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Review Article

## Lipid-Based Nanocarriers for Targeted Drug and Nutraceutical Delivery: Development, Characterization, Applications, and Industrial Challenges

Anjali Mishra \*<sup>1</sup> , Apoorva Kumari <sup>2</sup>, Pranjal Kumar <sup>2</sup>, Arya Kumari <sup>2</sup>, Manas Ranjan Nayak <sup>3</sup>, Rupam Vishwannaath <sup>2</sup>

<sup>1</sup> Department of Pharmacy, Sarala Birla University, Mahilong, Ranchi, Jharkhand 835103

<sup>2</sup> Department of Pharmaceutical Sciences, Jharkhand Rai University, Namkum, Ranchi, Jharkhand 835009

<sup>3</sup> NSHM Institute of Pharmaceutical technology (NIPT), NSHM Knowledge campus, Durgapur, West Bengal 713212

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#### For Correspondence:

Anjali Mishra, Department of Pharmacy, Sarala Birla University, Mahilong, Ranchi, Jharkhand 835103

### Abstract

**Background:** Traditional drug delivery systems often face problems like low permeability, quick metabolism, poor targeting, and lower effectiveness. Lipid-based carriers, due to their unique chemical structure, ability to break down over time, and compatibility with the body, provide a helpful way to improve drug absorption, protect active molecules from breaking down, and reduce toxicity through controlled distribution and targeted delivery.

**Aim:** This article aims to give a clear overview of lipid-based systems for delivering drugs and nutraceuticals, focusing on their development, how they are characterized, their applications, and the challenges faced in industry.

**Objectives:** The objectives include discussing different types of lipid-based carriers, methods for characterization, the delivery of plant-derived bioactive using lipid-based systems, their applications in managing metabolic disorders, how targeted and controlled release works, and the role of artificial intelligence in improving formulations.

**Conclusion:** Lipid-based delivery systems are a flexible and effective way to improve the delivery of drugs and nutraceuticals by enhancing bioavailability, enabling targeted release, and reducing toxicity. Despite the progress made, issues related to stability, scalability, regulatory approval, and industrial manufacturing still exist. This underscores the need for better lipid engineering and AI-driven formulation methods for future advancements.

**Keywords:** Lipid-based carriers, Liposomes, Targeted drug delivery, Nanotechnology, Controlled drug release, Functional foods.

## 1. Introduction

Delivery systems are extremely important in improving the efficacy and safety of medicinal and nutraceutical drugs through increasing the bioavailability, stability, and targeted delivery of drugs. Recent trends have seen a dramatic increase in the use of insoluble drugs that pose serious problems in formulation. The common problem associated with poor solubility is lack of absorption, fast metabolism, and consequently decreased efficacy of drugs<sup>1,2</sup>. Conventional delivery methods such as solutions, emulsions, and gel preparations rarely provide control over delivery, protection from rapid metabolism, and lack specificity to

target organs<sup>3</sup>. Therefore, there is a need for novel delivery systems.

Amphiphilic properties, biodegradability, and biocompatibility offered by the use of lipid-based carriers have made these a promising and effective tool for enhancing the solubility and availability of drugs that are less soluble in water<sup>4,5</sup>. They allow forming different structures like micelles, liposomes, nanoemulsions, and lipid nanoparticles, ensuring effective uptake of the drug, sustained release, and protection against enzymatic and chemical degradation<sup>6</sup>. Furthermore, it is possible to modulate the biodistribution of the drug

with the use of lipid carriers, thus reducing their toxicity while delivering them into target tissues. This makes lipid carriers perfect candidates for delivery through oral, dermal, and pulmonary routes of administration<sup>7</sup>. Another advantage of these vehicles is associated with the possibility of incorporating food-grade compounds<sup>8</sup>.

With respect to nanotechnology and formulations, there has been tremendous progress in the development of lipid carriers due to the possibility of controlling the size, loading, stability, and release rate of the liposomes<sup>9</sup>. In addition, the incorporation of artificial intelligence has proven promising for optimizing the formulation, stability, and scale up of the lipids<sup>10</sup>. However, despite all these developments, the problems of physical and chemical instability, manufacturing limitations, regulatory and commercialization challenges still present themselves.

