

## A Review Article on:Recent Advances in Nanocarrier-Based Drug Delivery Systems

Saklain Mushtaq Sheikh<sup>1</sup>, Nikhil Bansal<sup>2</sup>, Supreet Kaur<sup>3</sup>, Kuldeep Singh<sup>4</sup>, Hasandeep Singh<sup>5\*</sup>,  
Archana Rani<sup>6</sup>

<sup>1</sup>Centre for Research Innovation, Amritsar Group of Colleges, Amritsar,143109, Punjab

<sup>2</sup>Centre for Research Innovation, Amritsar Group of Colleges, Amritsar,143109, Punjab

<sup>3</sup>Centre for Research Innovation, Amritsar Group of Colleges, Amritsar,143109, Punjab

<sup>4</sup>Associate Professor, Centre for Research Innovation, Amritsar Group of Colleges, Amritsar,143109, Punjab

<sup>5</sup>Associate Professor, Centre for Research Innovation, Amritsar Group of Colleges, Amritsar,143109, Punjab

<sup>6</sup>Centre for Research Innovation, Amritsar Group of Colleges, Amritsar,143109, Punjab

**Corresponding Author**

**Kuldeep Singh**

Mail ID: [hasanpharma.rsh@gndu.ac.in](mailto:hasanpharma.rsh@gndu.ac.in)

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### ABSTRACT

Nanocarrier-based drug delivery systems have revolutionized modern therapeutics by enhancing the bioavailability, stability, and targeted delivery of drugs. Liposomes, niosomes, and solid lipid nanoparticles (SLNs) have emerged as prominent platforms due to their biocompatibility, controlled release characteristics, and ability to encapsulate diverse therapeutic agents. Recent advances include the development of surface-functionalized and stimuli-responsive carriers, hybrid nanosystems, and exosome mimetic nanoparticles, which allow for precision targeting and improved pharmacokinetics. These innovations have expanded applications across oncology, anti-inflammatory therapy, dermatology, and neurological disorders. Despite the rapid progress, challenges such as large-scale production, long-term stability, regulatory approval, and clinical translation remain critical hurdles. This review highlights the latest developments in liposomes, niosomes, and SLNs, discusses emerging nanocarrier platforms, and evaluates clinical and regulatory perspectives, providing a comprehensive overview of the current and future landscape of nanocarrier-based drug delivery systems.

**Keywords:** Nanocarriers Liposomes, Niosomes, Solid Lipid Nanoparticles. Stimuli-responsive Targeted Drug Delivery Clinical Translation.

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### INTRODUCTION:

The rapid advancement of nanotechnology has profoundly influenced the field of drug delivery, enabling the development of sophisticated nanocarrier systems that can improve therapeutic efficacy while minimizing systemic toxicity [1][41][61]. Conventional drug delivery approaches often suffer from poor solubility, limited bioavailability, rapid clearance, and off-target effects, which reduce clinical outcomes [2][25][31]. Nanocarrier-based systems, including liposomes, niosomes, and solid lipid nanoparticles (SLNs), provide solutions by encapsulating drugs within biocompatible matrices, offering controlled release, protection from enzymatic degradation, and the potential for targeted delivery [3][12][35].

Liposomes, composed of phospholipid bilayers surrounding an aqueous core, were among the first nanocarriers developed for clinical applications [1][2][3]. Their amphiphilic nature allows encapsulation of both hydrophilic and hydrophobic drugs, while surface modifications, such as PEGylation, enhance circulation time and reduce immunogenicity [5][6][7]. Niosomes, non-ionic surfactant-based vesicles, have emerged as an alternative to liposomes due to lower cost, higher chemical stability, and ease of production

[11][12][17]. They have been extensively explored for transdermal, ocular, and oral drug delivery, demonstrating improved bioavailability and targeted release profiles [13][14][18]. Solid lipid nanoparticles (SLNs) offer a solid lipid matrix that stabilizes encapsulated drugs, ensures controlled release, and enhances chemical stability compared to conventional colloidal systems [31][32][35]. SLNs have been widely applied for oral, topical, and parenteral drug delivery, including anticancer, anti-inflammatory, and antimicrobial therapies [36][37][40].

