

Lipid-Based Nanomedicines for Enhanced Drug Solubility, Bioavailability, and Targeted Delivery

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Abstract: *Despite these advantages, many therapeutic molecules suffer from several drawbacks such as poor aqueous solubility, limited bioavailability, high rate of degradation, non-specific biodistribution and dose-dependent toxicity. The lipid-based nanomedicines have proven to be versatile nanoplatfroms that can overcome these drawbacks by nanoscale drug encapsulation, protection of cargo, control of drug release, and modification of drug disposition. Liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), lipid nanoparticles (LNPs), nanoemulsions, and self-emulsifying lipid formulations are some of the major lipid-based systems. Depending on the structure of the drug and its composition, these carriers can hold hydrophobic drugs, hydrophilic molecules, peptides, proteins, and nucleic acids. The dose of poorly water soluble drugs can be kept in a solubilized or molecularly dispersed state by use of lipid matrices and can improve dissolution in the intestine, intestinal absorption and for appropriate drugs, lymphatic transport. The systemic level of nanoscale formulation can affect pharmacokinetics, resistance to enzymatic degradation of the labile cargo, circulation and tissue distribution. Passive targeting is due to the size of particles and disease-associated vascular properties, while active targeting is due to the modification of the surface with ligands that bind to selected cellular receptors. Examples of clinical translation of lipid nanomedicines include well-known liposomes-based drugs and lipid nanotechnology for nucleic acid delivery. However, there are several critical topics related to physical stability, drug leakage, lipid oxidation, protein corona, immune interactions, scale up, sterilisability, batch reproducibility, and regulatory characterization. This review summarizes the key classes, formulation principles, mechanisms, characterization parameters, therapeutic applications, the translational challenges and emerging areas of lipid-based nanomedicines with a special focus on their application for enhancing drug solubility, bioavailability, and targeted delivery.*

Keywords: lipid-based nanomedicines; lipid nanoparticles; liposomes; solid lipid nanoparticles; nanostructured lipid carriers; drug solubility; bioavailability; targeted drug delivery; controlled release; nanotechnology

I. INTRODUCTION

One of the major hurdles in drug development is to transform a pharmacologically active compound into a formulation that provides therapeutic concentrations at the targeted action site. It is a common characteristic of many promising drug candidates that they have low aqueous solubility, chemical or enzymatic instability, lack of membrane permeability, extensive first-pass metabolism, rapid systemic clearance or unfavorable tissue distribution. These properties may relate to variable absorption, low bioavailability, high dose requirements and increased risk of adverse effects.

This is a special situation for poorly water-soluble compounds. Drugs that fit into the Biopharmaceutics Classification System (BCS) classes II and IV have dissolution-limited absorption and the importance of formulation strategy on the



therapeutic performance is key. Nanotechnology is therefore an emerging strategy for the formulation of challenging drugs.

Lipid-based nanomedicines are especially appealing due to the ability to design biocompatible structures that can be used to encapsulate chemically diverse therapeutic agents. The systems employed in the present era are liposomes, SLNs, LNPs, nanoemulsions and lipid-based self-emulsifying systems. These carriers can enhance apparent solubility, prevent drug degradation, alter drug release profiles, enhance cellular uptake and affect the pharmacokinetic and biodistribution profile dependent on composition and architecture.

For instance, SLNs and NLCs have been studied for the enhancement of drug solubility and permeability, bioavailability, residence time, and targeted drug delivery. In addition to solid lipids, NLCs contain liquid lipids, which results in a more disordered lipid matrix, which can give a higher drug loading capacity and remove some of the limitations of the highly crystalline SLNs.

Small molecules are not the only ones that can be solubilized using lipid nanomedicine, since there are other aspects of clinical relevance to consider. Lipid nanoparticles have emerged as key vehicles for nucleic acids and liposomal formulations have long proven that modification of drug disposition through nanoscale lipid vehicles can lead to clinically relevant products. In addition, the FDA documents list examples such as liposomal doxorubicin and the LNP siRNA therapeutic patisiran, showing the versatility of lipid-based delivery for clinical applications.