Accordingly, this paper aims to comprehensively highlight lipid-based delivery systems of drugs and nutraceuticals, specifically in terms of classification, characterization, applications of bioactive compounds from plants and metabolic diseases, targeting and release methods, and the use of lipid technology in functional foods. Stability challenges and manufacturing challenges will also be considered together with artificial intelligence<sup>11</sup>.

## 2. Concept of Lipid-Based Drug and Nutraceutical Delivery Systems

Lipid-based delivery systems involve the use of physiological lipids or lipids analogs in order to improve the solubility, stability, bioavailability, and effectiveness of drug substances and bioactives. These carriers allow incorporation of hydrophobic or lipophilic molecules into a lipid matrix, thus improving their dissolution, absorption, and availability. Lipids as physiologically relevant substances with amphiphilic properties, biodegradability, and biocompatibility, have become popular in various drug delivery techniques<sup>12,13</sup>.

The main characteristic of lipid carriers is their ability to solubilize hydrophobic substances and to deliver them via biological membranes. Various lipid assemblies such as micelles, vesicles, emulsions, and nanoparticles may be utilized for enhancing drug dissolution and preventing enzymatic degradation of labile compounds in physiological conditions<sup>14</sup>. Lipid carriers also possess an important feature related to promoting lymphatic absorption and avoidance of first pass effect, resulting in better oral bioavailability<sup>15</sup>. These properties of lipid-based carriers make them efficient tools for delivery of bioactives, essential oils, vitamins, and difficult-to-dissolve pharmaceutical compounds of plant origin.

Other critical properties of the liposome system that have contributed to their utility in a number of

formulations include the ability to combine with pharmaceutical and nutritional grade compounds to produce nutraceutical and functional foods. They can incorporate antioxidants, polyphenols, fatty acids, and herbal components, among other bioactive molecules, improving stability and delivering such compounds with greater efficiency in the GI tract<sup>16</sup>. Additionally, the employment of natural lipids, such as phospholipids, triglycerides, and fatty acids, decreases toxicity and increases the safety profile of these compounds<sup>17</sup>.

In addition, the use of recent advances in formulation science and nanotechnology has led to the introduction of innovative types of lipid delivery systems, such as nanostructured lipid carriers, nanoemulsions, and self-emulsifying drug delivery systems, among others<sup>18</sup>. Such developments in the field have played a crucial role in the increasing application of lipid systems in the biomedical and pharmaceutical industry.

## 3. Classification of Lipid-Based Drug and Nutraceutical Delivery Systems

The delivery systems based on lipid technology can be classified considering their physical and chemical structure, their chemical composition, and the drug incorporation approach. From simple forms of drug carriers such as lipid emulsions and liposomes up to sophisticated nanostructured and self-emulsifying systems, various approaches were used for developing drug delivery systems aiming at improving drug solubility, availability, and targeted delivery<sup>19</sup>.

Overall, it is possible to distinguish conventional lipid systems from advanced nanostructured lipid delivery systems. The conventional lipid systems include mainly emulsions, microemulsions, and liposomes, and their major advantage is associated with increased stability and solubility of bioactive substances<sup>20</sup>.

Liposomes are one example of conventional lipid carriers which are phospholipidic vesicles that can accommodate both hydrophilic and lipophilic drugs, and therefore are widely used for different drug and nutraceuticals encapsulation. Emulsions and microemulsions are lipid carriers that increase the solubility and permeation potential of the drugs due to their oil-in-water structure. Stability and scalability problems of such systems led to the invention of advanced lipid-based carriers<sup>21</sup>.

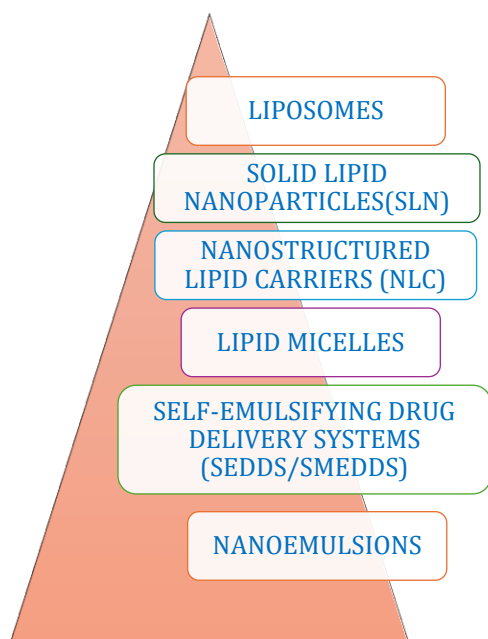
Second-generation lipid systems include SLN and NLC, which possess higher stability and drug encapsulation efficiency than their predecessors. SLN comprises solid lipid matrices, whereas NLC is based on a combination of solid and liquid lipids. Nanoemulsion and SEDDS have become increasingly popular for delivering compounds orally and as nutraceuticals owing to increased solubility and lymphatic absorption<sup>22</sup>.

