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# Lipid-Based Nanoformulation in Drug Delivery for Precision Targeting and Enhanced Efficacy: Formulation and its Application

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**Abstract:**

In the realm of drug delivery, the paradigm shift towards precision and efficacy has catalyzed the evolution of lipid-based nanoformulations. This review endeavors to provide an exhaustive exploration of lipid-based nanoformulations, elucidating their pivotal role in achieving effective and targeted drug delivery. The core essence of lipid-based nanoformulations lies in their ability to encapsulate therapeutic agents within lipidic matrices, offering a versatile platform for enhanced drug solubility, bioavailability, and targeted delivery. The paper synthesizes information from a plethora of studies to elucidate the unique properties of lipid-based nanostructures that enable precise targeting of therapeutics to specific cells, tissues, or organs. The review begins by exploring the diverse range of lipid materials employed in nanoformulations, highlighting their biocompatibility, versatility, and ability to encapsulate a wide variety of drugs. Emphasis is placed on lipid nanoparticles, liposomes, ethosomes, and lipid-based micelles, each offering distinct advantages in terms of drug loading, stability, and release kinetics. Special attention is given to the design principles governing lipid-based nanoformulations, such as size, surface charge, and functionalization, and their impact on target-specific drug delivery. Furthermore, the review delves into the mechanisms underlying the enhanced permeability and retention (EPR) effect, which plays a pivotal role in the passive targeting of lipid-based nanoformulations to tumor tissues. Strategies to augment active targeting, including ligand conjugation and surface modification, are extensively discussed to enhance the specificity of drug delivery systems. In addition to cancer therapy, the paper explores the application of lipid-based nanoformulations in various therapeutic areas, including cardiovascular diseases, infectious diseases, metabolic disorder, gene therapy, vaccination and neurological disorders. The safety profile of lipid-based nanocarriers and their potential for personalized medicine are also examined. As lipid-based nanoformulations continue to evolve, this review serves as a valuable resource for researchers, clinicians, and pharmaceutical scientists seeking a comprehensive understanding of the challenges, and future directions in the realm of lipid-based nanoformulations for effective targeting in drug delivery.

**Keywords:** Lipid Nanoparticles, Liposomes, SLN, NLC, Cancer, Drug Delivery System, Lipid based drug carrier, Lipid based formulation

**Introduction:**

In the dynamic landscape of pharmaceutical research, the quest for innovative drug delivery systems has led to the advent of lipid-based nanoformulations, offering a promising avenue for achieving targeted and efficient therapeutic outcomes. Engineered to overcome the challenges of conventional drug delivery, these lipid-based nanocarriers present a versatile platform with unique properties, such as biocompatibility, controlled release, and the ability to encapsulate diverse therapeutic agents. This review aims to provide a comprehensive overview of the current state of lipid-based nanoformulations, with a specific focus on their efficacy in targeted drug delivery. The choice of lipids as key components in nanoformulations is rooted in their inherent ability to self-assemble into nanostructures, forming liposomes, lipid nanoparticles, and micelles. These lipid-based carriers have garnered significant attention due to their capacity to encapsulate hydrophobic and hydrophilic drugs, offering a versatile platform for a wide range of therapeutic applications [1][2]. A critical aspect of the success of lipid-based nanoformulations lies in their ability to navigate through physiological barriers and selectively reach target tissues or cells. The enhanced permeability and retention (EPR) effect, particularly in tumor tissues, has been a cornerstone for passive targeting [3]. Concurrently, active targeting strategies, involving the functionalization of lipid-based nanocarriers with ligands or antibodies, have emerged as powerful tools to enhance specificity and improve therapeutic outcomes [4]. While the application of lipid-based nanoformulations in cancer therapy has been extensively explored, their potential extends to various therapeutic areas, including cardiovascular diseases, infectious diseases, and neurodegenerative disorders [5][6]. Moreover, the safety profile of these nanoformulations is of paramount importance, warranting a thorough examination of potential toxicities and immunogenicity. As researchers continue to unravel the intricate interplay of design parameters, surface modifications, and biological interactions, this review consolidates the current knowledge on lipid-based nanoformulations for effective targeting. By synthesizing findings from diverse studies, we aim to provide a holistic understanding of the advancements, challenges, and future directions in harnessing lipid-based nanoformulations for drug delivery to targeting sites. Lipid-based nanoparticles can also be sub categorized as follows in **Chart 1**. These lipid-based nanoformulations have attracted worldwide interest due to their advantages, given in **Table 1**.

