

Review Article

Lipid Nanocarrier Gel: Promising Novel Drug Delivery System



Shivam Singh^{1*}, Arpita Singh¹, Ritunja Singh¹, Anupama Maurya¹, Urmila Nishad¹, Priyanka Tyagi¹, Harshit Yadav¹

1. Department of Pharmaceutics, Seth Vishambhar Nath Institute of Pharmacy, Lucknow, India.

* Corresponding Author:

Shivam Singh

Address: Department of Pharmaceutics, Seth Vishambhar Nath Institute of Pharmacy, Lucknow, India.

Phone: +91 (931) 4782620

E-mail: shivamchotu08@gmail.com



Copyright © 2025 The Author(s);

This is an open access article distributed under the terms of the Creative Commons Attribution License (CC-BY-NC: <https://creativecommons.org/licenses/by-nc/4.0/legalcode.en>), which permits use, distribution, and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

Article info:

Received: 18 Mar 2025

Accepted: 03 May 2025

Keywords:

Nanocarrier, Lipid, Bioavailability, Lipid Nanocarriers (LNCs), Solid lipid nanoparticles (SLNs)

ABSTRACT

Background: Nanostructured lipid carriers (NLCs) are advanced colloidal drug delivery systems composed of a mixture of solid and liquid lipids. Compared to metallic or polymeric nanoparticles, NLCs are considered safer, non-toxic, and biocompatible, making them highly suitable for pharmaceutical applications.

Objectives: This study aimed to provide an in-depth overview of NLCs, focusing on their composition, structural characteristics, methods of preparation, advantages, and recent advancements, particularly in the formulation of lipid nanocarrier-based gels.

Methods: NLCs are formulated using various techniques, such as high-pressure homogenization, solvent evaporation, and microemulsion methods. These approaches, along with the use of appropriate solid and liquid lipids and surfactants, enable the customization of NLCs for specific therapeutic needs. The study reviewed recent literature to assess the performance and potential of NLCs in drug delivery.

Results: NLCs exhibit improved stability, enhanced drug loading, controlled and sustained drug release, and increased permeability of poorly water-soluble drugs. These characteristics make them effective for targeted delivery in the treatment of chronic and complex conditions, such as cancer, infections, neurological disorders, diabetes, hypertension, and pain management. Additionally, their application in gel-based formulations supports long-term treatment of skin and wound-related disorders.

Conclusion: Due to their biocompatibility, stability, and versatility, NLCs represent a promising platform for innovative drug delivery. However, comprehensive clinical evaluation of their long-term safety, toxicity, and bio-compatibility is essential. This review highlights the structure, classification, ingredients, formulation methods, and recent advancements in NLC technology, underlining their growing role in modern therapeutics.

Citation Singh Sh, Singh A, Singh R, Maurya A, Nishad U, Tyagi P. Lipid Nanocarrier Gel: Promising Novel Drug Delivery System. *Pharmaceutical and Biomedical Research*. 2025; 11(2):81-94. <http://dx.doi.org/10.32598/PBR.11.2.1378.1>

doi <http://dx.doi.org/10.32598/PBR.11.2.1378.1>

Introduction

In today's healthcare landscape, improving drug delivery requires innovative approaches that maximize therapeutic outcomes while minimizing side effects [1]. Traditional methods, such as oral tablets, injections, and topical creams deliver drugs without specialized carriers, which can lead to poor bioavailability, rapid clearance, and non-specific distribution [2-4]. For instance, oral drugs may degrade in the stomach or be cleared before reaching the target, reducing effectiveness. Lipids, commonly known as fats, are biologically important molecules involved in energy storage, membrane structure, and metabolic regulation [5, 6]. They include simple lipids (e.g. triglycerides, waxes), complex lipids (e.g. phospholipids), and related compounds, like sterols and fat-soluble vitamins. Their ability to dissolve in organic solvents while remaining insoluble in water has enabled their application in drug delivery systems [5]. Recently, lipids have been used to create nanoscale carriers that encapsulate active substances, offering protection and controlled release [7]. These lipid-based systems improve the delivery of drugs in medicine, cosmetics, and pharmacology [8, 9]. Lipid nanocarriers (LNCs) are an emerging class of drug delivery vehicles that combine lipid chemistry with nanotechnology to improve solubility, stability, and bioavailability of therapeutics [10]. Incorporating LNCs into gels results in lipid nanocarrier gels (LNC gels), which offer benefits, such as enhanced skin penetration, sustained drug release, and targeted delivery ideal for topical and transdermal use [11, 12].

Nanotechnology plays a major role across disciplines, particularly in enhancing drug delivery through precise targeting and efficient therapeutic action [13]. Nanocarriers, typically less than one micron in size, possess high surface-area-to-volume ratios and unique biodistribution profiles, making them suitable for diverse pharmaceutical applications [14, 15]. Their nanoscale properties allow for the modulation of drug kinetics, toxicity, and therapeutic index through surface and structural engineering [16]. However, despite progress, challenges, such as biological barriers, formulation complexity, and stability limit the widespread adoption of nanostructured lipid carriers (NLCs) [17-19]. NLCs are especially useful in chronic wound treatment, where sustained drug release is vital [20]. Their surface charge (zeta potential) and morphology (e.g. spheres, cones, and cylinders) significantly influence stability, targeting, and therapeutic performance [21, 22]. Nano-modification strategies are being explored to enhance drug action, especially in

wound healing applications [23]. NLCs protect therapeutic agents, provide controlled release, and improve drug absorption, making them effective for both synthetic and natural compounds [24, 25]. Preclinical and clinical research has demonstrated their ability to enhance wound healing outcomes by delivering consistent drug levels and supporting tissue regeneration [26, 27].

Composition of LNCs

LNCs, particularly NLCs, are composed of carefully selected lipids, surfactants, and other functional ingredients that collectively determine their physicochemical properties and therapeutic efficacy (Figure 1). The selection of lipids is critical, as their type and structure significantly influence the characteristics of the resulting nanoparticles, including stability, particle size, drug loading capacity, and release behavior [29]. Two important factors to consider during lipid selection are the solubility of the drug within the lipid matrix and the drug's partition coefficient, both of which affect encapsulation efficiency and the rate of drug release [30]. Additionally, the viscosity and melting point of the lipids play a crucial role in particle formation—lipids with higher viscosity and melting points tend to produce larger particles, impacting dispersion uniformity and system stability [31]. Surfactants are another key component in lipid nanocarrier systems. They serve multiple functions, most notably enhancing drug solubility, dissolution, and membrane permeability, which contributes to improved drug absorption and therapeutic outcomes [32]. The choice of surfactant is influenced by its hydrophilic-lipophilic balance (HLB), which affects not only emulsion formation but also particle size and the interaction between lipids and aqueous phases [33]. As emulsifiers, surfactants reduce the interfacial tension between lipid and water phases, promoting compatibility and preventing phase separation, thus enhancing the formulation's overall stability [34].