Recent research has focused on further enhancing nanocarrier performance through functionalization, hybrid systems, and stimuli-responsive designs [8][18][55][58]. Functionalization with ligands, antibodies, or aptamers enables active targeting to specific tissues or tumor cells, improving therapeutic index and reducing off-target effects [27][43][46]. Hybrid nanosystems, combining lipids with polymers or inorganic cores, provide multifunctionality, such as imaging and therapy in a single platform [53][59][60]. Stimuli-responsive nanocarriers can release drugs in response to specific triggers, including pH, temperature, redox potential, or enzymatic activity, enabling site-

specific delivery and minimizing systemic exposure [8][55][58].

Despite these advances, several challenges remain. Large-scale manufacturing, long-term stability, regulatory approval, and translation from preclinical models to human therapy are significant barriers [61][62][64]. Additionally, understanding in vivo pharmacokinetics, biodistribution, and toxicity is critical to ensure safety and clinical success [63][65].

This review provides a comprehensive analysis of recent advances in liposomes, niosomes, and SLNs, while also exploring emerging nanocarrier systems, including polymeric nanoparticles, dendrimers, micelles, exosomes, and hybrid nanosystems. The clinical applications, regulatory perspectives, and future directions of nanocarrier-based drug delivery are discussed to provide a holistic overview of this rapidly evolving field.

## 2. Nanocarrier Platforms

Nanocarriers are nanoscale delivery vehicles designed to improve drug solubility, stability, pharmacokinetics, and targeting [1][41][31]. Among the diverse nanocarrier systems, liposomes, niosomes, and solid lipid nanoparticles (SLNs) are most widely studied, while emerging platforms such as polymeric nanoparticles, dendrimers, micelles, and exosome-mimetic carriers are increasingly explored [41][43][44][51].

### 2.1 Liposomes

Liposomes are spherical vesicles consisting of one or more phospholipid bilayers encapsulating an aqueous core, allowing simultaneous delivery of hydrophilic and hydrophobic drugs [1][2][3]. The size, lamellarity, and surface properties of liposomes influence drug loading, release kinetics, and in vivo distribution [6][7].

#### Recent advances in liposomes include:

**PEGylated liposomes:** Surface modification with polyethylene glycol increases circulation time and reduces opsonization [5][6].

**Targeted liposomes:** Conjugation with ligands, antibodies, or peptides allows active targeting to specific tissues or tumor cells [8][9].

**Stimuli-responsive liposomes:** Engineered to release drugs in response to pH, temperature, or enzymatic triggers [8][55].

**Applications:** Liposomes have been extensively used in cancer therapy, antifungal treatment, gene delivery, and anti-inflammatory therapy [2][4][9].

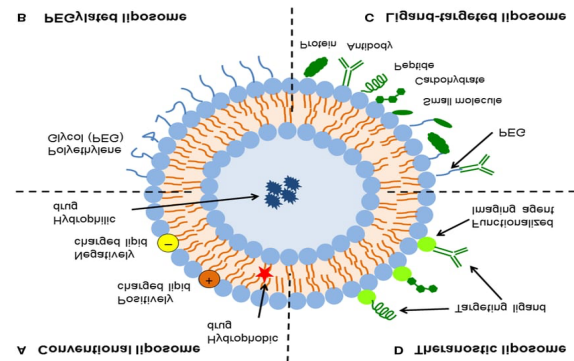


Fig.1 Schematic representation of liposome structure showing hydrophilic core, lipid bilayer, and PEGylation/ligand surface modification

### Niosomes

Niosomes are non-ionic surfactant vesicles similar to liposomes but composed of non-ionic surfactants and cholesterol [11][12][13]. They are chemically stable, cost-effective, and versatile in encapsulating hydrophilic and hydrophobic drugs [14][17].

#### Recent advances in niosomes include:

**Transdermal niosomes:** Enhanced skin permeation for anti-inflammatory and anticancer agents [12][14].

**Thermosensitive niosomes:** Controlled release triggered by temperature changes [23].

**Functionalized niosomes:** Targeted delivery using ligands or antibodies for tissue-specific therapy [16][27].

**Applications:** Niosomes have shown promise in transdermal, ocular, oral, and nasal drug delivery systems, particularly for anti-inflammatory, anticancer, and peptide-based therapies [13][15][18].

