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Original Article

Nanocarrier-Based Drug Delivery Systems: Revolutionizing Therapeutic Efficacy and Targeted Release

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ABSTRACT

The development of nanocarrier-based drug delivery systems (NDDS) represents a transformative advancement in modern pharmaceutical sciences. By engineering materials at the nanometer scale (1–1000 nm), it is possible to enhance therapeutic efficacy, optimize pharmacokinetics, and achieve controlled and targeted drug release. Nanocarriers—including liposomes, polymeric nanoparticles, dendrimers, solid lipid nanoparticles, niosomes, and metallic nanoparticles—provide unique benefits such as improved solubility, bioavailability, biocompatibility, and site-specific delivery. The ability of these systems to cross biological barriers and release drugs in a sustained or stimuli-responsive manner has revolutionized treatment strategies in cancer, neurological disorders, infectious diseases, and gene therapy. Despite significant achievements, challenges such as cytotoxicity, large-scale manufacturing, regulatory hurdles, and cost remain barriers to clinical translation. This comprehensive review provides an in-depth analysis of nanocarrier types, mechanisms of drug loading and release, targeting strategies, characterization parameters, applications, and recent technological advancements that are shaping the future of personalized and precision medicine.

Keywords: Nanocarriers, Targeted Drug Delivery, Nanoparticles, Liposomes, Polymeric Nanoparticles, Therapeutic Efficacy

INTRODUCTION

Traditional drug delivery methods often result in poor therapeutic efficiency due to the lack of controlled release and inability to target specific tissues. Drugs administered via oral, intravenous, or topical routes frequently exhibit low solubility, rapid metabolism, and nonspecific distribution, leading to undesirable side effects and poor patient compliance [1]. Nanotechnology offers an innovative solution by developing carriers at the nanoscale capable of transporting and releasing drugs in a controlled and targeted manner [2]. Nanocarrier-based drug delivery systems (NDDS) are designed to encapsulate active pharmaceutical ingredients (APIs) within nanosized materials ranging from 1–1000 nm. Their nanoscale dimensions allow for increased surface area, improved solubility of hydrophobic compounds, and enhanced permeability through physiological barriers such as the intestinal mucosa and blood–brain barrier [3]. The concept of using nanocarriers for drug delivery was first explored with the development of liposomes in the 1960s, followed by polymeric nanoparticles, dendrimers, and lipid-based systems [4]. Over time, advancements in material science, polymer chemistry, and nanofabrication have refined these systems for greater biocompatibility and targeted drug release. Moreover, surface modification with hydrophilic polymers such as polyethylene glycol (PEG) or targeting ligands such as folate, antibodies, or peptides further enhances selectivity and circulation time [5]. Nanocarriers play a crucial role in increasing drug residence time, reducing degradation, and achieving sustained release. For instance, liposomal formulations of doxorubicin and paclitaxel have demonstrated prolonged plasma half-life and reduced systemic toxicity in cancer therapy [6]. The integration of stimuli-responsive mechanisms—where release is triggered by pH, temperature, or enzymes—further personalizes treatment to disease-specific microenvironments [7]. Table 1 summarizes the key benefits of nanocarrier-based systems compared to conventional drug delivery approaches.

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Table 1: Comparison between Conventional and Nanocarrier-Based Drug Delivery Systems

Parameter	Conventional Systems	Nanocarrier-Based Systems
Drug solubility	Often poor; limited for hydrophobic drugs	Improved solubility via encapsulation
Bioavailability	Variable, often low	Significantly enhanced
Drug protection	Limited protection from degradation	Protects drug from enzymatic and environmental degradation
Targeting capability	Non-specific	Site-specific via passive or active targeting
Release profile	Rapid, uncontrolled	Sustained and controlled
Side effects	High due to systemic exposure	Reduced due to localized delivery
Patient compliance	Moderate	Improved due to reduced dosing frequency

NDDS are being extensively explored in oncology, neurology, cardiology, and infectious diseases for delivering small molecules, peptides, proteins, and nucleic acids [8]. Recent innovations such as multifunctional hybrid nanocarriers and nanotheranostic systems—combining therapy and diagnostics—illustrate the versatile potential of nanomedicine [9]. Therefore, understanding the classification, design principles, mechanisms of drug release, and evaluation parameters of nanocarriers is essential for their rational development and successful clinical translation.

