WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 15, Issue 1, 1624-1635. Research Article ISSN 2277–7105

LIPID-BASED NANOPARTICLES IN THE CLINIC AND CLINICAL TRIALS

Priya Roy*[1], Dr. Arun Patel[2], Shailendra Patel[3]

*[1]Student, Shri Ram Group of Institutions, Faculty of Pharmacy, Jabalpur (M.P).

[2]Principal and Professor, Shri Ram Group of Institutions, Faculty of Pharmacy, Jabalpur (M.P.)

[3]Assistant Professor, Shri Ram Group of Institutions, Faculty of Pharmacy, Jabalpur (M.P.)

Article Received on 21 Nov. 2025,
Article Revised on 11 Dec. 2025,
Article Published on 01 Jan. 2026,
https://doi.org/10.5281/zenodo.18221351

***Corresponding Author**
Priya Roy
Student, Shri Ram Group of Institutions, Faculty of Pharmacy, Jabalpur (M.P).

How to cite this Article: Priya Roy*[1], Dr. Arun Patel[2], Shailendra Patel[3]. (2026). Lipid-Based Nanoparticles in The Clinic and Clinical Trials. World Journal of Pharmaceutical Research, 15(1), 1624–1635.

ABSTRACT

Lipid-based nanoparticles (LBNs) represent one of the most clinically successful nanotechnology-driven drug delivery platforms, bridging the gap between experimental nanomedicine and real-world therapeutic application. Owing to their excellent biocompatibility, biodegradability, and structural similarity to biological membranes, lipid-based nanocarriers have demonstrated remarkable translational potential. These systems are capable of encapsulating small molecules, peptides, proteins, and nucleic acids, while improving pharmacokinetics, biodistribution, and therapeutic index. This review provides a comprehensive overview of lipid-based nanoparticles with a special emphasis on their clinical relevance and progression through clinical trials. Different classes of LBNs, including liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), lipid nanoparticles (LNPs), and nanoemulsions are discussed in detail. Clinically approved formulations, ongoing clinical trials in oncology, infectious diseases, neurological disorders, and genetic therapies are summarized. Key formulation components, mechanisms of action, advantages, limitations, regulatory considerations, and recent technological advancements are elaborated. Despite challenges such as large-scale manufacturing, long-term stability, and regulatory complexity,

lipid-based nanoparticles continue to dominate the nanomedicine landscape, offering promising solutions for personalized and precision medicine.

KEYWORDS: Lipid-based nanoparticles, Liposomes, Solid lipid nanoparticles, Nanostructured lipid carriers, Clinical trials, Nanomedicine, Gene delivery.

INTRODUCTION

The clinical success of any drug delivery system is determined not only by its therapeutic efficacy but also by its safety profile, reproducibility, scalability, and patient compliance. Conventional dosage forms frequently fail to achieve optimal therapeutic outcomes due to inherent limitations such as poor aqueous solubility of drugs, rapid presystemic metabolism, short biological half-life, dose-related systemic toxicity, and lack of site-specific targeting. These shortcomings often necessitate high or repeated dosing, leading to increased adverse effects and reduced patient adherence. To address these challenges, nanotechnology-based drug delivery systems have emerged as a powerful and transformative approach in modern pharmaceutical science. Among the various nanocarriers investigated, lipid-based nanoparticles (LBNs) have achieved exceptional clinical acceptance due to their biocompatibility, biodegradability, and strong translational potential.[1,2] Lipid-based nanoparticles are colloidal drug delivery systems typically ranging from 20 to 500 nm in size and are composed of physiological lipids such as phospholipids, triglycerides, fatty acids, and cholesterol. The lipid composition of these carriers closely resembles that of biological membranes, which contributes to their excellent tolerability, minimal immunogenicity, and enhanced cellular uptake via endocytic pathways. Furthermore, the nanoscale size of LBNs enables prolonged systemic circulation, improved biodistribution, and passive targeting through the enhanced permeability and retention (EPR) effect, particularly in tumor tissues and inflamed regions. These characteristics make LBNs highly suitable for both systemic and targeted drug delivery applications.[3] The remarkable translational success of lipid-based nanoparticles is evident from the approval of several lipid-based nanomedicines for clinical use. Liposomal formulations of anticancer drugs, such as doxorubicin and daunorubicin, have demonstrated reduced cardiotoxicity and improved therapeutic index. Similarly, liposomal antifungal agents, such as amphotericin B, have shown enhanced efficacy with significantly lower nephrotoxicity. Most notably, the recent global success of lipid nanoparticle–based mRNA vaccines has highlighted the unparalleled potential of LBNs in nucleic acid delivery, immunotherapy, and rapid vaccine development. These clinical achievements have not only

validated the safety and efficacy of lipid-based nanocarriers but have also accelerated academic research, industrial investment, and regulatory interest in lipid nanotechnology.[4]

