VOLUME 10 ISSUE 1 2024

ISSN 2454 – 3055

INTERNATIONAL JOURNAL OF ZOOLOGICAL INVESTIGATIONS

Forum for Biological and Environmental Sciences

Published by Saran Publications, India

International Journal of Zoological Investigations Vol. 10, No. 1, 811-823 (2024)

International Journal of Zoological Investigations
Contents available at Journals Home Page: www.ijzi.net
Editor-in-Chief: Prof. Ajai Kumar Srivastav
Published by: Saran Publications, Gorakhpur, India

ISSN: 2454-3055

Advancement in Lipid-Based Drug Delivery System: A Comprehensive Review

Kokate Shekhar V.*, Valvi Sanjana Vilas and Ushir Yogesh V.

S.M.B. T College of Pharmacy Nandi Hills, Dhamangaon, Tal. Igatpuri, Nashik 422403, Maharashtra, India

**Corresponding Author*

Received: 8th April, 2024; **Accepted:** 7th May, 2024; **Published online:** 17th May, 2024

https://doi.org/10.33745/ijzi.2024.v10i01.088

Abstract: Lipid-based drug delivery systems (LBDDS) have the potential to transform pharmaceutical delivery by providing a viable solution to the problems associated with poorly soluble drugs. They accommodate different medication kinds and administration routes while improving stability, absorption, and bioavailability. Notwithstanding their potential, difficulties remain in achieving optimal lipid selection and comprehending the intricate connection between lipids and pharmacological action. To overcome these challenges and fully utilize LBDDS is the aim of continuing research., opening the door to better patient care and more efficacious therapies. Scientists can solve the shortcomings of standard formulations by customizing drug delivery systems to specific therapeutic needs by utilizing the adaptability of LBDDS. LBDDS has the potential to revolutionize medicine distribution and satisfy changing pharmaceutical needs as long as research and innovation in the field are sustained.

Keywords: Permeability, Biodegradability, Lipid, Surfactant

Citation: Kokate Shekhar V., Valvi Sanjana Vilas and Ushir Yogesh V.: Advancement in lipid-based drug delivery system: A comprehensive review. Intern. J. Zool. Invest. 10(1): 811-823, 2024.

https://doi.org/10.33745/ijzi.2024.v10i01.088

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Introduction

These days, a lot of work has been put toward utilizing the potential of drug delivery methods based on lipids because they offer a convenient way to deliver drugs with different molecular weights – small or large – and bioactive chemicals at specific locations and within time constraints. Pharmaceuticals with poor solubility and bioavailability present challenges for formulation scientists. Because of its proven effective size-dependent properties, lipid-based medication delivery method has attracted a lot of attention (Bellefroid *et al*., 2019; Berthelsen *et al*., 2019). Drug delivery methods based on lipids, which employ lipids as carriers, are essential for delivering hydrophobic medications with low bioavailability. Micellar systems, lipid solutions, and self-emulsifying drug delivery systems are examples of LBDDSs, which are composed of a variety of physically different media. By solubilizing the medication in lipids, surfactants,

co-solvents, or combinations of these, the majority of LBDDSs deliver the medication to the GI tract in solution. Lipids are legitimately regarded as safe and practical medication delivery materials(*et al*., 2021). The reliability of system is closely connected to the distribution of particle sizes, the amount of lipid present, and the existence of a surfactant that can stabilize the dispersion. In accordance with the disease state, route of management cost, toxicity, or efficacy of the products, different lipid formulation adjustments can be made to satisfy a variety of product requirements(Muller *et al*., 2002).

Lipid-based drug delivery system have a good experience of user acceptance. Many drugs, including proteins, peptides, and nucleic acids, are delivered by LBDDS. Various methods are used to administer LBDDS, including oral, parenteral, ophthalmic, intranasal, dermal, transdermal, and vaginal (Pattewar *et al*., 2016). Similarly, LBDDS has seized the initiative because of its greater biocompatibility and adaptability, which are clear benefits. Pharmaceuticals can be commercially formulated using these techniques for parenteral, pulmonary, topical, or oral administration. Because lipid-based vehicles are effective and safe, these are attractive alternatives for vaccinations, medications, and nutritional formulation (Pund, 2021). It appears that lipid-based formulations are the most crucial in the efficient distribution of poorly water-soluble or insoluble drugs, despite having been utilized to minimize adverse outcomes and maximize targeted administration of active agents. This need to be mentioned that using formulation on lipid primarily determined by biological characteristics of the intended cell or tissue, the method of distribution, and nature and type of active ingredients (Pattewar *et al*., 2016). Despite their pharmacological efficacy, most novel drug candidates meant for oral administration have low oral bioavailability, which prevents them from moving on to further advanced phases of research and development (Patil and Deshpande, 2018). Consequently, it is necessary to provide DDSs with the necessary bioavailability so they can have the intended therapeutic impact (Zubair *et al*., 2021). In order to avoid the dissolving of crystalline material becoming the rate-limiting step in absorption, lipid-based drug delivery systems for oral use are usually intended to offer a poorly soluble molecule in a dispersed state (Cannon and Long, 2008). Medication delivery based on lipids have been thoroughly researched for the oral and transdermal delivery of ED medications due to their wide range of formulation options (Güven, 2020). Drug delivery formulations based on lipids have benefited from the development of new lipid excipients that have favorable safety and regulatory characteristics and can increase oral bioavailability. A number of factors influence how well a medicine is absorbed from lipid formulations, including particle dimension, the rate of dispersion of the emulsifier, and the precipitation of the drug during dispersing (Kalepu *et al*., 2013). Lipid-based systems can range from basic oil solutions to complicated mixes of oils, co-solvents, surfactants, and co-surfactants, depending on the type of excipients and formulation parameter (Zubair *et al*., 2021). These systems are actually transformed by various methods into solid intermediaries such as granules, pellets and powders which is thereafter pressable into tablets or filled into hard gelatin capsules after mixing with suitable tableting excipients (Kalepu *et al*., 2013)