**Table 1: Detailed description of different lipid systems**

Category	System	Description	Key Advantages	Applications
Conventional lipid systems	Liposomes	Phospholipid vesicles	Biocompatible, versatile	Drug and nutraceutical delivery
	Emulsions	Oil-water dispersions	Solubility enhancement	Oral and topical delivery
	Microemulsions	Thermodynamically stable systems	High stability and permeability	Nutraceuticals
Advanced lipid systems	SLN	Solid lipid core nanoparticles	Controlled release	Oral, topical, pulmonary
	NLC	Solid + liquid lipid matrix	High drug loading	Targeted delivery
	Nanoemulsion	Nanosized oil-water system	Improved bioavailability	Functional foods
	SEDDS/SMEDDS	Self-emulsifying system	Enhanced absorption	Oral delivery

#### 4. Types of Lipid-Based Drug and Nutraceutical Delivery Systems

Lipid based formulations for drug or nutraceutical delivery are an interesting array of formulations used for improving solubility, stability, and bioavailability of biologically active compounds. They vary depending on the structure, drug entrapment, and application area. Some of the most researched formulations include liposomes, solid lipid nanoparticles, nanostructured lipid carriers, nanoemulsions, self-emulsifying drug delivery systems, and lipid micelles. This array of formulations is characterized by unique benefits when it comes to loading and delivering drugs, hence making them highly applicable in pharmaceuticals and nutraceuticals<sup>23,24</sup>.

**Figure 1: Types of Lipids based drug delivery system**

#### Liposomes

Liposomes consist of one or more concentric phospholipid bilayers containing an aqueous interior that can accommodate both hydrophilic and hydrophobic drugs. Being analogous to natural membranes, liposomes are highly biocompatible, safe, and have a high loading efficiency<sup>25</sup>. Hydrophilic compounds are carried by the aqueous core inside the liposomes, whereas lipophilic compounds are included in the phospholipid bilayer, thereby providing dual functionality for drug delivery.

Liposomes contribute to increased stability of the drug, prolonged circulation time, and targeted delivery through the incorporation of ligands or polymers like polyethylene glycol (PEG) at the surface. Liposomes are extensively applied in pharmaceutical products for anticancer purposes, vaccine administration, and nutraceutical delivery since they offer protection of unstable compounds and increase their bioavailability<sup>26</sup>. Liposomes have some limitations as well, such as instability, high costs, and limited shelf-life<sup>27</sup>.

#### Solid Lipid Nanoparticles (SLN)

Solid lipid nanoparticles are submicron-size particles made up of solid lipids that are stabilized with surfactants to achieve targeted release and stability. The lipids used in SLNs remain solid at both room temperature and body temperature, making it easier to preserve the entrapped drugs and release them effectively. Solid lipid nanoparticles have many benefits, including being biocompatible, nontoxic, stable, and scalable<sup>28</sup>.

SLNs can be used for drug administration through the oral, topical, and pulmonary routes since they improve drug solubility, thus increasing the drug's bioavailability. This makes SLNs ideal for the delivery of natural products like phytochemicals and nutraceuticals since they easily encapsulate lipophilic compounds. However, some disadvantages associated with SLNs include low drug loading and lipid crystallization<sup>29</sup>.

### Nanostructured Lipid Carriers (NLC)

NLC is considered the second-generation lipid nanoparticles and is designed to address the shortcomings of SLN. NLC consists of a combination of solid and liquid lipids, resulting in a defective lipid matrix, which helps achieve better encapsulation and stability. This innovation improves the loading capacity and decreases drug leakage<sup>30</sup>.

NLC has received much recognition in pharmaceutical and nutraceutical industries because of their controlled release nature, good stability, and high bioavailability. The application areas include skin care products, orally delivered drugs, and target drug delivery applications. NLC is a suitable system owing to its capacity to encapsulate lipophilic as well as hydrophilic substances<sup>31</sup>.

