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LIPID BASED DRUG DELIVERY SYSTEM – A REVIEW

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Abstract:

Lipid-based drug delivery systems (LBDDS) have gained significant attention in recent times, owing to their ability to overcome the challenges limiting the oral delivery of poorly water-soluble drugs. Despite the successful commercialization of several LBDDS products over the years, a large discrepancy exists between the number of poorly water-soluble drugs displaying optimal in-vivo performances and the application of LBDDS to mitigate their various delivery challenges. The formation of drugs carried out with the principle objective of enhancing their bioavailability. Poorly water-soluble drugs are challenging for the formulation scientists with regard to solubility and bioavailability. However, the number of applications for lipid-based formulations has expanded as the nature and type of active drugs under investigation have become more varied. This paper mainly focuses on novel lipid-based formulations, namely, emulsions, vesicular systems, and lipid particulate systems and their subcategories as well as on their prominent applications in pharmaceutical drug delivery.

Key words: *Lipid-based drug delivery systems, poorly water-soluble drugs, in-vivo.*

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INTRODUCTION:

The concept of liposomal drug delivery system has revolutionised the pharmaceutical field. Alec Bangham, in1961, first described liposomes (Upendra Bulbake, *et al.,* 2017). In these modern days, many significant efforts have been applied to use the potentials of lipid-based drug delivery systems, as it provides the suitable means of site specific as well as time-controlled delivery of drugs with different molecular weight, either small or large, and also the bioactive agents. Lipid-based drug delivery systems (LBDDS) have shown the effective size dependent properties so they have attracted a lot of attention. Also LBBDS have taken the lead because of obvious advantages of higher degree of biocompatibility and versatility (Hina Shrestha, *et al.*, 2014).

The utility of such delivery systems is based on their ability to mimic the food (or postprandial) effect by creating a lipophilic microenvironment within the gastrointestinal tract (GIT), thereby favouring solubilization of poorly water-soluble drug molecules and providing a concentration gradient driving intestinal drug absorption processes (Tahnee J. Dening, *et al.*,2016). Lipid-based drug delivery systems (LBDDS) are the most well studied and well established formulation approaches for addressing solubility and permeability issues (Wai Ma, *et al.*,2018).Lipid-based drug delivery systems (LBDDS) are a wide-ranging designation for formulations containing a dissolved or suspended drug in lipidic excipients. Lipids are esters of fatty acids–lipophilic hydrocarbon chains linked to a hydrophilic group like glycerol, polyglycerol, or polyalcohol. The melting range, solubilization capacity, and miscibility properties of the excipient are defined by the fatty acid chain length and degree of unsaturation. The amphiphilicity or dual polar and non-polar nature of lipids is characterized by the Hydrophilic Lipophilic Balance (HLB), a measure of the excipient dispersibility in aqueous media (https://drug-dev.com, 2017).

Such formulations are self-emulsifying drug delivery system (SEDDS) or self-micro emulsifying drug delivery system (SMEDDS).LBDDS can be used as drinking solutions, filled into hard or soft capsules, or incorporated into tablets; they maybe liquids, semi-solids, or solids at room temperature (https://drug-dev.com, 2017). Liposomal formulations were first proposed as drug delivery vehicles in ophthalmology to enhance ocular drug penetration (Jean-Sebastien Garrigue, *et al.,* 2017). The significant contribution of liposomes as drug delivery systems in the healthcare sector is known by many clinical products, e.g., Doxil®, Ambisome®, DepoDur™, etc (Upendra Bulbake, *et al.,* 2017).

FORMULATIONS:

Lipid-Based delivery systems range from simple oil solutions to complex mixtures of oils, surfactants and co-solvents. They have a high potential for increasing solubility of BCS class II drugs. Drugs in LBF are already in a soluble form and thus the dissolution step is omitted in the GI tract. Moreover, these formulations should be able to form emulsions in the water environment and maintain the drug in the solubilised state without its precipitation (Soltysova.I, *et al.,* 2016).

