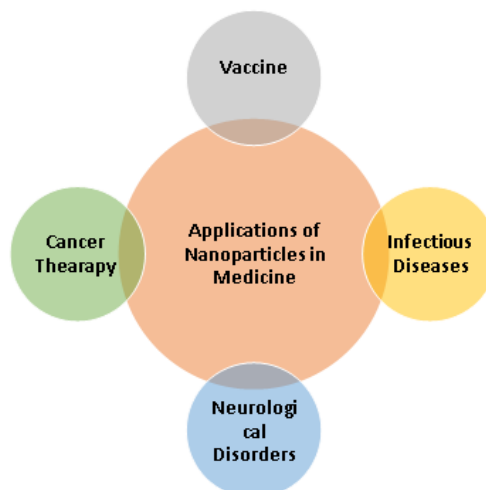
Fig: Challenges and Limitations of Nanoparticle Drug Delivery.

1. Toxicity and Biocompatibility Concerns

- Nanoparticles may accumulate in tissues and organs over time, causing toxicity.

- Unknown long-term effects on the immune system and metabolism.
 - Ensuring complete safety and compatibility with the human body is still a major challenge.
- 2. High Production Costs and Complex Manufacturing**
- Fabrication of nanoparticles requires advanced technology and precise conditions.
 - Large-scale production is difficult and expensive compared to conventional drugs.
 - Quality control and reproducibility remain concerns.
- 3. Regulatory and Standardization Challenges**
- Lack of universal guidelines for nanoparticle-based drugs.
 - Difficulties in meeting safety, efficacy, and ethical standards set by regulatory bodies.
 - Long and uncertain approval process delays clinical use.
- 4. Stability Issues During Storage and Transport**
- Nanoparticles may aggregate, degrade, or lose activity over time.
 - Sensitive to temperature, pH, and environmental conditions.
 - Maintaining stability for long-term storage and global distribution is challenging.
- 5. Rapid Clearance by the Reticuloendothelial System (RES)**
- The body's immune defense system (mainly liver and spleen macrophages) quickly removes foreign particles.
 - Reduces circulation time of nanoparticles in the bloodstream.
 - Leads to lower drug availability at the target site unless surface modifications (e.g., PEGylation) are used.

Applications of Nanoparticles in Medicine



1 Cancer Therapy

- **Precise Targeting:** Nanoparticles can carry chemotherapeutic drugs directly to tumor tissues using passive (EPR effect) and active targeting (ligands/antibodies).
- **Reduced Side Effects:** Healthy tissues are less affected, minimizing toxicity.
- **Example:** *Abraxane*® (*albumin-bound paclitaxel*) – FDA approved for breast cancer treatment.

2 Neurological Disorders

- **Crossing the Blood-Brain Barrier (BBB):** Nanoparticles can penetrate biological barriers due to their nanoscale size and surface modifications.
- **Applications:** Treatment of Alzheimer's, Parkinson's, brain tumors, and other CNS disorders.
- **Advantage:** Improves drug delivery to sites that conventional drugs cannot easily reach.

3 Infectious Diseases

- **Broad Use:** Nanoparticles are effective carriers for antifungal, antibacterial, and antiviral agents.
- **Improved Efficacy:** They enhance solubility, stability, and targeted delivery of antimicrobial drugs.
- **Example:** *Liposomal amphotericin B* – used in treatment of fungal infections with reduced toxicity compared to conventional forms.

4 Vaccine Delivery

- **Modern Vaccines:** Lipid nanoparticles (LNPs) are widely used in mRNA vaccine technology.
- **Mechanism:** LNPs protect fragile mRNA, facilitate cellular uptake, and trigger immune response.
- **Examples:** *Pfizer-BioNTech and Moderna COVID-19 vaccines*.
- **Advantage:** Safe, effective, and rapid development of vaccines against emerging diseases.

Future Prospects and Emerging Trends

1. Stimuli-Responsive Nanoparticles

- **Definition:** Nanoparticles engineered to release drugs in response to internal or external stimuli.
- **Types of Stimuli**

- **pH-sensitive:** Release drugs in acidic tumor environments.
- **Temperature-sensitive:** Trigger release during hyperthermia or localized heating.
- **Magnetic-sensitive:** Magnetic fields guide nanoparticles to specific tissues and trigger release.
- **Ultrasound-sensitive:** Use ultrasound waves for controlled release at the target site.
- **ADVANTAGES**
 - Ensures site-specific delivery.
 - Reduces side effects by avoiding premature release.
 - Improves therapeutic efficacy by timed release.
- **Example:** Thermo-sensitive liposomes for localized cancer chemotherapy.