### Nanoemulsions

A nanoemulsion is a thermodynamic or kinetic system involving the dispersion of oil or water in another phase. The average diameter of the dispersed phase is between 20 and 200 nm. This technology has been extensively employed to improve the solubility and bioavailability of hydrophobic substances such as drugs and nutraceutical ingredients<sup>32</sup>.

Nanoemulsions can effectively dissolve poorly soluble drugs and increase their surface area for better absorption across biological barriers. These formulations are very effective in delivering oral dosage forms or in functional foods. In addition, nanoemulsions are easily scalable and ideal for commercial manufacturing<sup>33</sup>.

### Self-Emulsifying Drug Delivery Systems (SEDDS/SMEDDS)

Self-emulsifying drug delivery systems represent isotropic solutions of oils, surfactants, and cosurfactants that, when coming into contact with gastro-intestinal juices, form emulsions automatically. This delivery system is known to increase solubility and absorption of the drug because they form tiny oil droplets that promote lymphatic transfer and decrease first pass effect<sup>34</sup>.

SEDDS and SMEDDS have found extensive application in oral delivery of drugs and nutraceuticals due to their higher bioavailability and sustained-release characteristics. The other benefits of this delivery system include simplicity of manufacture, greater stability, and better compliance<sup>35</sup>.

### Lipid Micelles

Lipid micelles constitute nanoscale colloidal structures consisting of amphiphilic molecules present in aqueous media, which have the core comprising the hydrophobic part while the hydrophilic part constitutes the outer shell. These are highly stable and effective in solubilizing drugs as well as increasing their bioavailability. They have found widespread applications in drug delivery,

delivery of nutraceuticals, and targeted drug therapies owing to their stability and tiny size<sup>36</sup>.

Lipid micelles are efficient in delivering bioactive compounds, antioxidant compounds, and hydrophobic drugs.

## 5. Components of Lipid based drug delivery system Lipids

Lipids constitute the essential building blocks in lipid-based systems, and they are primarily involved in the process of encapsulating and releasing drugs. Triglycerides, fatty acids, phospholipids, waxes, and glycerides are some of the frequently utilized lipids. The hydrophobic nature of lipids is employed to incorporate drugs that are not easily soluble in aqueous solutions, and natural lipids such as phosphatidylcholine and stearic acid are widely employed due to their biocompatible and biodegradable nature<sup>37,38</sup>.

Lipids have an immense impact on the drug-loading capacity, drug release profiles, and even stability of formulations. Solid lipids have been mostly applied in solid lipid nanoparticles for sustained drug release, while liquid lipids are used in nanoemulsions and nanostructured lipid carriers for increased bioavailability and dissolution of drugs. The employment of food-grade lipids further makes it possible to produce functional foods and nutraceuticals<sup>39,40</sup>.

### Surfactants

Surfactants are important agents that ensure the stability of lipid systems through the reduction of surface tension between oil and water components, ensuring that there is no aggregation. This helps form emulsions, nanoemulsions, and lipid nanoparticles by increasing interactions between lipid and aqueous phases. Some common surfactants are tween, span, lecithin, and sodium dodecyl sulfate, and they are commonly used in drugs<sup>41</sup>.

Surfactants affect the size of particles, rate of drug release, and absorption of lipid-based systems. Non-ionic surfactants should be preferred because of their low level of toxicity and biological compatibility. Selection and use of the right number of surfactants are very crucial in ensuring formulation stability and increasing bioavailability of the drug<sup>42</sup>.

### Co-Surfactants

Co-surfactants are used in lipids to further decrease interfacial tensions and improve emulsification properties. They increase the mobility of the interface, which enables the production of stable nanoscale droplets as well as drug solubilization. Examples of co-surfactants are ethanol, propylene glycol, polyethylene glycol, and short-chain alcohols<sup>43</sup>.

The use of co-surfactants increases thermodynamic stability of the self-emulsifying system and of the produced nanoemulsion. They improve drug

permeability and lymphatic drug transportation in the gastro-intestinal tract<sup>44</sup>.