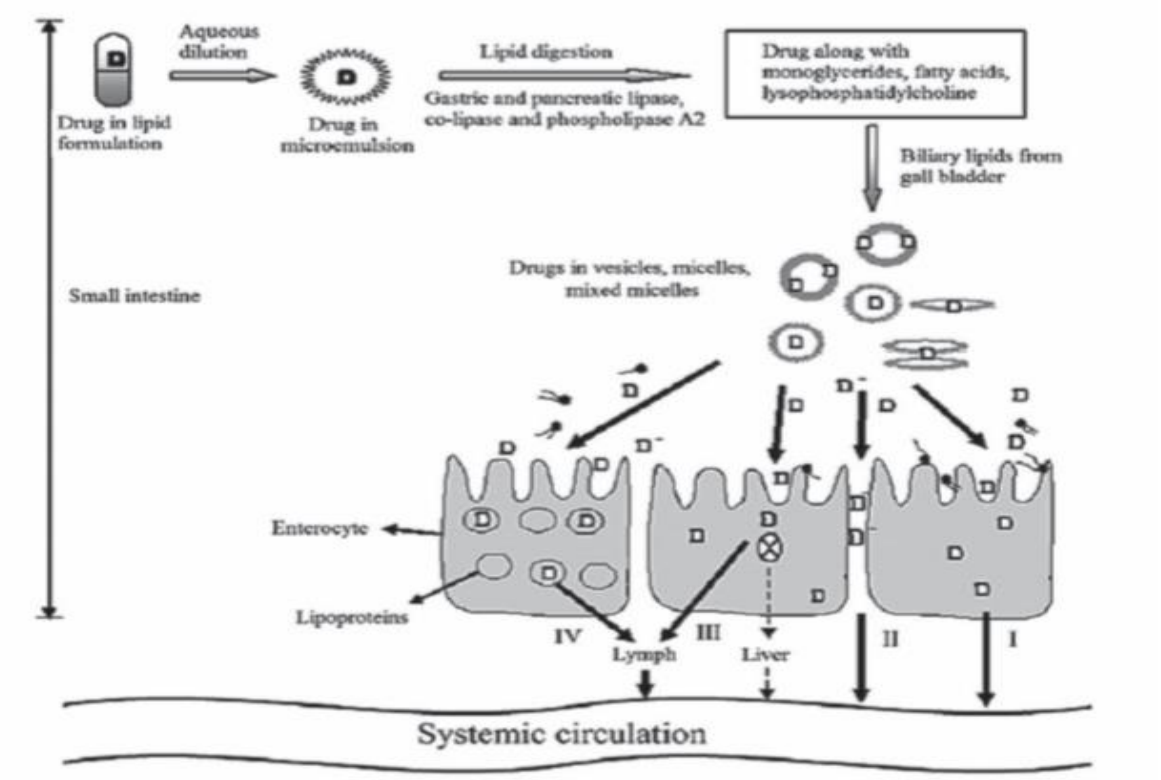

Figure 1: mechanism of intestinal transport of drug from LBF

General Routes of LBDDS:

Routes like oral, parenteral, ocular, intranasal, dermal/transdermal, and vaginal can be for the administration of the lipid based drug delivery systems (LBDDS). However, oral route is the most preferred route because of the properties like non-invasiveness, less expensive, and less prone to side effects, such as injection-site reactions. It is also considered as the easiest and the most convenient method of drug delivery for chronic therapies. But, at a very early stage of development, formulation strategies based on a rational and systematic approach need to be developed to avoid erratic and poor *in vitro/in vivo* correlations and thus increase the chances of success in formulation development (Hina Shrestha, *et al.*, 2014). Ayurveda, an ancient system of medicine originated from India during Vedic culture around 3000 years ago, has developed a group of lipid based formulations for hydrophilic molecules that are delivered through oral, nasal and topical routes (Selvakumar Duraipandi, *et al.*, 2018).

Advantages of LBDDS: (Hina Shrestha, *et al.*, 2014).

- Drug release in controlled and targeted way.
- Pharmaceutical stability.
- High and enhanced drug content (compared to other carriers).
- Feasibilities of carrying both lipophilic and hydrophilic drugs.
- Biodegradable and biocompatible.
- Excipients versatility.
- Formulation versatility.
- Low risk profile.
- Passive, non-invasive formation of vesicular system which is available for immediate commercialization.

Guidelines for Design of Lipid-Based Formulations: -

- It is critical to maintain drug solubility in the formulation, after dispersion, and after digestion.
- Properties of the colloidal species formed after processing in the GI milieu are probably more important than properties of the formulation itself in enhancing absorption.
- Higher proportions of lipid (>60%) and lower proportions of surfactant (<30%) and co-solvent (<10%) generally lead to more robust drug solubilization after dilution.
- Medium chain triglycerides may afford greater drug solubility and stability in the

formulation, but long chain triglycerides facilitate more efficient formation of bile salt lipid colloidal species and thus may afford higher bioavailability.

- Type IIIB SMEDDS formulations give lower droplet sizes after dispersion. However, they are more dependent on the surfactant properties employed, and non-digestible surfactants generally give higher bioavailability.
- Dispersion of type IV formulations (surfactant/co-solvent) is likely more efficient if two surfactants are used rather than a single one.
- Type IV formulations may give higher drug solubility but must be designed carefully to assure that drug does not precipitate after dispersion.