2. Hybrid Nanoparticles

- **Definition:** Nanoparticles combining different materials (e.g., polymer + lipid, metal + polymer) to create multifunctional systems.
- **Properties**
 - **Combine advantages of multiple materials (e.g., stability of polymers + biocompatibility of lipids).**
 - Allow for drug co-delivery (two or more drugs in one system).
 - Enable theranostics (therapy + diagnostics).
- **Applications**
 - Cancer therapy (drug + imaging agent).
 - Antimicrobial therapy (drug + silver nanoparticles).
- **ADVANTAGES**
 - Multi-functionality in a single carrier.
 - Better targeting and efficiency.
- **Example:** Lipid-polymer hybrid nanoparticles for cancer drug delivery and imaging.

3. Personalized Nanomedicine

- **Definition:** Designing nanoparticle drug delivery systems tailored to an individual's genetic, molecular, or disease profile.
- **Approach**
 - Use patient-specific biomarkers to select nanoparticle composition, drug type, and release mechanism.
 - Incorporate genomic and proteomic data for personalized therapy.

- **ADVANTAGES**

- Improves treatment effectiveness.
- Reduces risk of adverse reactions.
- Supports precision medicine strategies.

- **Applications**

- Personalized cancer therapy.
- Genetic disorder treatments using tailored gene delivery carriers.

- **Example:** Customized polymeric nanoparticles carrying siRNA tailored for a patient's tumor mutations.

4. AI and Machine Learning in Nanoparticle Design

- **Role of AI/ML**

- Predict nanoparticle behavior (drug release rates, biodistribution, toxicity).
- Optimize formulation parameters (size, surface charge, coating).
- Identify the best targeting ligands for specific diseases.

- **Applications**

- Designing smart nanoparticles with high precision.
- Accelerating drug development by simulating delivery outcomes.
- Reducing cost and time in nanoparticle optimization.

- **ADVANTAGES**

- Data-driven design ensures more effective carriers.
- Facilitates discovery of new nanoparticle structures.

- **Example:** AI-assisted modeling to predict nanoparticle clearance rates and targeting efficiency in cancer therapy.

CONCLUSION

Nanoparticles have emerged as one of the most powerful and versatile platforms in modern drug delivery systems, addressing the limitations of conventional therapeutic strategies. Their unique nanoscale dimensions, high surface-to-volume ratio, and tunable physicochemical properties allow them to encapsulate a wide range of therapeutic agents, from small-molecule drugs to complex biomolecules such as nucleic acids and proteins. By enabling both passive and active targeting, nanoparticles enhance site-specific delivery, reduce systemic side effects, and increase therapeutic efficiency. The ability to engineer nanoparticles with polymers, lipids, ligands, or antibodies has opened new horizons in precision medicine, where

treatments can be tailored to the specific needs of patients and disease types. A major advantage of nanoparticles lies in their ability to improve solubility, bioavailability, and stability of poorly soluble drugs while offering controlled and sustained release. This ensures prolonged circulation and steady therapeutic concentrations, improving patient compliance and minimizing dosing frequency. Furthermore, the capacity of nanoparticles to cross complex biological barriers, such as the blood–brain barrier, has paved the way for breakthroughs in the treatment of neurological disorders that were once considered untreatable. Clinically, their impact has already been demonstrated in several FDA-approved formulations, including liposomal amphotericin B for fungal infections and lipid nanoparticles in COVID-19 mRNA vaccines, underscoring their transformative role in global healthcare. Despite these successes, significant challenges remain before nanoparticle-based drug delivery becomes a universal clinical reality. Issues such as potential toxicity, long-term accumulation in tissues, high production costs, batch-to-batch variability, and the lack of standardized regulatory guidelines hinder widespread adoption. Stability during storage and transport, as well as rapid clearance by the reticuloendothelial system (RES), further complicate their clinical translation. These limitations highlight the importance of ongoing research aimed at developing next-generation carriers, including hybrid nanoparticles that combine the advantages of different materials, and stimuli-responsive systems that release drugs only under specific physiological or external triggers.

Looking ahead, the integration of advanced technologies such as artificial intelligence and machine learning in nanoparticle design is expected to accelerate the discovery and optimization of smart drug delivery systems. Personalized nanomedicine, guided by patient-specific genomic and proteomic profiles, holds particular promise for tailoring therapies that maximize efficacy and minimize adverse effects. The convergence of nanotechnology, biotechnology, and data-driven medicine is likely to transform nanoparticle-based delivery into a cornerstone of precision healthcare.

In conclusion, while challenges in safety, manufacturing, and regulation persist, the continuous advancements in material science, bioengineering, and computational modeling strongly suggest that nanoparticle drug delivery systems will play a central role in the future of medicine. They embody the potential to revolutionize therapeutics by making treatments more effective, safer, and highly personalized, ultimately reshaping how diseases are prevented, managed, and cured.

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