### Oils

Oils are the key components responsible for the solubility of hydrophobic drugs and nutraceuticals in lipids. Natural and artificial oils, including medium chain triglycerides, long chain triglycerides, and essential oils, are frequently utilized in the formulation design process. They improve the drug solubility and lymphatic uptake, thus enhancing the bioavailability of oral medications<sup>45</sup>.

The type of oil influences the droplet size, drug encapsulation, and stability of the formulation. Medium chain triglycerides are extensively utilized because of their fast absorption and enhanced drug uptake, whereas long chain triglycerides are more favourable for prolonged release and lymphatic uptake<sup>46</sup>.

### Stabilizers and Additives

Stabilizing agents and additives are used in lipid carriers for stabilization, prevention of oxidation, and increasing shelf life. The commonly used stabilizing agents include polymers, antioxidants, and preservatives, which increase the stability of lipid carriers by preventing their degradation<sup>47</sup>.

Examples of commonly used antioxidants include tocopherols and ascorbic acid, while polymers like polyethylene glycol are also used for the same purpose. The main function of these additives is to increase the stability of lipid-based formulations<sup>48</sup>.

## 6. Mechanism of Drug and Nutraceutical Delivery from Lipid-Based Systems

Various methods through which lipid-based formulations improve the therapeutic activity of bioactive molecules include solubility, absorption promotion, lymphatic delivery, release control, and site-specific delivery. All these contribute to improving the bioavailability and effectiveness of poorly soluble drugs and plant-derived bioactive molecules. The association between lipids and biological membrane structures as well as gut fluids helps promote drug delivery and absorption. Lipids are important for the development of both pharmaceuticals and nutraceuticals<sup>49,50</sup>.

### Solubilization Mechanism

Solubilization of poorly soluble drugs and nutraceuticals is one of the main actions of lipid-based delivery systems. Formation of micelles, emulsions, and nanoparticles allows lipids to solubilize lipophilic substances and keep them in a solubilized form, which enhances drug solubility and absorption from the gastrointestinal tract<sup>51</sup>. After administration of lipids, the process of lipid digestion by lipases and bile salts results in formation of mixed micelles, which contributes to the process of drug solubilization and improves drug absorption<sup>51</sup>.

This action is crucial for delivery of lipophilic drugs and natural bioactive substances (polyphenols, essential oils, vitamins, etc.) that are characterized by low solubility and bioavailability due to their lipophilicity. The solubilization effect ensures drug presence in a solubilized form, which prevents precipitation and further enhances absorption of the drug<sup>52</sup>.

### Absorption Enhancement

The use of liposomal delivery systems improves drug absorption because they improve membrane permeability and interact with biological membranes. Lipids and surfactants act on tight junctions in the intestinal epithelial cells to increase paracellular permeation for efficient drug delivery. Lipid digestion products, including fatty acids and mono-glycerols, improve membrane fluidity to promote the transcellular transport of drugs and nutraceuticals<sup>53</sup>.

Lipid-based drug carriers further increase the dwell time of drugs in the GIT and the interactions with the absorption surfaces. The use of nanoparticles improves the contact between drugs and the absorption surfaces because of the increased surface areas created<sup>54</sup>.

### Lymphatic Transport

The other method by which lipid carriers provide drug delivery to the site of action is lymphatic transport, especially for hydrophobic drugs. Lymphatic transport of drugs involves the use of lipids that promote the formation of chylomicrons in intestinal cells and thus transport the drug in the lymphatic network rather than in the portal vein network, thereby circumventing first-pass effect and enhancing the systemic bioavailability of the drug<sup>55</sup>.

The most effective lipids for lymphatic transport include long chain triglycerides, which facilitate chylomicron production and lymphatic drug transport. This mode of transport is used in lipid nanoparticles and self-emulsifying drug delivery systems for delivering antineoplastic drugs, hormones, and nutraceuticals<sup>56</sup>.

### Controlled Release

Controlled release of drugs in lipid-based systems can be achieved by controlling the diffusion of the drug out of the lipid system. The use of solid lipid nanoparticles and nanostructured lipid carriers enables the formation of a stable lipid system where the drug is slowly released over time to ensure that the drug level remains constant in the body. This release process is controlled by altering the composition of the lipids, particle size, and surfactant concentration<sup>57</sup>.

The benefit of controlled release in drug therapy involves minimizing the number of doses administered, ensuring that patients adhere to the regimen, and reducing the side effects associated with sudden changes in drug levels in the blood stream.