LIPID FORMULATION CLASSIFICATION SYSTEM:

The lipid formulation classification system (LFCS) was introduced as a working model in 2000 and an extra "type" of formulationwasaddedin2006. In recent years the LFCs have been discussed more widely within the pharmaceutical industry to seek a consensus which can be adopted as a framework for comparing the performance of lipid-based formulations (Hina Shrestha, *et al.*, 2014; Maulik Patel, *et al.*, 2011). Group III has been divided into Type IIIA and Type IIIB, to distinguish between formulations which contain a significant proportion of oils (Type IIIA) and which are predominantly water soluble (Type IIIB) (Maulik Patel, *et al.*, 2011).

Formulation type	Material	Characteristics	Advantages	Disadvantages
Type I	Oils without surfactants (e.g. tri, di- and monoglycerides)	Non-dispersing, requires digestion	GRAS status; simple; excellent capsule compatibility	Formulation has poor solvent capacity unless drug is highly lipophilic
Type II	Oils and water insoluble Surfactants	SEDDS formed without water-soluble components	Unlikely to lose solvent capacity on dispersion	Turbid o/w dispersion (particle size 0.25–2 μm)
Type IIIA (Fine emulsion)	Oils, surfactants, co-solvents (both water-insoluble and water-soluble excipients)	SEDDS/SMEDDS formed with water-soluble components	Clear or almost clear dispersion; drug absorption without digestion	Possible loss of solvent capacity on dispersion; less easily digested
Type IIIB (Micro emulsion)	Oils, surfactants, co-solvents (both water-insoluble and water-soluble excipients)	SEDDS/SMEDDS formed with water-soluble components and low oil content	Clear dispersion; drug absorption without digestion	Likely loss of solvent capacity on dispersion
Type IV	Water-soluble surfactants and co-solvents (no oils)	Formulation disperses typically to form a micellar solution	Formulation has good solvent capacity for many drugs	Likely loss of solvent capacity on dispersion; may not be digestible

Table 1: lipid formulation classification system

Drug absorption:

In practice, lipid formulations can be obtained as a result of blending of excipients such as pure triglyceride oils, mixed glycerides, lipophilic surfactants, hydrophilic surfactants and water-soluble co-solvents. These systems increase absorption from the gastrointestinal tract by accelerating the dissolution process, facilitating the formation of solubilized phases by reduction of particle size to the molecular level, yielding a solid-state solution within the carrier, changing drug uptake, efflux and disposition by altering enterocyte-based transport, and enhancing drug transport to the systemic circulation via intestinal lymphatic system (Sandeep Kalepu, *et al.*, 2013).

Lymphatic system:

The lymphatic system plays an important role in the transport of drugs to the systemic circulation, given its extensive drainage network throughout the body.

Some of the advantages of lymphatic transport of drug are avoidance of first-pass metabolism and targeting of specific diseases which are known to spread via lymphatics, such as certain lymphomas and HIV (Sandeep Kalepu, *et al.,* 2013). Those lymphatic systems inside solid tumours are dysfunctional (Lan Feng, *et al.*, 2013).

Digestion and solubilization:

The balance between a drug's solubility in the aqueous environment of the gastrointestinal lumen and its permeation across the lipophilic membrane of enterocytes determines its rate and extent of absorption (Sandeep Kalepu, et al., 2013).

