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Solid Lipid Nanoparticles and Nanostructured Lipid Carriers: A Review on Their Role in Targeted Drug Delivery Systems

Smita P. Borkar[1*], Snehal Pawar[1], Swaranjali Mohite[1]

[1]**Arvind Gavali College of Pharmacy, Jaitapur, Satara, Maharashtra**

Pin:415001

***Corresponding Email: smita.borkaragcop@gmail.com**

Abstract

This review is an overview of the Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs) as the advanced lipid-based drug delivery systems with emphasis on the preclinical animal studies. Their physicochemical properties and formulation strategies and therapeutic uses are explored with a particular focus on how they can be used to enhance drug stability, controlled release and bioavailability. The stable lipid matrix of SLNs can be used to deliver drugs slowly, whereas the partially disordered lipid phase of NLCs offers more space to load drugs, less expulsion of drugs and improved in vivo properties. Comparative studies have shown that NLCs are normally more effective than SLNs in therapeutic efficacy especially in poorly water-soluble or targeted drugs. The review also addresses the existing limitations, such as complexities of formulation and storage stability, and determines the gaps in research, in toxicity evaluation, pharmacokinetics and scalability, and offers directions to guide future preclinical and translation research.

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Key Words:

Solid Lipid Nanoparticles, Nanostructured Lipid Carriers, Targeted Drug Delivery, Lipid-Based Nanoparticles

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1. INTRODUCTION

Nanotechnology has become a revolutionary subject in the pharmaceutical sciences and especially in drug delivery systems[1]. Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs) are among the different nanocarriers which have attracted great interest as a new generation of lipid-based drug delivery systems. Such nanoparticles offer a flexible platform that

can entrap both hydrophilic and lipophilic drugs with the potential to increase drug stability, extend circulation time, and allow controlled/targeted release[2]. Introduced in the early 1990s, SLNs were aimed at overcoming the shortcomings of the traditional carriers like liposomes and polymeric nanoparticles. The second generation, NLCs, overcame some of the drawbacks of SLNs, mainly low drug loading capacity and expulsion of drug during storage, by making use of a blend of solid and liquid lipids to create a less ordered structure with improved performance[3].

1.1. Background information and context.

The preclinical animal studies have shown the potential of SLNs and NLCs in various treatment fields such as anticancer, anti-inflammatory, antimicrobial and neuroprotective therapy[4]. This can be demonstrated by their capacity to permeate biological barriers, enhance the bioavailability of poorly water-soluble drugs, and minimize systemic toxicity, which makes them promising in future clinical practice. Nevertheless, issues of complexity of formulations, long-term stability and thorough toxicology testing remain as obstacles to complete clinical translation[5].

1.2. Objectives of the Review

The main objectives of this review are to:

- Provide an in-depth analysis of the structural characteristics, preparation methods, and advantages of SLNs and NLCs.
- Critically evaluate the therapeutic applications of SLNs and NLCs in preclinical animal studies, with emphasis on drug stability, release kinetics, and bioavailability.
- Compare the performance of SLNs and NLCs to identify their strengths, limitations, and potential clinical implications.
- Highlight existing research gaps and propose directions for future studies to enhance their translational potential in drug delivery.

1.3. Importance of the Topic

The importance of the study of SLNs and NLCs is that they can transform targeted drug delivery systems, particularly in poor water-soluble drugs (poorly soluble drugs), drugs with short half-life and drugs with high systemic toxicity[6]. These nanocarriers have a great potential in the unmet medical needs in oncology, infectious diseases, inflammation, and central nervous system disorders by enhancing stability, solubility, and therapeutic efficacy. Moreover, the increasing worldwide need in safer, more effective, and patient-friendly drug delivery systems evidences the necessity of investigating SLNs and NLCs as possible alternatives to conventional carriers[7]. They can be further optimized and evaluated, thus, filling the gap between preclinical success and clinical translation, and, thus, personalized medicine and next-generation therapeutics.