Delivery systems based on lipids provide a wide range of choices. They can be made into self-emulsifying drug delivery systems (SEDDS), dry emulsion, microemulsions, solutions, suspensions, or emulsions. In addition, mixtures of many excipients can be created, such as mixtures of different triglyceride (TG), diglyceride (DG), monoglyceride (MG) or pure triglyceride (TG) oils. Furthermore, hydrophilic co-solvents and various surfactant types (lipophilic and hydrophilic) can be added (Pouton, 2006) It is necessary to assess the feasibility of alternative lipid-based formulations because the absence of improved absorption in one of the aforementioned main formulations does not always imply ineffectiveness. Generally speaking, the lipid-based delivery system must preserve the

medication in liquid throughout the gastrointestinal system and optimize pace and extent of drug dissolution in order to successfully boost oral absorption. Therefore, there is a great demand for techniques to monitor the drug's solubilization state following the dispersal of various delivery mechanisms based on lipids in the GI tract (Muller *et al*., 2002). LBDDS is one class of facilitating DDS designed to bypass the gradual disintegration procedure and make the medication appear soluble in GI fluids. Micellar system, lipid solution, and self-emulsifying DDS are among relatively diverse physical systems that make up LBDDS. The majority of LBDDS transport the medication to the GI tract in solution since it is soluble in lipids, surfactants, co-solvents, or mixtures of these substances. GI fluids can better absorb the medication due to its apparent solubility, and one kind of permitting DDS called LBDDS is made to avoid the sluggish dissolution process. The comparatively varied physical systems that comprise LBDDS include micellar systems, lipid solutions, and self-emulsifying DDS (SEDDS) (Berthelsen *et al*., 2019).

Most medication delivery techniques based on lipids involve lipid vesicles or excipients to solubilize lipophilic medicines, which are inherently poorly water-soluble, hence enhancing medication absorbance in the body. However, hydrophilic pharmaceuticals are dissolved in the system when it comes to water-in-oil emulsions or microemulsions, and phase inversion typically occurs later *in vivo*. Pharmaceutical scientists in various phases of drug research have faced numerous obstacles due to the special properties of lipid-excipients and lipid-based delivery methods (Chen, 2008). Lipid driven methods enhance storage and distribution although preventing oxidation of APIs, breakdown, additionally degradation (Pouton, 2006). The ability of Drug delivery techniques based on lipids to navigate the blood brain barrier, blood vessels, stomach, and gastrointestinal tract is its main benefit. Drug delivery using lipids is an increasingly expanding field. Liposomes are lipid-based delivery systems, as are self-micro-/nanoemulsifying drug delivery systems, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs). Lipids have favorable physicochemical properties, such as biocompatibility, low sensitivity to erosion events, and slow water uptake, making them an ideal nanocarrier system to improve the aqueous solubility, bioavailability, and effective therapy of APIs (Kumar, 2019).