Lipid-based nanoparticles are particularly advantageous for the delivery of

- Poorly water-soluble drugs, by improving dissolution rate and oral or parenteral bioavailability
- Drugs with a narrow therapeutic index, by reducing peak-related toxicity and maintaining controlled plasma concentrations
- Macromolecules such as proteins, peptides, siRNA, and mRNA, by protecting them from enzymatic degradation and facilitating intracellular delivery
- Targeted and controlled drug delivery, through surface modification, ligand conjugation, and controlled release mechanisms.

In light of these advantages, lipid-based nanoparticles have become one of the most extensively investigated and clinically advanced nanocarrier systems. This review therefore focuses on the clinical applications of lipid-based nanoparticles, with particular emphasis on their approved formulations and progress in ongoing clinical trials across oncology, infectious diseases, neurological disorders, and genetic therapies.

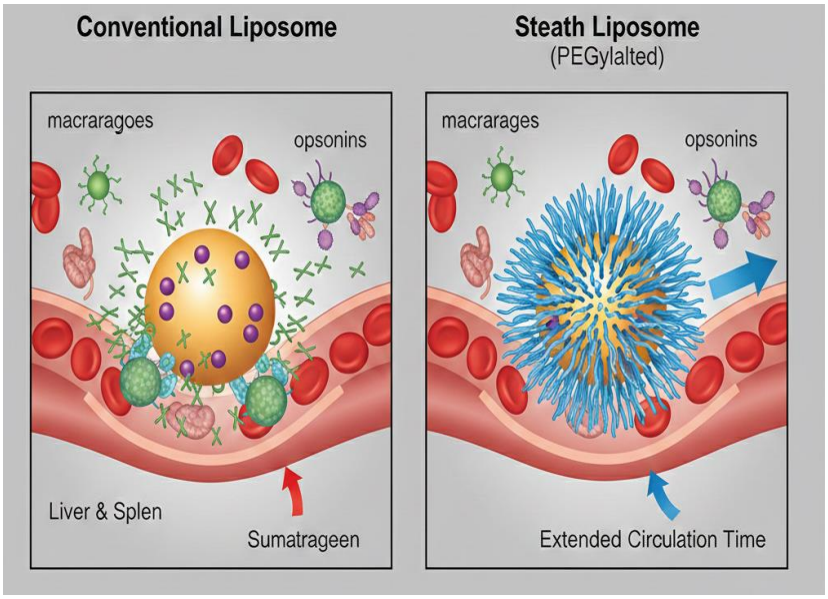

Figure I: Conventional Liposome vs. Stealth (PEGylated) Liposome: Mechanism of Opsonization and Blood Circulation Time.

CLASSIFICATION OF LIPID-BASED NANOPARTICLES

1. Liposomes

Liposomes are the earliest and most extensively studied lipid-based nanocarriers. They consist of one or more phospholipid bilayers surrounding an aqueous core. Depending on size and lamellarity, liposomes are classified as small unilamellar vesicles (SUVs), large unilamellar vesicles (LUVs), and multilamellar vesicles (MLVs).[5]

Liposomes can encapsulate

- Hydrophilic drugs in the aqueous core
- Lipophilic drugs within the lipid bilayer
- Amphiphilic drugs at the bilayer interface

Surface modification with polyethylene glycol (PEGylation) results in stealth liposomes that evade reticuloendothelial system (RES) clearance, thereby prolonging circulation time.[6]

Clinically approved liposomes

- Doxil® (pegylated liposomal doxorubicin)
- AmBisome® (liposomal amphotericin B)
- DaunoXome® (liposomal daunorubicin).