2. SOLID LIPID NANOPARTICLES (SLNS)

Solid Lipid Nanoparticles (SLNs) are submicron colloidal vehicles, with typical diameters of 50 to 1000 nm, made of lipids that are solid at ambient and physiologic temperatures. The physical property of lipid core is solid and thus a stable matrix that can be filled with a wide range of drugs such as hydrophobic and lipophilic drugs and this property makes SLNs very suitable to pharmaceutical uses. In contrast to the conventional carriers like liposomes or polymeric

nanoparticles, SLNs have the benefits of lipid carriers and the stability of solid matrix, which provide controlled release and protection of labile drugs.

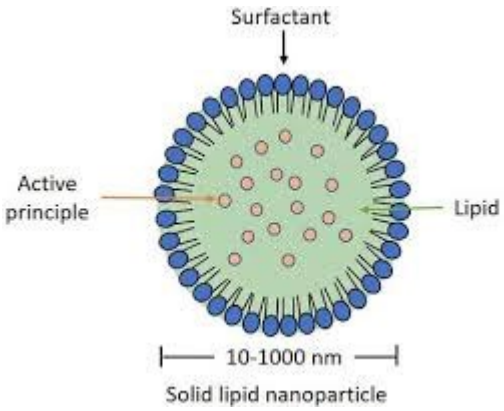

Figure 1: Solid Lipid Nanoparticles[8]

2.1. Preparation Methods

There are various methods to prepare Solid Lipid Nanoparticles (SLNs) and each method influences the size of the particle, encapsulation efficiency, and the stability of drugs as well as the release profile. The choice of an appropriate method is based on physicochemical characteristics of the drug, therapeutic effect required, and animal model to be studied.

1. **High-Pressure Homogenization (HPH)**

The method used is to push a molten mixture of lipid-drug through tiny pores under very high pressures, resulting in nanoparticles of homogenous size distribution. HPH is very scalable and reproducible and thus a popular preclinical research method. SLNs prepared by HPH have been shown in animal studies to enable the sustained release of anticancer drugs like paclitaxel and doxorubicin, as well as improved biodistribution and tumor targeting.

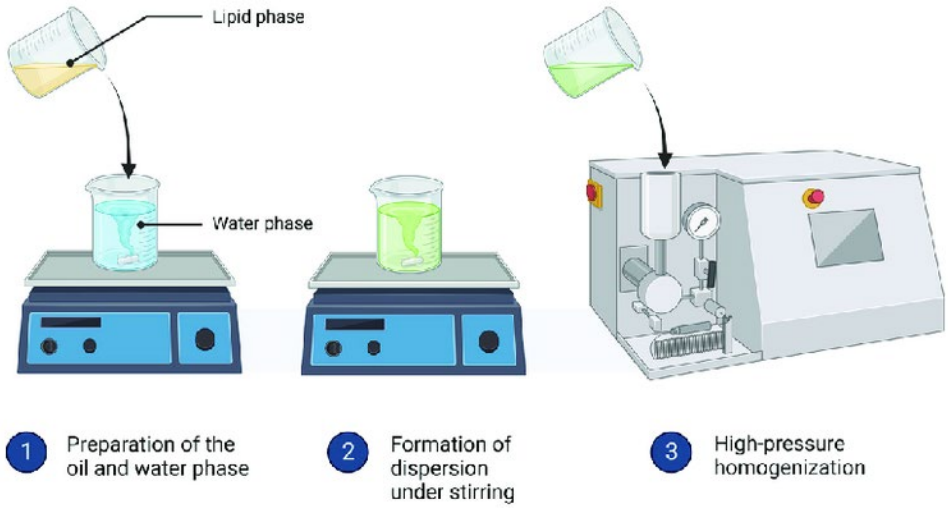

Figure 2: Preparation of SLN using high-pressure homogenization techniques[9]

2. Microemulsion Method

Microemulsion technique: This is a high temperature technique that produces a microemulsion of lipids, surfactants and occasionally co-surfactants. The microemulsion solidifies to SLNs on cooling. The technique enables us to narrowly regulate the size of the particles, their shape, and the encapsulation efficiency. Microemulsion-prepared SLNs have been effectively administered in preclinical studies in rodents to deliver antifungal and anti-inflammatory drugs with long-lasting therapeutic effect and improved bioavailability.

