

A REVIEW ON LIPID NANOPARTICLES AS CARRIERS FOR ENHANCING BIOAVAILABILITY OF POORLY SOLUBLE DRUGS**Ravi Kumar, Rashmi Pandey*, Saurabh Sharma, Pranjul Shrivastava, Sandip Prasad Tiwari****Faculty of Pharmacy, Kalinga University, Naya Raipur, Chhattisgarh India (492101)***Corresponding Author's E mail: rashmi.pandey@kalingauniversity.ac.in

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ABSTRACT

Considering lipid-based nanotransporters have several advantages, such as biocompatibility, biodegradability, low toxicity, and non-immunogenicity, nanomaterials have undergone extensive research for the delivery of drugs. However, the efficacy of therapy or the effectiveness of delivering the medication are limited by the disadvantages that accompany traditional lipid-based nanocarriers as particularly inappropriate aiming for, procurement by the system of Endothelial cells in reticulum, and rapid clearance. To contribute to facilitate identify and address the causes of a variety of diseases, a number of multifunctional nanocarriers constructed from lipids have been created constructed that improve the development of pharmaceuticals in the area of the lesions. Everyone described the latest advances along with applications of nanocarriers made with lipids in this review, wrapping both traditional and intriguing operational a lipid formulation.

Keywords: Bioavailable Drug, Self-micro Emulsifying drug delivery system

INTRODUCTION

The bioavailability of a drug, which refers to the proportion of the administered drug that reaches the systemic circulation in an active form, is a critical factor in determining its therapeutic efficacy. High bioavailability ensures that a sufficient amount of the drug reaches its target site to exert its intended pharmacological effect. However, many drugs, particularly those with poor water solubility, face significant challenges in achieving adequate bioavailability. Poorly soluble drugs often exhibit low absorption rates, limited bioavailability, and variable therapeutic outcomes. These challenges can hinder

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Poor water solubility is one of the primary obstacles in the formulation and delivery of many pharmaceutical compounds. Drugs with low solubility often have poor dissolution rates, which are crucial for absorption in the gastrointestinal tract. This limitation can result in suboptimal drug concentrations in the bloodstream, necessitating higher doses to achieve therapeutic levels, which in turn can lead to increased side effects and patient non-compliance. Addressing the solubility issue is, therefore, a critical aspect of pharmaceutical research and development. Various strategies have been employed to enhance the solubility and bioavailability of these drugs, including the use of prodrugs, salt formation, complexation with cyclodextrins, and the development of novel drug delivery systems ².

Among these strategies, lipid nanoparticles have emerged as a promising solution for enhancing the bioavailability of poorly soluble drugs. Lipid nanoparticles, including solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), offer several advantages over traditional delivery systems. These nanoparticles are composed of biocompatible and biodegradable lipid materials, which can encapsulate hydrophobic drugs, enhancing their solubility and stability. The lipid matrix of these nanoparticles can protect the drug from degradation, improve its absorption through the gastrointestinal tract, and facilitate controlled release, thereby enhancing bioavailability ³.

Lipid nanoparticles also offer versatility in administration routes, including oral, intravenous, transdermal, and pulmonary, broadening their application potential. Their small size and large surface area contribute to better interaction with biological membranes, promoting more efficient drug delivery. Furthermore, lipid nanoparticles can be engineered to target specific tissues or cells, enhancing the therapeutic efficacy and reducing systemic side effects. The use of lipid nanoparticles in drug delivery is supported by a growing body of research demonstrating their potential to improve the pharmacokinetic and pharmacodynamic profiles of poorly soluble drugs ⁴.

This review aims to provide a comprehensive overview of lipid nanoparticles as carriers for poorly soluble drugs. It will discuss the importance of drug bioavailability, the challenges associated with poorly soluble drugs, and the various types of lipid nanoparticles used in drug delivery. By examining the current state of research and highlighting successful applications, this review will underscore the potential of lipid nanoparticles to revolutionize the delivery and efficacy of poorly soluble drugs, paving the way for more effective and patient-friendly therapeutic options ⁶.