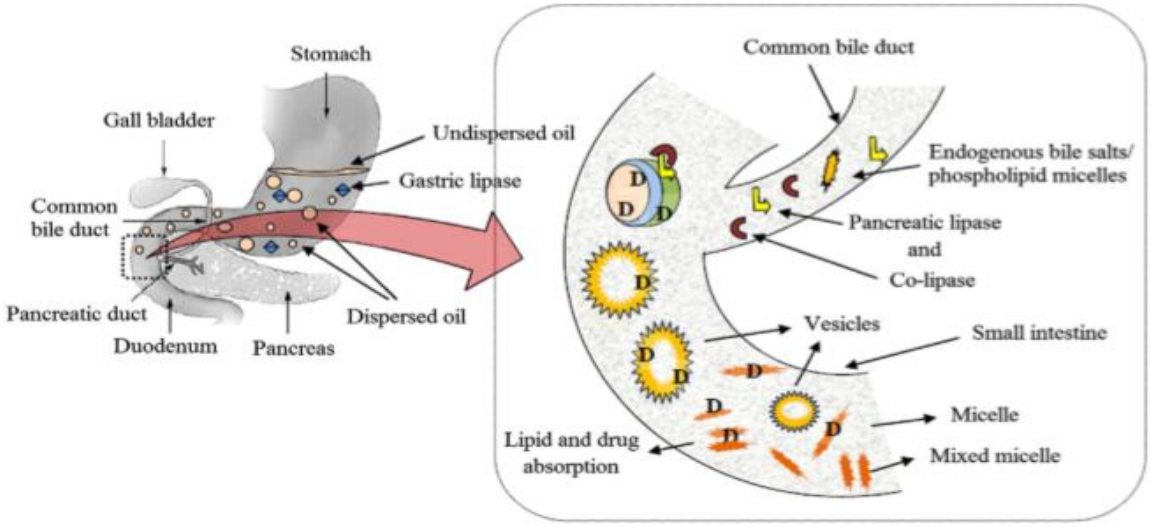

Figure 2 Lipid digestion and drug solubilization process in the small intestine.

Lipid excipients:

A wide range of lipid excipients are triglycerides, partial glycerides, semi synthetic oily esters, and semi-synthetic non-ionic surfactants esters are available from excipient suppliers. The factors that determine the choice of excipients for lipid-based formulations include miscibility; solvent capacity; self-dispersibility and ability to promote self-dispersion of the formulation; digestibility and fate of digested products; regulatory issues – irritancy, toxicity, purity, chemical stability; capsule compatibility; melting point, and cost (Sandeep Kalepu, *et al.*, 2013; Maulik Patel, *et al.*, 2011).Excipients are essential components of drug products. They may be also potential toxicants. Examples of known excipients-induced toxicities include renal failure and death caused by di-ethylene glycol, or cardio toxicity induced by propylene glycol (Soltysova.I, *et al.*, 2016).

Water-insoluble excipients	Triglycerides	Surfactants
Bees wax, Oleic acid, Soy fatty acids, d- α -tocopherol (vitamin E), Corn oil mono-di-tri-glycerides, Medium chain (C8/C10) mono and diglycerides, Propylene glycol esters of fatty acids.	***Long-chain triglycerides*** Corn oil, Olive oil, Pea nut oil, Rape seed oil, Sesame oil, soya bean oil, Hydrogenated soya bean oil, Hydrogenated vegetable oil. ***Medium-chain triglycerides*** Caprylic/capric triglycerides derived from coconut oil or palm seed oil	Glyceryl mono-oleate, Polyoxyl 35 castor oil (cremophor EL), Polyoxyl 40/60 hydrogenated castor oil (cremophor RH40/60), Polysorbate 20/80 (tween 20/80), d-α-tocopheryl PEG 1000 succinate (TPGS), Sorbitan monolaurate (Span 20) PEG 300 oleic/linoleic glycerides (Labrafil® M-1944/2125CS), PEG 400 Caprylic/capric Glycerides (Labrasol®), PEG 1500 lauric glycerides (Gelucire®44/14).

Factors affecting the choice of excipients for lipid-based formulations:
(Maulik Patel, *et al.*, 2011)

- ✓ Regulatory issues-irritancy, toxicity, knowledge and experience
- ✓ Solvent capacity
- ✓ Miscibility
- ✓ Morphology at room temperature (i.e., melting point)
- ✓ Self dispersibility and role in promoting self-dispersion of the formulation
- ✓ Digestibility, and fate of digested products
- ✓ Capsule compatibility
- ✓ Purity, chemical stability
- ✓ Cost of goods

PROBLEMS SOLVED BY LBDDS:

Solubilization of Poorly Water-Soluble Drugs:
Oral lipid-based formulations, which are by no means a recent technological innovation, have not only proven their utility for mitigating the poor and variable gastrointestinal absorption of poorly soluble, lipophilic drugs, but in many cases have shown the ability to reduce or eliminate the influence of food on the absorption of these drugs(David J.Hauss, *et al.*,). Hauss has pointed out that over 70% of new drug candidates have low solubility values in water. Approximately 40% of lipophilic drug candidates that demonstrate good pharmacological activity do not reach market because low aqueous solubility compromises bioavailability and leads to poor pharmacokinetic performance and low exposure. LBDDS provide the drug in a fully to partly solubilized state, and most importantly, maintain solution of the drug until it is absorbed. The drugs remain in the solubilized state because LBDDS self-emulsify, and/or form emulsions upon digestion. During digestion, oils in the LBDDS undergo lipolysis to form fatty acids and monoglycerides, which combine with components in the gastrointestinal fluids to form mixed micelles that can assist in maintaining the drug in solutions(https://drug-dev.com, 2017).