3. Double-Emulsion Technique (w/o/w)

This is mainly applicable in encapsulation of hydrophilic or macromolecular drugs and the resultant product is a w/o/w emulsion. The hydrophilic drug is present in the internal aqueous phase and is emulsified in a lipid phase prior to being re-emulsified in an external aqueous phase. When cooled the lipid solidifies, trapping the hydrophilic medicine. In animal studies, it has been found that this method is very effective in delivering peptides, proteins, and nucleic acids in an enhanced bioavailability and lower systemic degradation.

2.2. Advantages of Solid Lipid Nanoparticles (SLNs)

- **Improved Drug Stability**

SLNs also offer a good lipid matrix that offers good protection on encapsulated drugs against chemical, enzymatic and environmental destruction[10]. This characteristic is especially significant in case of labile or weakly stable molecules like curcumin, paclitaxel or other chemotherapeutic agents. In animal studies it has been shown that SLNs are capable of preserving the biological activity of these drugs in circulation and delivery to target tissues. Indeed, in murine tumor models, paclitaxel-loaded SLNs maintained a greater drug potency than free drug administration, minimizing premature degradation to increase therapeutic efficacy.

- **Controlled and sustained drug release**

The ability of the solid lipid core of SLNs to release the drug gradually over time is important in the reduction of dosing frequency and sustaining therapeutic drug levels. In preclinical experiments, anticancer-loaded SLNs delivered to mice resulted in extended circulation times, increased tumor targeting and lower off-target toxicity. Likewise, anti-inflammatory agents such as dexamethasone administered through SLNs in rat models showed a long-lasting anti-inflammatory effect, and this shows the promise of SLNs to offer long term therapeutic responses.

- **Biocompatibility and Low Toxicity**

SLNs consist of physiological lipids glyceryl monostearate, stearic acid, or triglycerides, and are generally tolerated well in vivo. In rodent toxicology studies, there have been minimal immunogenicity, insignificant organ toxicity and overall tolerability. These characteristics render SLNs as safe and biocompatible in preclinical drug delivery investigations.

2.3. Limitations of Solid Lipid Nanoparticles

→ **Low Drug Loading Capacity**

Extremely crystalline nature of solid lipid matrix can limit the amount of drug that can be fitted hence high dose or highly potent drugs may be a problem. Expulsion of drugs or unstable can occur as a result of overloading. Cases of rapid drug leakage and subsequent loss in therapeutic efficacy have been observed in animal studies to be common in SLNs with high drug loading and necessitate optimisation of lipid composition[11].

→ **Drug Expulsion During Storage**

SLNs are also vulnerable to polymorphic transitions during storage that may result in crystallization of the lipid matrix and outflux of the encapsulated drug. Stability tests in animal formulations show that formulating lipid types, surfactants and storage conditions carefully is needed to retain the drug and efficacy during time.

2.4. Therapeutic Applications in Animal Models

SLNs have been extensively evaluated in preclinical animal studies for diverse therapeutic applications. Key examples include:

Table 1: Preclinical Evaluation of Bioactive Compounds Across Therapeutic Areas[12]

Therapeutic Area	Drug Examples	Animal Model	Observed Outcomes
Anticancer Therapy	Doxorubicin, Paclitaxel, Curcumin	Murine tumor models	Enhanced tumor targeting, prolonged circulation, reduced systemic toxicity, improved survival
Anti-inflammatory Therapy	Ibuprofen, Dexamethasone	Rat arthritis and paw edema models	Sustained drug release, significant reduction in inflammation, prolonged therapeutic effects
Antimicrobial Therapy	Amphotericin B, Fluconazole	Mice and rat infection models	Improved bioavailability, enhanced penetration at infection site, higher therapeutic efficacy for poorly soluble drugs

a) Anticancer Therapy

Chemotherapeutics, such as paclitaxel and doxorubicin, have been loaded into SLNs, which have demonstrated better tumor accumulation in mice than free agents, thus minimizing systemic drug toxicity. SLNs loaded with curcumin in mouse tumor models also showed increased anti-tumor effect and increased survival rates.