Types of Lipid Nanoparticles

Lipid nanoparticles have gained significant attention in recent years as versatile and effective carriers for enhancing the bioavailability of poorly soluble drugs. The primary types of lipid nanoparticles include Solid Lipid Nanoparticles (SLNs), Nanostructured Lipid Carriers (NLCs), Lipid-Drug Conjugates (LDCs), and Liposomes. Each type offers unique properties and benefits, making them suitable for various drug delivery applications. This section will explore these different types of lipid nanoparticles, their characteristics, and their advantages in drug delivery systems.

Solid Lipid Nanoparticles (SLNs)

Solid Lipid Nanoparticles (SLNs) are among the first generation of lipid nanoparticles developed to overcome the limitations of traditional colloidal carriers such as emulsions, liposomes, and polymeric nanoparticles. SLNs are composed of solid lipids that remain solid at room and body temperatures, providing a stable matrix for drug encapsulation. The solid lipid core can incorporate lipophilic and hydrophilic drugs, enhancing their solubility and stability. SLNs offer several advantages, including controlled drug release, protection of sensitive drugs from degradation, and improved bioavailability. Additionally, SLNs are biocompatible and biodegradable, reducing the risk of toxicity and side effects. Their small size allows for efficient cellular uptake and targeted delivery, making them suitable for a wide range of pharmaceutical applications ⁷.

Nanostructured Lipid Carriers (NLCs)

Nanostructured Lipid Carriers (NLCs) represent the second generation of lipid nanoparticles, designed to address some of the limitations associated with SLNs. NLCs are composed of a mixture of solid and liquid lipids, resulting in a nanostructured lipid matrix with improved drug loading capacity and stability. The inclusion of liquid lipids creates imperfections in the solid lipid matrix, providing more space for drug accommodation and reducing drug expulsion during storage. NLCs offer enhanced drug release profiles and higher encapsulation efficiency compared to SLNs. They also exhibit better physical stability and reduced risk of polymorphic transitions. NLCs are particularly useful for delivering poorly soluble drugs, as the combination of solid and liquid lipids can solubilize and stabilize a broader range of drug molecules. Their versatility and improved performance make NLCs a promising platform for drug delivery ⁸.

Lipid-Drug Conjugates (LDCs)

Lipid-Drug Conjugates (LDCs) are a novel approach to lipid-based drug delivery, where the drug molecules are chemically conjugated to lipid moieties. This strategy enhances the solubility and stability

Pandey *et al.* A review on lipid nanoparticles as carriers for enhancing bioavailability of poorly soluble drugs by covalently attaching them to lipids. The resulting conjugates can self-assemble into nanoparticles, micelles, or other nanostructures, depending on the lipid-drug combination and formulation conditions. LDCs offer several advantages, including improved drug loading, enhanced stability, and targeted delivery. The lipid component of the conjugate can facilitate cellular uptake and protect the drug from degradation. Additionally, LDCs can be designed to release the drug in a controlled manner, improving therapeutic efficacy and reducing side effects. This approach is particularly beneficial for drugs with poor solubility and bioavailability, as it provides a means to enhance their pharmacokinetic profiles ⁹.

Liposomes

Liposomes are spherical vesicles composed of one or more phospholipid bilayers, encapsulating an aqueous core. They are one of the most widely studied and utilized lipid-based carriers for drug delivery. Liposomes can encapsulate both hydrophilic and lipophilic drugs, offering protection from degradation and enhancing bioavailability. The lipid bilayer structure of liposomes mimics biological membranes, allowing for biocompatibility and efficient cellular uptake. Liposomes can be modified with surface ligands, such as antibodies or peptides, to achieve targeted delivery to specific tissues or cells. They also offer controlled release properties, which can be tailored by adjusting the lipid composition and preparation method. Liposomes have been successfully used in various therapeutic applications, including cancer therapy, gene delivery, and vaccination. Their versatility, biocompatibility, and ability to encapsulate a wide range of drugs make liposomes a valuable tool in drug delivery systems ¹⁰.

Other Lipid-Based Carriers

In addition to SLNs, NLCs, LDCs, and liposomes, there are other lipid-based carriers that have been explored for drug delivery. These include lipid nanocapsules, lipid micelles, and lipid-based nanoemulsions. Lipid nanocapsules are vesicular systems with an oily core surrounded by a solid lipid shell, offering a stable environment for drug encapsulation and controlled release. Lipid micelles are formed by the self-assembly of amphiphilic lipids in aqueous solutions, creating a hydrophobic core that can solubilize poorly soluble drugs. Lipid-based nanoemulsions are fine oil-in-water emulsions stabilized by surfactants, providing a means to enhance the solubility and bioavailability of lipophilic drugs. Each of these carriers has unique properties and advantages, making them suitable for specific drug delivery applications. The choice of lipid-based carrier depends on the drug's physicochemical properties, the desired release profile, and the target site of action ¹¹.