Classification of Nanocarrier Systems

Nanocarriers can be classified based on their composition, structural organization, and method of drug incorporation. Each system possesses distinct characteristics influencing its pharmacokinetic behavior, stability, and therapeutic performance [10]. The major types of nanocarrier systems are discussed below and summarized in Table 2.

1. Liposomes

Liposomes are spherical vesicles composed of one or more phospholipid bilayers enclosing an aqueous core [11]. They can encapsulate both hydrophilic drugs (in the aqueous phase) and lipophilic drugs (within the bilayer). Their size generally ranges from 50 to 1000 nm, and surface modification with PEG or ligands enhances circulation time and targeting ability [12]. Liposomal formulations like Doxil® and Ambisome® are FDA-approved for cancer and fungal infections. Advantages include biocompatibility, biodegradability, and versatility in drug encapsulation, whereas limitations involve stability issues and high production costs [13].

2. Polymeric Nanoparticles

Polymeric nanoparticles are solid colloidal particles prepared from biodegradable polymers such as poly (lactic-co-glycolic acid) (PLGA), chitosan, and polycaprolactone (PCL) [14]. These particles can encapsulate or adsorb drugs, providing controlled release and protection from degradation. The surface of polymeric nanoparticles can be modified with targeting ligands or hydrophilic polymers to enhance site specificity and circulation time [15]. Their biocompatibility and controlled release kinetics make them particularly useful for anticancer and peptide drug delivery.

3. Dendrimers

Dendrimers are highly branched, tree-like polymers with nanometric dimensions and well-defined architecture. Their internal cavities allow encapsulation of drugs, while terminal functional groups permit surface modification for targeted delivery [16]. Generations (G1–G10) define their size and branching complexity. Poly(amidoamine) (PAMAM) dendrimers are among the most widely studied types due to their water solubility and low toxicity [17]. They have shown promising applications in gene delivery, antimicrobial therapy, and imaging.

4. Solid Lipid Nanoparticles (SLNs)

SLNs are composed of physiologically compatible solid lipids that remain solid at room and body temperature [18]. They provide controlled drug release, excellent biocompatibility, and protection of labile drugs from degradation. Compared to polymeric nanoparticles, SLNs offer higher physical stability and scalability [19]. However, limitations include drug

expulsion during storage and low loading efficiency for hydrophilic drugs.

5. Nanostructured Lipid Carriers (NLCs)

To overcome SLN limitations, nanostructured lipid carriers (NLCs) were developed by blending solid and liquid lipids. This combination improves drug loading and prevents crystallization, enhancing stability and release control [20]. NLCs are used in transdermal and oral delivery of poorly soluble drugs.

6. Polymeric Micelles

Polymeric micelles are formed by the self-assembly of amphiphilic block copolymers in aqueous media, creating a hydrophobic core and hydrophilic shell [21]. They are ideal for solubilizing poorly water-soluble drugs like paclitaxel and curcumin. Additionally, micelles can be engineered for stimuli-responsive behavior, releasing drugs under specific pH or temperature conditions [22].

7. Metallic and Magnetic Nanoparticles

Metal-based nanocarriers, such as gold, silver, and iron oxide nanoparticles, are utilized for both therapeutic and diagnostic purposes [23]. Magnetic nanoparticles can be directed to target sites using external magnetic fields and also serve as contrast agents in imaging [24]. Surface modification enhances their stability and biocompatibility.