Furthermore, lipid crystallization behavior, modulated by surfactants and other factors, can influence the morphology, size, and surface characteristics of colloidal particles parameters that directly affect the nanocarrier's drug delivery performance and physical stability under varying conditions [35]. Beyond lipids and surfactants, other ingredients are often incorporated to enhance the performance of NLCs. Surface modifiers improve the physical stability and biocompatibility of the formulation while facilitating targeted drug delivery across epithelial barriers [36]. These surface modifications also contribute to immune evasion by reducing the likelihood of phagocytic uptake by macrophages in the reticuloen-

Structure of Nanostructured lipid carrier

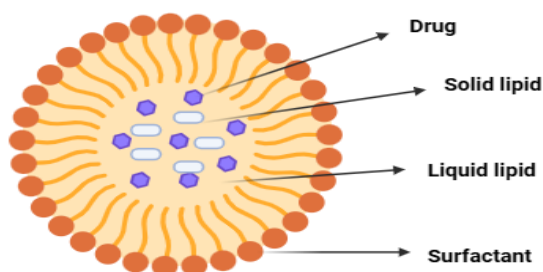


Figure 1. Structure of the nanostructured lipid carrier [28]

PBR

dothelial system (RES), thereby prolonging systemic circulation and enhancing therapeutic outcomes [37]. Because lipid-based drug delivery systems utilize biodegradable and biocompatible lipids, they are well-suited for applications requiring controlled drug release, targeted delivery, and protection of pharmaceuticals from degradation [38]. Moreover, these systems provide versatility in delivering a wide range of therapeutic agents, including growth factors, gene therapies, and cytokines offering more adaptability than traditional drug delivery methods [39]. They are also capable of targeting specific cells and tissues, enabling the delivery of complex therapeutic entities, such as nucleic acids, peptides, and proteins [40]. Lipid-based delivery systems can be broadly categorized into vesicular systems and lipid nanoparticles. Vesicular systems are formed when amphiphilic molecules self-assemble in aqueous environments into highly structured arrangements containing one or more concentric lipid bilayers [41]. Lipid nanoparticles, on the other hand, include several types, such as lipid-drug conjugates (LDCs), solid lipid nanoparticles (SLNs), and NLCs [42]. NLCs are further subclassified based on their internal structural organization into multiple oil/fat/

water (O/F/W) systems, amorphous types, and highly imperfect crystalline structures. These variations influence the drug loading capacity and release behavior of the formulation, making NLCs a highly adaptable platform for advanced drug delivery applications [29] (Figure 2, Tables 1 and 2).

Preparation method of LNCs

High-pressure homogenization techniques (hot and cold methods)

In the hot homogenization method, the drug is initially blended into a melted lipid mixture. At the same time, a heated surfactant solution is prepared. These two components are combined and processed using a high-pressure homogenizer, resulting in the formation of nanostructured lipid carriers. In the cold homogenization method, the drug is also first mixed with molten lipids, but this blend is rapidly cooled and then mechanically ground into fine particles. These particles are then mixed with a chilled surfactant solution and further processed under high pressure to yield the final nanocarriers.

Advantages of Nano Lipid Carrier

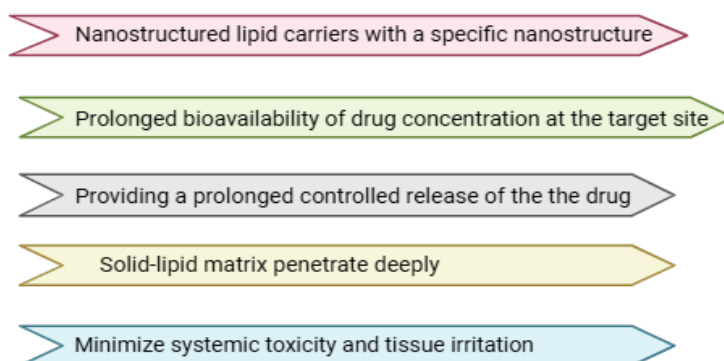


Figure 2. Advantages of nano-lipid carriers [19, 44]

PBR

Table 1. Ingredients used in LNCs

Component	Name	Ref.
Solid lipid	Polyethylene glycol monoesterate	[45]
	Monostearin	[46]
	Compritol	[47]
	Soy lecithin	[48]
	Olive oil	[49]
Liquid lipid	Coconut oil	[50]
	Isopropyl myristate	[51]
	Pumpkin seed oil	[52]
	Tween 80	[53]
Surfactant	Tween 20	[54]
	Poloxamer	[55]
	Lecithin	[28]

PBR

Solvent-based techniques (evaporation and diffusion)

The solvent evaporation technique involves dissolving the drug and lipid in a water-insoluble organic solvent, which is then combined with a surfactant solution. This mixture is heated to remove the solvent through evaporation, leading to the production of lipid nanoparticles. On the other hand, in the solvent diffusion method, the drug-lipid mixture is dissolved in a water-soluble organic solvent, and then blended with a surfactant solution. This mixture is diluted with water to initiate solvent diffusion.

The final nanocarrier formulation is obtained by drying the system through freeze-drying or filtration [61-64, 53] (Figure 3).

Lipid nano-carrier gel

Lipid core

Lipid molecules (micelles or liposomes) will be grouped in a spherical shape in the center. Phospholipids, which have hydrophilic heads and hydrophobic tails, would normally make up these lipids. A bilayer or monolayer

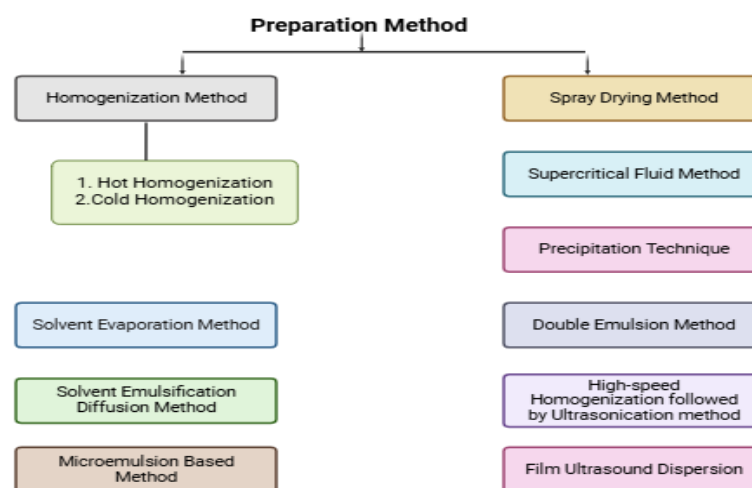
**Figure 3.** Preparation method**PBR**

Table 2. Characteristics of lipid-based nanocarriers [56-60]

Lipid Nanocarrier	Description	Components
Liposomes	Spherical vesicles with bilayer membranes enclosing aqueous cores	Natural/synthetic phospholipids (e.g. phosphatidylcholine, and sphingomyelin)
Ethosomes	Ethanol-rich liposomes enhancing skin penetration	Phospholipids, ethanol, cholesterol, and glycols
Transfersomes	Highly deformable vesicles that adapt to stress and penetrate deeply	Phospholipids, edge activators, surfactants, and alcohols
Cubosomes	Nanostructured particles with cubic liquid crystalline phases	Amphiphilic lipids and stabilizers
Niosomes	Non-ionic surfactant-based vesicles	Nonionic surfactants, cholesterol, and charge inducers
Glycerosomes	Glycerol-modified liposomes with improved flexibility	Phospholipids, glycerol, and water
Invasomes	Vesicles with penetration enhancers for deep skin delivery	Phosphatidylcholine, terpenes, and ethanol
Bilosomes	Bile salt-integrated vesicles resistant to GI tract conditions	Bile salts, nonionic surfactants, and cholesterol
Cerasomes	Ceramic-coated liposomes for improved stability	Polyorganosiloxane, phospholipids, polymers, and steroids
Phytosomes	Vesicles formed by complexing plant extracts with phospholipids	Phosphatidylcholine, plant extracts, and nonpolar solvents
Glycerosomes (elastic)	Glycerol-rich liposomes that hydrate the stratum corneum	Phospholipids, high-conc, glycerol, and water
Pharmacosomes	Drug-lipid conjugates forming vesicular systems	Drug-lipid esters and solvents
Emulsomes	Hybrid of liposomes and emulsions with solid/semi-solid lipid cores	Phospholipids, lipids, surfactants, and antioxidants
Photosomes	Light-activated liposomes releasing content upon irradiation	Light-sensitive lipids and solvents
Vesosomes	Multicompartment liposomes for extended drug release	Phospholipids, polymers, steroids, and solvents
Novasomes	Multilamellar vesicles with unique surfactants	Cholesterol, polyoxyethylene fatty acid esters, fatty acids, and solvents
Cryptosomes	Stealth liposomes containing poloxamers	Phospholipids, poloxamers
Hyalurosomes	Hyaluronan-containing vesicles aiding skin healing	Phospholipids and sodium hyaluronate
Nanoemulsions	Fine oil-water dispersions stabilized by surfactants	Oil, water, and surfactants
Solid lipid nanocarrier	Nanocarriers made from solid lipids dispersed in water	Solid lipids, triglycerides, fatty alcohols, and surfactants
Nanostructured lipid carriers	Mixed solid-liquid lipid carriers with disordered internal structure	Solid lipids, liquid lipids, emulsifiers, and water

PBR

structure is created with the hydrophilic heads oriented outward and the hydrophobic tails directed inward [28].