The kind of lipid component used in the delivery mechanism significantly affects how well it increases absorption. The intestinal lumen does not absorb mineral oil, sucrose polyesters, or other non-digestible lipids. It stays in the gastrointestinal lumen and have a tendency to hold the lipophilic medication in the oil, which could restrict the drug's absorption. Digestible lipids are appropriate oils for lipophilic compound medication delivery methods. These consist of cholesterol, fatty acids, phospholipids, triglycerides, and diglycerides, among other synthetic compounds. These lipids are commonly classified based on their degree of saturation, interaction with water, lipid class (TG, DG, MG, or FA), carbon chain length (LCT or MCT), and degree of saturation. This is because the lipidic component's capacity to increase oral absorption is reliant on the medication, and substances with varying lipidic components have varied effects on the three chemo physical characteristics (Dahan and Hoffman, 2008). For example, ethylico-sapentate, tocopherol nicotinate, teprenone, indomethacin, farnesyl, and dronabinol are examples of oily drugs that can be prepared as lipid-based formulations in cases where the medicine is water insoluble or if oral bio-availability is not improved by conventional formulation methods like granulation or soluble liquids in capsules. After being combined with the proper tableting excipients, these systems can actually go through a number of conversion procedures to produce solid intermediates such powders, granules, and pellets, that can subsequently be crushed into tablets or filled into hard gelatin capsules (Berthelsen *et al*., 2019). This review describes how the effectiveness of a

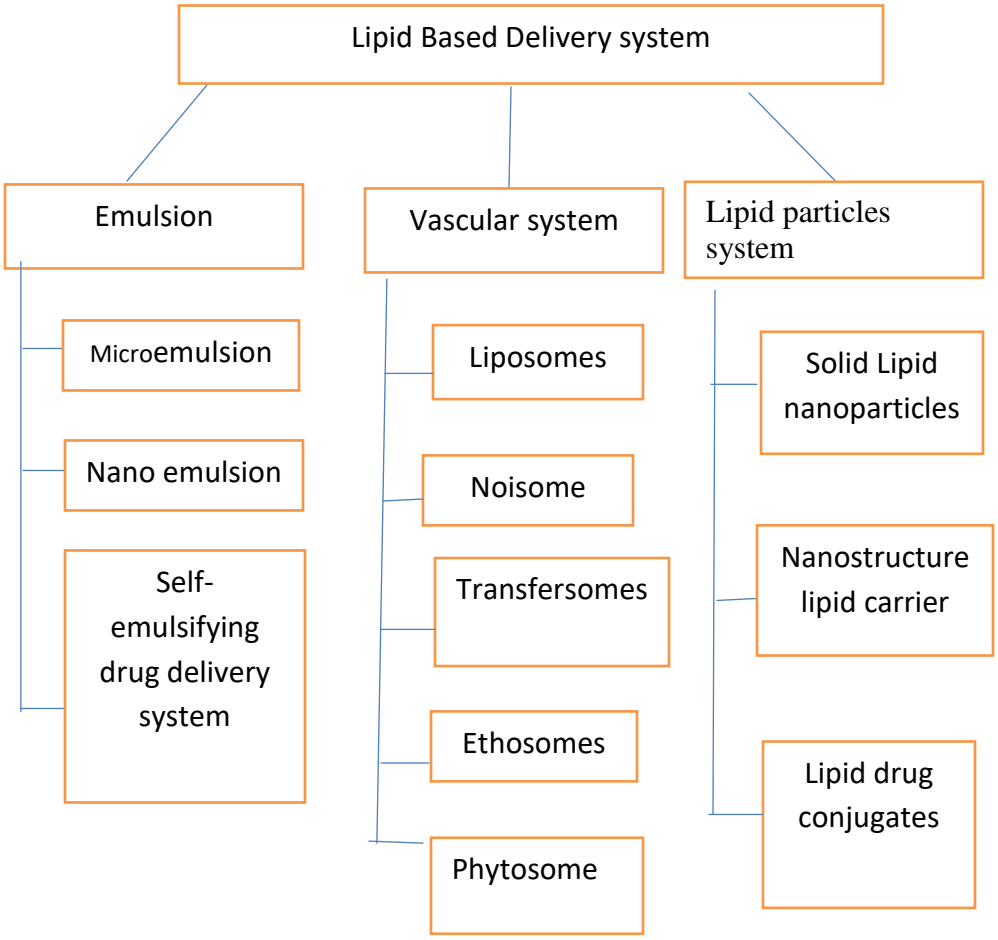

Fig.1: Types of lipid-based drug delivery.

lipid-based delivery system is attributed to the careful design of a specific drug candidate and the suitable selection of vehicle composition. In general, for a lipid-based delivery system to maximize oral absorption, the drug must be kept in solution throughout the GI tract and the rate and amount of drug dissolution must be optimized. Therefore, there is a great demand for techniques to monitor the condition of the medicine solubilization subsequent to dispersal of various different GI tract lipid-based delivery method (Dahan and Hoffman, 2008).