8. Niosomes

Niosomes are nonionic surfactant-based vesicles similar to liposomes but more stable and cost-effective [25]. They encapsulate both hydrophilic and hydrophobic drugs and are widely used in topical, transdermal, and ocular delivery systems [26].

Table 2: Summary of Major Nanocarrier Systems and Their Characteristics

Type	Composition	Drug Type	Advantages	Limitations
Liposomes	Phospholipids, cholesterol	Hydrophilic/ lipophilic	Biocompatible, clinically approved	Expensive, stability issues
Polymeric nanoparticles	PLGA, PCL, chitosan	Small molecules, peptides	Controlled release, versatile	Solvent residues possible
Dendrimers	PAMAM, PPI	DNA, proteins, small molecules	Multivalency, precision	Synthesis complexity, toxicity
SLNs	Solid lipids	Lipophilic	Stable, biodegradable	Limited hydrophilic loading
NLCs	Solid + liquid lipids	Hydrophobic	Higher loading, stable	Moderate scalability
Polymeric micelles	Amphiphilic copolymers	Hydrophobic	Solubilization, stimuli-responsive	Low drug loading
Metallic nanoparticles	Gold, silver, Fe_3O_4	Anticancer, imaging	Magnetic targeting, imaging	Cytotoxicity concerns
Niosomes	Nonionic surfactants	Broad range	Stable, economical	Limited clinical data

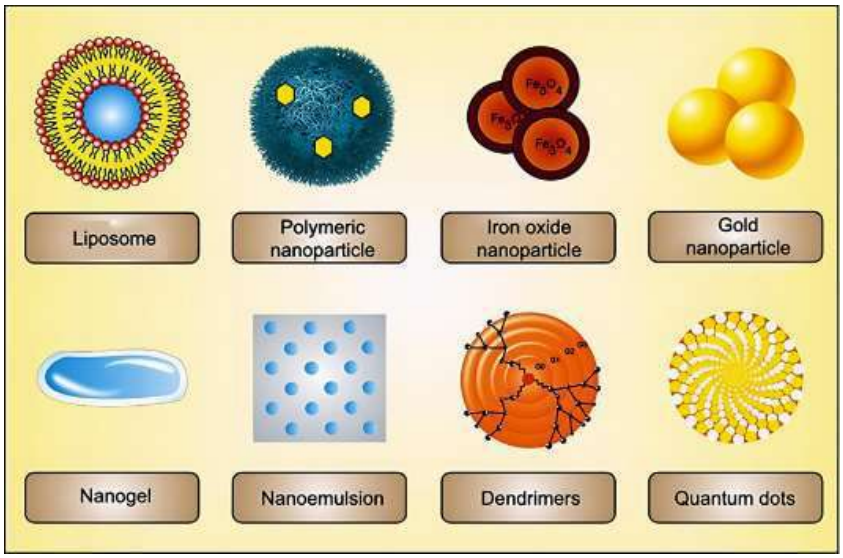

Figure 1: Morphological and Structural Diversity of Major Nanocarrier Systems

Mechanisms of Drug Loading and Release:

The efficiency of nanocarrier systems is largely dependent on how effectively a drug is loaded and subsequently released at the target site [20]. Drug loading mechanisms vary with the type of carrier, the physicochemical nature of the drug, and the method of preparation.

1. Drug Loading Mechanisms

Drugs can be incorporated into nanocarriers through **physical entrapment**, **chemical conjugation**, or **adsorption** [21].

1. **Physical Entrapment:** Common in liposomes, polymeric nanoparticles, and SLNs, where drugs are either encapsulated in the core (hydrophilic) or embedded within the lipid or polymer matrix (lipophilic).

2. **Chemical Conjugation:** Drug molecules are covalently bonded to the carrier surface or backbone, often through cleavable linkers responsive to environmental stimuli such as pH or enzymes [22].

3. **Adsorption:** Drugs adhere to the carrier surface via electrostatic or hydrophobic interactions, a simple but less stable method.