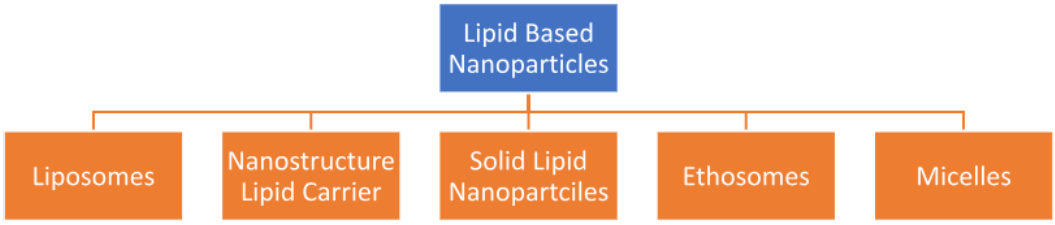



**Chart 1:** Different types of lipid-based nanoparticles

| Sr.no | Types of Lipids Nanoformulation | Advantages | References |
|---|---|---|---|
| **1** | **Liposomes** | • They are composed of natural phospholipids, making them biocompatible and generally well-tolerated in biological systems.<br>• Encapsulate a wide range of drugs, both hydrophilic and hydrophobic, providing versatility in drug delivery.<br>• Have the ability for modification to achieve targeted drug delivery by incorporating ligands or antibodies on their surface. | 7, 8, 9, 10, 11, 12 |

| | | | |
|---|---|---|---|
| | | • Liposomes can improve the pharmacokinetics of drugs, protecting them from degradation and increasing circulation time.<br>• Provide controlled drug release, contributing to sustained therapeutic effects.<br>• The liposomal drug formulations can help minimize side effects by targeting drugs to specific tissues and reducing exposure to healthy tissues. | |
| **2** | **Nanostructure Lipid Carrier** | • NLCs have higher drug loading capacities compared to traditional lipid nanoparticles, enabling the encapsulation of a greater amount of therapeutic agents.<br>• It provides improved stability for encapsulated drugs, protecting them from degradation and enhancing their shelf life.<br>• Post incorporation of drug show controlled and sustained release, contributing to optimize therapeutic outcomes.<br>• Exhibit biocompatibility, minimizing potential adverse effects and allowing for their safe use in drug delivery.<br>• Enhance the bioavailability of poorly water-soluble drugs by promoting their absorption and distribution. | 13, 14, 15, 16, 17 |
| **3** | **Solid Lipid Nanoparticles** | • They provide enhanced stability for encapsulated drugs, protecting them from degradation and improving shelf life.<br>• Exhibit a high drug loading capacity, allowing for the encapsulation of a substantial amount of therapeutic agents.<br>• SLN protects labile compounds from degradation, allowing for the delivery of sensitive drugs or bioactive molecules.<br>• Enhance the bioavailability of poorly water-soluble drugs by promoting their absorption and improving systemic circulation.<br>• They are relatively easy to produce and are scalable, making them suitable for large-scale manufacturing. | 18, 19, 20, 21, 22 |
| **4** | **Ethosomes** | • Have the ability to enhance the permeation of drugs through the skin, allowing for improved transdermal drug delivery.<br>• Ethosomes facilitate the absorption of drugs through the stratum corneum, leading to increased drug bioavailability.<br>• They have higher drug loading capacity compared to some other topical delivery systems.<br>• Show generally biocompatibility, and the addition of ethanol may help reduce skin irritation associated with certain drugs.<br>• They have been employed for the delivery of a variety of molecules, including lipophilic and hydrophilic drugs, as well as peptides and proteins.<br>• Ethosomes have demonstrated the ability to penetrate not only the stratum corneum but also the hair follicles, providing an additional route for drug delivery. | 23, 24, 25, 26, 27, 28 |
| **5** | **Micelles** | • Micelles can solubilize hydrophobic drugs, enhancing their bioavailability and allowing for effective delivery.<br>• They protect encapsulated drugs from degradation, improving their stability and prolonging their shelf life. | 29, 30, 31, 32, 33 |

| | | | |
|---|---|---|---|
| | | • Designed in such a way for targeted drug delivery by incorporating ligands or modifying their surface properties, improving drug accumulation at specific sites.<br>• They are composed of biocompatible materials that are generally well-tolerated in biological systems, minimizing potential adverse effects.<br>• Micelles can be designed to incorporate imaging agents, allowing for simultaneous drug delivery and diagnostic imaging. | |