## Targeted Delivery

The mechanism of targeted delivery is one of the sophisticated methods that are used by lipid-based systems in order to deliver medications and nutraceuticals to certain body parts. Surface modification of lipid vehicles using ligands, antibodies, or polymers allows the process of site-specific drug delivery to be performed. The example of site-specific lipid-based formulations includes pegylated liposomes or ligand functionalized nanoparticles that target only certain cell types, e.g., cancer cells or inflamed tissue. Nano-scale lipids can use the EPR effect to perform their delivery to diseased areas passively<sup>58-59</sup>.

## 7. Characterization of Lipid-Based Drug and Nutraceutical Delivery Systems

The characterization of lipid-based drug and nutraceutical delivery systems is a necessary process in the design and optimization of the formulations due to its importance in ensuring their stability, safety, effectiveness, and consistency. Characterization allows the determination of the physicochemical and physical parameters of lipid carriers that include liposomes, nanoemulsions, solid lipid nanoparticles, and nanostructured lipid carriers in terms of their size, surface charge, morphology, thermal behaviour, crystallinity, molecular interaction, and stability, which in turn define the performance of these carrier systems in pharmaceutical and nutraceutical applications<sup>60</sup>.

A number of analytical techniques are routinely employed for characterizing lipid-based carrier systems, and some of these include particle size analysis, measurement of zeta potential, morphological studies, encapsulation efficiency analysis, thermal behaviour analysis, spectroscopic studies, crystallinity studies, and stability analysis among others.

### Particle Size Analysis

Particle sizes are some of the essential parameters of lipid drug delivery systems. This parameter affects the process of drug absorption, stability, biodistribution, and effectiveness of the administered drug. When the particle sizes are small, the process of dissolution, diffusion, and bioavailability becomes better and faster. The normal range of nanoemulsion and lipid nanoparticles is usually from 10 nm to 500 nm since it enhances the interaction of the particles with intestinal and cellular membranes.

Dynamic light scattering (DLS) is a common method for evaluating the sizes and polydispersity indexes (PDI) of particles in such drug delivery systems. A low PDI value (<0.3) confirms uniform dispersion and stability of the prepared formulations<sup>61</sup>.

### Zeta Potential

Zeta potential is responsible for the surface charge on lipid particles, and it is essential for determining the formulation stability. The higher the zeta potential value (>±30 mV), the more stable the system, since it prevents

aggregation or sedimentation of the particles due to repulsive force.

Zeta potential is also an important property with respect to uptake and biological effects, including mucoadhesion. Positive charges on lipids improve the interaction with negatively charged cell membranes.

### Exterior surface Morphology

Analysis of morphology reveals details regarding shape, structure, and surface properties of liposomal drug carriers. Scanning electron microscopy (SEM), transmission electron microscopy (TEM), and atomic force microscopy (AFM) have been extensively used for imaging lipids and liposomes<sup>62</sup>.

### Encapsulation Efficiency

The encapsulation efficiency is defined as the proportion of drug or nutraceutical entrapped into the lipid vesicles. It is an important factor that indicates how much drug will be entrapped in the lipid vesicle. High encapsulation efficiency means low amount of leakage of drug.

Encapsulation efficiency is generally determined by UV spectrophotometry, HPLC, and centrifugation technique. The encapsulation efficiency is expressed as follows:

$$\text{Encapsulation Efficiency (\%)} = \left( \frac{\text{Entrapped Drug}}{\text{Total Drug}} \right) \times 100$$

### Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) helps to investigate the thermal characteristics of the drugs and lipids included in the preparation. DSC provides information about the melting point, crystallinity, phase transition, and the interaction between drug and lipid.

### Fourier Transform Infrared Spectroscopy (FTIR)

FTIR is applied for studying molecular interaction between lipids and drugs or nutraceuticals. FTIR allows us to understand the functionality and bonding of the molecules in formulation,

### X-ray Diffraction (XRD)

X-Ray Diffraction (XRD) techniques are applied to ascertain whether the sample is crystalline or amorphous. This technique is helpful in knowing how lipids and drugs change structurally during formulation.

### Stability Studies

Stability studies play an important role in the determination of shelf-life and overall performance of lipid-based drug delivery and nutraceuticals. Such stability studies include the examination of physical, chemical, and thermal stabilities under various environmental conditions like temperature, humidity, and light.