2. Solid Lipid Nanoparticles (SLNs)

Solid lipid nanoparticles are composed of lipids that remain solid at both room and body temperature. The drug is dispersed or dissolved within the solid lipid matrix, which is stabilized by surfactants.[7]

- **Advantages of Solid Lipid Nanoparticles (SLNs):** High physical and chemical stability: The solid lipid core provides a rigid matrix that protects the encapsulated drug from chemical degradation, oxidation, and hydrolysis during storage and in biological environments**.**
- **Controlled and sustained drug release:** The crystalline lipid matrix allows modulation of drug diffusion, enabling prolonged and predictable release profiles that help maintain therapeutic drug levels and reduce dosing frequency.
- **Protection of labile drugs:** SLNs effectively shield sensitive molecules such as peptides, proteins, and chemically unstable drugs from enzymatic degradation and harsh physiological conditions**.**

- **Use of physiological and biodegradable lipids:** The use of biocompatible lipids minimizes toxicity and improves patient safety.
- **Versatile routes of administration:** SLNs are suitable for oral, topical, ocular, pulmonary, and parenteral delivery.
- **Improved bioavailability:** SLNs enhance lymphatic uptake and bypass first-pass metabolism, particularly beneficial for poorly water-soluble drugs.

Limitations of Solid Lipid Nanoparticles (SLNs)

- **Low drug loading capacity**: The highly ordered crystalline structure of solid lipids restricts space for drug incorporation, especially for hydrophilic drugs.
- **Drug expulsion during storage:** Polymorphic transitions of lipids from less stable to more stable crystalline forms can lead to drug leakage over time.
- **Initial burst release:** Surface-associated drug may cause an undesired burst effect, affecting release uniformity.
- **Limited compatibility with high-dose drugs:** High drug concentrations may compromise matrix integrity and stability.
- **Scale-up challenges:** Maintaining particle size uniformity and reproducibility during large-scale manufacturing can be difficult.

3. Nanostructured Lipid Carriers (NLCs)

NLCs are second-generation lipid nanoparticles developed to overcome the limitations of SLNs. They consist of a mixture of solid and liquid lipids, creating a less-ordered lipid matrix that accommodates higher drug loading.[8]

Types of NLCs

- Imperfect crystal type
- Amorphous type
- Multiple type

NLCs exhibit improved stability, enhanced drug encapsulation efficiency, and controlled release profiles. Several NLC formulations are currently in clinical and preclinical development for cancer and CNS disorders.

4. Lipid Nanoparticles (LNPs)

LNPs are advanced lipid systems specifically optimized for nucleic acid delivery. They typically consist of ionizable lipids, phospholipids, cholesterol, and PEG-lipids. At

physiological pH, ionizable lipids remain neutral, reducing toxicity, but become positively charged in acidic endosomes, facilitating endosomal escape.[9]

5. Nano-emulsions

Nano-emulsions are kinetically stable dispersions of oil and water stabilized by surfactants, with droplet sizes typically below 200 nm. They improve drug solubility and absorption, especially for lipophilic drugs.[10]

Nanoemulsions are widely used in

- Parenteral nutrition
- Anesthesia (Propofol)
- Vaccin adjuvants.

MECHANISMS OF DRUG DELIVERY

Lipid-based nanoparticles (LBNs) enhance therapeutic efficacy and clinical performance through multiple complementary mechanisms that influence drug absorption, distribution, metabolism, and elimination.

- **Enhanced Permeability and Retention (EPR) Effect**: LBNs preferentially accumulate in tumor tissues and inflamed sites due to leaky vasculature and impaired lymphatic drainage. Their nanoscale size allows passive targeting, resulting in higher local drug concentration at the disease site while minimizing exposure to healthy tissues.
- **Prolonged Systemic Circulation:** Surface modification, particularly PEGylation, reduces opsonization and uptake by the reticuloendothelial system (RES). This prolongs blood circulation time, enhances bioavailability, and increases the probability of drug accumulation at the target site.
- **Cellular Uptake via Endocytosis:** LBNs are efficiently internalized by cells through endocytic pathways such as clathrin-mediated, caveolae-mediated, and macropinocytosis. This facilitates intracellular delivery of drugs, including nucleic acids, and enhances therapeutic action at the cellular and subcellular levels.
- **Controlled and Sustained Drug Release:** The lipid matrix of nanoparticles allows controlled diffusion and gradual drug release, maintaining consistent plasma drug levels and reducing dosing frequency. This is particularly beneficial for chronic diseases requiring long-term therapy.