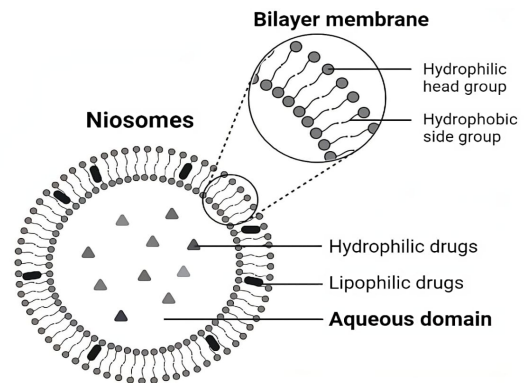


Fig. 2 Structure of a niosome showing surfactant bilayer, cholesterol, and drug encapsulation

### Solid Lipid Nanoparticles (SLNs)

SLNs consist of a solid lipid core stabilized by surfactants, offering controlled drug release, high stability, and biocompatibility [31][32][35]. SLNs can encapsulate lipophilic drugs and protect labile molecules from degradation [36][37].

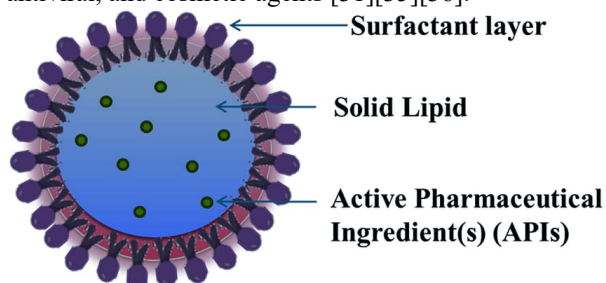
#### Recent advances in SLNs include:

**Hybrid SLNs:** Combining lipids with polymers or inorganic materials for multifunctional delivery [53][59].

**Targeted SLNs:** Surface modification with ligands for tumor-specific delivery [36][37].

**Stimuli-responsive SLNs:** Drug release triggered by pH, temperature, or redox conditions [55][58].

**Applications:** SLNs are applied in oral, topical, and parenteral delivery of anticancer, anti-inflammatory, antiviral, and cosmetic agents [31][35][36].



**Fig. 3** Solid lipid nanoparticle structure showing lipid core, surfactant layer, and encapsulated drug molecules.

### Emerging Nanocarrier Platforms

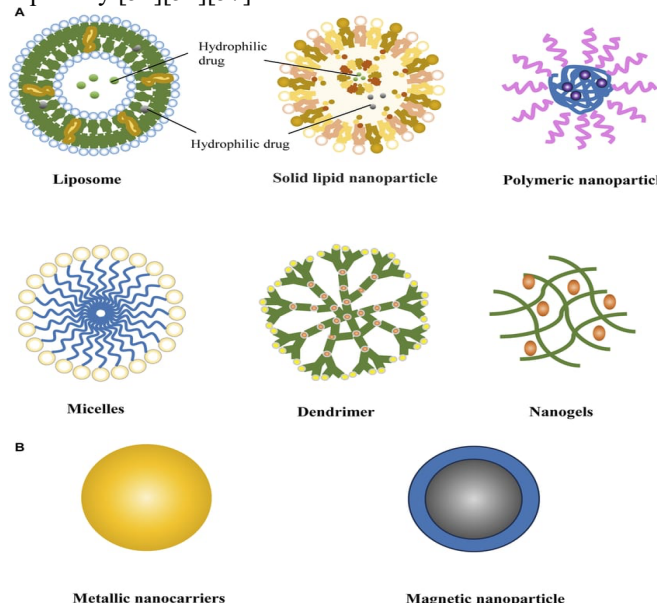
While liposomes, niosomes, and SLNs dominate current research, emerging nanocarriers such as polymeric nanoparticles, dendrimers, micelles, and exosome-mimetic nanoparticles offer additional advantages:

**Polymeric nanoparticles (PLGA, PLA, PEG):** Biodegradable, controllable release, and versatile surface modification [41][42][45].

**Dendrimers:** Highly branched polymers providing precise drug encapsulation and functionalization [43][46].

**Micelles:** Amphiphilic structures ideal for solubilizing hydrophobic drugs [44][48][50].

**Exosomes and extracellular vesicles:** Natural carriers with high biocompatibility and intrinsic targeting capability [51][52][57].