b) Anti-inflammatory Therapy

Ibuprofen or dexamethasone-based drugs entrapped in SLNs showed a prolonged release in rat arthritis and paw edema models. The SLN formulations gave sustained anti-inflammatory activity, and this implies that they can be used in the treatment of chronic inflammatory diseases.

c) Antimicrobial Therapy

SLNs loaded with antifungal (e.g., amphotericin B) or antibacterial agents (e.g., ciprofloxacin) have been evaluated in rodent models. These formulations increased the solubility of drugs, their tissue penetration and enhanced their therapeutic effectiveness, especially of drugs with low water solubility or in vivo stability.

3. NANOSTRUCTURED LIPID CARRIERS (NLCS)

Nanostructured Lipid Carriers (NLCs) are the second generation of nanoparticles based on lipids, which have been developed in order to solve some of the limitations inherent to Solid Lipid Nanoparticles (SLNs) including low drug loading capacity and drug expulsion during storage[13]. A combination of solid lipids and liquid lipids (oils), NLCs form an imperfect or less ordered crystalline structure in the lipid core. The chaotic matrix can accommodate drugs better, inhibits the possibility of drug leakage, and increases the stability of nanoparticles. NLCs are generally between 50 and 1000 nm in diameter, and are produced in a similar manner to SLNs (e.g. high-pressure homogenization, ultrasonication, and microemulsion) but often optimized to animal studies.

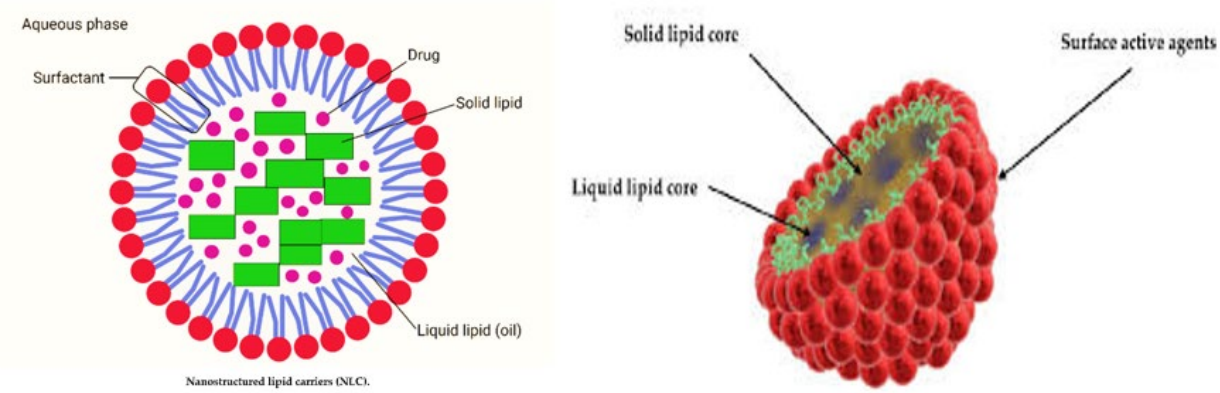

Figure 3: Nanostructured Lipid Carriers (NLCs)[14]

3.1. Preparation Techniques and Formulation

NLCs can be prepared by numerous methods and each method influences the size of the particles, the drug loading, stability and release properties. The choice of the method to use is based on the properties of the drug, the required size of the particles and the intended usage of the animal studies.

1. High-Pressure Homogenization (HPH)

The scalability and reproducibility of HPH has made it a common method of production of NLC. In this technique, the lipid blend (solid and liquid lipids) is melted and emulsified in an aqueous surfactant solution and forced to pass through a small orifice under high pressures to produce nanoparticles of homogeneous size distribution. In animal models, NLCs made by HPH have been demonstrated to offer better drug delivery, biodistribution and longer circulation in cancer and inflammation models.