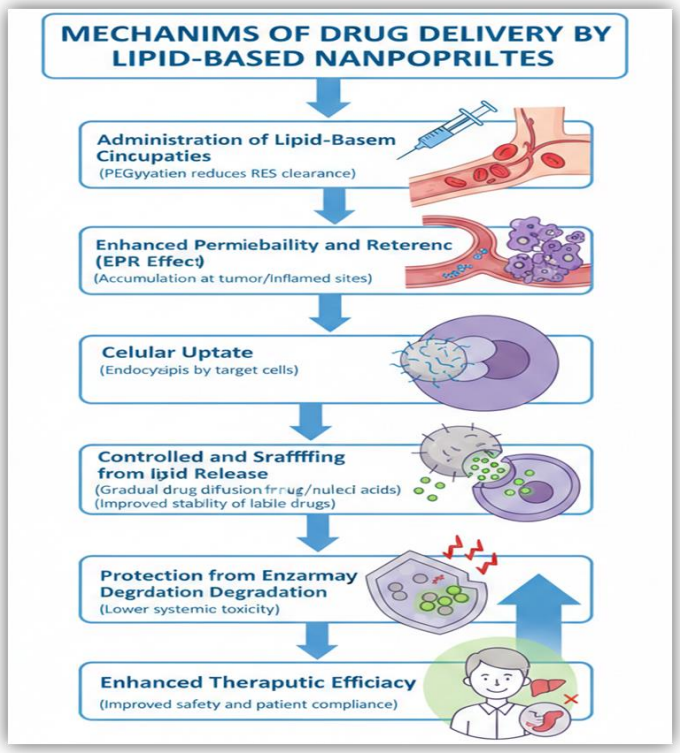

Figure II: Mechanism of Drug Delivery

- **Protection from Enzymatic Degradation:** Encapsulation within lipid nanocarriers protects drugs from enzymatic and chemical degradation in biological fluids, improving stability and therapeutic effectiveness. This is especially critical for peptides, proteins, siRNA, and mRNA.

CLINICALLY APPROVED LIPID-BASED NANOMEDICINES

Table No. I: Approved lipid-based nanoparticle formulations.

PRODUCT	DRUG	CARRIER	INDICATION
Doxil®	Doxorubicin	Liposome	Ovarian, breast cancer
AmBisome®	Amphotericin B	Liposome	Systemic fungal infections
Abraxane®	Paclitaxel	Albumin–lipid NP	Cancer
Onpattro®	Patisiran	LNP	Amyloidosis
Comirnaty®	mRNA	LNP	COVID-19

LIPID-BASED NANOPARTICLES IN CLINICAL TRIALS

Lipid-based nanoparticles (LBNs) have been extensively evaluated in clinical trials across multiple therapeutic areas due to their biocompatibility, versatility, and proven ability to improve drug efficacy and safety.

Oncology

- **Liposomal irinotecan (Onivyde®):** Enhanced tumor targeting, reduced gastrointestinal toxicity, and improved pharmacokinetics for pancreatic cancer.
- **Liposomal cisplatin**: Reduced nephrotoxicity and improved tumor accumulation in solid tumors.
- **siRNA-loaded LNPs targeting oncogenes:** Early-phase trials demonstrate gene silencing of tumor-promoting genes with minimal off-target effects.

Infectious Diseases

- Liposomal antibiotics: Liposomal formulations of amphotericin B (AmBisome®) and vancomycin improve pharmacokinetics and reduce nephrotoxicity.
- LNP-based vaccines: Moderna and Pfizer–BioNTech COVID-19 mRNA vaccines demonstrated rapid clinical translation; LNP-based influenza and HIV vaccines are in Phase I–II trials.

Neurological Disorders

- **LNPs for Parkinson's and Alzheimer's disease:** Lipid nanocarriers facilitate blood–brain barrier (BBB) penetration, enabling delivery of neuroprotective agents and RNA therapeutics.
- **Brain-targeted lipid nanocarriers:** Functionalized LBNs with ligands (e.g., transferrin, lactoferrin) enhance CNS uptake and improve therapeutic outcomes.[19]

Genetic and Rare Diseases

- **CRISPR/Cas9 delivery via LNPs:** Ongoing trials explore safe in vivo gene editing for monogenic disorders.
- **mRNA therapies for enzyme replacement:** Trials for lysosomal storage disorders demonstrate transient expression of missing enzymes with minimal immunogenicity.[12–15]

ADVANTAGES OF LBNs

- **Excellent biocompatibility:** Lipids are often physiological or biodegradable, minimizing immune reactions and systemic toxicity.
- **Enhanced drug solubility:** LBNs improve the solubility of poorly water-soluble drugs, increasing oral bioavailability and therapeutic efficacy.
- **Reduced systemic toxicity:** Targeted delivery and controlled release limit off-target drug exposure.