In this paper, the scientific principles of lipid-based nanomedicines and their applications for improving solubility, bioavailability, controlled release and targeted delivery are therefore discussed.

II. OBJECTIVES

- To study the main classes and structural features of lipid-based nanomedicines such as liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), lipid nanoparticles (LNPs) and nanoemulsions.
- To study the mechanism of increase in the solubility of the poorly water soluble therapeutic agents in the presence of lipid based nanocarriers.
- To assess the use of lipid based nanomedicines for enhancing the dissolution, degradation and pharmacokinetic properties to improve drug absorption and bioavailability.
- To evaluate the prospective for lipid based nanocarriers in passive and active targeted drug delivery; receptor-mediated and ligand-based targeting approaches.
- To be able to compare different lipid based nanocarrier systems in terms of their structure, drug loading capacity, stability, drug release profile, advantages and limitations.

III. REVIEW OF LITERATURE

Rakibe and Yadav (2026)¹ reviewed the use of lipid nanoparticles as a platform technology for translational nanomedicine. They highlighted the modularity of LNPs and its applications in RNA therapeutics, vaccines and gene therapy. High RNA encapsulation efficiency and formulation characteristics were considered as significant advantages of the review. But limitations in manufacturing scalability, cold-chain considerations, extrahepatic targeting, and repeat-dose safety remain to impact broader clinical translation. Their work reflects a move from single use of LNPs to creating flexible therapeutic delivery systems.

Iqbal, Hwang, and Costain (2026)² reviewed blood–brain barrier (BBB) lipid nanoparticle (LNP) delivery of biotherapeutics and gene therapies. Their review points to the promise of LNPs to surmount one of the most

¹ Rakibe, U., & Yadav, K. S. (2026). Lipid nanoparticles as a platform technology for translational nanomedicine. *Journal of Drug Delivery Science and Technology*. Advance online publication.

² Iqbal, U., Hwang, R. W., & Costain, W. J. (2026). Recent developments in lipid nanoparticle-mediated delivery of biotherapeutics and gene therapy across the blood–brain barrier. *BioDrugs*, 40, 407–431. <https://doi.org/10.1007/s40259-026-00782-0> Springer



challenging biological barriers for drug delivery, and outlines the strategies developed for enhancing the delivery of therapeutic macromolecules into the central nervous system. Development of targeted lipid nanomedicines for neurological applications and precision delivery are of particular relevance to the study.

Kambanis et al. (2026)³ summarized the latest developments and shortcomings in LNP drug delivery. The formulation design, along with the manufacturing reproducibility, stability, transfer to the endosomes and efficiency of the intracellular delivery were identified as important limitations. The authors also covered organ- and cell-specific targeting, hybrid extracellular-vesicle/LNP systems, microfluidic manufacturing, and formulation optimization using artificial intelligence. The advances are a move toward more precisely engineered, scaled and biologically efficient systems of lipids.

The authors of **Bahmani et al. (2025)**⁴ gave a new review of nanostructured lipid carriers as novel drug delivery platforms. Their research highlighted the current developments in NLC formulation and therapeutic uses, demonstrating the ongoing research focus on NLC as potential alternatives to lipid-based systems. NLCs are particularly relevant since they have a less ordered matrix due to the mixed solid liquid lipid structure which allows the incorporation of therapeutic molecules more readily and thus provides for drug loading and controlled delivery. The study continues the evolution of NLCs towards a new generation of pharmaceutical applications.

Kashyap et al. (2025)⁵ investigated NLCs as a novel approach to improving drug delivery systems. The authors pointed out that NLC formulations have many beneficial features, such as improved stability, controlled drug release, and increased bioavailability. They also reviewed other applications like those in dermatology and cancer therapy, as well as scale-up and regulatory considerations, and Quality-by-Design (QbD) approaches. The results indicate that NLCs need to be optimized simultaneously with regard to therapeutic performance, manufacturing processes, product quality, and regulatory acceptability for successful translation.