Schematic representation of various types of nanocarriers used commonly for nano-drug delivery systems. (A) Organic nanocarriers: liposome, solid lipid

nanoparticle, polymeric nanoparticle, micelles, dendrimer, nanogels, (B) Inorganic nanoparticle carrier: metallic nanocarriers and magnetic nanoparticle

### Mechanisms & Targeting Strategies

Nanocarrier-based drug delivery relies on multiple mechanisms to enhance therapeutic efficacy, including controlled release, cellular uptake, and site-specific targeting. Understanding these mechanisms is essential for designing effective nanomedicines [1][2][27].

#### Passive Targeting

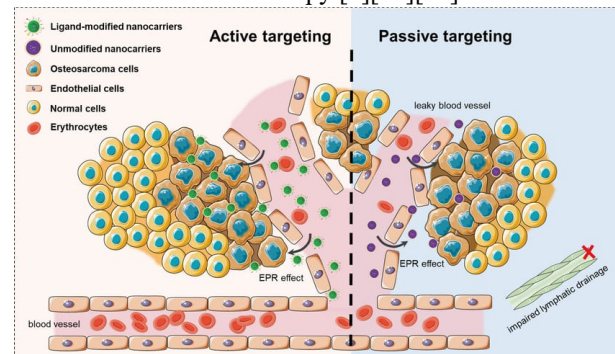
Passive targeting exploits the enhanced permeability and retention (EPR) effect, a phenomenon in which nanoparticles preferentially accumulate in tumor or inflamed tissues due to leaky vasculature and impaired lymphatic drainage [2][9][41].

#### Key features of passive targeting include:

**Size-dependent accumulation:** Nanocarriers between 50–200 nm can effectively accumulate in target tissues [6][36].

**Surface properties:** Neutral or slightly negative surfaces minimize opsonization and prolong circulation [5][6].

**Application:** Widely used in oncology, inflammation, and infectious disease therapy [4][14][29].



**Fig.5** passive targeting via EPR effect showing nanoparticle accumulation in tumor tissue.

### Cellular Uptake Mechanisms

Nanocarriers can enter cells via multiple pathways depending on their physicochemical properties, size, and surface modifications [41][42][46].

#### Primary mechanisms include:

**Endocytosis:** Clathrin-mediated, caveolae-mediated, or macropinocytosis

**Phagocytosis:** Mainly for larger particles by immune cells

**Direct penetration:** Observed for ultra-small or highly lipophilic nanoparticles [2][41][42]

### Controlled and Stimuli-Responsive Drug Release

Nanocarriers are engineered to release drugs in a controlled or stimuli-responsive manner, ensuring site-specific therapy and reduced systemic toxicity [8][18][55][58].

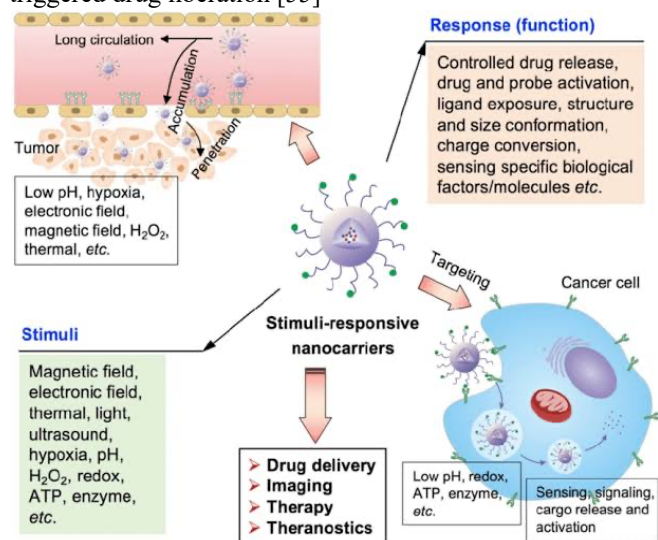
#### Common stimuli include:

**pH-sensitive carriers:** Release drugs in acidic tumor microenvironments or lysosomes [55]

**Temperature-sensitive carriers:** Thermosensitive liposomes or niosomes for local hyperthermia-triggered release [23][58]

**Redox-sensitive carriers:** Drug release triggered by intracellular glutathione levels [55]

**Enzyme-sensitive carriers:** Protease- or esterase-triggered drug liberation [55]



**Fig. 6** Stimuli-responsive nanocarrier releasing drug under pH, temperature, or redox triggers

**Pharmacokinetic and Biodistribution Considerations**

Nanocarrier design strongly influences pharmacokinetics, biodistribution, and clearance [5][31][36].