Mechanisms of Bioavailability Enhancement

Enhancing the bioavailability of poorly soluble drugs is a critical challenge in pharmaceutical development. Various mechanisms have been employed to improve the delivery and efficacy of these drugs, ensuring they reach therapeutic levels in the systemic circulation. Key mechanisms include increasing the surface area of drug particles, improving absorption, enabling targeted drug delivery, and avoiding first-pass metabolism. Each of these mechanisms plays a crucial role in optimizing the bioavailability of drugs, leading to better therapeutic outcomes ¹².

Increased Surface Area

One of the fundamental mechanisms for enhancing drug bioavailability is increasing the surface area of drug particles. By reducing the particle size to the nanometer range, the total surface area of the drug exposed to the dissolution medium is significantly increased. This enhancement facilitates a higher dissolution rate according to the Noyes-Whitney equation, which states that the dissolution rate is directly proportional to the surface area of the drug. Nanoparticles, including lipid-based carriers like Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs), provide an extensive surface area for interaction with the gastrointestinal fluids. This increased surface area enhances the dissolution of poorly soluble drugs, making more drug available for absorption. Moreover, the small particle size allows for a more uniform distribution of the drug throughout the gastrointestinal tract, further enhancing absorption and bioavailability ¹³.

Improved Absorption

Improved absorption is another critical mechanism for enhancing bioavailability. Poorly soluble drugs often face challenges in permeating the biological membranes of the gastrointestinal tract, limiting their absorption into the systemic circulation. Lipid nanoparticles, such as liposomes and lipid nanocapsules, can encapsulate hydrophobic drugs and enhance their solubility, facilitating their transport across cell membranes. These lipid-based carriers can merge with the lipid bilayers of the cell membranes, promoting the uptake of the encapsulated drug through endocytosis or direct fusion. Additionally, lipid nanoparticles can protect the drug from degradation in the harsh gastrointestinal environment, ensuring that a higher proportion of the drug remains intact and available for absorption. This improved absorption translates to higher bioavailability and more consistent therapeutic effects ¹⁴.

Targeted Drug Delivery

Targeted drug delivery is a sophisticated mechanism that not only enhances bioavailability but also improves therapeutic efficacy and reduces side effects. Lipid nanoparticles can be engineered to target

Pandey *et al.* A review on lipid nanoparticles as carriers for enhancing bioavailability specific tissues or cells by modifying their surface with ligands such as antibodies, peptides, or small molecules. This targeting ensures that the drug is delivered directly to the site of action, increasing the local drug concentration and minimizing systemic exposure. For example, in cancer therapy, lipid nanoparticles can be functionalized to recognize and bind to specific receptors overexpressed on cancer cells, allowing for precise delivery of chemotherapeutic agents to the tumor site. This targeted approach not only enhances the bioavailability of the drug at the desired location but also reduces the risk of off-target effects and toxicity, leading to a more effective and safer treatment ¹⁵.

Avoidance of First-Pass Metabolism

First-pass metabolism, which occurs primarily in the liver, is a significant barrier to the bioavailability of many orally administered drugs. During first-pass metabolism, a substantial portion of the drug is metabolized and inactivated before it reaches the systemic circulation, resulting in reduced bioavailability. Lipid nanoparticles can help circumvent this issue by facilitating alternative routes of administration, such as oral mucosal, transdermal, or pulmonary delivery. These routes allow the drug to enter the systemic circulation directly, bypassing the liver and avoiding extensive first-pass metabolism. For example, liposomal formulations designed for sublingual or buccal administration can rapidly deliver the drug into the bloodstream through the highly vascularized mucosal tissues in the mouth. Similarly, transdermal patches incorporating lipid nanoparticles can deliver drugs through the skin directly into the systemic circulation. By avoiding first-pass metabolism, these alternative delivery routes can significantly enhance the bioavailability of the drug, ensuring a higher proportion of the administered dose reaches the target site ¹⁶.