IV. METHODOLOGY

The present study was a narrative literature-based review of the development and pharmaceutical applications of lipid-based nanomedicines for solubility, bioavailability and targeted delivery. The scientific literature related to liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carrier (NLCs), lipid nanoparticles (LNPs), nanoemulsions and self-emulsifying systems was reviewed. The focus of this analysis was on their structural features, formulation principles, mechanism of drug incorporation, enhancement of solubility, protection against degradation, improvement of absorption and targeted delivery. The scope of the paper is such that these systems were compared in terms of drug loading capacity, stability, release characteristics, advantages and limitations. Preparation methods included thin-film hydration, high-pressure homogenization, spontaneous emulsification, ultrasonication, solvent emulsification and microfluidics and were discussed in detail. The physicochemical properties of the particles, such as particle size, lipid composition, surface features and carrier architecture, were critically synthesized and evaluated for their impact on the therapeutic performance. The reviewed evidence was then categorized to find out the key applications in the pharmaceutical industry, formulation issues, translational hurdles and new possibilities of developing efficient lipid-based nanomedicines.

³ Kambanis, L., Zeng, S., Yong, K.-T., Zhu, L., & Shen, Y. (2026). Lipid nanoparticles in drug delivery: Overcoming challenges and unlocking new frontiers. *Small Structures*, 7(3), e202500583. <https://doi.org/10.1002/ssstr.202500583> [Wiley Online Library](#)

⁴ Bahmani, K., Nasa, P., Tushir, S., Malik, J., Devi, M., & Devi, S. (2025). An updated review on nanostructured lipid carriers used in drug delivery systems. *Current Physical Chemistry*, 16. <https://doi.org/10.2174/0118779468417653251129100607> [Bentham Science Publishers](#)

⁵ Kashyap, K., Sharma, A., Mittal, V., & Malhotra, H. (2025). Nanostructured lipid carriers: A modern approach to optimizing drug delivery systems. *Current Drug Delivery*. Advance online publication. <https://doi.org/10.2174/0124054615360932250721110031> [Bentham Science Publishers](#)



Result:

Table 1. Comparative Performance of Major Lipid-Based Nanomedicine Systems

Scoring scale: 1 = Very Low, 2 = Low, 3 = Moderate, 4 = High, 5 = Very High

Lipid-Based System	Solubility Enhancement	Bioavailability Enhancement	Drug-Loading Potential	Targeted Delivery Potential	Formulation Stability
Liposomes	4	4	4	5	3
Solid Lipid Nanoparticles (SLNs)	4	4	3	4	4
Nanostructured Lipid Carriers (NLCs)	5	5	5	4	4
Lipid Nanoparticles (LNPs)	4	4	5	5	3
Nanoemulsions	5	4	4	3	3

Interpretation:

The comparative performance of the main systems of lipid-based nanomedicine is shown in Table 1. The highest overall scores are obtained for nanolipid carriers (NLCs) for the solubility enhancement, the bioavailability as well as the drug-loading potential. The solubility enhancement is a second important characteristic of nanoemulsions, which also have relatively low targeted-delivery potential and formulation stability. The drug-loading, targeted-delivery potential, and stability score of lipid nanoparticles (LNPs) are high. The targeted delivery properties are excellent and the solubility and bioavailability are also good, with the characteristics of drug-loading also being good in liposomes. Solid lipid nanoparticles (SLNs) exhibit relatively balanced qualities; they are relatively stable and have relatively lower drug loading capacity. In general, the table reflects specific functional benefits of lipid based nanocarriers⁶.