Surface modification (e.g., PEGylation) prolongs circulation

Particle size and shape determine tissue penetration

Surface charge affects protein corona formation and opsonization

Optimizing these parameters ensures higher accumulation in target tissues, reduced clearance, and improved therapeutic index [5][6][36][37].

**Recent Advances in Nanocarrier-Based Drug Delivery**

Recent years (2020–2025) have witnessed significant innovations in nanocarrier design and application, driven by the need for precision, efficiency, and multifunctionality in drug delivery systems [1][2][41]. Advances encompass improvements in liposomes, niosomes, SLNs, polymeric nanoparticles, dendrimers, micelles, and hybrid systems.

**Liposomal Innovations**

Liposomes remain the most clinically established nanocarriers, with recent developments focusing on enhanced targeting, multifunctionality, and stimuli-responsiveness [5][8][9].

**Key advances include:**

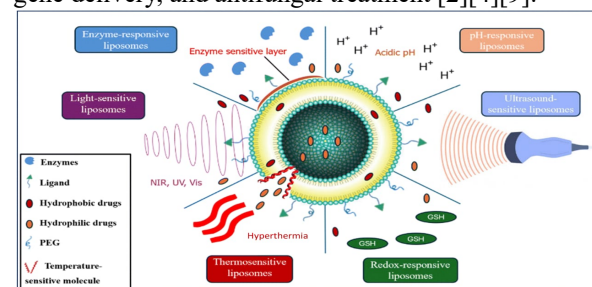
**Multifunctional liposomes:** Co-delivery of chemotherapeutics and immunomodulators for synergistic anti-cancer therapy [8][9][53].

**Theranostic liposomes:** Incorporation of imaging agents for real-time monitoring of drug distribution [7][53].

**Stimuli-responsive liposomes:** pH, temperature, and enzyme-sensitive formulations allow site-specific drug release, reducing systemic toxicity [8][55][58].

**Surface-engineered liposomes:** PEGylation, ligand conjugation, or antibody functionalization enhances circulation, targeting, and cellular uptake [5][6][27].

**Applications:** Oncology, anti-inflammatory therapy, gene delivery, and antifungal treatment [2][4][9].



**Fig.7** Recent innovations in liposome-based nanocarriers including theranostic and stimuli-responsive systems.

**Niosomal Developments**

Niosomes have gained attention due to their chemical stability, ease of production, and cost-effectiveness [11][12][16]. Recent advances focus on improving permeability, controlled release, and targeted delivery:

**Innovations include:**

**Transdermal niosomes:** Enhanced skin permeation of anti-inflammatory and anticancer agents [12][14][22].

**Thermosensitive and stimuli-responsive niosomes:** Release drugs in response to temperature or pH changes [23][18].

**Functionalized niosomes:** Surface modification with ligands, antibodies, or polymers enables active targeting [16][27].

**Nano-niosomes:** Ultra-small vesicles with improved stability and enhanced bioavailability [14][19].

**Applications:** Dermatology, transdermal therapy, ocular delivery, and oral peptide delivery [12][14][16].

**Solid Lipid Nanoparticle (SLN) Progress**

SLNs provide a solid lipid matrix for drug encapsulation, offering controlled release, enhanced stability, and biocompatibility [31][32][35].

**Recent advances include:**

**Hybrid SLNs:** Combining lipids with polymers or inorganic materials to create multifunctional carriers for imaging and therapy [53][59][60].

**Targeted SLNs:** Ligand-conjugated formulations for tumor-specific or tissue-specific delivery [36][37].

**Stimuli-responsive SLNs:** pH-, redox-, or temperature-sensitive release for site-specific therapy [55][58].

**Oral and topical SLNs:** Optimized for improved bioavailability and skin permeation [36][40].

**Applications:** Anti-inflammatory, anticancer, antiviral, and cosmetic formulations [35][36][37].

#### **Polymeric and Hybrid Nanocarriers**

Polymeric nanoparticles, dendrimers, and micelles offer complementary advantages in stability, biodegradability, and functionalization [41][43][44].

#### **Recent innovations:**

PLGA/PLA nanoparticles: Biodegradable carriers with controlled drug release [41][42].