Enhancement of intestinal permeability:
Earlier studies, based on the in vitro cell-based model, pointed to membrane fluidity and efflux inhibition as other potential mechanisms driving intestinal permeability. A subsequent imbalance created between the initial solubilized drug concentration in the GI fluids and drug solubility in the colloidal species formed post-dispersion and digestion is another factor contributing to API super saturation. Meanwhile, the lipid metabolites are absorbed contributing to further reduction in the solubilization capacity of the remaining colloidal phases during digestion, thus promoting on-going super saturation.
To be absorbed into the systemic circulation, a drug molecule must pass through the GI wall (https://drug-dev.com, 2017). While the main advantage of LBDDS have been recognized as increasing GI solubility of poorly soluble molecules, it is also increasingly clear that LBDDS may provide other key advantages such as decreasing food effect, increasing permeability and, under some circumstances, avoiding first-pass metabolism, and with some possibilities to influence absorption pathways (Wai Ma, *et al*., 2018).

Protection from Enzymatic/Chemical Degradation:
Hetényi and co-workers recently demonstrated that therapeutic peptides, leuprorelin, insulin, and desmopressin could be paired with sodium docusate and loaded into a SEDDS formulation. The researchers exposed the formulated peptides to intestinal proteases (α-chymotrypsin, trypsin, and elastase) and glutathione. They observed that no degradation of the peptides occurred in the SEDDS formulation, which was consistent with observation that the proteases and glutathione were ≤ 0.1% soluble in the oily SEDDS. This work strongly suggests that a LBDDS can protect sensitive peptide APIs from water-soluble reactants and degradation mechanisms that require an aqueous environment (https://drug-dev.com, 2017).

Reduction of First-Pass Metabolism:
The triglycerides in a LBDDS are digested by the natural lipolysis process in the GI tract to form fatty acids and monoglycerides. Fatty acids can be absorbed by the hepatic and/or lymphatic route, and the distribution between the routes is dependent on the hydrocarbon chain length. Fatty acids with hydrocarbon chains below 12C tend to bind to albumin, which renders them water soluble. The unsaturated long-chain fatty acids (LCFA), in particular, are known to stimulate chylomicron secretion and increase the lymphatic uptake. Enhanced lymphatic absorption is important in oral delivery primarily for highly lipophilic drugs (LogP > 5) with high solubility in triglycerides (Cs > 50 mg/mL), i.e., APIs that are candidates for lymphatic absorption (https://drug-dev.com, 2017).

NEW TRENDSINLBDDS:

Creation of Lipophilic Salts/Ion Pairs of Drugs for Solubilization in Lipidic Excipients:
Despite the vast array of excipients to enable development of a LBDDS in which the drug is fully solubilized, some molecules will not dissolve in

lipidic excipients at their required unit dose. While suspensions in LBDDS can provide good exposure and are commercially available, for example Cipro™ Oral Suspension, typically, the best exposure from LBDDS is achieved when the drug is fully solubilized in the dosage form. The inability to solubilize an active agent in lipidic excipients has led formulators to rule out LBDDS as a viable technology for the drug. This unfortunate circumstance has restricted the use of this very versatile LBDDS approach to enable formulation of drugs with high formulation barriers, including poor bioavailability (https://drug-dev.com, 2017).

Use of LBDDS for oral delivery of peptides of proteins:

Liposomes are effectively suitable for the delivery of peptides and proteins by surface modification and biocompatibility, these delivers the peptides and proteins. Lipid nanoparticles are new and innovative model for the delivery of recombinant proteins (N. Tejeswari, *et al.*, 2014). Lipid formulations are used for several high molecular weight molecules including peptides and peptidomimetics. Insulin and glucagon like peptide 1 (GLP-1) analogs are typically administered by subcutaneous injections. These peptides have high molecular weights, short half-lives and high clearance. However, these improved peptides must still be injected (Ronak Savla, *et al.*, 2017). Hydrophobic ion pairing of the peptides with anionic surfactants sodium docusate, dodecyl sulfate, and oleate was performed to enable solubilization of these highly water-soluble peptides into the oily SEDDS formulations. The hydrophobic ion pairs were evaluated by measuring the quantity of the complex formed, the n- octanol/water partition coefficient and the zeta potential of the complexes. For all three peptides, the ion pair formed with docusate gave the best combination of properties. It was observed that the docusate ion pairs of these peptides were soluble in all SEDDS formulations at greater than 10% by weight. Here, we see again, how pairing of compounds with lipophilic salts enables high loading of fully solubilized therapeutic agents into a LBDDS (https://drug-dev.com, 2017).