- **Controlled and targeted delivery:** Enables sustained release and preferential accumulation at disease sites via passive (EPR) or active targeting (ligand functionalization).
- **Capability to deliver nucleic acids**: LBNs protect siRNA, mRNA, and DNA from enzymatic degradation and facilitate intracellular delivery.
- **Strong clinical and regulatory acceptance:** Multiple FDA/EMA-approved LBNs validate their translational potential.[18]

LIMITATIONS AND CHALLENGES

- **Physical and chemical instability:** Lipid oxidation, hydrolysis, and polymorphic transitions may affect particle integrity and drug retention.
- **High manufacturing cost:** Specialized equipment, cleanroom facilities, and complex formulation processes increase production expenses.
- **Scale-up and batch-to-batch variability:** Ensuring reproducible size, charge, and encapsulation efficiency at industrial scale remains challenging.
- **PEG-associated immunogenicity:** Anti-PEG antibodies may lead to accelerated blood clearance (ABC phenomenon) and reduce efficacy.[16]

REGULATORY AND QUALITY CONSIDERATIONS

Regulatory approval for LBN-based nanomedicines requires extensive physicochemical and biological characterization to ensure quality, safety, and reproducibility. Key requirements include.[18]

Physicochemical characterization

- Particle size and size distribution
- Zeta potential (surface charge)
- Encapsulation efficiency and drug loading
- Morphology (TEM/SEM)
- Lipid polymorphism and crystallinity.[19]

Stability and sterility

- Short- and long-term stability under defined storage conditions
- Resistance to aggregation or fusion
- Sterility and endotoxin testing for parenteral formulations

Biological evaluation

- Pharmacokinetics and biodistribution
- Immunogenicity and toxicity assessment
- Targeting efficiency and therapeutic efficacy.

Quality-by-Design (QbD) and risk-based approaches

- Identification of critical quality attributes (CQAs) and critical process parameters (CPPs)
- Systematic optimization of formulation and manufacturing processes

Implementation of robust control strategies to ensure reproducibility and regulatory compliance.[17,20]

Table No. II: Summary Table of Clinical.

DISEASE AREA	DRUG / LBN TYPE	PHASE	NCT NUMBER	KEY OUTCOME
Pancreatic Cancer	Liposomal irinotecan	III	NCT01509056	Improved overall and progression-free survival
Solid Tumors	siRNA-loaded LNPs (KRAS)	I/II	NCT03076385	Effective gene silencing, early tumor regression
COVID-19	mRNA-LNP vaccines	III	NCT04368728	>90% efficacy, robust neutralizing antibodies
Visceral Leishmaniasis	Liposomal amphotericin B	IV	NCT00178408	Enhanced therapeutic outcomes, reduced toxicity
Huntington's Disease	LNP-siRNA	I	NCT04120493	Safe CNS delivery, effective gene knockdown
Parkinson's Disease	SLNs	I/II	NCT04584565	Improved brain ioavailability, favorable tolerability
Amyloidosis	Patisiran (siRNA-LNP)	III	NCT01960348	Reduced serum TTR, improved neuropathy scores
Fabry Disease	mRNA-LNP enzyme replacement	I/II	NCT04172592	Safe enzyme delivery, transient restoration of enzyme activity
Influenza / HIV	LNP-based vaccines	I/II	NCT04557882	Promising immunogenicity and safety

CONCLUSION

Lipid-based nanoparticles (LBNs) have firmly established themselves as one of the most clinically relevant and versatile nanocarrier systems in modern medicine. Their ability to enhance solubility, improve bioavailability, enable targeted delivery, and protect labile molecules has led to significant breakthroughs across oncology, infectious diseases, neurological disorders, and rare genetic conditions. The clinical success of formulations such as liposomal chemotherapeutics, LNP-based mRNA vaccines, and siRNA therapeutics

underscores their transformative impact on patient care.Advances in lipid chemistry, surface functionalization, and controlled-release strategies have expanded the scope of LBNs from small-molecule drugs to macromolecules, nucleic acids, and gene-editing tools, paving the way for precision and personalized medicine. Furthermore, innovative manufacturing approaches, including microfluidics, high-pressure homogenization, and 3D printing, are enabling scalable, reproducible, and customizable formulations tailored to individual patient needs. Despite challenges related to stability, immunogenicity, high production costs, and regulatory complexity, ongoing research and regulatory harmonization are addressing these barriers, facilitating broader clinical translation. Future directions include targeted LBNs for tissue-specific delivery, stimuli-responsive nanoparticles, combination therapies, and integration with digital health platforms for real-time monitoring of therapeutic outcomes. In conclusion, lipid-based nanoparticles represent a robust and adaptable platform that not only enhances drug efficacy and safety but also redefines the landscape of modern therapeutics. With continued innovation and clinical validation, LBNs are poised to become central to the next generation of precision, personalized, and gene-based therapies, ultimately improving patient outcomes across a wide spectrum of diseases.