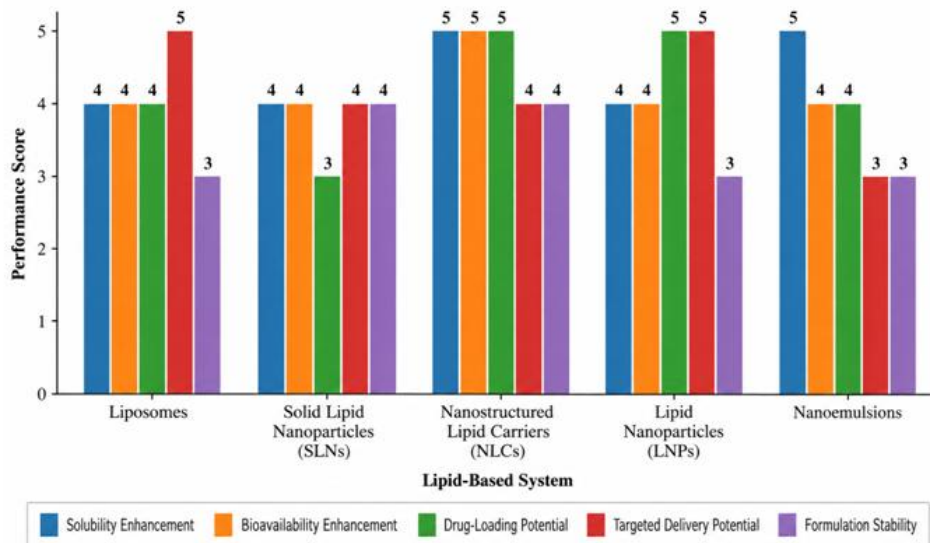


Figure 1. Comparative Performance of Major Lipid-Based Nanomedicine Systems

⁶ Makkar, S., Sharma, A., Rathore, C., Joshi, G., & Rawat, S. (2025). Recent update on applications of nanostructured lipid carriers and solid lipid nanocarriers in drug delivery systems: A narrative review. *Current Nanomedicine*, 15(5), 503–522. <https://doi.org/10.2174/0124681873299903240723112436> EurekaSelect



V. LIPID-BASED NANOMEDICINES: CONCEPT AND CLASSIFICATION

Nanomedicines are nanotechnology-based delivery systems containing mainly physiological, synthetic or semi-synthetic lipids and suitable stabilisers and, when needed, functional excipients. The physicochemical properties are highly related to their manufacturing process, morphology, particle size, surface charge, particle architecture, and lipid composition.⁷

Table 2. The big three lipid-based drug-delivery systems.

System	Basic structure	Major advantage	Important limitation
Liposomes	Phospholipid bilayer surrounding aqueous core	Encapsulation of hydrophilic and lipophilic agents	Leakage and physical instability can occur
SLNs	Predominantly solid lipid matrix	Controlled release and protection of incorporated drug	Crystallization may reduce drug loading
NLCs	Mixed solid and liquid lipid matrix	Higher loading and reduced drug expulsion	More complex formulation optimization
LNPs	Organized lipid particles, often containing ionizable lipids	Highly effective nucleic-acid delivery	Stability and biological interactions require careful control
Nanoemulsions	Nanoscale oil/water dispersion	Strong solubilization of lipophilic drugs	Physical instability may develop over time
Self-emulsifying systems	Lipid/surfactant mixtures forming fine dispersions in GI fluids	Enhanced oral delivery of poorly soluble drugs	Formulation depends strongly on drug/lipid compatibility

Recent reviews highlight the possibility of making lipid nanoformulations for both conventional drugs and therapeutic macromolecules. The use of manipulation of lipid composition and nanoscale structure has expanded the use of lipids from poorly soluble small molecules to proteins and nucleic-acid therapeutics progressively.