Table 3: Drug Loading Mechanisms in Different Nanocarriers

Nanocarrier Type	Loading Method	Nature of Interaction	Example
Liposomes	Physical entrapment	Hydrophilic/hydrophobic partitioning	Doxorubicin
Polymeric nanoparticles	Entrapment or adsorption	Diffusion within polymer matrix	Paclitaxel
Dendrimers	Chemical conjugation	Covalent bonding	Methotrexate
Metallic nanoparticles	Surface adsorption	Electrostatic/hydrophobic	Cisplatin

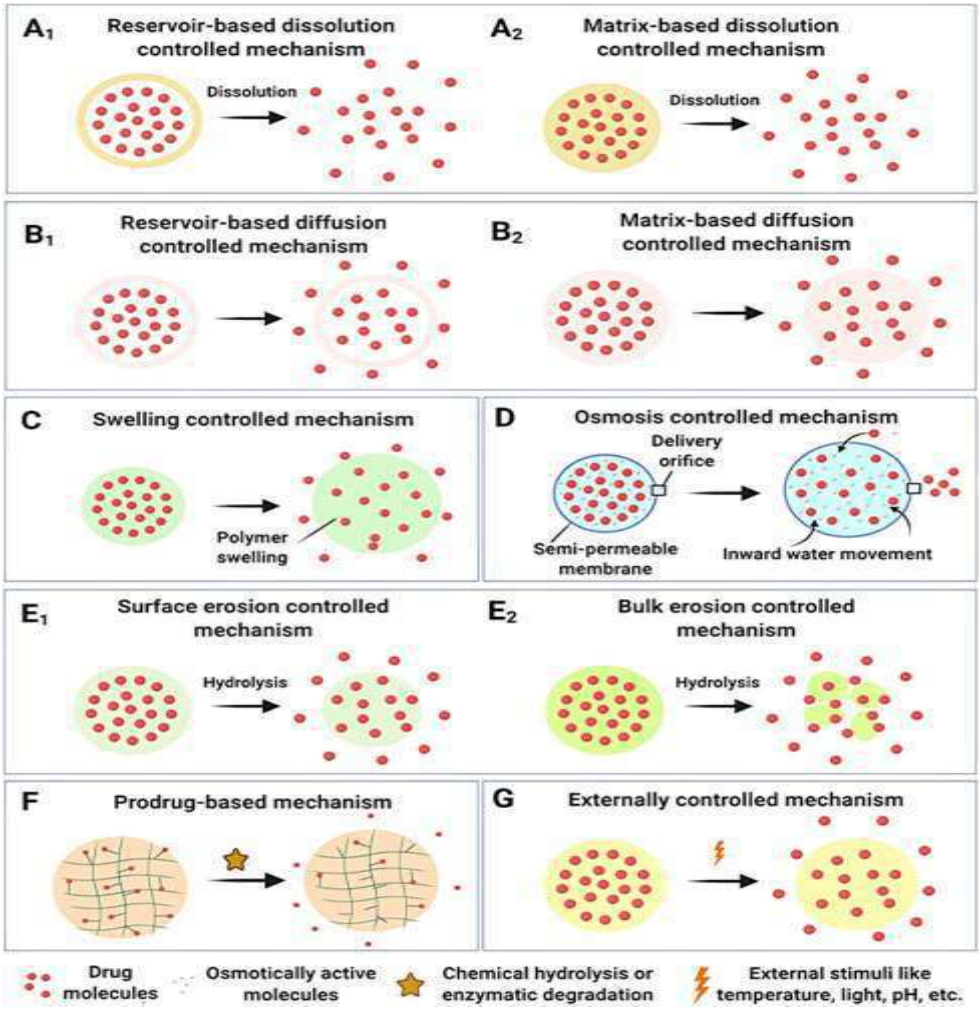

Figure 2: Key Mechanisms for Drug Loading and Controlled Release

2. Drug Release Mechanisms

Controlled drug release is the hallmark of NDDS, ensuring therapeutic concentration over extended periods and minimizing side effects [23].