Types of LBDDS:

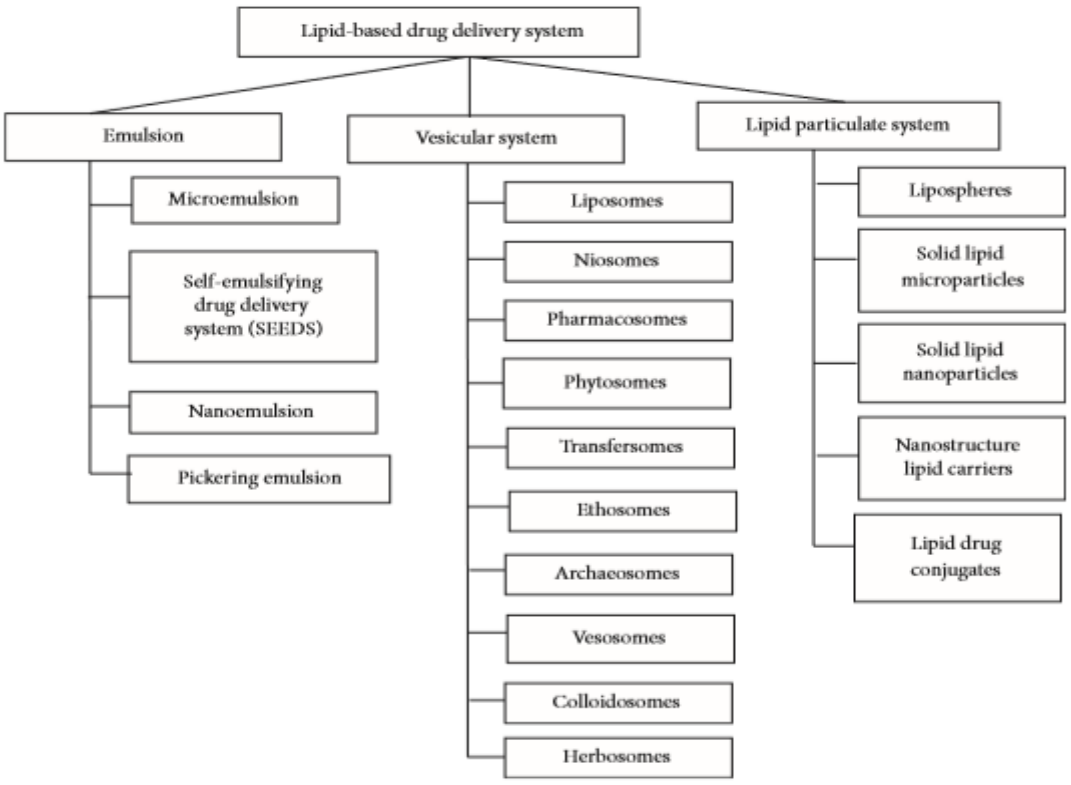

Figure 3: types of LBDDS

Formulation approaches for LBDDS:

- **Spray Congealing:**
  This is also referred to as spray cooling. In this method, molten lipid is sprayed into a cooling chamber and, on contact with the cool air, congeals into spherical solid particles. The solid particles are collected from the bottom of the chamber, which can be filled into hard gelatin capsules or compressed into tablets (Sandeep Kalepu, *et al.,* 2013). Ultrasonic atomizers are frequently used to generate solid particles in this spray cooling process (Hina Shrestha, *et al.*, 2014).
- **Spray drying:**
  In this method the drug solution is sprayed into a hot air chamber, where the organic solvent and water evaporates giving rise to solid microparticles of drug (Sandeep Kalepu, *et al.,* 2013). During this process, along with the lipid excipients, solid carriers like silicon dioxide can be used. Gelucire (lipid excipient) enhances the drug release process by forming hydrogen bonds with the active substance, leading to the formation of stable solids of amorphous drug in microparticles (Madhu Gudipati and Ramarao Nadendla, 2016).
- **Adsorption onto Solid Carrier:**
  This is a simple and economical process (in the context of equipment investment) in which a liquid-lipid formulation is adsorbed onto solid carrier like silicon dioxide, calcium silicate, or magnesium alumina Metasilicate. The liquid-lipid formulation is added to the carrier by mixing in a blender (Sandeep Kalepu, *et al.,* 2013). Gentamicin and erythropoietin with caprylocaproyl Polyoxyl glycerides (Labrasol) formulations were successfully converted into solid intermediates whose bioavailability was maintained even after adsorption on carriers (Hina Shrestha, *et al.,* 2014).
- **Melt Granulation:**
  This is also referred to as pelletization, which transforms a powder mix (with drug) into granules or pellets. In this method a melt able binder (molten state) is sprayed onto the powder mix in presence of high shear mixing (Sandeep Kalepu, *et al.,* 2013). This process can be referred to as a "pump on" technique. Alternatively, the meltable binder is blended with powder mix and, due to the friction of particles (solid/semisolid) during the high-shear mixing, the binder melts. The melted binder forms liquid bridges between powder particles and forms small granules which transform into spheronized pellets under controlled conditions (Hina Shrestha, *et al.,* 2014).
- **Super critical Fluid-Based Method:**
  This method uses lipids for coating drug particles to produce solid dispersions. In this method, the drug and lipid-based excipients are dissolved in an organic solvent and super critical fluid (carbon dioxide) by elevating the temperature and pressure (Sandeep Kalepu, *et al.*, 2013). The coating process is facilitated by a gradual reduction in pressure and temperature in order to reduce the solubility of the coating material in the fluid and hence precipitate onto the drug particles to form a coating. The solubility of the formulation components in the super critical fluid and stability of the substance during the process are important considerations of this method (Hina Shrestha, *et al.,* 2014).