Types of Lipid-Based Delivery System:

(1) *Emulsion*:

(a) *Microemulsion*:

The state of some LBDDS following dispersion is frequently referred to as a microemulsion (Fig. 1). Microemulsions (MEs) are not emulsions, despite the term suggesting an emulsion with extremely small particles (Souto *et al*., 2011). The state of some LBDDS following dispersion is frequently referred to as a "microemulsion (Cannon and Long, 2008). MEs are defined as optically transparent, low viscosity, and thermodynamically stable dispersions of water and oil that have been micro-emulsify by a surfactant. Typically, a cosurfactant--a polyhydroxy compound and another surfactant-- is added to the mix to enhance the interfacial film's ability to curve at the oil/water interface. Microemulsion are well researched as a method of transdermal medication administration because of its various benefits, including improved skin penetration, ease of manufacture, high solubilization ability, thermodynamic stability, and attractive appearance (Anton and Vandamme, 2011). High

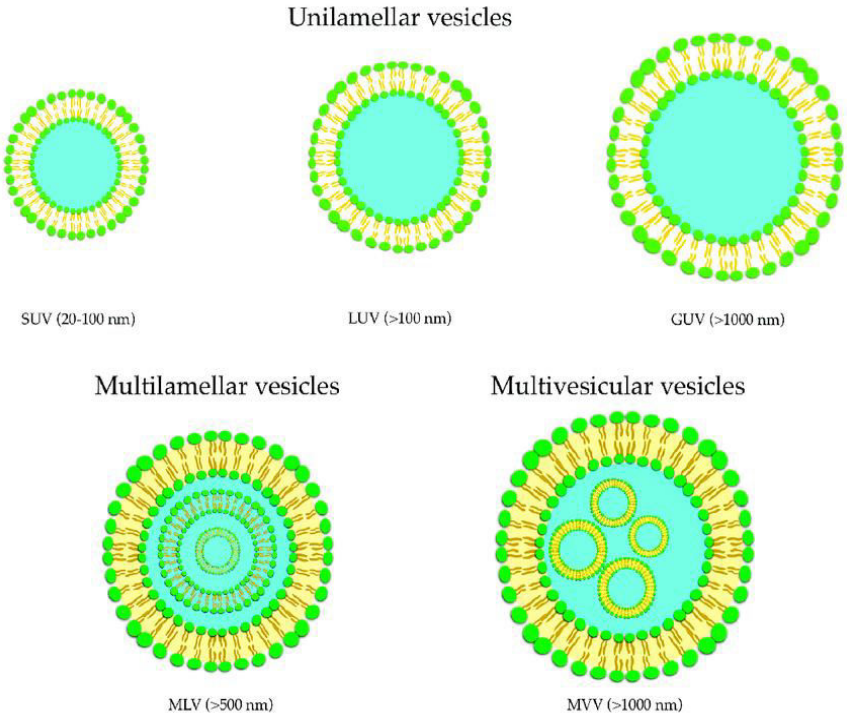

Fig. 2: The three types of liposomes are unilamellar vesicles, multivesicular vesicles (100–2000 nm), and multilamellar vesicles (100–2000 nm).

emulsifier content and cosurfactants are required when using pharmaceutically approved lipids to create a formulation that can form a microemulsion (Pund, 2021).

(b) *Nano emulsion*:

Nano emulsions are translucent, thermo-dynamically stable mixtures of water and oil that are stabilized by an extremely small droplet size (usually 20–200 nm) interfacial coating of surfactant and co-surfactant molecules (Sharma and Baldi, 2018). Nano emulsions are fine emulsions that are either water in oil or oil in water. These forms seem transparent to milky white to the unaided eye because of their droplet size range which is roughly between a few and 200 nanometers. When administered orally, parenterally, or topically, these innovative formulations improve medication delivery. In contrast to microemulsions, water-diluted nano emulsions maintain their stability without altering the droplet size distribution; temperature and pH variations can have an impact on this stability. Researchers in pharmaceuticals were driven to focus on nano-emulsion due to factors such as less toxic formulation, kinetically stable systems, targeted applications, and aesthetic aspects. higher solubilizing ability, consistency over the long run, ease of production and extended shelf life are some of the advantages of using nano emulsions (Sharma and Baldi, 2018).

(c) *A self-emulsifying drug delivery system* (*SEEDS*):

An easily dispersible isotope combination of medication, surfactant, and co-surfactant combined with agitation results in an oil-in-water emulsion with droplet size of less than 1000 nm. This is known as a self-emulsifying drug delivery system (Pund, 2021) as bioavailability of APIs with limited water solubility is improved by self-emulsifying drug-delivery systems (SEDDSs). When compared to powder formulations, they demonstrated a significant improvement in bioavailability (Patil and Deshpande, 2018). The SEDDS features are influenced by various aspects, including size, drug release, and bioavailability. When it comes to increasing bioavailability, SNEDDSs outperform SMEDDSs because of their

nanosized droplets' large interface surface area for drug absorption (Zubair *et al*., 2021).