Applications in Drug Delivery

Lipid nanoparticles have revolutionized the field of drug delivery by offering versatile and effective platforms for the administration of poorly soluble drugs. These nanoparticles enhance the bioavailability and therapeutic efficacy of drugs through various routes of administration, including oral, topical, transdermal, parenteral, pulmonary, and other specialized routes. This section will explore the applications of lipid nanoparticles in these different drug delivery systems, highlighting their advantages and potential in improving patient outcomes.

Oral Drug Delivery

Oral administration is the most preferred route for drug delivery due to its convenience, patient compliance, and cost-effectiveness. However, many drugs suffer from poor solubility and stability in the gastrointestinal tract, leading to low bioavailability. Lipid nanoparticles, such as Solid Lipid

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Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs), address these issues by enhancing the solubility and stability of poorly soluble drugs. These nanoparticles protect the encapsulated drug from the harsh gastrointestinal environment and promote its absorption through the intestinal epithelium. Additionally, lipid nanoparticles can be engineered to release the drug in a controlled manner, ensuring sustained therapeutic levels. Their ability to improve the oral bioavailability of drugs makes lipid nanoparticles a promising platform for the development of effective oral drug delivery systems ¹⁷.

Topical and Transdermal Delivery

Topical and transdermal delivery systems are designed to deliver drugs directly to the skin or through the skin into the systemic circulation, respectively. These routes offer several advantages, including bypassing the gastrointestinal tract and first-pass metabolism, reducing systemic side effects, and providing sustained drug release. Lipid nanoparticles enhance the penetration of drugs through the skin by interacting with the lipid matrix of the stratum corneum, the outermost layer of the skin. Liposomes, NLCs, and SLNs are commonly used in topical and transdermal formulations due to their ability to encapsulate both hydrophilic and lipophilic drugs. These nanoparticles can improve the therapeutic efficacy of drugs used in the treatment of skin disorders, such as acne, psoriasis, and dermatitis, as well as systemic conditions requiring transdermal drug delivery ¹⁸.

Parenteral Delivery

Parenteral delivery involves the administration of drugs via injections or infusions, providing a rapid onset of action and precise control over drug dosing. Lipid nanoparticles are highly suitable for parenteral delivery due to their biocompatibility, biodegradability, and ability to protect the drug from enzymatic degradation in the bloodstream. Liposomes and lipid-based nanocarriers can encapsulate a wide range of drugs, including anticancer agents, peptides, and proteins, improving their solubility and stability. These nanoparticles can be engineered to release the drug in a controlled or targeted manner, enhancing therapeutic efficacy and reducing toxicity. For instance, liposomal formulations of chemotherapeutic agents, such as doxorubicin, have shown significant improvements in targeting tumor cells while minimizing adverse effects on healthy tissues ¹⁹.

Pulmonary Delivery

Pulmonary delivery is an effective route for the administration of drugs intended for the treatment of respiratory diseases, such as asthma, chronic obstructive pulmonary disease (COPD), and cystic fibrosis. Lipid nanoparticles can improve the delivery of drugs to the lungs by enhancing their solubility, stability, and bioavailability. These nanoparticles can be incorporated into inhalable formulations, such as dry

Pandey *et al.* A review on lipid nanoparticles as carriers for enhancing bioavailability powders or aerosols, providing targeted delivery to the respiratory tract. Lipid nanoparticles can also protect the drug from degradation by pulmonary enzymes and promote its absorption across the alveolar epithelium. This route of administration offers the advantage of rapid drug action and reduced systemic side effects, making it highly suitable for both local and systemic therapies ²⁰.

Other Routes of Administration

Beyond the conventional routes, lipid nanoparticles are also explored for their potential in other specialized routes of drug delivery. These include ocular, nasal, buccal, and vaginal delivery systems. For ocular delivery, lipid nanoparticles can enhance the solubility and bioavailability of drugs used in the treatment of eye diseases, such as glaucoma and macular degeneration. Nasal delivery systems utilizing lipid nanoparticles can provide a non-invasive route for the delivery of drugs to the systemic circulation or directly to the brain, bypassing the blood-brain barrier. Buccal delivery involves the administration of drugs through the mucous membranes of the mouth, providing rapid absorption and avoiding first-pass metabolism. Vaginal delivery systems can benefit from lipid nanoparticles' ability to enhance the solubility and stability of drugs used in the treatment of local infections and systemic conditions ²¹.

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