Characterization ofLipid-Based Drug Delivery Systems (LBDDS):

- **Appearance:**
  The appearance can be check edit graduated glass cylinder or transparent glass container for its uniformity and colorant equilibrium (Hina Shrestha, *et al.,* 2014; Maulik Patel, *et al.*, 2011). Particle size is an important parameter for the purpose of quality control, especially quality assurance, as particle size along with particle size distribution can influence the physical stability of vesicle dispersion (Rajan Rajabalaya, *et al.,* 2017).
- **Color, Odor, and Taste**:
  These characteristics are especially important in orally administered formulation. Variations in taste, especially of active constituents, can often be accredited to changes in particle size, crystal habit, and subsequent particle dissolution. Changes in color, odor, and taste can also indicate chemical instability (Hina Shrestha, *et al.,* 2014; Maulik Patel, *et al.,* 2011).
- **Density:**
  Specific gravity or density of the formulation is an essential parameter. A decrease in density often indicates the entrapment air within the structure of the formulation (Hina Shrestha, *et al.,* 2014). Density measurements at a given temperature can be made using high precision hydrometers (Maulik Patel, *et al.,* 2011).
- **pH Value:** The Ph value of aqueous formulation should be taken at a given temperature using pH meter and only after settling equilibrium has been reached, to minimize "pH drift" and electrode surface coating with suspended particles. Electrolyte should not be added to the external phase of the formulation to stabilize the pH, because neutral electrolytes disturb the physical stability of the suspensions (Hina

Shrestha, *et al.*, 2014; Maulik Patel, *et al.*, 2011).

- **Self-Dispersion and Sizing of Dispersions:**
  Assessment of the dispersion rate and resultant particle size of lipid-based systems is desirable so attention has been given to measuring dispersion rate (Hina Shrestha, *et al.*, 2014).
- **Droplet Size and Surface Charge (Zeta Potential):**
  The droplet size distribution of microemulsion vesicles can be determined by either electron microscopy or light-scattering technique. The dynamic light-scattering measurements are takenat90∘ in a dynamic light-scattering spectrophotometer which uses a neon laser of wavelength 632nm. The surface charge is determined using a zeta potential analyser by measuring the zeta potential (ZP) of the preparations. ZP characterizes the surface charge of particles and thus it gives information about repulsive forces between particles and droplets (Hina Shrestha, *et al.*, 2014; Maulik Patel, *et al.*, 2011).
- **Viscosity Measurement:**
  Brook field type rotary viscometer can be used to measure the viscosity of lipid-based formulations of several compositions at different shear rates at different temperatures. The samples for the measurement are to be immersed in it before testing and the sample temperaturemustbemaintainedat37 ± 0.2∘Cbyathermobath. The viscometer should be properly calibrated to measure the apparent viscosity of the suspension at equilibrium at a given temperature to establish suspension reproducibility (Hina Shrestha, *et al.*, 2014; Maulik Patel, *et al.*, 2011).
- ***In vitro* studies:**
  A preliminary guideline for formulation development and assessment of drug release can be obtained from *in vitro* studies (Sandeep Kalepu, *et al.*, 2013). In vitro evaluation of lipid-based drug delivery systems can be done with the use of lipid digestion models. In order to assess the performance of an excipient during formulation development and to predict in vivo performance, it is necessary to design an *in vitro* dissolution testing method. This can be termed as "simulated lipolysis release testing" (Hina Shrestha, *et al.*, 2014; Maulik Patel, *et al.*, 2011). In vitro release studies were undertaken in SGF (pH 1.2) and SIF (pH 7.4) and sustained drug release profiles were obtained in both media over a 9 h period, attributed to the ion-exchange process between intercalated drug molecules and alkali metal cations present in the release media (Tahnee J. Dening, *et al.*, 2016).
- ***In vivo* studies:**
  The impact of excipients on the bioavailability and pharmacokinetic profile of drugs can be estimated by designing of appropriate *in vivo studies* (Sandeep Kalepu, *et al.*, 2013). A detailed study of intestinal lymphatic absorption is required, since lipid based formulations enhance bioavailability by improving the intestinal uptake of drug. Due to insufficient clinical data and differences in methods and animal models used, studies related to the drug transport by lymphatic system have become difficult (Hina Shrestha, *et al.*, 2014; Maulik Patel, *et al.*, 2011).
- **In Vitro-In Vivo Correlation (IVIVC):**
  The in vivo oral bioavailability of two model drugs, griseofluvin, and dexamethasone, was predicted by designing an in vitro lipolysis and ex vivo intestinal permeability model (Sandeep Kalepu, *et al.*, 2013). In vitro -in vivo correlation will help to maximize the development potential and commercialization of lipid-based formulations. A shortened drug development period and improved product quality could be achieved by developing a model that correlates the in vitro and in vivo data. Determining the solubility, dissolution, lipolysis of the lipid excipient, and intestinal membrane techniques (isolated animal tissue and cell culture models) are various in vitro techniques that can be used to assess lipid-based formulations (Hina Shrestha, *et al.*, 2014;Maulik Patel, *et al.*, 2011).