Accelerated stability tests have been carried out under varying conditions of 25°C, 40°C, and 75% relative humidity for the evaluation of formulation stability. The formulations of lipids, which remain stable, exhibit

consistent performance throughout the storage period due to stability in particle size, composition, and structure<sup>63</sup>.

## 8. Future Scope and Challenges of Lipid-Based Drug and Nutraceutical Delivery Systems

The utilization of lipid-based drug and nutraceutical delivery systems has been recognized because of their potential to improve solubility, bioavailability, stability, and specific targeting of drugs that are poorly soluble in water. The use of liposome, nanoemulsion, solid lipid nanoparticles, and nanostructured lipid carrier is one such effective means of improving therapeutic action and lowering the toxicity of the drug. In spite of great technological advances in lipid nanotechnology, a number of challenges like instability, low loading, scalability, and regulation continue to limit their industrial implementation. Meanwhile, innovations like artificial intelligence technology, eco-friendly lipid materials, and intelligent drug delivery systems present a promising avenue for the future development of lipid-based drug delivery.

One of the problems associated with lipid-based drug delivery is physical and chemical instability. Lipid-based drug delivery systems tend to undergo degradation as a result of oxidative or hydrolytic reactions or phase separation. Such changes may cause loss of drug content and aggregation, resulting in poor shelf life. This may be exacerbated by environmental conditions such as temperature and humidity. Consequently, the creation of lipid formulations with better antioxidant performance and suitable storage conditions is necessary to ensure quality control and efficacy.

The limited drug-loading capability of lipid formulations, especially for lipophilic drugs and nutraceuticals, represents another drawback of the technique. In case of excess inclusion of the drug, it affects the stability and the encapsulation process and negatively influences the drug-release profile from the carrier. The balancing of lipid content, surfactants, and drug solubility is a crucial step during the preparation of formulations. Novel lipid engineering and hybrid nanocarrier design represent promising approaches to address this issue and optimize drug loading efficiency.

The industrial scale-up process poses additional challenges for lipid-based drug carriers and nutraceuticals. While laboratory-level methods like high-pressure homogenization, ultrasonic treatment, and microfluidization provide uniform results, it is challenging to maintain particle size, encapsulation efficiency, and stability on an industrial level. Besides, the cost associated with specialized equipment for large-scale production limits industrial feasibility. Microfluidization and continuous processing techniques have emerged as potential solutions for ensuring the reproducibility and scale-up of lipid formulations.

Other issues related to regulations and safety measures constitute a critical barrier for the further research of lipid-based systems and their implementation. To

receive an approval, it is necessary to assess all potential toxicity risks as well as the biocompatibility and safety of all the excipients used. Moreover, the lack of regulatory measures in regard to nutraceutical products in different states makes the matter even more difficult. Hence, the creation of regulatory framework for liposomal drug delivery systems is needed to ensure their safe usage in the pharmaceutical industry.

However, despite all these difficulties, the future perspective of using lipid-based systems looks extremely bright, especially because of the use of artificial intelligence in the development of formulations. The use of AI and machine learning may help to enhance formulations in terms of optimizing lipids content and properties as well as the behavior of the particles. Such techniques may save researchers much time and effort in creating new formulations.

Moreover, advancements in developing lipid-based delivery systems capable of selective and efficient drug delivery will transform the landscape of pharmaceutical and nutraceutical formulations. These stimuli-sensitive systems have the ability to release drugs based on changes in pH, temperature, enzymes, or other external cues. Targeted delivery of drugs via ligands-based approach and functionalization of lipid nanoparticles have become popular options in cancer treatment, metabolic disorders and delivery of plant derived bioactives.

Lastly, the increasing popularity of functional foods and nutraceuticals is anticipated to lead to the growth in demand for lipid-based delivery systems in plant derived bioactives like curcumin, polyphenols, essential oils, and vitamins. Formulations based on nanodroplets, lipid vesicles (liposomes), and solid-lipid nanoparticles offer superior stability and improved bioavailability of these bioactives. This aspect will promote lipid-based formulations as part of functional foods. The future trends in the area of lipid-based delivery systems include the development of novel eco-friendly and sustainable lipids using plant oils, marine lipids and biodegradable components. Formulation of lipid delivery systems by green formulation processes and green manufacturing methods will lower toxicity and adverse environmental impacts.

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