**Table 1:** Different types of lipid formulations with of advantages

## Lipid Based Nanoparticles

***Liposomes:*** First introduced by Alec Bangham in 1961, are phospholipid-based vesicles characterized by a lipid bilayer structure. Mimicking cell membranes, liposomes have proven to be versatile drug delivery systems with applications in pharmaceuticals, cosmetics, and research. It consists of phospholipids, forming a lipid bilayer with an aqueous core. The amphipathic nature of phospholipids allows liposomes to encapsulate both hydrophobic and hydrophilic compounds. In the composition of liposomes phospholipids used include phosphatidylcholine, phosphatidylserine, and cholesterol. They can be categorized based on size, lamellarity, and preparation methods. Common classifications include multilamellar vesicles (MLVs), small unilamellar vesicles (SUVs), and large unilamellar vesicles (LUVs). Stealth liposomes, PEGylated to increase circulation time, and cationic liposomes, used in gene delivery, are notable variations. Various methods are employed for liposome preparation, such as thin-film hydration, reverse-phase evaporation, and extrusion. These methods allow control over size, lamellarity, and drug encapsulation efficiency. Liposomes encapsulate a diverse range of drugs, including small molecules, peptides, and nucleic acids. The encapsulation is influenced by factors such as lipid composition, drug solubility, and preparation method. They exhibit controlled drug release, influenced by factors like liposomal composition, size, and surface charge. Passive release through diffusion and active release through stimuli-responsive liposomes contribute to their versatility. Liposomal drug delivery system is used for various anticancer drugs encapsulation, such as Doxorubicin (Doxil), minimize side effects and enhance drug delivery to tumor tissues **[34],** Antibiotic, Antiviral, antifungal to improve drug efficacy and reduce toxicity **[35],** Vaccine and immunotherapy for vaccine antigens and adjuvants, enhancing immune response **[36],** Gene delivery to facilitating the transport of genetic material into cells **[37].**

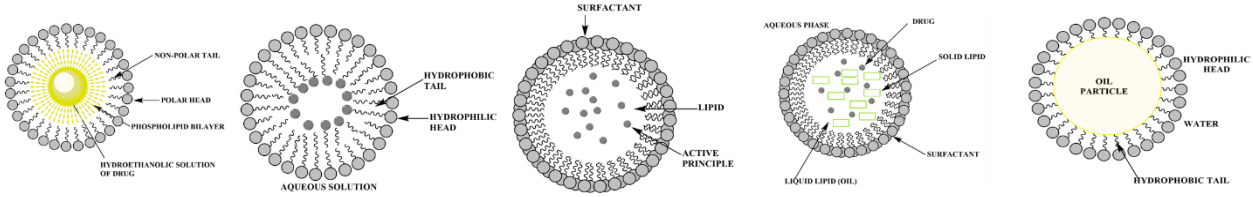
***Nanostructure Lipid Carrier:*** Nanostructured Lipid Carriers (NLCs) represent a novel generation of lipid nanoparticles developed to overcome limitations associated with traditional lipid-based drug delivery systems. Introduced in the early 2000s, NLCs have gained prominence for their unique structure and enhanced drug delivery capabilities. They consist of a blend of solid and liquid lipids, creating a hybrid structure with an amorphous core. The inclusion of solid lipids prevents the crystalline structure found in Solid Lipid Nanoparticles (SLNs), leading to increased drug loading capacity and improved stability. Nanostructured Lipid Carriers (NLCs) can be prepared using various methods, each influencing the characteristics of the final formulation. There are some commonly used preparation methods for NLCs are High- Pressure Homogenization (involves high shear forces to reduce the particle size of the lipid blend, followed by cooling to induce solidification) **[41]**, Solvent Emulsification and Evaporation Method (in which Lipids are dissolved in an organic solvent, emulsified in an aqueous phase, and then the solvent is evaporated, leading to NLC formation) **[42],** Microemulsion Technique (formed by preparing a microemulsion containing lipids, surfactants, and water, followed by solvent removal) **[43],** Melt Emulsification-High Pressure Homogenization (in which Lipids are melted, and a drug is dispersed in the molten lipid. The mixture is then homogenized under high pressure) **[44],** Double Emulsion Method (this involves the formation of a primary water-in-oil emulsion, followed by a second emulsification step in an aqueous phase) **[45],** Coacervation Method (involves the separation of a phase into two liquid phases, with the drug being incorporated into one phase, followed by hardening to form nanoparticles) **[46].** This lipid blend (NLCs) drug delivery system is used in various therapy such as anticancer drug to improve efficacy by encapsulation into this carrier **[38],** dermal and transdermal delivery to enhance drug permeation **[39],** ocular drug delivery to improve drug delivery in to the eye **[40].**

***Solid Lipid Nanoparticles***: Solid Lipid Nanoparticles (SLNs) represent a class of colloidal drug delivery systems that offer a versatile platform for the encapsulation and controlled release of various therapeutic agents, providing