Encapsulated active ingredients

Inside the lipid core or in the surrounding gel matrix, there may be encapsulated substances, like drugs, vitamins, or other therapeutic agents. These molecules are usually hydrophobic and interact with the hydrophobic core of the lipid bilayer [65].

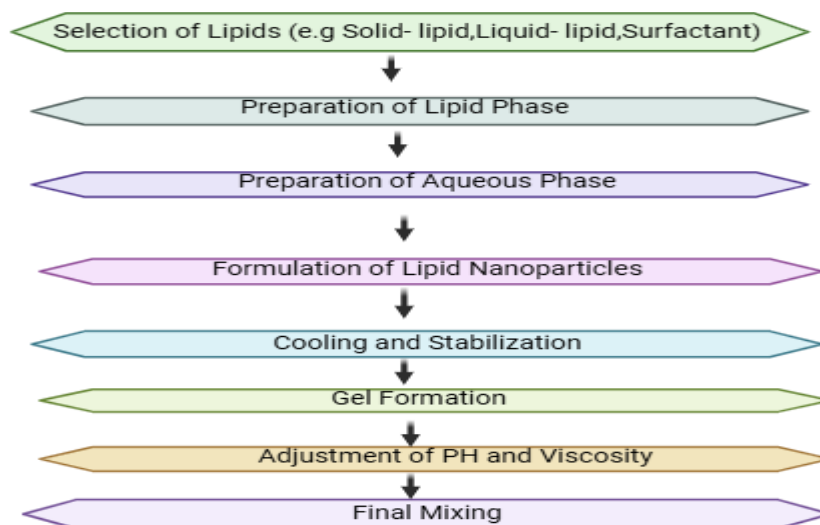
Gel matrix

Surrounding or embedding these lipid nanoparticles, the gel matrix could be a clear or slightly opaque net-

work, composed of polymers such as hydroxyethyl cellulose or carbomers. This gel structure aids in controlling the release of the encapsulated materials and stabilizing the lipid carriers [66].

Nanoscale size

The lipids themselves are nanoscale in size, resembling small, compact spheres or vesicles dispersed throughout the gel matrix. This would appear as a cloudy or translucent gel when viewed under a microscope [67] (Figure 4).

Flow Chart - Preparation of Lipid Nanocarrier Gel

Figure 4. Flow chart for the preparation of lipid nanocarrier gel

PBR

Advantages of lipid nanocarrier gels

LNC gels offer several significant advantages in drug delivery systems. One of the primary benefits is enhanced bioavailability. Drugs that are poorly water-soluble can achieve improved solubility and stability when incorporated into LNC gels, which leads to better absorption and more effective therapeutic outcomes [69]. These gels also enable targeted and controlled drug delivery. The release of the active substance can be precisely modulated through diffusion or stimuli-responsive mechanisms, such as pH or temperature sensitivity, ensuring the medication reaches the intended site efficiently [70]. Additionally, by encapsulating active agents within lipid carriers, LNC gels help reduce the toxicity of drugs and minimize adverse side effects [71]. LNC gels are particularly effective in enhancing skin penetration. Due to their nanoscale size, lipid carriers can transport drugs deeper into the skin, increasing efficacy in treating conditions, like psoriasis, acne, and localized pain [72, 73]. Furthermore, the lipid matrix protects the drug from environmental degradation, such as oxidation or enzymatic breakdown, enhancing the overall stability of the formulation [74].

Applications of LNC gels

LNC gels have wide-ranging applications in modern therapeutics and cosmetics. In topical drug delivery, they are highly valued for delivering medications directly to the skin to treat conditions, such as psoriasis, eczema,

fungal infections, and acne [75]. In transdermal drug delivery, these gels enable systemic absorption through the skin, offering a non-invasive alternative for managing conditions, like chronic pain and hormonal imbalances [76, 47]. The cosmetic industry also utilizes LNC gels due to their ability to protect and release active ingredients, such as vitamins and anti-aging compounds. These gels provide sustained delivery and better skin compatibility, making them suitable for skincare formulations [78, 79]. In oncology, LNC gels are being explored as targeted systems for localized delivery of anticancer drugs, reducing systemic side effects and improving drug accumulation at tumor sites [80].

Challenges and limitations

Despite their advantages, LNC gels present several challenges. One major limitation is the long-term stability of LNCs within gel formulations. Under certain storage conditions, issues, like phase separation and particle aggregation can compromise the system's effectiveness [81]. Additionally, the gel base and surfactants used may cause skin irritation in sensitive individuals, particularly with long-term use or high concentrations, necessitating thorough safety testing [66]. Scaling up production for commercial manufacturing also poses difficulties. Maintaining consistent particle size, drug distribution, and reproducibility on a large scale requires complex formulation controls [82]. Furthermore, regulatory hurdles exist for nanotechnology-based products. Agencies, such as the Food and Drug Administration (FDA) and European

Table 3. FDA-approved lipid nanocarrier-based formulations [35, 69]

Lipid Nanocarrier Type	Brand Name	Drug	Route	Indication
Vesicular (liposomes)	AmBisome	Amphotericin B	Intravenous	Fungal infections, visceral leishmaniasis
	Doxil	Doxorubicin	Intravenous	Breast & ovarian cancer, multiple myeloma, Kaposi's sarcoma
	Amphotec	Amphotericin B	Intravenous	Fungal infections, invasive aspergillosis, leishmaniasis
Nonvesicular (nanoemulsions)	Ropion	Flurbiprofen axetil	Intravenous	Osteoarthritis and rheumatoid arthritis symptoms
	Lipfen	Flurbiprofen axetil	Oral	Osteoarthritis and rheumatoid arthritis symptoms
	Cleviprex	Clevidipine	Intravenous	Hypertension

PBR

Medicines Agency (EMA) demand extensive safety and efficacy data before approving new nano-formulations for clinical use [83] (Table 3).

Recent advancements

Indomethacin-loaded NLCs (IND-NLC) demonstrated exceptional encapsulation efficiency of over 99%, with a low polydispersity index (PDI=0.139), a particle size of 168.1 nm, and a surface charge of -30.1 mV. The formulation maintained its stability for over 60 days at both 4 °C and 25 °C. At a dose of 15.7 µM, IND-NLC exhibited potent anticancer activity by significantly inhibiting the proliferation of MDA-MB-468 breast cancer cells,

confirming its potential as an effective anticancer drug delivery system [84].