(2) *Vesicular system*:

(a) *Liposomes*:

Liposomes is polar, circular vesicles made of cholesterol and phospholipid that have several concentric layers. Drugs with varying solubility and partition coefficients can be encapsulated in liposomes, either hydrophilic or lipophilic (Shegokar *et al*., 2017) . Since they were discovered and characterized over the past few decades, liposomes, which are considered to be first-class drug carriers, have shown promise as a carrier system with good biocompatibility, lower toxicity, reduced immunogenicity, and tailored delivery properties (Anton and Vandamme, 2011).

Chole-134 terol and phospholipids comprise the structural elements of liposomes. The liposome is, in its fullest sense, a fat structure that can be encapsulated. Natural or synthesized phospholipids can form liposomes, which are tiny vesicles sizes from nanometers to several micrometers. The natural forms of phospholipids are phosphatidylcholine, phosphatidylethanol-amine, phosphatidylglycerol, phosphatidylserine, and phosphatidylinositol. It is also possible to employ cholesterol to enhance the liposome's bilayer properties. Closed, spherical bilayer vesicles make up liposomes. There have been reports of liposomes that can encapsulate several API types despite differences in size, composition, charge, and feasibility (Patel *et al*., 2013). There are three different types of liposomes unilamellar 135 liposomes, multilamellar liposomes, and multivesicular liposomes (Fig. 2). The lipid species and preparation method 137, which have a significant impact on the sizes and shapes, determine the categorization foundation. Due to the fact that liposomes have the ability to perform many roles after topical application, they were one of the earliest transdermal delivery techniques (Parashar *et al*., 2020). The hydrophilic core of the liposomal construct may help with the loading of hydrophilic medications and their subsequent encapsulation by the lipid bilayer, which may trap the lipophilic candidates and form the vesicular structure (Dhaval *et al*., 2022).

(b) *Niosomes*:

Niosomes are multilayered vesicles made mainly of nonionic surfactants, hydration, medium, and lipids such as cholesterol. Niosomes consist of a hydrated blend of nonionic surfactants like amides, esters, and alkyl-ether. Niosomes alternatively referred to as vesicles containing nonionic surfactant, provide several benefits, such as excellent stability, inexpensive, wide availability of nonionic surfactants, and ease of storage (Patel *et al*., 2013). It has been demonstrated that niosomes offer consistent medication encapsulation and have clear benefits over unencapsulated medicines. They are far more stable than lipids because their main constituents, nonionic surfactants, are more stable in terms of both chemical and physical stability. Furthermore, the PEG on the liposome surface that may have extended the half-life after treatment was limited since the lipid bilayer has a limited capacity (Zubair *et al*., 2021).

(c) *Transfersomes*:

During the 1990s, Cevc and Blume created new lipid vesicles called deformable, elastic, and flexible liposomes to address liposomes' incapacity to penetrate skin (Sharma and Baldi, 2018).Transfersome are among the most effective carriers for skin distribution and are the original class of ultra deformable vesicles. Compared to liposomes, transfersomes are more pliable and stretchers, which are typically five to eight times larger and are typically smaller than 300 nm, making them ideal for skin penetration. Their primary constituents consist of edge activators and phospholipids. These edge activators disrupt the bilayer and give the vesicles extreme flexibility, which improves their ability to pass through the skin's tiny openings. The concentration of edged stimulator in the preparation, usually in the range of 10 to 20 per cent, must be present in sub-lytic amounts, which

means that it cannot degrade vesicles. Their primary constituents consist of edge activators and phospholipids. These edge activators disrupt the bilayer and give the vesicles extreme flexibility, which improves their ability to pass through the skin's tiny openings. It is imperative that the concentration of top stimulator in the formulation typically ranges 10 and 20 pe rcent, be present at sub lytic concentrations, meaning it should not destroy vesicles (Zubair *et al*., 2021)

(d) *Ethosomes*:

Ethosomes, like transfersomes, have the ability to increase transdermal flow and quickly penetrate the stratum corneum barrier (Parashar *et al*., 2020). These spherical lipid blisters, which are mostly made of phospholipids, ethanol, and water, are an example of the second generation of new vesicular drug carriers. The key characteristic that sets them apart from liposomes is their high alcohol content, which can reach up to 45%. This allows for a reduction in size and elasticity while using the same preparation technique. Additional adjuvants included in the ethosomal formulation include gel markers for longer residence duration or cholesterol to enhance stability (Zubair *et al*., 2021).

(e) *Phytosome*:

Phospholipids (phosphatidylcholine, phosphatidylethanolamine, and phosphatidylserine) with naturally occurring bioactive compounds (plant extracts or water-soluble phytoconstituents) make up phytosomes, also known as herbosomes. Phytosomes and liposomes are exactly the same. Phytosomes are a particular type of liposome since they are liposomes that have been loaded with phytocompounds (Sedaghat Doost *et al*., 2020).