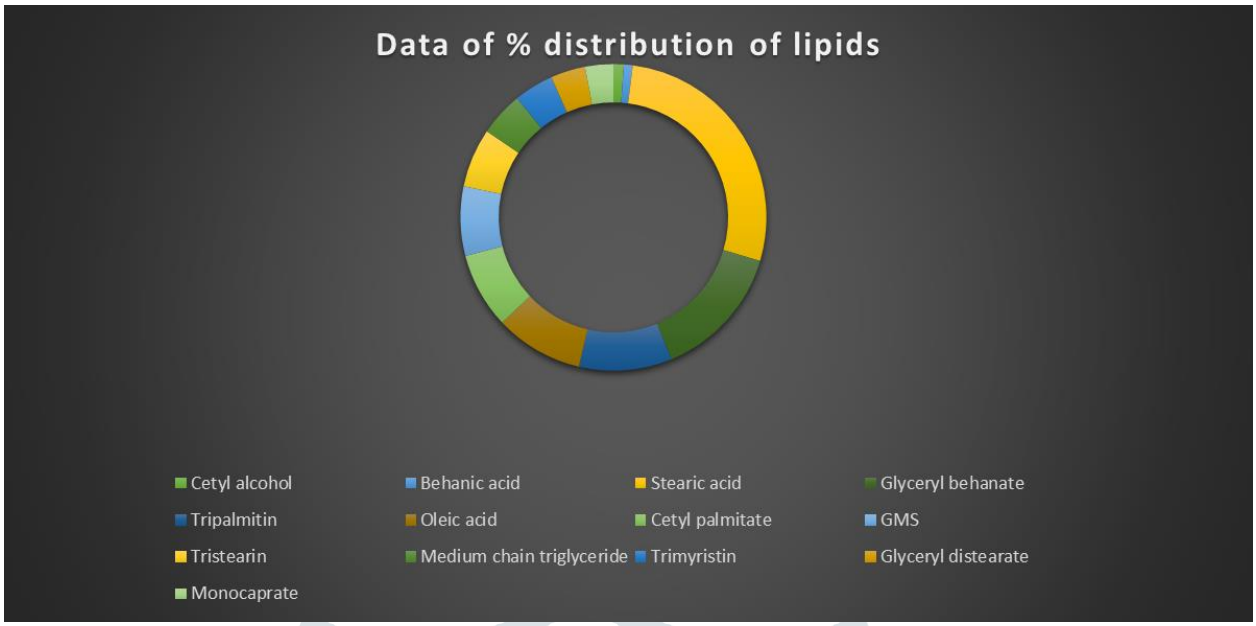
advantages over traditional drug delivery systems. They are composed of lipids that are solid at room temperature, usually in the form of lipids or lipid mixtures. The lipid matrix forms a colloidal nanoparticle structure with a diameter typically in the range of 10 to 1000 nanometers. Surfactant is used to stabilize its solid core in the preparation along with the choice of lipids because it influences the properties including drug loading capacity and release kinetics as well as the selection of surfactant is crucial due to its impairment in stability of SLNs **[47].** Likewise, NLCs, they can also be prepared by different methods such as High Shear Homogenization and Ultrasonication (Lipids are melted, and the drug is dispersed in the melted lipid. The mixture is then homogenized at high shear, followed by ultrasonication to reduce particle size). **[48],** Hot Homogenization and Cold Homogenization (Lipids are melted, and the drug is dispersed in the melted lipid. The mixture is then homogenized at an elevated temperature or hot homogenization. Subsequently, the hot homogenized mixture is cooled rapidly to room temperature and this phase is called cold homogenization. **[49],** Emulsification–Solvent Evaporation Method (Lipids are dissolved in an organic solvent, and the drug is added to the solution. This solution is emulsified in an aqueous phase, and the organic solvent is evaporated to form SLNs). **[50],** Supercritical Fluid Technology (SLNs are formed by precipitating the lipid and drug from a solution by using supercritical fluid such as carbon dioxide as antisolvent) **[51],** Microemulsion Technique (dispersion of lipids in a mixture of water and surfactants as a result of solidification of the microemulsion leads to the formation of SLNs) **[52],** Double Emulsion Method (this involves the formation of a primary water-in-oil emulsion, followed by a second emulsification step in an aqueous phase) **[53],** Coacervation Method (involves the separation of a phase into two liquid phases, with the drug being incorporated into one phase results hardening leads to SLN formation) **[54].**