2. Ultrasonication

Ultrasonication uses high frequency ultrasonic waves in the reduction of particle size and in the formation of homogenous dispersions. This method is particularly applicable in producing drugs in the laboratory scale and has been used in preclinical studies in the administration of drugs that are poorly soluble in water. The rodent studies showed that NLCs prepared by ultrasonication increased bioavailability, therapeutic efficacy and stored stability of the particles.

3. Microemulsion-Based Approach

In this method, hot or cold microemulsion of the lipids and surfactants is prepared and then cooled to obtain solid NLCs. The technique offers a fine control of particle size, morphology and encapsulation efficiency of drug making it applicable in animal studies that demand reproducible and stable formulations. In preclinical studies, NLCs based on microemulsions showed repeatable drug delivery and a high level of therapeutic effectiveness in cancer, inflammation, and microbial infection models.

Table 2: Advantages of NLCs[15]

Feature	Explanation	Evidence from Animal Studies
Enhanced Drug Loading Capacity	The imperfect lipid matrix accommodates more drug molecules compared to crystalline SLNs.	NLCs encapsulating curcumin and paclitaxel in mice and rat models showed higher drug concentrations in target tissues and enhanced therapeutic effects.
Reduced Drug Expulsion	The disordered structure minimizes crystallization-induced leakage during storage or circulation.	Rodent studies demonstrated higher drug retention for NLCs over SLNs after 30–60 days of storage.
Improved Stability	Combination of solid and liquid lipids reduces aggregation and enhances physical stability.	NLCs circulating in animal models maintained consistent particle size and drug content over prolonged periods, improving bioavailability and tissue targeting.
Versatile Drug Delivery	Suitable for hydrophobic, lipophilic, and poorly soluble drugs.	Delivery of anticancer, anti-inflammatory, and antimicrobial agents showed improved therapeutic efficacy in murine tumor, arthritis, and infection models.

3.2. Therapeutic Applications in Animal Models

Nanostructured Lipid Carriers (NLCs) have been shown repeatedly in animal models to be versatile and effective in the delivery of a wide variety of therapeutic agents. NLCs can enhance drug solubility, stability, and bioavailability because of the unique lipid matrix that consists of solid and liquid lipids, and thus NLCs are a good choice when conducting preclinical studies[16]. The major applications are:

1. Anticancer Therapy

NLCs have also found extensive use to administer hydrophobic chemotherapeutic drugs like paclitaxel, docetaxel and curcumin in mouse tumors. The chaotic lipid structure of NLCs increases drug entrapment and allows sustained drug release, which leads to circulation of the drug in vivo. Preclinical research revealed that NLCs were preferentially accumulated in tumor tissue with the help of the enhanced permeability and retention (EPR) effect. This purposeful build-up resulted in enhanced tumor control, less systemic toxicity, and few side effects relative to free drug delivery. As an example, NLCs loaded with paclitaxel in murine models of breast cancer showed increased tumor uptake and great decrease in tumor volume when compared to conventional formulations.

2. Anti-inflammatory Therapy

NLCs loaded with anti-inflammatory agents (diclofenac and dexamethasone) exhibited improved treatment results in rodent models of arthritis, paw edema and other inflammatory disorders. The lipid matrix allowed prolonged drug release, which kept the therapeutic levels at the inflamed area over longer time. Results of animal studies demonstrated remarkable decreases in swelling, inflammatory parameters, and analgesia, which reflects the possibility of NLCs to control chronic inflammation and decrease the frequency of dosing.

3. Antimicrobial Therapy

NLCs have been tested in the treatment of antibacterial and antifungal agents in different animal infection models[17]. They are nanoscale and contain lipids, which increases drug penetration into biological barriers, increasing bioavailability at the infection site. As an example, NLC formulations of poorly water-soluble antifungal agents, like itraconazole, clotrimazole, exhibited better tissue penetration and efficacy in murine models of cutaneous and systemic fungal infections than conventional forms. On the same note, antibacterial NLCs prepared against infections in rodent models exhibited a long drug residence and increased microbial clearance.