Common release mechanisms include:

- **Diffusion-controlled release**: Drug diffuses through the carrier matrix (common in polymeric systems).
- **Degradation-controlled release**: Carrier material gradually degrades to release the encapsulated drug.
- **Stimuli-responsive release**: Triggered by environmental factors such as pH, temperature, redox potential, or external stimuli like light and magnetic fields [24].

Table 4: Mechanisms of Drug Release

Mechanism	Trigger/Factor	Example Carrier	Drug Released
Diffusion-controlled	Concentration gradient	PLGA nanoparticles	Curcumin
Degradation-controlled	Hydrolysis, enzymatic cleavage	Chitosan nanocapsules	5-Fluorouracil
pH-sensitive	Acidic tumor microenvironment	Liposomes with pH-labile linkers	Doxorubicin
Thermo-responsive	Local temperature rise	Hydrogel-based nanocarriers	Cisplatin

3. Targeting Strategies in Nanocarrier Systems

The ultimate goal of nanocarrier design is to ensure selective accumulation of the therapeutic agent at the desired site while minimizing systemic distribution [25]. Targeting can be **passive**, exploiting physiological phenomena, or **active**, achieved via surface modification.

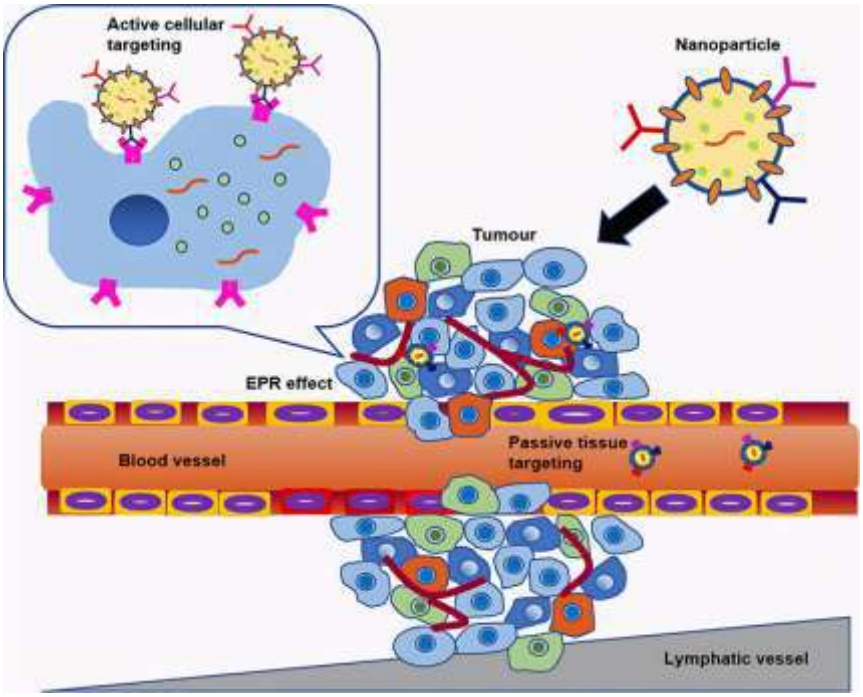

Figure 3: Passive vs. Active Targeting Strategies in Tumor Nanomedicine

3.1 Passive Targeting

Passive targeting takes advantage of the **Enhanced Permeability and Retention (EPR) effect**, a property of tumor tissues that allows nanoparticles (100–400 nm) to preferentially accumulate due to leaky vasculature and impaired lymphatic drainage

[26]. This principle has been widely exploited in anticancer nanomedicine.