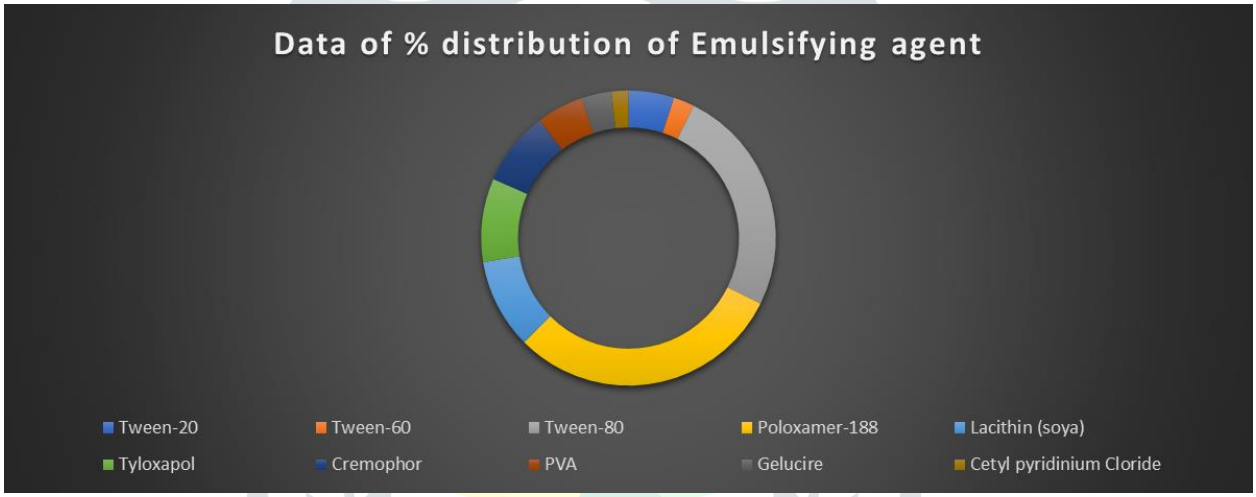
***Ethosomes:*** They are specialized lipid-based vesicular carriers developed for enhanced transdermal and topical drug delivery. They are characterized by the inclusion of high concentrations of ethanol, which imparts unique properties facilitating improved drug permeation through the skin. It consists of phospholipids, high concentrations of ethanol (usually 20-45%), water, and occasionally other components. The high ethanol content imparts fluidity to the vesicle membrane, enhancing its flexibility and permeability. Ethosomes can be formulate by various method such as cold method (Lipids and ethanol are mixed at room temperature, followed by the addition of an aqueous phase and then the mixture undergoes ultrasonication or mechanical stirring) **[55],** Hot Method (Lipids and ethanol are heated until a clear solution is formed, followed by the addition of water with continuous stirring then allowed for cooled to form ethosomes) **[56],** Reversed Phase Evaporation (A water-in-oil emulsion is formed by adding an aqueous phase to a lipid phase containing ethanol, the emulsion is then evaporated under reduced pressure) **[57],** Microwave-Assisted Method (Lipids, ethanol, and water are mixed and heated using microwave irradiation then the resulting mixture is sonicated to form ethosomes) **[58],** Dual Asymmetric Centrifugation (Lipids, ethanol, and water are combined and subjected to dual asymmetric centrifugation to form ethosomes) **[59],** Hot High-Pressure Homogenization (Lipid and ethanol are mixed at an elevated temperature, followed by homogenization at high pressure then the resulting mixture is allowed to cooled to form ethosomes) **[60].**

***Micelles:*** Micelles are colloidal structures formed by the self-assembly of amphiphilic molecules in a solvent. These structures, commonly in the form of spherical aggregates, play a crucial role in solubilizing and delivering hydrophobic drugs, enhancing their bioavailability. They are typically composed of amphiphilic molecules, such as surfactants or lipids, which have both hydrophobic and hydrophilic regions. In an aqueous environment, these molecules arrange themselves to form a core-shell structure, with the hydrophobic tails oriented toward the center, creating a hydrophobic core where hydrophobic drugs can be encapsulated. They are formed by various methods such as Solvent Evaporation Method (drug and amphiphilic molecules are dissolved in an organic solvent, and the solvent is then evaporated, leading to micelle formation) **[61],** Spontaneous Emulsification (A mixture of surfactant and co-surfactant is introduced to an aqueous phase with the drug, leading to the spontaneous formation of micelles) **[62].**