Thymol-loaded NLCs were incorporated into various gel formulations to enable sustained release. Among these, carbomer-based gels showed superior skin retention, especially within the dermis and epidermis. While the NLC-thymol gels displayed prolonged efficacy against *Cutibacterium acnes*, their performance against *Staphylococcus epidermidis* was slightly lower than that of free thymol. Nonetheless, the thymol-loaded NLC gel formulation successfully maintained beneficial skin microbiota, establishing its potential as a promising topical therapy for acne vulgaris [76].

Table 4. Market formulation of LNCs and clinical trials [90-101]

LNC Type	Active Substance	Disease	Product(s)/Clinical Trial(s)	Description
Nanostructured lipid carriers	Acitretin	Psoriasis	Acitretin NLC (precirrol ATO 5/oleic acid/tween 80) (RCT)	Treats chronic skin conditions with improved delivery and less irritation
	All-trans retinoic acid	Keratinization disorders	NLCs with oleic acid, cetyl palmitate, cineole, etc.	Enhances delivery for treating rough/scaly skin
	Self-amplifying RNA (saRNA)	COVID-19 vaccine	THEMBA II T-cell vaccine (phase I/II trial)	Advanced RNA vaccine with higher potency at lower dose
Solid lipid nanoparticles	Mitoxantrone	Hepatocarcinoma	DHAD-PBCA-NPs (phase II clinical trial)	Targeted cancer therapy with reduced systemic toxicity
	Oxiconazole	Fungal infection (tinea)	Oxiconazole-loaded SLN gel (phase I clinical trial)	Improved skin delivery for antifungal treatment
	siRNA (patisiran)	Amyloidosis	Onpattro (FDA-approved)	First RNAi drug for rare protein disorder
Lipid-polymer hybrid NPs	Docetaxel	Pancreatic cancer	Docetaxel polymeric nanoparticle (phase I clinical trial)	Boosts chemo with prolonged circulation
	Docetaxel	Lung cancer (KRAS mutation)	BIND-014 (phase II clinical trial)	Mutation-specific targeted delivery
	Docetaxel	Prostate cancer	BIND-014 (phase II clinical trial)	Precise and sustained chemotherapy
Nanoemulsions	Etomidate/Propofol	Anesthesia	Etomidat-Lipuro, diprivan	Fast-acting, safe anesthetic formulations
	Ibuprofen	Pain relief	Ibuprofen nanoemulsion gel	Localized topical relief with fast absorption
	Ritonavir	HIV-1 (children)	Norvir	Pediatric-friendly HIV treatment with enhanced bioavailability

PBR

Magnolol-loaded NLCs (MA-NLC) were successfully synthesized with a particle size of 19.67 nm, a PDI of 0.21, and a zeta potential of -5.18 mV. These physicochemical properties contributed to enhanced safety and reduced pulmonary irritation. When administered via nebulization, MA-NLC showed improved lung targeting and prolonged retention, effectively overcoming issues related to low solubility and bioavailability. In animal models of chronic obstructive pulmonary disease (COPD), MA-NLC significantly improved oxidative stress markers and reduced inflammation, highlighting its therapeutic promise [85].

Bergenin-loaded NLCs (BNNLCo) were developed to enhance oral drug delivery efficiency. The formulation achieved an encapsulation efficiency of 80.6%, with a particle size of 174.3 nm, a PDI of 0.086, and a zeta potential of -35.6 mV. Compared to pure bergenin, BNNLCo demonstrated a 4.27-fold increase in relative bioavailability, a 3.2-fold enhancement in intestinal permeability, and a sustained drug release profile of 74.2% over 12 hours. Additionally, it achieved significant edema reduction (71.78% at 6 hours) and maintained prolonged therapeutic effects, suggesting its value in improving oral treatment outcomes [86].

Quercetin-loaded NLCs incorporated into chitosan hydrogels showed over 95% encapsulation efficiency and excellent long-term stability, retaining 88.63% of quercetin after ten months under natural daylight. Electrostatic interactions helped stabilize the NLCs within the chitosan matrix. In vitro studies demonstrated improved skin penetration and greater deposition of hydrophobic active compounds, establishing the NLC–chitosan hydrogel system as a promising vehicle for topical drug delivery [77].

Ketoconazole (KTZ)-loaded NLCs exhibited significantly improved retention in the skin, including a 2.58-fold increase in the stratum corneum, a 6.35-fold rise in the viable epidermis, and a 6.41-fold enhancement in transdermal permeation. The formulation displayed strong antifungal activity with effective inhibition of *Candida albicans* in planktonic, hyphal, and biofilm phases. NLC-based hydrogels also offered optimal spreadability, shear-thinning behavior, and minimal cytotoxicity on human skin fibroblasts, supporting their use in candidiasis treatment [87].

Luteolin-loaded NLCs (LUT-NLC) showed sustained drug release for up to 36 hours, with a particle size of 199.9 nm and encapsulation efficiency of 99.81%. Compared to conventional luteolin gel, LUT-NLC demon-

strated superior skin penetration (78.89 $\mu\text{g}/\text{cm}^2$). Fluorescent dye-tracking confirmed drug accumulation in the dermis, epidermis, and hair follicles. In an imiquimod-induced psoriasis model, LUT-NLC gels significantly reduced inflammatory cytokines (TNF- α , IL-6, IL-17, and IL-23) and alleviated both cutaneous and systemic symptoms, making it a promising therapeutic for psoriasis [88].

Zingiber officinale extract (ZOE)-loaded NLCs displayed excellent stability at 0.4% concentration, with particle sizes ranging from 302–344 nm and PDI values between 0.14 and 0.23 over 28 days. At 2% ZOE concentration, high encapsulation efficiency was achieved. Morphological assessments revealed well-formed, uniformly distributed particles. Compared to conventional topical formulations, ZOE-NLC gels exhibited enhanced rheological properties and improved stability, reinforcing their potential for effective topical drug delivery [89] (Table 4).

Conclusion

Featuring several uses in dermatology, cosmetics, and pharmaceuticals, LNC gels are a promising and adaptable drug delivery technology. LNC gels can enhance a range of pharmaceuticals' solubility, stability, and effectiveness by combining the benefits of LNCs with the stability and controlled-release characteristics of gel matrices. Even while issues, like scalability, stability, and skin irritation still exist, more research and technical developments might eventually allow LNC gels to reach their full clinical and commercial potential. NLCs have been shown to greatly increase the effectiveness of drugs used to promote wound healing. Numerous studies demonstrate that NLCs are efficient at carrying a range of materials, such as hydrophobic chemicals, essential oils, plant extracts, and physiologically active molecules, like proteins and nucleic acids, which are essential for the repair of wounds. NLCs speed up wound healing and regeneration by improving these chemicals' stability, absorption, and regulated release. NLC formulations are flexible enough to be customized to meet individual therapeutic demands since they may include a range of surfactants, lipids, and preparations, both liquid and solid techniques, such solvent evaporation, high-pressure homogenization, and microemulsion procedures. Because NLCs may administer medications at a steady, sustained pace, they are very useful for treating chronic wounds that need prolonged therapy periods. To investigate the usage of NLCs for a larger variety of medications, including more recent synthetic and natural substances, more study is necessary. Furthermore, thorough safety

to ensure the long-term security and efficacy of NLCs, research is required, particularly in the management of long-term injuries, like as burns, diabetic ulcers, and other chronic wounds.

Ethical Considerations

Compliance with ethical guidelines

As this is a review article, there were no ethical issues or human/animal involvement requiring ethical approval.

Funding

This study did not receive financial support from any public, private, or non-profit funding organizations.

Authors' contributions

All authors equally participated in the study's conception, design, data acquisition and analysis, interpretation of findings, and preparation of the manuscript.

Conflict of interest

The authors declared no conflict of interest.