Dendrimer-based delivery: Targeted therapy and precise drug encapsulation [43][46].

Micellar nanocarriers: Solubilization of hydrophobic drugs with enhanced tumor accumulation [44][48].

Hybrid systems: Lipid-polymer hybrids or inorganic-organic carriers enable multifunctionality and theranostic applications [53][59][60].

**Applications:** Oncology, anti-inflammatory therapy, transdermal, and gene delivery [41][43][48][53].

#### **Exosome-Mimetic and Emerging Platforms**

Exosomes and extracellular vesicle-inspired nanocarriers represent a new frontier, offering natural targeting and high biocompatibility [51][52][57].

#### **Highlights include:**

Exosome-mimetic nanoparticles: Combining natural vesicles with synthetic modifications for targeted delivery [57].

Stimuli-responsive exosomes: Triggered drug release in tumor or inflamed microenvironments [55].

**Clinical translation:** Early-phase studies demonstrate safety, targeted delivery, and therapeutic efficacy [51][52].

**Applications:** Oncology, neurological disorders, and regenerative medicine [51][52][57].

#### **Clinical Applications of Nanocarriers:**

Nanocarrier-based drug delivery has transitioned from preclinical studies to clinical applications in oncology, anti-inflammatory therapy, transdermal drug delivery, and neurological disorders. Their unique properties, including targeted delivery, controlled release, and reduced systemic toxicity, have accelerated their use in modern therapeutics [1][2][4][41].

#### **Oncology**

Cancer treatment benefits significantly from nanocarrier-based delivery systems due to the need for high efficacy and minimal off-target toxicity [2][4][9].

#### **Key applications:**

Liposomal chemotherapeutics: Doxil® (liposomal doxorubicin) reduces cardiotoxicity while maintaining antitumor activity [2][3].

Niosomal anticancer agents: Targeted delivery of chemotherapeutics enhances cellular uptake and reduces systemic side effects [14][22].

SLNs and polymeric nanoparticles: Co-delivery of multiple drugs and combination therapy with stimuli-responsive release improve therapeutic outcomes [36][41][53].

Exosome-mimetic carriers: Offer intrinsic targeting capabilities for tumors with minimal immune recognition [51][57].

#### **Anti-Inflammatory Therapy**

Nanocarriers improve the bioavailability and efficacy of anti-inflammatory drugs, particularly in arthritis and localized inflammation [12][14][29].

#### **Applications:**

Transdermal niosomes and SLNs: Enhanced skin penetration of NSAIDs like diclofenac and curcumin [12][14][29].

Stimuli-responsive carriers: Controlled drug release triggered by pH or temperature at inflammatory sites [18][23][55].

Functionalized carriers: Targeting inflamed tissue reduces systemic exposure and improves therapeutic index [16][27].

#### **Transdermal and Topical Delivery**

Transdermal drug delivery benefits from nanocarrier systems by overcoming the stratum corneum barrier [12][14][36].

#### **Key advances:**

Niosomal gels: Improved permeability and sustained release of hydrophilic and lipophilic drugs [12][14].

SLN and NLC-based creams: Enhanced skin retention and stability [36][40].

Liposomes and polymeric micelles: Delivery of hydrophobic drugs with controlled release and minimal irritation [2][44][48].

#### **Neurological Disorders**

Crossing the blood-brain barrier (BBB) is a major challenge in CNS drug delivery [41][51].

#### **Applications:**

Liposomal and polymeric nanoparticles: Facilitate brain-targeted delivery of chemotherapeutics, neuroprotective agents, and anti-Alzheimer drugs [2][41][42].

Exosome-based carriers: Naturally cross the BBB, enabling delivery of small molecules, RNA, and proteins [51][52][57].

Stimuli-responsive systems: pH or enzyme-triggered release improves drug concentration at the site of pathology [55][58].

#### **Gene and Vaccine Delivery**

Nanocarriers, particularly lipid-based systems, have enabled breakthroughs in nucleic acid delivery and vaccination [66][67][68].

#### **Applications:**

mRNA vaccines: Lipid nanoparticles (LNPs) protect mRNA, facilitate cellular uptake, and enhance immune response [66][67][68].

siRNA and gene therapy: SLNs, polymeric nanoparticles, and exosome-mimetic carriers deliver

nucleic acids effectively while minimizing degradation [41][43][57].