**Percentage distribution of lipids and emulsifying agents used in preparation of SLNs/NLCs**




**Pre-formulation preparation strategies for lipid based nanoformulation approaches:**

Pre-formulation preparation for lipid-based nano approaches involves the development of stable and effective formulations for drug delivery, offering advantages for drug delivery due to their biocompatibility, versatility, and ability to improve drug solubility. Here are some preformulation strategies for lipid based nanoformulation approaches. Choose lipids based on their biocompatibility, stability, and ability to encapsulate the drug [100]. Perform compatibility studies to ensure that the drug is stable within the selected lipid matrix [101]. Optimization of particle size to enhance drug encapsulation and improve bioavailability [102], Surface modification allow to improve stability, prevent aggregation, and control drug release [103], Using of such stabilizing excipients such as surfactants and co-solvents to enhance formulation stability [104]. In-vitro release studies to understand the drug release profile from the lipid-based nanoparticles [105]. Stability studies under different storage conditions to assess long-term stability [106].

**Physicochemical properties and optimization of lipid based nanoformulation:**

**Particle Size:**

The particle size of lipid-based nanoformulations is a critical parameter influencing their behavior in biological systems. Nano-sized particles (typically in the range of 20-200 nm) are preferred for drug delivery due to their improved bioavailability and tissue penetration. Nanoparticles with smaller sizes (typically in the range of 1-100 nanometers) can penetrate biological barriers more effectively, allowing for improved drug delivery to target tissues and cells and also the smaller particle size favor the high surface area-to-volume ratio influence the drug solubility, bioavailability, and targeted delivery, leading to improved therapeutic outcomes **[63,64].** There are some techniques to minimize the particle size of the formulations such as high-pressure homogenization, sonication, or microfluidization are commonly employed to control and optimize particle size.

**Zeta Potential (Surface charge)**

Zeta potential (ZP) is a measure of the surface charge of nanoparticles, it influences the stability and colloidal behavior of the nanoformulation. ZP reflects the surface charge of nanoparticles. Nanoparticles with a higher zeta potential (positive or negative) experience stronger electrostatic repulsion, preventing them from aggregating as a result homogeneous and dispersed state in suspension formed and lead to increased electrostatic repulsion, reducing sedimentation and promoting stability. In biological systems, nanoparticles with a stable zeta potential are less likely to aggregate or be recognized by the reticuloendothelial system (RES), contributing to improved circulation and bioavailability **[65,66,67,68].** Zeta potential can be modified by incorporating charged lipids or surfactants during the formulation process.

**Drug Loading Capacity:**

Drug loading capacity is a crucial aspect of nanoformulation that influences the efficiency of drug encapsulation and subsequent release. The ability of nanoparticles to carry and deliver therapeutic agents is dependent on their drug loading capacity, which is influenced by factors such as the composition of the nanoparticles, the physicochemical properties of the drug, and the method of nanoparticle preparation. Optimal drug loading is essential to achieve therapeutic efficacy while minimizing adverse effects. For instance, lipid-based nanoparticles, including liposomes and lipid nanoparticles, have gained attention for their ability to encapsulate both hydrophobic and hydrophilic drugs. Researchers often explore various lipid formulations and ratios to enhance drug loading capacity, allowing for the delivery of a diverse range of therapeutic compounds. Optimization involves selecting suitable lipids and adjusting their ratios to maximize drug loading while maintaining stability **[69].**

**Drug Release Kinetics:**

The drug release kinetics of nanoformulations play a pivotal role in determining the therapeutic efficacy and safety of nanoparticle-based drug delivery systems. The controlled release of drugs from nanoparticles influences their pharmacokinetics and therapeutic outcomes. Various mathematical models, such as zero-order, first-order, Higuchi, and Korsmeyer-Peppas, are employed to describe the release kinetics of drugs from nanoparticles. The selection of an appropriate model depends on the characteristics of the nanoformulation and the desired release profile **[70, 71, 72, 73].**

**Stability:**

The stability of nanoformulations is a critical aspect that influences their performance and suitability for various applications, including drug delivery. Stability encompasses several factors such as physical stability, chemical stability, and oxidative stability, which determine the ability of nanoparticles to maintain their intended properties over time. Physical stability refers to the ability of nanoparticles to resist changes in size, shape, and aggregation over time **[74].** Chemical stability involves maintaining the integrity of the nanoparticle structure and preventing degradation of the encapsulated drug or other payload **[75].** Oxidative stability is particularly relevant for lipid-based nanoformulations, and antioxidants may be incorporated to prevent lipid oxidation **[76].**