References

- [1] Ezike TC, Okpala US, Onoja UL, Nwike CP, Ezeako EC, Okpara OJ, et al. Advances in drug delivery systems, challenges and future directions. *Heliyon*. 2023; 9(6):e17488. [DOI:10.1016/j.heliyon.2023.e17488] [PMID]
- [2] Jain KK. Drug delivery systems - an overview. *Methods Mol Biol*. 2008; 437:1-50. [DOI:10.1007/978-1-59745-210-6_1] [PMID]
- [3] Homayun B, Lin X, Choi HJ. Challenges and recent progress in oral drug delivery systems for biopharmaceuticals. *Pharmaceutics*. 2019; 11(3):129. [DOI:10.3390/pharmaceutics11030129] [PMID]
- [4] Lee VH, Dodda-Kashi S, Grass GM, Rubas W. Oral route of peptide and protein drug delivery. In: Lee V, editor. *Peptide and protein drug delivery*. Boca Raton: CRC Press; 2024. [DOI:10.1201/9781003573715-18]
- [5] Duché G, Sanderson JM. The chemical reactivity of membrane lipids. *Chem Rev*. 2024; 124(6):3284-30. [DOI:10.1021/acs.chemrev.3c00608] [PMID]
- [6] Reszcyńska E, Hanaka A. Lipids composition in plant membranes. *Cell Biochem Biophys*. 2020; 78(4):401-14. [DOI:10.1007/s12013-020-00947-w] [PMID]
- [7] Ren R, Lim C, Li S, Wang Y, Song J, Lin TW, et al. Recent advances in the development of lipid-, metal-, carbon-, and polymer-based nanomaterials for antibacterial applications. *Nanomaterials*. 2022; 12(21):3855. [DOI:10.3390/nano12213855] [PMID]
- [8] Sonawane D, Pokharkar V. Quercetin-loaded nanostructured lipid carrier in situ gel for brain targeting through intranasal route: formulation, in vivo pharmacokinetic and pharmacodynamic studies. *AAPS PharmSciTech*. 2024; 25(2):30. [DOI:10.1208/s12249-024-02736-7] [PMID]
- [9] Iqbal MA, Md S, Sahni JK, Baboota S, Dang S, Ali J. Nanostructured lipid carriers system: Recent advances in drug delivery. *J Drug Target*. 2012; 20(10):813-30. [DOI:10.3109/1061186X.2012.716845] [PMID]
- [10] Khan S, Sharma A, Jain V. An overview of nanostructured lipid carriers and its application in drug delivery through different routes. *Adv Pharm Bull*. 2023; 13(3):446-60. [DOI:10.34172/apb.2023.056] [PMID]
- [11] Gilani SJ, Jumah MNB, Zafar A, Imam SS, Yasir M, Khalid M, et al. Formulation and evaluation of nano lipid carrier-based ocular gel system: Optimization to antibacterial activity. *Gels*. 2022; 8(5):255. [DOI:10.3390/gels8050255] [PMID]
- [12] Kumbhar PS, Manjappa AS, Shah RR, Nadaf SJ, Disouza JI. Nanostructured lipid carrier-based gel for repurposing simvastatin in localized treatment of breast cancer: formulation design, development, and in vitro and in vivo characterization. *AAPS PharmSciTech*. 2023; 24(5):106. [DOI:10.1208/s12249-023-02565-0] [PMID]
- [13] Saxena SK, Nyodu R, Kumar S, Maurya VK. Current advances in nanotechnology and medicine. In: Saxena SK, Khurana SMP, editors. *NanoBioMedicine*. New York: Springer; 2020. [DOI:10.1007/978-981-32-9898-9_1]
- [14] Majumder J, Taratula O, Minko T. Nanocarrier-based systems for targeted and site specific therapeutic delivery. *Adv Drug Deliv Rev*. 2019; 144:57-77. [DOI:10.1016/j.addr.2019.07.010] [PMID]
- [15] Wu H, Tang L, Dong H, Zhi M, Guo L, Hong X, et al. Shape and size dependence of pharmacokinetics, biodistribution, and toxicity of gold nanoparticles. *Mol Pharm*. 2025; 22(1):196-208. [DOI:10.1021/acs.molpharmaceut.4c00832] [PMID]
- [16] Bourquin J, Milosevic A, Hauser D, Lehner R, Blank F, Petri-Fink A, et al. Biodistribution, clearance, and long-term fate of clinically relevant nanomaterials. *Adv Mater*. 2018; 30(19):e1704307. [DOI:10.1002/adma.201704307] [PMID]
- [17] Jaiswal P, Gidwani B, Vyas A. Nanostructured lipid carriers and their current application in targeted drug delivery. *Artif Cells Nanomed Biotechnol*. 2016; 44(1):27-40. [DOI:10.3109/21691401.2014.909822] [PMID]
- [18] Singhvi G, Patil S, Girdhar V, Dubey SK. Nanocarriers for topical drug delivery: Approaches and advancements. *Nanosci Nanotechnol Asia*. 2019; 9(3):329-36. [DOI:10.2174/2210681208666180320122534]
- [19] Mall J, Naseem N, Haider MF, Rahman MA, Khan S, Siddiqui SN. Nanostructured lipid carriers as a drug delivery system: A comprehensive review with therapeutic applications. *Intelligent Pharm*. 2024 [Unpublished]. [DOI:10.1016/j.iph.2024.09.005]