5.1 Liposomes

Liposomes are vesicles with a spherical shape formed by one or more phospholipid bilayers that encase an aqueous core. They are able to incorporate the hydrophilic drugs into the aqueous compartment and the hydrophobic ones into the lipid bilayer. PEG or targeting ligands can be applied on the surface to enhance circulation properties and receptor-mediated targeted drug delivery properties.⁸

5.2 Solid Lipid Nanoparticles

Solid lipid nanoparticles (SLNs) are composed of lipids which are solid at physiological temperature and are typically stabilized by a surfactant. They can be used for the protection of incorporated drugs, for sustained release and enhance

⁷ Alkhamach, D., Khan, S. A., Greish, K., Hassan, H. A. F. M., & Haider, M. (2025). Nanostructured lipid carriers in cancer therapy: Advances in passive and active targeting strategies. *International Journal of Pharmaceutics*, 678, 125736. <https://doi.org/10.1016/j.ijpharm.2025.125736> PubMed

⁸ Biswas, U. K., Bose, A., & Parmanik, A. (2025). Recent advances in the preparation, properties, and applications of solid lipid nanoparticles in drug delivery. *Pharmaceutical Nanotechnology*, 13(3), 512–527. <https://doi.org/10.2174/0122117385333634240911075833> PubMed



bioavailability and targeted delivery. However, over time, lipid crystallization may cause a decrease in drug loading capacity and therapeutic compounds expulsion from the liposome.⁹

5.3 Nanostructured Lipid Carriers

Nanostructured lipid carriers (NLCs) are carriers that are made from a mixture of solid and liquid lipids to create a less ordered lipid matrix. This matrix contains structural defects that can incorporate additional drug, and therefore have better loading capacity and lower drug expulsion. NLCs can be used to help deliver poorly soluble drugs with good release characteristics and stability.¹⁰

5.4 Lipid Nanoparticles

Advanced carriers for the intracellular delivery of nucleic acids are called lipid nanoparticles (LNPs). They typically include ionizable lipids, phospholipids, cholesterol and PEG lipids. Ionizable lipids help to encapsulate nucleic acids and allow for release within cells, enabling the delivery of therapeutic agents such as siRNA, mRNA, and components for gene editing¹¹.

5.5 Nanoemulsions and Self-Emulsifying Systems

Nanoemulsions are nano-scale dispersion of immiscible liquids stabilized with surfactant with special significance in solubilization of lipophilic drugs. Self-emulsifying systems are those that spontaneously make fine emulsified dispersions once they come in contact with gastrointestinal fluids. These formulations can help keep poorly water-soluble drugs in a solubilised form to aid dissolution and absorption from the gastrointestinal tract¹².

VI. TARGETED DRUG DELIVERY

Targeted delivery aims to maximise and optimise the amount of drug delivered to the desired tissues or cells, while minimising the exposure to other tissues or cells.

6.1 Passive Targeting

Passive targeting relies on physicochemical and pathophysiological properties and not on a specific ligand-receptor interaction. Accumulation could be influenced by particle size, circulation behavior, vascular permeability and clearance mechanisms.

The abnormal vasculature and enhanced permeability and retention concept are often talked about in the context of tumour delivery. The accumulation, however, is not homogenous among tumor types and patients and passive targeting should not, therefore, be considered to be universally successful.¹³

⁹ Bharti, S., Sharma, G., Sarwal, A., & Katare, O. P. (2026). Nano lipid carriers (NLCs): Potential and promises in drug delivery. *Critical Reviews in Therapeutic Drug Carrier Systems*, 43(1), 97–142. <https://doi.org/10.1615/CritRevTherDrugCarrierSyst.2025056948> PubMed

¹⁰ Biswas, U. K., Sen, S., Sharma, S., Paul, M., Nayak, A. K., & Bose, A. (2025). Nanostructured lipid carrier-based topical gels as novel drug delivery system: A comprehensive overview. *Current Drug Delivery*, 22(8), 1092–1111. <https://doi.org/10.2174/0115672018335655241015062436> PubMed

¹¹ Patel, D., Solanki, J., Kher, M. M., & Azagury, A. (2024). A review: Surface engineering of lipid-based drug delivery systems. *Small*, 20(43), e2401990. <https://doi.org/10.1002/smll.202401990> PubMed