**Applications of lipid based nanoformulation:**

**Cancer Targeting:**

Lipid-based nanoformulations have shown significant promise in the field of cancer targeting, offering advantages such as improved drug solubility, enhanced bioavailability, and the ability to encapsulate a variety of chemotherapeutic agents. Some of the lipid-based nanoparticles that are able to target the cancer cell effectively are discussed here: Liposomes, can encapsulate both hydrophobic and hydrophilic drugs, providing a versatile platform for cancer targeted therapy. Surface modifications with ligands, such as antibodies or peptides, enable specific targeting of cancer cells, minimizing off-target effects **[77].** Likewise, SLNs and NLCs have been explored for cancer targeting, with the potential to encapsulate a range of anticancer drugs. Their biocompatibility and ability to evade the reticuloendothelial system (RES) contribute to improved drug delivery to tumor sites **[78].** Lipid-based micelles, are also having potential cancer targeting ability. Surface modifications can enhance their stability and enable active targeting to specific cancer cells or tissues **[79].**

**Infectious disease**

Lipid-based nanoparticles, including liposomes, are utilized for the targeted delivery of antibiotics that allowing for enhanced drug delivery to infection sites while minimizing systemic side effects **[80],** they are also explored for antiviral, antifungal and antiparasitic drug delivery, aiming to improve the therapeutic index of active agents. These nanoformulations can encapsulate a variety of drugs, protecting them from degradation and facilitating targeted delivery to infected sites **[81,82,83].**

**Neurological disorder**

Lipid-based nanoparticles, such as liposomes and lipid nanocarriers, are designed to enhance the delivery of drugs across the blood-brain barrier. These nanoformulations can encapsulate therapeutic agents, protecting them during transit and facilitating their transport to the central nervous system and also treatment of neurodegenerative diseases, such as Alzheimer's and Parkinson's disease through targeting specific areas in the brain **[84,85]**

**Cardiovascular disease**

Lipid-based nanoparticles are explored for the targeted delivery of drugs to treat atherosclerosis. These nanoparticles can encapsulate anti-inflammatory or anti-atherosclerotic drugs, improving their solubility and allowing for controlled release at the site of inflammation and also, they are involved in many other cardiovascular diseases such as Thrombosis, protect heart tissue to mitigate damage caused by ischemia, in treatment of hypertension **[86,87,88,89]**

**Metabolic disorder**

Lipid-based nanoformulations play a significant role in addressing metabolic disorders by enhancing the delivery of therapeutic agents and improving the treatment outcomes. These formulations are employed for the delivery of anti-diabetic drugs by improving their solubility and bioavailability, delivery of weight management agent and nutrients delivery for malabsorption conditions **[90,91,92,93].** Lipid-based nanoformulations have emerged as innovative tools in addressing metabolic disorders, offering a targeted and efficient approach for drug delivery and therapeutic interventions. The unique properties of lipid nanoparticles (LNPs) make them particularly suited for navigating the complexities of these conditions. One significant application of lipid-based nanoformulations in metabolic disorders is in the delivery of insulin for diabetes management. Encapsulation of insulin in LNPs enhances its stability, prolongs its release, and facilitates targeted delivery to specific cells, potentially improving patient compliance and treatment outcomes. Moreover, lipid-based nanocarriers can offer protection to therapeutic agents against enzymatic degradation, ensuring the integrity of the delivered drugs **[110].**

**Gene therapy**

Lipid-based nanoparticles serve as effective carriers for the delivery of nucleic acids, including DNA, mRNA, and siRNA. These nanoformulations protect nucleic acids from degradation, enhance cellular uptake, and facilitate their delivery to the target cells **[94].** Lipid-based nanoformulations have emerged as promising vehicles for advancing gene therapy, providing an efficient and versatile approach to deliver genetic material to target cells. The application

of these nanostructures in gene therapy holds immense potential for addressing various diseases at the molecular level. This innovative strategy harnesses the unique properties of lipids, such as biocompatibility and the ability to encapsulate nucleic acids, to overcome challenges associated with gene delivery. Lipid-based nanoparticles (LNPs) offer a protective and stable environment for nucleic acids, shielding them from enzymatic degradation while navigating biological barriers. This protective encapsulation enhances the stability and bioavailability of the genetic cargo during transit, ensuring effective delivery to the intended cells. Moreover, the biocompatible nature of lipid carriers minimizes the risk of adverse reactions, making them suitable for clinical applications. Several studies have contributed significantly to the understanding and development of lipid-based nanoformulations in gene therapy. A comprehensive review by Alamoudi et al. (2015) explores the targeting of the cell cycle using lipid gene nanocarriers, shedding light on the potential of lipid-based platforms in regulating cellular processes. Wang et al. (2004) discuss the co-delivery of drugs and DNA using cationic core–shell nanoparticles, showcasing the versatility of lipid-based systems for multifunctional applications in gene therapy. The review by Zhang et al. (2012) delves into lipid-based vectors specifically designed for siRNA delivery, elucidating the role of lipids in facilitating the delivery of small RNA molecules. Additionally, the work of Yin et al. (2014) provides a comprehensive overview of non-viral vectors, including lipid-based ones, emphasizing their significance in gene-based therapy.