- [20] Ullah A, Ullah M, Lee GJ, Lim SI. A review of recent advances in nanotechnology for the delivery of therapeutics in wound healing. *J Pharm Invest.* 2024; 55:33-54. [DOI:10.1007/s40005-024-00692-9]
- [21] Shrestha S, Wang B, Dutta P. Nanoparticle processing: Understanding and controlling aggregation. *Adv Colloid Interface Sci.* 2020; 279:102162. [DOI:10.1016/j.cis.2020.102162] [PMID]
- [22] Stolarczyk JK, Deak A, Brougham DF. Nanoparticle assemblies: nanoparticle clusters: Assembly and control over internal order, current capabilities, and future potential (*Adv. Mater.* 27/2016). *Adv Mater.* 2016; 28(27):5764. [DOI:10.1002/adma.201505350] [PMID]
- [23] Wang W, Lu KJ, Yu CH, Huang QL, Du YZ. Nano-drug delivery systems in wound treatment and skin regeneration. *J Nanobiotechnology.* 2019; 17(1):82. [DOI:10.1186/s12951-019-0514-y] [PMID]
- [24] Beloqui A, Solinís MÁ, Rodríguez-Gascón A, Almeida AJ, Prést V. Nanostructured lipid carriers: Promising drug delivery systems for future clinics. *Nanomedicine.* 2016; 12(1):143-61. [DOI:10.1016/j.nano.2015.09.004] [PMID]
- [25] Goel R, Mishra R, Singh N, Rajora A, Singh R, Gaur PK. Nanostructured lipid carriers: Enhancing herbal medicine delivery. In: Baghel Chauhan S, Singh I, Singh Grewal A, Kaur R, editors. *Lipid based nanocarriers for drug delivery.* New York: Nova; 2024. [Link]
- [26] Faheem S, Hameed H, Paiva-Santos AC, Zaman M, Sarwar HS, Majeed I. Niosome-based gels: A smart nano-carrier for effective and advanced transdermal drug delivery. *Int J Polym Mater Polym Biomater.* 2024; 74.4:1-9. [DOI:10.1080/00914037.2024.2335169]
- [27] Abdel-Mageed HM, Abd El Aziz AE, Mohamed SA, AbuelEzz NZ. The tiny big world of solid lipid nanoparticles and nanostructured lipid carriers: an updated review. *J Microencapsul.* 2022; 39(1):72-94. [DOI:10.1080/02652048.2021.2021307] [PMID]
- [28] Wathoni N, Suhandi C, Elamin KM, Lesmana R, Hasan N, Mohammed AFA, et al. Advancements and challenges of nanostructured lipid carriers for wound healing applications. *Int J Nanomedicine.* 2024; 19:8091-113. [DOI:10.2147/IJN.S478964] [PMID]
- [29] Tamjidi F, Shahedi M, Varshosaz J, Nasirpour A. Nanostructured lipid carriers (NLC): A potential delivery system for bioactive food molecules. *Innov Food Sci Emerg Technol.* 2013; 19:29-43. [DOI:10.1016/j.ifset.2013.03.002]
- [30] Pan Y, Tikekar RV, Nitin N. Distribution of a model bioactive within solid lipid nanoparticles and nanostructured lipid carriers influences its loading efficiency and oxidative stability. *Int J Pharm.* 2016; 511(1):322-30. [DOI:10.1016/j.jip-harm.2016.07.019] [PMID]
- [31] Westesen K. Novel lipid-based colloidal dispersions as potential drug administration systems-expectations and reality. *Colloid Polym Sci.* 2000; 278:608-18. [DOI:10.1007/s003969900257]
- [32] Souto EB, Baldim I, Oliveira WP, Rao R, Yadav N, Gama FM, et al. SLN and NLC for topical, dermal, and transdermal drug delivery. *Expert Opin Drug Deliv.* 2020; 17(3):357-77. [DOI:10.1080/17425247.2020.1727883] [PMID]
- [33] Hogarth C, Arnold K, Wright S, Elkateb H, Rannard S, McDonald TO. Navigating the challenges of lipid nanoparticle formulation: The role of unpegylated lipid surfactants in enhancing drug loading and stability. *Nanoscale Adv.* 2023; 6(2):669-79. [DOI:10.1039/D3NA00484H] [PMID]
- [34] Das R, Mallik N, Adhikari A, Bhattarai A. A comprehensive review on the creation, description, and utilization of surfactants containing multiple hydroxyl groups. *Int J Polym Sci.* 2024; 2024(1):6120535. [DOI:10.1155/2024/6120535]
- [35] Mittal P, Singla M, Smriti, Kapoor R, Kumar D, Gupta S, et al. Paclitaxel loaded Capmul MCM and tristearin based nanostructured lipid carriers (NLCs) for glioblastoma treatment: Screening of formulation components by quality by design (QbD) approach. *Discov Nano.* 2024; 19(1):175. [DOI:10.1186/s11671-024-04132-3] [PMID]
- [36] Xie Y, Li P, Fu D, Yang F, Sui X, Huang B, et al. CBD-loaded nanostructured lipid carriers: Optimization, characterization, and stability. *ACS Omega.* 2024; 9(39):40632-43. [DOI:10.1021/acsomega.4c04771] [PMID]
- [37] Patel D, Solanki J, Kher MM, Azagury A. A review: Surface engineering of lipid-based drug delivery systems. *Small.* 2024; 20(43):e2401990. [DOI:10.1002/smll.202401990] [PMID]
- [38] Satapathy BS, Mishra A, Mohanty K, Pattnaik S, Tripathy S, Biswal B. Lipid nanocarrier-based bigel of piper betel oil for analgesic and anti-inflammatory applications. *J Microencapsul.* 2025; 42(1):47-69. [DOI:10.1080/02652048.2024.2430651] [PMID]
- [39] Li H, Lin Z, Ouyang L, Lin C, Zeng R, Liu G, et al. Lipid nanoparticle: Advanced drug delivery systems for promotion of angiogenesis in diabetic wounds. *J Liposome Res.* 2025; 35(1):76-85. [DOI:10.1080/08982104.2024.2378962] [PMID]
- [40] Lin Y, Chen X, Wang K, Liang L, Zhang H. An overview of nanoparticle-based delivery platforms for mRNA vaccines for treating cancer. *Vaccines.* 2024; 12(7):727. [DOI:10.3390/vaccines12070727] [PMID]
- [41] Kang Y, Zhang S, Wang G, Yan Z, Wu G, Tang L, et al. Nanocarrier-based transdermal drug delivery systems for dermatological therapy. *Pharmaceutics.* 2024; 16(11):1384. [DOI:10.3390/pharmaceutics16111384] [PMID]
- [42] Arora R, Katiyar SS, Kushwah V, Jain S. Solid lipid nanoparticles and nanostructured lipid carrier-based nanotherapeutics in treatment of psoriasis: A comparative study. *Expert Opin Drug Deliv.* 2017; 14(2):165-77. [DOI:10.1080/17425247.2017.1264386] [PMID]
- [43] Singhal GB, Patel RP, Prajapati BG, Patel NA. Solid lipid nanoparticles and nano lipid carriers: As novel solid lipid based drug carrier. *Int Res J Pharm.* 2011; 2(2):20-52. [Link]
- [44] Schoenfelder H, Wiedemann Y, Lunter DJ. Development and characterization of topical formulation for maintenance therapy containing sorbitan monostearate with and without PEG-100-stearate. *Int J Cosmet Sci.* 2025; 47(2):223-33. [DOI:10.1111/ics.13023] [PMID]
- [45] Wang Y, Deng Y, Mao S, Jin S, Wang J, Bi D. Characterization and body distribution of beta-elemene solid lipid nanoparticles (SLN). *Drug Dev Ind Pharm.* 2005; 31(8):769-78. [DOI:10.1080/03639040500216329] [PMID]