4. Additional Potential Applications

In addition to these main areas of therapeutic interest, NLCs have been investigated preclinically as a neuroprotective therapy, a brain-targeted drug delivery system, and as a topical dermatological vehicle. NLCs could penetrate the blood brain barrier with higher success than SLNs in rodent models of neurodegenerative diseases to deliver neuroprotective agents such as curcumin and resveratrol to the brain. In dermatological applications, NLCs enhanced skin penetration and hydration, therefore, suggesting NLCs as carriers of anti-inflammatory, antimicrobial, and cosmetic agents.

3.3. Critical Evaluation

NLCs have a great benefit over SLNs, especially in drug loading, stability and in vivo performance. In vivo studies on animals confirm that NLCs give a prolonged release of drugs and increase their bioavailability, which translates to better treatment results. But there are still issues:

- **Large-Scale Manufacturing:** Standardization of particle size and loading drug in large-scale batches is still a complicated process.

- **Long-Term Storage Stability:** In spite of the fact that this has been enhanced as compared to SLNs, there are still formulations that experience stability problems during long-term storage.
- **Comprehensive Toxicity Evaluation:** There are systematic long-term toxicity assessments in several animal models.

Recent studies have been aimed at the optimization of lipid composition, surfactant and surface functionalization to target delivery to enhance efficacy and safety. NLCs functionalized with ligands including peptides, antibodies, or folic acid have demonstrated successful preclinical studies of targeted delivery of tumor sites and inflammatory sites.

4. COMPARATIVE ANALYSIS AND APPLICATIONS

Nanostructured Lipid Carriers (NLCs) and Solid Lipid Nanoparticles (SLNs) are two extensively studied nano-lipid delivery systems to achieve targeted drug delivery[18], but they have some significant differences in structural composition, drug loading capacity, stability, and in vivo activity. Animal studies conducted preclinically have emphasized that although SLNs have good physical stability and drug release, NLCs have several advantages over SLNs because of their partially disordered lipid matrix that increases drug loading capacity and decreases expulsion of drugs. These differences are essential to understand to choose a suitable nanocarrier system according to the physicochemical characteristics of the therapeutic agent and targeted pharmacokinetic profile.

4.1. Comparative Evaluation

- **Drug Loading Capacity**

The lipid core of SLNs is relatively crystalline, which may restrict the drug loading, especially hydrophobic or high doses drugs. Mixed solid-liquid lipid structure of NLCs provides a more disordered matrix, which can accommodate more drug payload. In vivo experiments using anticancerous agents such as paclitaxel and curcumin or antifungal agents have shown that NLCs ensured a higher concentration of the drug at the target locations over a long duration, which enhanced therapeutic efficiency[19].

- **Stability**

SLNs and NLCs both shield the drugs against chemical and enzymatic breakdown. Nevertheless, NLCs have a better physical stability in vivo as there is less crystallization of lipids and therefore reduced leakage of drugs during storage and circulation. The increased stability results in long-term bioavailability of the drug and uniform therapeutic effects in animal models.

- **Controlled Release Profiles**

The solid lipid matrix offers sustained release of drugs by SLNs, and this makes them ideal in chronic or maintenance treatment. The heterogeneous lipid core of NLCs can be shaped into more tunable and flexible release profiles. Preclinical studies have demonstrated that NLCs have longer circulation times and greater tissue accumulation than SLNs, which is especially beneficial when poorly soluble drugs are to be targeted, or when drugs need to be directed to a specific tissue such as a tumor or inflamed area.

- **Therapeutic Outcomes**

According to animal-based research, NLCs tend to lead to an improvement in the therapeutic outcomes. As an illustration, NLC-based delivery of chemotherapeutic agents was found to be more effective in targeting tumors, less toxic in the systemic circulation, and more effective in survival in murine cancer models than SLNs. In the same way, NLCs displayed enhance pharmacological effects and extended bioavailability in inflammatory and microbial models.