(3) *Lipid Particles System*:

(a) *Solid lipid nanoparticles* (*SLN*):

By the end of 20th century's, the conventional colloid carrier systems began to replace such emulsions, liposomes, and polymer particles (Kumar, 2019). SLN is produced using 217 medically acceptable solid lipid components. SLN is produced using 217 medically acceptable solid lipid components. Since they are known to improve the penetration of active chemical, fatty alcohols, fatty acids, and fatty acid esters are among the lipids that are suitable for SLN synthesis (Souto *et al*., 2011). Solid lipids took the place of liquid lipids due to their many benefits. The most efficient colloidal carriers are SLNs. Their great biocompatibility, low toxicity, and ease of scaling up and sterilizing make them extremely beneficial. Since the lipid matrix of SLNs and the epidermal lipids in skin share a similar structure, SLNs have proven to be exceptional transdermal medication transporters in the rapidly expanding field of nanotechnology (Kumar, 2019). The small size range of SLNs (between 100 and 200 nm) allows them to pass through the blood-brain barrier's (BBB) tight endothelial cells during digestion. It bypasses the liver and escapes the reticuloendothelial system. SLNs have an average diameter between 50 to 1000 nm, which is in the submicron range. They are made up of lipids that are dispersed across an aqueous surfactant phase and digested by the body. These nanoparticles in particular show a lot of promise as appropriate drug delivery vehicles. The advantages of SLNs include low prices, ease of use, biodegradability and biocompatibility, better percentages of EE and DL, enhanced stability, compatibility with hydrophilic and lipophilic medications, controlled drug release, and applicability for industrial applications (Zubair *et al*., 2021).

(b) *Nanostructure lipid carriers*:

NLCs are thought to be a better form of SLNs since they have an unstructured lipid matrix created by combining liquid and solid lipids rather than a tightly packed collection of uniformly organized solid lipids. Eventually, this makes more space available for loading medication candidates. The distinct advantages of NLCs include their long-term release, great biocompatibility, and biodegradable nature. The fundamental building block of contemporary nanotechnology is nanoparticles. To increase encapsulation and

drug-loading effectiveness, NLCs, a form of modified lipid nanoparticle, are made by partially integrating a low-melting liquid into a high-melting lipid, resulting in lipid defects (Kumar, 2019). The goal was to design a lipid carrier for nanoparticulate with a particular nanostructure to increase payload and prevent drug expulsion (Ozlen Sahin, 2007).

(c) *Lipid drug conjugates*:

In some cases, the filling capability of SLNs is not enough to fully encapsulate hydrophilic medications because hydrophilic chemicals are poorly soluble in the lipidic phase and the lipid matrix is crystalline. Because of this, lipid-drug bioconjugates can be used to graft drug functional groups (like amine groups) onto fatty acid carboxylic acids (like stearic acid and oleic acid) to transform hydrophilic pharmaceuticals into water-insoluble medications. The conjugate is then melted and homogenized under high pressure to create the lipid-drug bioconjugates. Because of lipid-drug conjugates' superior drug loading capacity over SLNs, much more drug molecules can be transported into target cells with a significantly less quantity of lipid-drug conjugate NPs, allowing for maximum medication delivery with the least number of adverse effects. Targeted gene and medication delivery using lipid-based technology (Pattwar *et al*., 2016).

Advantages (*Pund, 2021*):

1. Increased oral bioavailability that permits dosage adjustment,
2. Selective drug delivery to a certain GIT absorption window
3. Improved consistency in the absorption of drugs throughout time
4. Targeting and regulating the release of drugs
5. Defense of the medication(s) against the intestinal environment
6. Regulating delivery profiles.
7. Decreased unpredictability, encompassing the impact of nutrition
8. Preserving delicate pharmaceutical substances
9. Drug content that is higher and better than other carriers
10. Possibilities of transporting hydrophilic and lipophilic drugs
11. Both biocompatible and biodegradable
12. The versatility of the excipient

Disadvantages (*Vaishnavi et al., 2024*):

1. Drug delivery methods based on lipids have a tendency to experience premature drug release or drug leakage, which could result in less effective and subpar medication delivery.

2. Phase separation or degradation are two unstable lipid-based drug delivery technologies that might impact the formulation's shelf life and efficacy.

3. The formulation or manufacture of drug delivery methods based on lipids can be challenging, requiring specialized equipment and knowledge that can increase production costs and limit scalability.

4. Drug delivery techniques based on lipids occasionally have the capacity to cause the body to mount an immunological response, which could result in negative side effects or diminished medication efficacy.

Application (*Rawat et al., 2006*):

(i) Observational research has largely been used to develop efficient lipid-based delivery strategies. The development of novel and enhanced formulations can be accelerated by systematic physicochemical study of structure and stability, which can also aid in the clarification of the intricate mechanisms underlying the interaction between lipid carriers and live cells. As a result, they aimed to be precise, effective, and safe medication and gene carriers.