- [46] D'Souza A, Shegokar R. Nanostructured lipid carriers (NLCs) for drug delivery: Role of liquid lipid (oil). *Curr Drug Deliv.* 2021; 18(3):249-70. [DOI:10.2174/1567201817666200423083807] [PMID]
- [47] Arezoumand KS, Alizadeh E, Esmaeillou M, Ghasemi M, Alipour S, Pilehvar-Soltanahmadi Y, Zarghami N. The emu oil emulsified in egg lecithin and butylated hydroxytoluene enhanced the proliferation, stemness gene expression, and in vitro wound healing of adipose-derived stem cells. *In Vitro Cell Dev Biol Anim.* 2018; 54(3):205-16. [DOI:10.1007/s11626-018-0228-8] [PMID]
- [48] Dobрева M, Stefanov S, Andonova V. Natural lipids as structural components of solid lipid nanoparticles and nanostructured lipid carriers for topical delivery. *Curr Pharm Des.* 2020; 26(36):4524-35. [DOI:10.2174/138161282666200514221649] [PMID]
- [49] Dalwadi S, Thakkar V, Prajapati B. Optimizing neuroprotective nano-structured lipid carriers for transdermal delivery through artificial neural network. *Pharm Nanotechnol.* 2025; 13(1):184-98. [DOI:10.2174/0122117385294969240326052312] [PMID]
- [50] Fitriani EW, Avanti C, Rosana Y, Surini S. Nanostructured lipid carriers: A prospective dermal drug delivery system for natural active ingredients. *Pharmacia.* 2024; 71:e115849. [DOI:10.3897/pharmacia.71.e115849]
- [51] Ahmed OAA, Fahmy UA, Bakhaidar R, El-Moselhy MA, Alfaleh MA, Ahmed AF, et al. Pumpkin oil-based nanostructured lipid carrier system for antiulcer effect in NSAID-induced gastric ulcer model in rats. *Int J Nanomedicine.* 2020; 15:2529-39. [DOI:10.2147/IJN.S247252] [PMID]
- [52] Alatawi HM, Alhwiti SS, Alsharif KA, Albalawi SS, Abu-saleh SM, Sror GK, et al. Nanostructured lipid carriers (NLCs) as effective drug delivery systems: Methods of preparation and their therapeutic applications. *Recent Pat Nanotechnol.* 2024; 18(2):179-89. [DOI:10.2174/1872210517666230120142439] [PMID]
- [53] Kanojiya PS, Wadettwar RN, Atole PG, Thakrani KC, Gawande NP. Sustained delivery of statistically optimized transdermal gel of miconazole nitrate for vaginal candidiasis. *J Dispers Sci Technol.* 2025; 46(2):333-50. [DOI:10.1080/01932691.2023.2289621]
- [54] Elbardisy B, Boraie N, Galal S. Tadalafil nanoemulsion mists for treatment of pediatric pulmonary hypertension via nebulization. *Pharmaceutics.* 2022; 14(12):2717. [DOI:10.3390/pharmaceutics14122717] [PMID]
- [55] Gupta P, Mazumder R, Padhi S. Glycosomes: Advanced liposomal drug delivery system. *Indian J Pharm Sci.* 2020; 82(3):385-97. [DOI:10.36468/pharmaceutical-sciences.661]
- [56] Karami Z, Saghatchi Zanjani MR, Hamidi M. Nanoemulsions in CNS drug delivery: Recent developments, impacts and challenges. *Drug Discov Today.* 2019; 24(5):1104-115. [DOI:10.1016/j.drudis.2019.03.021] [PMID]
- [57] Khosa A, Reddi S, Saha RN. Nanostructured lipid carriers for site-specific drug delivery. *Biomed Pharmacother.* 2018; 103:598-613. [DOI:10.1016/j.biopha.2018.04.055] [PMID]
- [58] Tan C, Hosseini SF, Jafari SM. Cubosomes and hexosomes as novel nanocarriers for bioactive compounds. *J Agric Food Chem.* 2022; 70(5):1423-37. [DOI:10.1021/acs.jafc.1c06747] [PMID]
- [59] Lohumi A. A novel drug delivery system: Niosomes review. *J Drug Deliv Ther.* 2012; 2(5):129-35. [DOI:10.22270/jddt.v2i5.274]
- [60] Chinthaginjala H, Bogavalli V, Hindustan AA, Pathakamuri J, Pullaganti SS, Gowni A, et al. Nanostructured lipid carriers: A potential era of drug delivery systems. *Ind J Pharm Educ Res.* 2024; 58(1):21-33. [DOI:10.5530/ijper.58.1.3]
- [61] Qian L, Cook MT, Dreiss CA. In situ gels for nasal delivery: Formulation, characterization and applications. *Macromolecular Materials and Engineering.* 2025; 2400356. [DOI:10.1002/mame.202400356]
- [62] Jahan S, Aqil M, Ahad A, Imam SS, Waheed A, Qadir A, et al. Nanostructured lipid carrier for transdermal gliclazide delivery: Development and optimization by box-behnken design. *Inorganic and Nano-Metal Chemistry.* 2024; 54(5):474-87. [DOI:10.1080/24701556.2021.2025097]
- [63] Soni S, Maheshwari RK, Sah AK. Nanostructured lipid carrier: Beneficial role in oral drug delivery system. *BioNanoScience.* 2024; 14:3988-4005. [DOI:10.1007/s12668-024-01416-x]
- [64] Duong VA, Nguyen TT, Maeng HJ. Preparation of solid lipid nanoparticles and nanostructured lipid carriers for drug delivery and the effects of preparation parameters of solvent injection method. *Molecules.* 2020; 25(20):4781. [DOI:10.3390/molecules25204781] [PMID]
- [65] Munir M, Zaman M, Waqar MA, Khan MA, Alvi MN. Solid lipid nanoparticles: A versatile approach for controlled release and targeted drug delivery. *J Liposome Res.* 2024; 34(2):335-48. [DOI:10.1080/08982104.2023.2268711] [PMID]
- [66] Swami AB, Nagoba SN. Design, development and optimization of nanostructured lipid carrier containing anticancer drug. *Afr J Biomed Res.* 2024; 27(s3):1406-15. [DOI:10.53555/AJBR.v27i3S.2312]
- [67] Taher SS, Al-Kinani KK. In vivo brain pharmacokinetics of dolutegravir sodium-loaded nanostructured lipid carrier in situ gel: Comparative study with an intravenous drug solution. *Al-Rafidain J Med Sci.* 2025; 8(1):115-25. [DOI:10.54133/ajms.v8i1.1692]
- [68] Singh A, Iqbal MK, Mittal S, Qizilbash FF, Sartaz A, Kumar S, et al. Designing and evaluation of dermal targeted combinatorial nanostructured lipid carrier gel loaded with curcumin and resveratrol for accelerating cutaneous wound healing. *Particulate Sci Technol.* 2024; 42(1):88-106. [DOI:10.1080/02726351.2023.2205348]
- [69] Domingues Bianchin M, Borowicz SM, da Rosa Monte Machado G, Pippi B, Stanisçuaski Guterres S, et al. Lipid core nanoparticles as a broad strategy to reverse fluconazole resistance in multiple Candida species. *Colloids Surf B Biointerfaces.* 2019; 175:523-9. [DOI:10.1016/j.colsurfb.2018.12.011] [PMID]
- [70] Pal P, Sambhakar S, Paliwal S. Revolutionizing ophthalmic care: A review of ocular hydrogels from pathologies to therapeutic applications. *Curr Eye Res.* 2025; 50(1):1-17. [DOI:10.1080/02713683.2024.2396385] [PMID]
- [71] Yu G, Jie K, Huang F. Supramolecular amphiphiles based on host-guest molecular recognition motifs. *Chem Rev.* 2015; 115(15):7240-303. [DOI:10.1021/cr5005315] [PMID]