Table 3: Reference Table

Author(s) & Year	Focus / Topic	Type of Study	Methods	Key Findings / Contribution
Viegas et al., 2023[20]	Comparative review of SLNs and NLCs	Review	Literature review of formulation methods, animal studies	Highlighted advantages and limitations of SLNs and NLCs, including drug loading, stability, and controlled release; emphasized animal-based preclinical studies.
Jnaidi et al., 2020[21]	SLNs and NLCs in glioblastoma treatment	Animal-based preclinical	High-pressure homogenization, ultrasonication	Demonstrated enhanced drug delivery and targeting to glioblastoma cells using lipid-based nanoparticles.
Ghasemiyeh& Mohammadi-Samani, 2018[22]	SLNs and NLCs as drug delivery systems	Review	Compilation of HPH, microemulsion, double-emulsion studies	Discussed applications, advantages, and limitations; included animal studies showing improved therapeutic outcomes.
Yoon, Park & Yoon, 2013[23]	Advances in SLNs and NLCs	Review	Overview of preparation techniques including HPH and microemulsion	Provided detailed insights into formulation methods, physicochemical properties, and preclinical applications in animal models.
Akbari et al., 2022[24]	Methods of manufacture and administration routes	Review	HPH, ultrasonication, microemulsion, oral and topical routes	Focused on preparation techniques and animal-based studies showing improved biodistribution and therapeutic effects.
Iqbal et al., 2012[25]	Advances in NLC systems	Review	HPH, microemulsion, formulation optimization	Emphasized NLC advantages over SLNs in drug loading, stability, and bioavailability, with examples from animal studies.

4.2. Applications in Animal Models

Solid Lipid Nanoparticles (SLNs) as well as Nanostructured Lipid Carriers (NLCs) have proven to be highly versatile in preclinical studies, and differ significantly in their therapeutic efficacy, bioavailability, and tissue targeting. Table 4 summarizes the comparative performance of SLNs and NLCs in the different areas of application.

Table 4: Comparative Applications of SLNs and NLCs in Preclinical Animal Studies[26]

Application Area	SLNs	NLCs	Key Observations from Animal Studies
Targeted Drug Delivery	Provides controlled release; moderate drug accumulation	Higher drug accumulation; improved tissue targeting	NLCs conjugated with folate or peptide ligands achieved enhanced tumor site delivery in murine models, reducing systemic toxicity.
Gene Delivery	Encapsulates nucleic acids; moderate transfection efficiency	Enhanced encapsulation and transfection; sustained gene expression	NLCs achieved higher mRNA and siRNA delivery efficiency in rodents, with prolonged gene expression compared to SLNs.
Cosmetic / Dermatological	Good skin penetration; stable formulations	Superior hydration; enhanced retention	In murine and porcine skin models, NLCs provided better penetration and prolonged drug presence in dermal layers.
Anti-inflammatory & Antimicrobial	Sustained release; moderate efficacy	Enhanced bioavailability and therapeutic effect	NLCs demonstrated superior anti-inflammatory activity in arthritis models and improved antifungal activity in cutaneous infection models.
Neuroprotective Therapy	Limited brain targeting	Enhanced brain delivery	NLCs crossed the blood-brain barrier more effectively in rodent neurodegenerative disease models, supporting potential for CNS-targeted therapies.

Preclinical investigations reveal that, although SLNs are useful in controlled release of drugs and moderate therapeutic uses, NLCs have always been superior to SLNs in drug loading, tissue targeting, bioavailability and sustained therapeutic effects. Such benefits are especially notable in such applications where there is a need to deliver to a specific tissue, e.g. tumors, inflamed areas, or the brain[27]. The excellent results of NLCs in animal models point to their potential as multifunctional delivery agents of complex therapies, such as anticancer, gene, dermatological, anti-inflammatory, antimicrobial, and neuroprotective functions.