Analysis of excipients in lipid-based drug delivery system:

Chemical Analysis:

Composition of lipid-based excipients i.e., esters, ethers and distribution of fatty acid can be assayed by HPLC and GC methods. For hygroscopic or high HLB value excipients moisture content must be analysed (N. Tejeswari, *et al.*, 2014).

Physical Analysis:

Lipids have higher chemical composition and leads to broad melting point as opposed to a single melting point. DSC (Differential scanning calorimetry) used for the study of thermal behaviour of excipients like melting, crystallization, solid to solid transition temperatures. Solid fat content of the excipient related to temperature can be assayed by nuclear magnetic resonance (NMR) (N. Tejeswari, *et al.*, 2014).

Analysis of physiological effects of excipients:

Oral absorption had various physiological effects

such as retarding gastric emptying and stimulation of bile flow, secretion of pancreatic juice, enhancing the membrane lipid fluidity or acting directly on to the enterocytes based drug transport and disposition, inhibiting efflux transporters like p-glycoprotein (P-gp) in-vitro models assess these effects by using liver and intestinal slices. These effects occurred due to the increase in the oral absorption by lipid based excipients (N. Tejeswari, *et al.,* 2014).

APPLICATIONS: (Hina Shrestha, *et al.,* 2014).

- So far, the design of successful lipid-based delivery systems has been based largely upon empirical experiences.
- Systematic physicochemical investigations of structure and stability do not only help to speed up the development of new and improved formulations, but may also aid in the understanding of the complex mechanisms governing the interaction between the lipid carriers and the living cells.
- Hence they sought to be safe, efficient, and specific carriers for gene and drug delivery.
- LBDDS can be used to deliver various types of drugs from new chemical entities to more recent new developments for proteins and peptides, nucleic acids (DNA, siRNA), and cellular site specific delivery
- The utility of lipid-based formulations to enhance the absorption of poorly water-soluble, lipophilic drugs has been recognized for many years.
- Lipids are perhaps one of the most versatile excipients classes currently available, providing the formulator with many potential options for improving and controlling the absorption of poorly water-soluble drugs.
- These formulation options include lipid suspensions, solutions, and emulsions, microemulsions, mixed micelles, SEDDS, SMEDDS, thixotropic vehicles, thermo softening matrices, and liposomes.

CONCLUSION:

Lipid-based drug delivery systems provide the vast array of possibilities to formulations as they potentially increase the bioavailabilityofnumberofpoorlysolubledrugsalongwith the formulations of physiologically well tolerated class. The development of these systems requires proper understanding of the physicochemical nature of the compound as well as the lipid excipients and gastrointestinal digestion. One of the major challenges of lipid excipients and delivery systems is the varying range of compounds they contain. Proper characterization and evaluation of these delivery systems, their stability, classification, and regulatory issues consequently affect the number of these formulations. On the way of conclusion, the prospect of these delivery systems looks promising.

Lipid based drug delivery systems may include a board range of oils, surfactants and co-solvents. This diversity makes comparison of lipid based formulations difficult. The lipid formulation classification system identifying the factors which are likely to affect performance *in-vivo*. There is known a need to establish performance criteria which will facilitate *in in vitro-iv vivo* correlation studies.

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