3.2 Active Targeting

Active targeting involves decorating the nanocarrier surface with **specific ligands**, **antibodies**, or **aptamers** that bind to receptors overexpressed on target cells [27]. For instance:

- **Folate receptor targeting** for ovarian and breast cancer
- **Transferrin-mediated targeting** for brain and tumor delivery
- **Hyaluronic acid targeting** for CD44-overexpressing tumor cells

Table 5. Active Targeting Ligands Used in Nanocarrier Systems

Ligand	Target Receptor	Application	Example Drug
Folic acid	Folate receptor	Cancer	Doxorubicin
Transferrin	Transferrin receptor	Brain targeting	Curcumin
Hyaluronic acid	CD44 receptor	Tumor targeting	Paclitaxel
Antibody fragments	HER2 receptor	Breast cancer	Docetaxel

3.3 Stimuli-Responsive and Dual-Targeted Systems

Emerging NDDS research focuses on **smart nanocarriers** capable of releasing drugs only under specific physiological or external conditions [28]. Examples include:

- **pH-responsive carriers** that release drugs in acidic tumor microenvironments
- **Thermo- and magneto-responsive carriers** activated by local heat or magnetic fields
- **Dual-targeted systems** combining ligand-based and stimuli-responsive mechanisms for enhanced precision [29]

4. Characterization and Evaluation of Nanocarriers

Thorough characterization is essential to ensure reproducibility, efficacy, and safety of nanocarrier formulations. Characterization includes **physicochemical**, **morphological**, and **biological** evaluations [30].

4.1 Physicochemical Characterization:

Table 6: Physicochemical Characterization

Parameter	Method	Significance
Particle size & PDI	Dynamic Light Scattering (DLS)	Determines uniformity and stability
Zeta potential	Electrophoretic mobility	Indicates surface charge and colloidal stability
Drug loading & entrapment efficiency	UV/Vis spectrophotometry, HPLC	Determines drug incorporation capacity
Surface morphology	SEM, TEM, AFM	Examines shape and surface characteristics
Thermal analysis	DSC, TGA	Studies thermal stability and crystallinity

4.2 In Vitro Evaluation

In vitro studies assess drug release kinetics, stability, and cytotoxicity. Techniques include:

- Dialysis method for release profiling
- MTT or SRB assays for cell viability
- Hemolysis and stability tests for biocompatibility [31]

4.3 In Vivo Evaluation

In vivo studies evaluate pharmacokinetics, biodistribution, and therapeutic response. Techniques such as fluorescence imaging, radiolabeling, and magnetic resonance imaging (MRI) are commonly used to track nanocarrier behavior in living organisms [32].

Table 7. Evaluation Parameters of Nanocarrier Systems

Evaluation Type	Parameters	Common Techniques
Physicochemical	Particle size, zeta potential	DLS, TEM
In vitro	Release, cytotoxicity	Dialysis, MTT assay
In vivo	Biodistribution, targeting	MRI, PET, fluorescence

5. Therapeutic Applications of Nanocarrier-Based Systems

Nanocarriers have significantly impacted multiple therapeutic domains by improving drug selectivity, reducing toxicity, and allowing controlled release [33].

5.1 Cancer Therapy

Cancer remains the most explored area for nanocarrier applications. Liposomes (e.g., Doxil®), polymeric nanoparticles, and gold nanoshells are employed for tumor-targeted therapy [34]. Nanocarriers enable enhanced accumulation at tumor sites via the EPR effect and reduce systemic toxicity of chemotherapeutic drugs such as doxorubicin and paclitaxel [35].

5.2 Neurological Disorders

The **blood–brain barrier (BBB)** poses a major challenge for CNS drug delivery. Nanocarriers such as polymeric micelles, solid lipid nanoparticles, and liposomes have demonstrated the ability to cross the BBB and deliver neurotherapeutics [36]. Drugs like dopamine and rivastigmine have been successfully encapsulated in lipid-based nanoparticles for improved brain bioavailability [37].