**Combination therapies:** Co-delivery of drugs and nucleic acids for synergistic effects [53][59].

#### **Challenges and Future Directions:**

Despite significant progress in nanocarrier-based drug delivery, several challenges limit their widespread clinical translation. Addressing these issues is crucial for advancing nanomedicine from bench to bedside [61][62][64].

#### **Manufacturing and Scale-Up**

Large-scale production of nanocarriers remains challenging due to complexity in reproducibility, particle size control, and batch-to-batch consistency [61][63].

#### **Key considerations:**

Process standardization: Ensuring uniform size, drug loading, and surface functionalization [31][36].

Cost-effectiveness: Developing scalable, economically viable methods for industrial production [62].

Quality control: Maintaining sterility, stability, and reproducibility across large batches [61].

#### **Stability and Shelf-Life**

Nanocarrier stability is influenced by aggregation, degradation, and drug leakage during storage [31][35][36].

#### **Strategies to improve stability:**

Lyophilization or freeze-drying for long-term storage [31][36]

Surface modification with polymers like PEG to reduce aggregation [5][6]

Optimization of lipid or surfactant composition to maintain integrity [12][36]

#### **Regulatory and Safety Considerations**

Regulatory approval of nanocarrier-based therapeutics requires extensive safety and efficacy evaluation [61][62][64].

#### **Challenges include:**

Defining standardized characterization methods for particle size, zeta potential, and encapsulation efficiency [61][62].

Evaluating long-term toxicity, immunogenicity, and biodistribution [61][63].

Navigating differing regulations across regions, such as FDA and EMA guidelines [62][63][64].

#### **Clinical Translation**

Translating nanocarriers from preclinical models to humans faces multiple hurdles [61][65]:

Variability in in vivo biodistribution and pharmacokinetics [36][37].

Immune recognition and clearance mechanisms [5][6].

High development costs and complex clinical trial design [62][65].

#### **Future strategies:**

Personalized nanomedicine: Tailoring nanocarrier design to patient-specific biomarkers and disease profile [27][41].

Hybrid and multifunctional systems: Combining therapy, imaging, and diagnostics in a single platform [53][59].

Stimuli-responsive and smart nanocarriers: Enhancing site-specific release and minimizing off-target effects [8][18][55].

#### **Emerging Perspectives**

Recent trends emphasize:

Integration of artificial intelligence and machine learning for nanocarrier design and optimization [66][67].

Combination of natural and synthetic nanocarriers, such as exosome-mimetic nanoparticles, for enhanced targeting and safety [51][57].

Expanding clinical applications beyond oncology to CNS disorders, immunotherapy, and regenerative medicine [41][51][52].

#### **Conclusion**

Nanocarrier-based drug delivery systems have transformed the therapeutic landscape by enabling targeted, controlled, and efficient delivery of a wide range of drugs. Liposomes, niosomes, and solid lipid nanoparticles (SLNs) remain the cornerstone of clinical and preclinical nanomedicine due to their biocompatibility, versatility, and ability to encapsulate hydrophilic and hydrophobic drugs [1][11][31]. Emerging platforms, including polymeric nanoparticles, dendrimers, micelles, hybrid systems, and exosome-mimetic carriers, offer multifunctionality, stimuli-responsiveness, and enhanced targeting potential [41][43][51][53][57].

Recent innovations have focused on improving therapeutic efficacy, site-specific delivery, and patient compliance through advanced targeting strategies, functionalization, and controlled release mechanisms [8][16][27][55]. Clinical applications span oncology, anti-inflammatory therapy, transdermal delivery, neurological disorders, and nucleic acid-based therapies, demonstrating the translational potential of nanocarrier systems [2][12][51][66].

Despite these advances, challenges remain in large-scale manufacturing, long-term stability, regulatory approval, and clinical translation [61][62][64]. Addressing these hurdles will be critical for realizing the full potential of nanocarriers in personalized medicine. Future directions point toward hybrid multifunctional carriers, stimuli-responsive smart systems, and integration of artificial intelligence for optimized design and therapy [53][55][66].

In summary, nanocarrier-based drug delivery continues to evolve rapidly, offering unprecedented opportunities for precise, safe, and effective therapeutic interventions. With ongoing research and regulatory support, these systems are poised to revolutionize modern medicine and expand the boundaries of targeted therapeutics.

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