¹² Mehraji, S., & DeVoe, D. L. (2024). Microfluidic synthesis of lipid-based nanoparticles for drug delivery: Recent advances and opportunities. *Lab on a Chip*, 24(5), 1154–1174. <https://doi.org/10.1039/D3LC00821E> PubMed

¹³ Godase, S. S., Kulkarni, N. S., & Dhole, S. N. (2024). A comprehensive review on novel lipid-based nano drug delivery. *Advanced Pharmaceutical Bulletin*, 14(1), 34–47. <https://doi.org/10.34172/apb.2024.012> PubMed



6.2 Active Targeting

Active targeting is the functionalization of the surface of the nanoparticle with a molecule present that targets a biological target.

Possible targeting ligands are:

antibodies and antibody fragments;

peptides;

folate;

carbohydrates;

aptamers; and

receptor-specific small molecules The basic strategy can be represented as:

The targeting ligand binds to the receptor, resulting in cellular association and internalization of the complex formed by the drug-loaded nanoparticle to the receptor. The targeting ligand recognizes the receptor, which leads to cellular association of the drug-nanoparticle complex¹⁴.

Surface engineering is therefore an important direction to research to modify the specificity, circulation and biological interaction of all lipid-based systems.¹⁵

6.3 Stimuli-Responsive Delivery

Advanced formulations can also react to internal and/or external stimuli, such as pH, enzymes, redox potential, temperature, light, magnetic field and ultrasound.

These strategies are designed to provide more controlled and targeted spatial and temporal drug delivery.

VII. CONCLUSION

Lipid-based nanomedicines are one of the most promising drug delivery systems used in today's era. Liposomes, SLNs, NLCs, LNPs, nanoemulsions and self-emulsifying systems are complementary approaches to address the challenges caused by poor aqueous solubility, poor stability, poor absorption, rapid clearance and poor tissue distribution.

Lipid carriers may keep poorly soluble drugs in solubilized or dispersed state and enhance the absorption condition for such pharmaceuticals. SLNs and NLCs can achieve drug protection and controlled release and the NLCs can give less ordered lipid matrix which can enhance loading properties. In contrast to liposomes which can encapsulate both hydrophilic and lipophilic compounds, modern LNPs are especially useful for delivering nucleic acids intracellularly.

The potential of these systems can be even further expanded by targeting strategies. However, the properties of the particles can affect passive biodistribution and surface ligands can promote receptor-mediated interactions. The use of stimuli responsive technologies could offer further control of drug release.

In a clinical application, lipid nanomedicine has been shown to be more than just an idea. Concurrently, there is a need for strict control of particle size, composition, drug loading, stability, release, biological interactions, manufacturing reproducibility, and safety in order to be successful as a translation. These specific factors are increasingly being acknowledged by regulatory guidance.

Going forward, designing more complicated nanoparticles is not enough; establishing reliable connections between the composition of the formulation, critical quality attributes, biological characteristics, therapeutic efficacy and manufacturability is essential. In the era of the modern era of lipid chemistry, microfluidics, computational formulation

¹⁴ Rehman, M., Tahir, N., Sohail, M. F., Qadri, M. U., Duarte, S. O. D., Brandão, P., Esteves, T., Javed, I., & Fonte, P. (2024). Lipid-based nanoformulations for drug delivery: An ongoing perspective. *Pharmaceutics*, 16(11), 1376. <https://doi.org/10.3390/pharmaceutics16111376> PubMed

¹⁵ Kumar, S., Singh, A., Pandey, P., Khopade, A., & Sawant, K. K. (2024). Application of sphingolipid-based nanocarriers in drug delivery: An overview. *Therapeutic Delivery*, 15(8), 619–637. <https://doi.org/10.1080/20415990.2024.2377066> PubMed



design, surface engineering and precision targeting, lipid-based nanomedicines are poised to continue to be an important platform for the advancement of delivery of conventional drugs and emerging biological therapeutics.

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