(ii) Lipophilic medications that are poorly soluble in water can benefit from lipid-based formulations, as has long been known. Undoubtedly, lipids represent one of the broadest

categories of excipients currently accessible, offering formulators a plethora of possibilities to enhance and regulate the process by which drugs with limited water solubility are absorbed.

(iii) Systems of medication delivery based on lipids have the potential to improve the solubility and bioavailability of drugs with limited water solubility, which makes them a promising concept for the pharmaceutical industry. The apparent benefits of their biocompatibility and adaptability have also drawn a lot of attention to them. Lipid-based nanoparticles are generally well tolerated, non-toxic, and generate harmless breakdown products since they are made of physiological lipids. Lipid-oriented medication supply a variety of formulation choices, as they consequently were thoroughly researched for the oral and transdermal delivery of ED medications. Newer methods have been the focus of research lately.

(iv) Cytoplasmic antigen distribution is essential for achieving cross-presentation via the "cytosolic pathway." Because of their capacity to destabilize endosomal membranes and release content in a pH-responsive manner, pH-sensitive liposomes have been extensively employed for this purpose. Conjugating pH-sensitive substances with antigen-loaded liposomes is one method of producing pH-sensitive liposomes.

(v) When taken by mouth at a dosage of paclitaxel 10 mg/kg, the 22 nm paclitaxel nano emulsions containing labrasol, d-α-tocopheryl succinate polyethylene glycol 1000, and labrafil have quickly absorbed or reached the steady-state value in 30 min. The absolute bioavailability remained constant for eighteen hours at 70.62%. The increased oral bioavailability of paclitaxel may be associated with the repression of P-glycoprotein efflux caused by dα-tocopheryl polyethylene glycol 1000 succinate and labrasol.

Challenges with lipid-based drug delivry system (*Cannon and Long, 2008*):

(a) *Physical Stability and Gelatin Compatibility*:

Physical stability is one of the difficulties that come up frequently while creating lipid-based formulations. Formulations containing liquids frequently encounter problems with contact and leakage from the capsule shell. Water, ethanol, propylene glycol, glycerol (often a trace amount in fatty excipients), and other hydrophilic substances can move between the fillings and capsule shells. The ensuing alteration in the shell composition may cause the capsule to become brittle or soften, compromising its physical integrity and perhaps altering the product's dissolving profile. Information regarding the compatibility of excipients with hard gelatin capsules has been compiled by Cole (1999). Additionally, changes to the fill's composition may affect the medication's solubility, which could cause the drug to precipitate and have a lower bioavailability.

Because semisolid formulations are dynamic structures with both solid and liquid phases, they pose significant challenges. It is necessary to take into account the matrix's crystallinity, which can be greatly influenced by the distribution of chain lengths, lipid polymorphism, and lipid purity. Glycerides, for instance, can display three phases: triclinic (β), orthorhombic (β), and hexagonal (α). While the first two are common yet metastable phases, the latter is the most stable polymorph. The polymorph ratios can be impacted by storage and manufacturing conditions (such as mixing, melting, and cooling speeds). Moreover, drug crystallization is typically enhanced by matrix crystallization, which might have detrimental effects on behavior both *in vitro* and *in vivo*. Constantly keeping an eye on the crystalline nature is crucial.

(b) *Toxicological Consideration for Lipid Based Drug Delivery*:

Toxicity is less problem with oral lipid-based formulations than with parenteral ones. Considered generally recognized as safe (GRAS) lipids, the majority of them are derived from meals; in fact, it is easier to absorb monoglycerides, diglycerides, and long-chain triglycerides from food than pill versions. Dietary ingestion of up to 1 g/kg of MCTs has found to be safe in human clinical studies, despite claims that

Table1: Classification system for lipid formulation

Categories	Contents	Feature	Lists of drug products approved
I	Mono- and mixed-glycerides and diglycerides	Unless the substance is extremely lipophilic, non-dispersing and low solvent capacity. Bile salt mixed micelles are formed when digestion converts triglycerides into fatty acids and monoglycerides.	Rocaltrol Amitiza
II	Low-HLB surfactants and oils	There is little chance that turbid O/W dispersion of water insoluble SEDDS will cause them to lose their solvent capacity.	Neoral Sandimmune
III	Hydrophilic cosolvents, surfactants with high HLB, and oils	SEDDS/SMEDDS components include those that are water-soluble or dispersible, have bluish or clear dispersions, may lose solvent capacity during dispersion, and have lower digestibility.	Kaletra Xtandi Lipofen
IV	Hydroalcoholic cosolvents, Low-HLB surfactants, and High-HLB surfactants	Micellar solutions are the least digestible formulation type; they have a considerable solvent capacity for many medications but lose it when they disperse.	Norvir Agenerase

MCTs can increase small intestinal transit time and cause diarrhea. For lipid formulations that are given orally as liquids, considerations relating to taste, flavor, and mouthfeel must be taken in addition to toxicity.