- [72] Ganta S, Talekar M, Singh A, Coleman TP, Amiji MM. Nanoemulsions in translational research-opportunities and challenges in targeted cancer therapy. *AAPS PharmSciTech*. 2014; 15(3):694-708. [DOI:10.1208/s12249-014-0088-9] [PMID]
- [73] Puri A, Loomis K, Smith B, Lee JH, Yavlovich A, Heldman E, et al. Lipid-based nanoparticles as pharmaceutical drug carriers: From concepts to clinic. *Crit Rev Ther Drug Carrier Syst*. 2009; 26(6):523-80. [DOI:10.1615/CritRevTherDrugCarrierSyst.v26.i6.10] [PMID]
- [74] Passos JS, Apolinario AC, Ishida K, Martins TS, Lopes LB. Nanostructured lipid carriers loaded into in situ gels for breast cancer local treatment. *Eur J Pharm Sci*. 2024; 192:106638. [DOI:10.1016/j.ejps.2023.106638] [PMID]
- [75] Elsewedy HS, Shehata TM, Genedy SM, Siddiq KM, Asiri BY, Alshammari RA, et al. Enhancing the topical antibacterial activity of fusidic acid via embedding into cinnamon oil nano-lipid carrier. *Gels*. 2024; 10(4):268. [DOI:10.3390/gels10040268] [PMID]
- [76] Folle C, Marqués AM, Díaz-Garrido N, Carvajal-Vidal P, Sánchez López E, Suñer-Carbó J, et al. Gel-dispersed nanostructured lipid carriers loading thymol designed for dermal pathologies. *Int J Nanomedicine*. 2024; 19:1225-48. [DOI:10.2147/IJN.S433686] [PMID]
- [77] Sun R, Xia Q, Sun Y. A novel strategy for topical administration by combining chitosan hydrogel beads with nanostructured lipid carriers: Preparation, characterization, and evaluation. *Gels*. 2024; 10(3):160. [DOI:10.3390/gels10030160] [PMID]
- [78] Jamshaid U, Anton N, Elhassan M, Conzatti G, Vandamme TF. Novel hydrogels based on the nano-emulsion formulation process: Development, rheological characterization, and study as a drug delivery system. *Pharmaceutics*. 2024; 16(6):812. [DOI:10.3390/pharmaceutics16060812] [PMID]
- [79] Ghasemiyeh P, Mohammadi-Samani S. Solid lipid nanoparticles and nanostructured lipid carriers as novel drug delivery systems: Applications, advantages and disadvantages. *Res Pharm Sci*. 2018; 13(4):288-303. [DOI:10.4103/1735-5362.235156] [PMID]
- [80] Zhang F, Zhang J, Zhang W. Recent advances in nanotechnology for the treatment of fungal keratitis. *Eur J Ophthalmol*. 2024; 34(1):18-29. [DOI:10.1177/11206721231174653] [PMID]
- [81] Mirza R, Shah KU, Khan AU, Fawad M, Rehman AU, Ahmed N, et al. Statistical design and optimization of nano-transfersomes based chitosan gel for transdermal delivery of cefepime. *Drug Dev Ind Pharm*. 2024; 50(6):511-23. [DOI:10.1080/03639045.2024.2353098] [PMID]
- [82] Moazeni M, Kelidari H, Kazeminejad A, Gholizadeh N, Haghani I, Saravani A, Parsay S, Nasirzadeh Y, Mofarragh R, Amini A. Addressing filamentous fungi-related onychomycosis in the era of antifungal resistance: Assessment of *Zataria multiflora* nanostructured lipid carrier topical gel in a double-blinded clinical trial. *Current Med Mycol*. 2025; 11. [Link]
- [83] Montenegro L, Lai F, Offerta A, Sarpietro MG, Micicche L, Maccioni AM, Valenti D, Fadda AM. From nanoemulsions to nanostructured lipid carriers: A relevant development in dermal delivery of drugs and cosmetics. *J Drug Deliv Sci Technol*. 2016; 32:100-12. [DOI:10.1016/j.jddst.2015.10.003]
- [84] Thiruchenthoooran V, Espina M, Świtalska M, Bonilla-Vidal L, Wietrzyk J, Garcia ML, et al. Combination of indomethacin with nanostructured lipid carriers for effective anticancer therapy. *Int J Nanomedicine*. 2024; 19:7033-48. [DOI:10.2147/IJN.S464239] [PMID]
- [85] Jia B, He J, Zhang Y, Dang W, Xing B, Yang M, et al. Pulmonary delivery of magnolol-loaded nanostructured lipid carriers for COPD treatment. *Int J Pharm*. 2024; 662:124495. [DOI:10.1016/j.ijpharm.2024.124495] [PMID]
- [86] Zafar A, Yasir M, Panda DS, Singh L. Bergenin nano-lipid carrier to improve the oral delivery: development, optimization, in vitro and in vivo evaluation. *J Drug Deliv Sci Technol*. 2024; 96:105655. [DOI:10.1016/j.jddst.2024.105655]
- [87] Chilamakuri SN, Kumar A, Nath AG, Gupta A, Selvaraju S, Basrani S, et al. Development and in-vitro evaluation of eugenol-based nanostructured lipid carriers for effectual topical treatment against *C. albicans*. *J Pharm Sci*. 2024; 113(3):772-84. [DOI:10.1016/j.xphs.2023.11.031] [PMID]
- [88] Xu H, Hu H, Zhao M, Shi C, Zhang X. Preparation of luteolin loaded nanostructured lipid carrier based gel and effect on psoriasis of mice. *Drug Deliv Transl Res*. 2024; 14(3):637-54. [DOI:10.1007/s13346-023-01418-4] [PMID]
- [89] Shazwani SS, Marlina A, Misran M. Development of nano-structured lipid carrier-loaded flavonoid-enriched zingiber officinale. *ACS Omega*. 2024; 9(15):17379-88. [DOI:10.1021/acsomega.4c00091] [PMID]
- [90] Agrawal Y, Petkar KC, Sawant KK. Development, evaluation and clinical studies of Acitretin loaded nanostructured lipid carriers for topical treatment of psoriasis. *Int J Pharm*. 2010; 401(1-2):93-102. [DOI:10.1016/j.ijpharm.2010.09.007] [PMID]
- [91] Charoenputtakun P, Pamornpathomkul B, Opanasopit P, Rojanarata T, Ngawhirunpat T. Terpene composited lipid nanoparticles for enhanced dermal delivery of all-trans-retinoic acids. *Biol Pharm Bull*. 2014; 37(7):1139-48. [DOI:10.1248/bpb.b14-00015] [PMID]
- [92] Hadinoto K, Sundaresan A, Cheow WS. Lipid-polymer hybrid nanoparticles as a new generation therapeutic delivery platform: A review. *Eur J Pharm Biopharm*. 2013; 85(3 Pt A):427-43. [DOI:10.1016/j.ejpb.2013.07.002] [PMID]
- [93] Zhou Q, Sun X, Zeng L, Liu J, Zhang Z. A randomized multicenter phase II clinical trial of mitoxantrone-loaded nanoparticles in the treatment of 108 patients with unresected hepatocellular carcinoma. *Nanomedicine*. 2009; 5(4):419-23. [DOI:10.1016/j.nano.2009.01.009] [PMID]
- [94] Holtze C. Large-scale droplet production in microfluidic devices an industrial perspective. *J Phys D*. 2013; 46(11):114008. [DOI:10.1088/0022-3727/46/11/114008]
- [95] Maeki M, Okada Y, Uno S, Sugiura K, Suzuki Y, Okuda K, et al. Mass production system for RNA-loaded lipid nanoparticles using piling up microfluidic devices. *Appl Mater Today*. 2023; 31:101754. [DOI:10.1016/j.apmt.2023.101754]
- [96] Carvajal-Vidal P, González-Pizarro R, Araya C, Espina M, Halbaut L, Gómez de Aranda I, et al. Nanostructured lipid carriers loaded with Halobetasol propionate for topical treatment of inflammation: Development, characterization, biopharmaceutical behavior and therapeutic efficacy of gel dosage forms. *Int J Pharm*. 2020; 585:119480. [DOI:10.1016/j.ijpharm.2020.119480] [PMID]

- [97] Luzzati V, Tardieu A, Gulik-Krzywicki T. Polymorphism of lipids. *Nature*. 1968; 217(5133):1028-30. [DOI:10.1038/2171028a0] [PMID]
- [98] Vetten MA, Yah CS, Singh T, Gulumian M. Challenges facing sterilization and depyrogenation of nanoparticles: effects on structural stability and biomedical applications. *Nanomedicine*. 2014; 10(7):1391-9. [DOI:10.1016/j.nano.2014.03.017] [PMID]
- [99] Packer M, Gyawali D, Yerabolu R, Schariter J, White P. A novel mechanism for the loss of mRNA activity in lipid nanoparticle delivery systems. *Nat Commun*. 2021; 12(1):6777. [DOI:10.1038/s41467-021-26926-0] [PMID]
- [100] Mayer M, Doenicke A, Nebauer AE, Hepting L. [Propofol and etomidate-Lipuro for induction of general anesthesia. Hemodynamics, vascular compatibility, subjective findings and postoperative nausea (German)]. *Anaesthesist*. 1996 Nov;45(11):1082-4. [DOI:10.1007/s001010050343] [PMID]
- [101] Patel HH, Pearn ML, Patel PM, Roth DM. General anesthetics and therapeutic gases. In: Brunton LL, Hilal-Dandan R, Knollmann BC, editors. *Goodman & Gilman's: The pharmacological basis of therapeutics*, 13e. New York: McGraw Hill; 2025. [Link]

This Page Intentionally Left Blank