5.3 Infectious Diseases

Nanocarriers improve the delivery of antibiotics, antivirals, and antifungals by enhancing tissue penetration and sustained release [38]. For example, silver nanoparticles show strong antimicrobial activity, while liposomal amphotericin B minimizes renal toxicity compared to conventional formulations [39].

5.4 Gene and Nucleic Acid Delivery

Gene therapy applications utilize nanocarriers such as cationic liposomes, dendrimers, and polymeric nanoparticles to deliver DNA, siRNA, or mRNA safely into cells [40]. Recent advances include **lipid nanoparticles (LNPs)** for mRNA-based COVID-19 vaccines, which represent a major clinical success of nanocarrier technology [41].

5.5 Vaccine Delivery

Nanocarriers enhance antigen stability and promote sustained immune activation. Lipid nanoparticles and polymeric carriers have been integrated into modern vaccine platforms, improving both efficacy and immune response [42].

6. Challenges and Limitations of Nanocarrier Systems

Despite significant advances, the translation of nanocarrier-based systems from laboratory research to clinical practice faces numerous obstacles. These include physicochemical instability, cytotoxicity, complex manufacturing processes, high cost, and regulatory uncertainties [43].

6.1 Stability and Scale-Up Issues

The stability of nanocarriers during storage and upon administration remains a concern. Physical instability such as aggregation, fusion, or leakage can alter drug release and bioavailability [44]. Scale-up from laboratory to industrial production is challenging due to the need for reproducible particle size, drug loading, and sterility under Good Manufacturing Practice (GMP) conditions [45].

6.2 Toxicity and Biocompatibility Concerns

Toxicological assessment is crucial since nanocarriers may interact with cells and organs differently than bulk materials [46].

- **Metallic nanoparticles**, while effective, may cause oxidative stress and inflammation.
- **Cationic polymers** (e.g., polyethyleneimine) can be cytotoxic at higher concentrations [47].

- Accumulation in the reticuloendothelial system (RES) can lead to long-term toxicity [48].

6.3 Regulatory and Ethical Considerations

The absence of harmonized international regulatory guidelines for nanomedicine complicates approval processes [49]. Agencies such as the **U.S. FDA** and **EMA** require extensive physicochemical, pharmacokinetic, and safety evaluations. Ethical issues related to nanomedicine—particularly in gene and neurological delivery—also warrant attention [50].

6.4 Cost and Commercialization

Although nanocarrier-based formulations such as *Doxil*® and *Abraxane*® have achieved commercial success, most remain economically unfeasible for low-resource healthcare systems due to high production and characterization costs [51]. Investment in scalable technologies and public-private partnerships could enhance accessibility [52].

FUTURE PERSPECTIVES

The next generation of NDDS is anticipated to integrate **multi-functional, stimuli-responsive**, and **biomimetic** designs [53]. Key directions include:

- **Personalized nanomedicine:** Tailoring carriers based on genetic and metabolic profiles.
- **Hybrid systems:** Combining organic and inorganic nanomaterials for synergistic properties.
- **Artificial-intelligence-guided formulation design:** Using computational models to predict optimal carrier parameters [54].
- **Green nanotechnology:** Employing eco-friendly materials and synthesis methods to improve sustainability [55].

The future also lies in **theranostics**, where nanocarriers simultaneously deliver drugs and enable real-time imaging for disease monitoring [56].

CONCLUSION:

Nanocarrier-based drug delivery systems have transformed modern therapeutics by offering controlled, targeted, and efficient delivery of a wide range of pharmacological agents. Through precise engineering at the nanoscale, these systems overcome limitations of conventional dosage forms, including poor solubility, nonspecific distribution, and short half-life. While the field faces hurdles related to safety, cost, and regulatory compliance, ongoing innovations—particularly in personalized and intelligent nanocarriers—hold immense potential to redefine global healthcare. Collaboration between academia, industry, and regulatory agencies is essential for translating these advances into safe, affordable, and effective nanomedicines.

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