Formulation (*Pund, 2021*):

A further "type" of formulation was introduced in 2006 to the classification system for lipid formulation (LFC), it was initially shown as a functional model in 2000. The pharmaceutical industry has been debating LFCs more extensively in recent years in an effort to reach an agreement that can be used as a model for evaluating an effectiveness of lipid formulations. The primary goal of LFCs is to make it easier to interpret *in vivo* research, which will in turn make it easier to determine which formulations are best for a given medicine in light of its physiochemical features, which are shown in Table 1.

Lipid-based formulation design guidelines (*Vaishnavi et al., 2024*):

An important technique for producing medications that are not sufficiently soluble is a lipid-based plan, and developing a plan of this kind is a highly challenging undertaking.

1. The drug's solubility in the schedule, after dispersion, and after processing must be monitored.

2. In the process of furthering assimilation, the characteristics of the colloidal species that are framed after being manipulated in the GI media

are most likely more important than the characteristics of the real details.

3. After attenuation, more abundant drug solubilization is initiated by a higher amount of lipids (>60%) and a smaller content of surface-active agent (<30%) and cosolvent (<10%).

4. While medium-chain fatty oils have the potential to offer greater medication solubility and safety, long-chain fatty substances have the potential to yield more exceptional bioavailability through their ability to facilitate the successful synthesis of colloidal lipid species from bile salts.

5. The Type IIIB self-emulsifying drug system (SMEDDS) forms a tiny droplet following dispersion. In any event, the characteristics of the surfactants determine the concept of the drops, and indigestible surfactants typically result in better bioavailability.

6. For Type IV detailing, the use of two surfactants yields a more effective dispersion than the use of one alone.

7. Improved medication solubility is offered by type IV regimens. To ensure that there is no precipitation of the medication following dispersion, they should be legitimately designed and executed with great care.

Conclusion

Drug delivery methods based on lipids offer a practical way to get beyond the problems caused by poorly soluble pharmaceuticals and transform the medicine delivery industry. Their potential importance in pharmaceutical formulations is highlighted by their capacity to improve bioavailability, absorption, and stability while supporting a variety of drug kinds and administration routes. Nonetheless, there are still difficulties, especially in maximizing therapeutic efficacy through lipid selection optimization and comprehending the complex link between lipid properties and drug behavior in the body. However, the key to realizing the full potential of LBDDS, paving the path for more stronger treatments, and easing the difficulties associated with poorly soluble medications lies in the ongoing research efforts directed towards overcoming these obstacles. LBDDS are ready to bring in a new age of medication development as long as improvements continue. Drug delivery systems based on lipids represent a flexible and exciting approach to pharmaceutical delivery, providing a wide range of formulations to address the issues raised by poorly water-soluble medicines. Through classes such as emulsions, microemulsions, vesicular systems, drug delivery methods that self-emulsify, and lipids particle networks across numerous administration routes, LBDDS offer customizable approaches for raising the permeability of drugs, stability, as well as targeted distribution. The versatility and promise of LBDDS in overcoming obstacles to drug solubility and absorption are highlighted by the incorporation of cutting-edge technologies including liposomes, niosomes, transfersomes, ethosomes, and phytosomes. Drug distribution methods based on lipids hold great potential for enhancing the provision of medications, especially for those with low water solubility. LBDDS have many benefits, such as increased oral bioavailability, controlled drug release, and adaptable formulation possibilities, but they also have drawbacks, including a low loading capacity, stability problems, complicated production processes, possible immunological reactions, and regulatory obstacles. Ongoing studies, however, are concentrated on finding solutions for these drawbacks and developing LBDDS technology. Through investigating physicochemical characteristics and refining the relationship between lipid carriers and cells, researchers want to create more accurate, efficient, and secure LBDDS for drug and gene delivery. With further research and development, LBDDS holds the promise of revolutionizing medication delivery and improving treatment outcomes for a wide range of conditions. The potential applications of LBDDS are numerous and include improving solubility and bioavailability as well as enabling diverse drug delivery methods like transdermal and topical applications. Scientists can customize

drug delivery systems to meet therapeutic demands, improving therapy efficacy and patient outcomes, by thoroughly studying the variety of choices within LBDDS and their distinctive qualities. When it comes to drugs that are not very soluble in water, where conventional formulations frequently fall short, this adaptability is very helpful in addressing the problems. LBDDS demonstrate great potential to transform pharmaceutical delivery through continued research and innovation, providing better patient care and more effective treatments. LBDDS's ability to get over obstacles to drug solubility and absorption is still a key component of pharmaceutical research and a means of satisfying changing needs as researchers continue to examine and improve these technologies.

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