REFERENCES

1. Allen, T.M. & Cullis, P.R., 2013. Liposomal drug delivery systems: From concept to clinical applications. Advanced Drug Delivery Reviews, 65(1): 36–48.
2. Barenholz, Y., 2012. Doxil®—The first FDA-approved nano-drug: Lessons learned. Journal of Controlled Release, 160(2): 117–134.
3. Immordino, M.L., Dosio, F. & Cattel, L., 2006. Stealth liposomes: Review of the basic science, rationale, and clinical applications, existing and potential. International Journal of Nanomedicine, 1(3): 297–315.
4. Sercombe, L., Veerati, T., Moheimani, F., Wu, S.Y., Sood, A.K. & Hua, S., 2015. Advances and challenges of liposome assisted drug delivery. Frontiers in Pharmacology, 6: 286.
5. Pattni, B.S., Chupin, V.V. & Torchilin, V.P., 2015. New developments in liposomal drug delivery. Chemical Reviews, 115(19): 10938–10966.
6. Kulkarni, S.A. & Feng, S.S., 2013. Effects of particle size and surface modification on cellular uptake and biodistribution of polymeric nanoparticles for drug delivery. Pharmaceutical Research, 30(10): 2512–2522.

7. Mehnert, W. & Mäder, K., 2001. Solid lipid nanoparticles: Production, characterization and applications. Advanced Drug Delivery Reviews, 47(2–3): 165–196.
8. Müller, R.H., Radtke, M. & Wissing, S.A., 2002. Nanostructured lipid matrices for improved microencapsulation of drugs. International Journal of Pharmaceutics, 242(1–2): 121–128.
9. Pardi, N., Hogan, M.J., Porter, F.W. & Weissman, D., 2018. mRNA vaccines — a new era in vaccinology. Nature Reviews Drug Discovery, 17(4): 261–279.
10. Mishra, V. & Rani, V., 2020. Lipid nanoparticles for targeted drug delivery: Advances and clinical perspectives. Journal of Drug Delivery Science and Technology, 60: 102010.
11. Mahmud, A., Faruque, M.R.I. & Ahmed, F., 2021. Lipid nanoparticles: Mechanisms, applications, and clinical advances. Pharmaceutical Nanotechnology, 9(1): 1–19.
12. Adams, D. et al., 2018. Patisiran, an RNAi therapeutic for hereditary transthyretin amyloidosis. New England Journal of Medicine, 379: 11–21.
13. Onpattro® (patisiran) prescribing information, Alnylam Pharmaceuticals, 2018. Available at: https://www.fda.gov [Accessed 6 Jan. 2026].
14. Feldman, R., Gaertner, J. & Schätzlein, A., 2019. Lipid-based nanoparticles for brain delivery of therapeutics. Drug Delivery and Translational Research, 9(6): 1002–1018.
15. Zhu, X. et al., 2020. CRISPR–Cas9 delivery using lipid nanoparticles for in vivo gene editing. Nature Biomedical Engineering, 4: 899–912.
16. Weissig, V., Pettinger, T.K. & Murdock, N., 2014. Nanopharmaceuticals (part 1): Products on the market. International Journal of Nanomedicine, 9: 4357–4373.
17. European Medicines Agency (EMA), 2021. Guideline on quality, non-clinical and clinical aspects of medicinal products containing nanoparticles. Available at: https://www.ema.europa.eu [Accessed 6 Jan. 2026].
18. Zhao, Y., Zhi, X. & Li, X., 2019. Lipid nanoparticles: Advances, clinical applications, and regulatory perspectives. Frontiers in Bioengineering and Biotechnology, 7: 487.
19. Akbarzadeh, A. et al., 2013. Liposome: Classification, preparation, and applications. Nanoscale Research Letters, 8: 102.
20. Pattni, B.S., Chupin, V.V. & Torchilin, V.P., 2015. New developments in liposomal drug delivery. Chemical Reviews, 115(19): 10938–10966.