4.3. Critical Insights

Although SLNs are easier to prepare and can be sufficient in some moderate therapeutic uses, NLCs have some unique benefits when it comes to complex therapies that need high drug loading, extended circulation and specific targeting[28]. Choice of the suitable system must be based on the physicochemical characteristics of the drug, the route of administration and kind of release kinetics intended. Tissue specific delivery may also be improved with functionalization of the targeting ligands or surface modifications and this has been successful in animal models.

It is possible to note that both SLNs and NLCs are useful materials in the preclinical drug delivery studies, and NLCs show better performance in the majority of therapeutic applications. Further

optimization of the formulation parameters, scalability, and thorough preclinical safety testing will be key to translating these nanocarriers to animal models to potential clinical settings.

5. DISCUSSION

5.1. Interpretation of Findings

As the discussion of preclinical animal studies shows[29], Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs) are both promising drug delivery platforms in terms of targeted delivery. Drugs encapsulated in SLNs are physically and chemically stable as the encapsulated drug is surrounded by a stable lipid matrix that shields the drug against chemical and enzyme degradation, resulting in controlled and sustained release[30]. Compared to SLNs, NLCs with its partially disorganized lipid composition have greater drug loading capacity, less drug loss, and better physical stability[31]. Animal models invariably demonstrate that NLCs are superior to SLNs in their ability to sustain therapeutic drug levels at their target sites, their extended circulation and enhanced bioavailability, especially of the poorly water-soluble drugs[32].

5.2. Implications and Significance

The results of animal model studies show the possibility of lipid-based nanoparticle application in various therapeutic fields[33]. Encapsulation of hydrophobic drugs and nucleic acid, as well as anti-inflammatory or antimicrobial agents, by SLNs and NLCs is of considerable importance in preclinical research and drug development[34]. Ligand-functionalized nanoparticles can be used to target delivery of drugs to tumors, improving therapeutic efficacy and reducing systemic toxicity by accumulating drugs at the site of disease. Further, the effective delivery of gene therapy agents in rodents highlights the flexibility of such carriers in the next-generation therapeutics[35]. Their translational potential to be used clinically and commercially is further evidenced by their application in dermatological and cosmetic models.

5.3. Research Gaps and Future Directions

Although there is a lot of research on animals, there are still a number of research gaps:

- **Full Toxicity Profiles:** The majority of studies are short-term toxicity. There is limited long-term safety data such as immunogenicity and organ-specific effects[36].
- **Streamlining of Targeting Strategies:** Ligand functionalization can be used to improve targeting[37], however, a systematic analysis of the efficiency and specificity of various ligands in various disease models is required.
- **Pharmacokinetic and Biodistribution Studies:** Further studies of the pharmacokinetics of SLNs and NLCs in animal models and the mechanisms of tissue distribution and clearance are needed to establish the clinical behavior[38,39].
- **Scalability and Manufacturing:** Despite the well-established production at laboratory-scale, scalable and reproducible manufacturing strategies require additional development to allow clinical translation in the future.
- **Comparative Effectiveness Across Disease Models:** Comparative effectiveness across disease models could be done to give a better guide on the selection of most appropriate carrier in specific therapeutics.

Well-designed animal studies to address these gaps will offer a better basis to clinical development, and ensure safe and effective application of SLNs and NLCs in site-specific drug delivery[40].

6. CONCLUSION

The two promising platforms in targeted drug delivery are Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs), which have better drug stability, release, and bioavailability as evidenced in most animal studies. Although SLNs offer easy and stable delivery system, NLCs overcome most of the limitations of SLNs due to the greater drug loading and drug expulsion, and enhanced in vivo activity, especially of the poorly water-soluble or targeted drugs. This review summarizes the importance of these lipid-based carriers in future preclinical drug delivery research and the possible future translational uses. Long-term safety, pharmacokinetics, targeted delivery strategies, and scalable production methods are the areas that require additional research to fully harness their therapeutic potential, and thus it is recommended to achieve effective and safe clinical translation of these versatile nanocarriers.

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