**Vaccination**

They contribute to prolonged shelf life and improved antigen stability in vaccine formulations, enhanced antigen delivery, adjuvant incorporation, targeted antigen delivery to immune cells and mRNA vaccine delivery **[95,96,97,98,99].** Lipid-based nanoformulations have emerged as a groundbreaking approach in the field of vaccination, offering a versatile platform for the delivery of antigens and other immunomodulatory agents. These nanostructures, particularly lipid nanoparticles (LNPs), have gained prominence for their ability to enhance the stability, bioavailability, and immunogenicity of vaccines. The encapsulation of antigens within lipid-based carriers provides several advantages, including protection against degradation, targeted delivery to immune cells, and the induction of robust immune responses. One notable example of the application of lipid-based nanoformulations in vaccination is the development of mRNA vaccines, such as the Pfizer-BioNTech and Moderna COVID-19 vaccines. These vaccines employ LNPs to encapsulate and deliver mRNA encoding viral spike proteins, triggering an immune response that confers protection against the virus. The success of these vaccines highlights the efficacy of lipid-based nanoformulations in facilitating the delivery of genetic material and eliciting potent immune responses **[107, 108, 109]**

**Discussion:**

The review begins by delving into the various lipid-based nanoformulations employed in drug delivery, such as liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), Ethosomes and lipid-based micelles. Each formulation is scrutinized for its unique attributes, encompassing biocompatibility, controlled release capabilities, and the ability to encapsulate a diverse range of hydrophobic and hydrophilic drugs. A detailed exploration of formulation strategies, including lipid composition, surface modifications, and drug loading techniques, sheds light on the versatility of lipid-based carriers. This review is highly rational and scientifically justified for several reasons such as Lipid-based nanoformulations have garnered attention for their potential to overcome challenges associated with conventional drug delivery systems, making the review relevant and timely. They have direct implications for improving the clinical efficacy of pharmaceuticals by emphasizing their potential to enhance drug solubility, stability, bioavailability, and targeted delivery, which are critical factors in achieving therapeutic success. This aspect highlights the practical relevance of these formulations in addressing specific medical challenges, including cancer therapy, neurological disorders, infectious diseases, and inflammatory conditions also justifiably explores the various lipid-based nanoformulations, such as liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and lipid-based micelles. This approach acknowledges the diverse range of carriers available and their unique properties, allowing for a nuanced understanding of formulation strategies.

**Conclusion:**

In conclusion, lipid-based nanoformulations have emerged as versatile and effective tools in the realm of drug delivery, offering a myriad of benefits for achieving precise and efficient targeting. The formulation of lipid-based nanostructures involves intricate design strategies to optimize properties such as size, surface charge, and drug loading capacity. These formulations encompass various delivery systems, including liposomes, solid lipid

nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and lipid-based micelles, each tailored to address specific challenges in drug delivery. The application of lipid-based nanoformulations spans across diverse therapeutic areas, showcasing their potential for targeted drug delivery. From cancer therapy to infectious diseases, neurological disorders, and cardiovascular diseases, lipid-based nanoformulations have demonstrated promising outcomes. Their ability to encapsulate a wide range of therapeutic agents, protect sensitive drugs, and enhance bioavailability contributes to their efficacy in disease management. Despite their remarkable potential, challenges persist, including issues related to biocompatibility, stability, and scale-up for industrial production. Future perspectives in this field involve the integration of advanced materials, personalized medicine approaches, and the incorporation of smart nanotechnologies. The development of multifunctional nanoformulations, continuous manufacturing technologies, and combination therapies will further shape the landscape of lipid-based drug delivery. In essence, lipid-based nanoformulations represent a cornerstone in the evolution of targeted drug delivery, bringing us closer to the realization of personalized and effective therapeutic interventions. As research continues to unravel new possibilities and overcome existing challenges, lipid-based nanoformulations stand poised to revolutionize the way we approach drug delivery, offering a paradigm shift towards precision medicine and improved patient outcomes.

**Future perspective:** The future of lipid-based nanoformulations is characterized by a convergence of cutting-edge technologies, personalized approaches, and a commitment to sustainability. As these formulations continue to advance, their impact on targeted drug delivery and therapeutic precision is poised to redefine the landscape of modern medicine, offering novel solutions for improved patient outcomes.

**Conflicts of Interest:** The authors declare no conflict of interest.

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