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PROPOSAL FOR LIPID-BASED DRUG DELIVERY SYSTEM: DEFINITION, RECOMMENDATIONS, FORMULATION STRATEGIES, FEATURES AND FUTURE ASPECTS

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ABSTRACT
The principle objective of formulation of lipid-based drugs is to reinforce their bioavailability. the utilization of lipids in drug delivery is not any more a replacement trend now but remains the promising concept. Lipid-based drug delivery systems are one of the emerging strategies designed to deal with challenges just like the solubility and bioavailability of poorly water-soluble drugs. These formulations are synthesized to meet a huge range of product specifications largely determined by sign of disease, route of administration, cost consideration, product security, toxicity and effectiveness. These formulations also are a commercially viable strategy to formulate pharmaceuticals, for topical, oral, pulmonary, or parenteral delivery. Additionally, lipid-based formulations are shown to scale back the toxicity of varied drugs by changing the biodistribution of the drug faraway from sensitive organs. However, the amount of applications for lipid-based formulations has expanded because the nature and sort of active drugs under investigation became more varied. This paper mainly focuses on novel lipid-based formulations, namely, emulsions, vesicular systems, and lipid particulate systems and their subcategories also as on their prominent applications in pharmaceutical drug delivery.

KEYWORDS: Drug, Lipid based formulation, Bioavailability, Administration.

INTRODUCTION
In these modern days, many significant efforts are applied to use the potentials of lipid-based drug delivery systems, because it provides the acceptable means of site specific also as time controlled delivery of medicine with different relative molecular mass, either small or large, and also the bioactive agents.[1,2] Poorly water-soluble drugs are challenging for the formulation scientists with reference to solubility and bioavailability. Lipid-based drug delivery systems (LBDDS) have shown the effective size dependent properties in order that they have attracted tons of attention. Also LBBDS have taken the lead due to obvious advantages of upper degree of biocompatibility and flexibility. These delivery systems are commercially to formulate pharmaceuticals of topical, oral, pulmonary, or parenteral dosage form. Lipid formulations are often modified in various ways to satisfy a good range of product requirements as per the disease condition, route of administration, and also cost product stability, toxicity, and efficacy. Lipid-based carriers are safe and efficient hence they need been proved to be attractive candidates for the formulation of pharmaceuticals, also as vaccines, diagnostics, and nutraceuticals.[3] Hence, lipid-based drug delivery (LBDD) systems have gained much importance within the recent years thanks to their ability to enhance the solubility and bioavailability of medicine with poor water solubility.

General Routes of LBDDS
Routes like oral, parenteral, ocular, intranasal, transdermal, and vaginal are often for the administration of the lipid-based drug delivery systems.[4,5] However, oral route is that the most preferred route due to the properties like non invasiveness, less costly, and fewer susceptible to side effects, like injection-site reactions. it's also considered because the easiest and therefore the most convenient method of drug delivery for chronic therapies. But, at a really early stage of development, formulation strategies supported a rational and systematic approach got to be developed to avoid erratic and poor in vitro/in vivo correlations and thus increase the probabilities of success in formulation development. Various useful guidelines regarding the convenient routes and formulation strategies are published by several authors.[6–9]

Lipid Formulation Classification System
The lipid formulation classification system (LFC) was introduced as a working model in 2000 and an extra

"type" of formulation was added in 2006.[10] 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. The main purpose of the LFCs is to enable in vivo studies to be interpreted more readily and subsequently to facilitate the identification of the most appropriate formulations for specific drugs, that is, with reference to their physiochemical properties as depicted in Table 1.

Table 1: Lipid Formulation Classification System

Formulation type	Material	Characteristics	Advantages	Disadvantages
Type I	Oils without surfactants (e.g., tri-, di-, and monoglycerides)	Nondispersing requires digestion	Generally recognized as safe (GRAS) status; simple; and 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 m)
Type III	Oils, surfactants, and cosolvents (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 IV	Water-soluble surfactants and cosolvents	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

Points to Be Considered for the Formulation

Main factors affecting the choice of excipients for lipid-based formulations are as follows:

- Solubility
- Dispersion
- Digestion
- Absorption.
- Other factors are as follows:
- 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.

1. Solubility- While the lipids (fatty acid derivatives) are the core ingredient of the formulation, one or more surfactants, also as perhaps a hydrophilic cosolvent, could also be required to assist solubilization and to enhance dispersion properties. Surfactants are categorized by their hydrophilic-lipophilic balance (HLB) number, with a coffee value (≤10) like greater lipophilicity and a better value (≥10) like higher hydrophilicity. As a suggestion as a start line for formulation design, most of the lipids utilized in these oral formulations have a known "required HLB" value (generally available from the vendors), which corresponds to the optimal HLB for the surfactant blend necessary to emulsify the oil in water. Various emulsifiers are often used for the varied formulations counting on their HLB values as depicted in Table 2.[11,13]

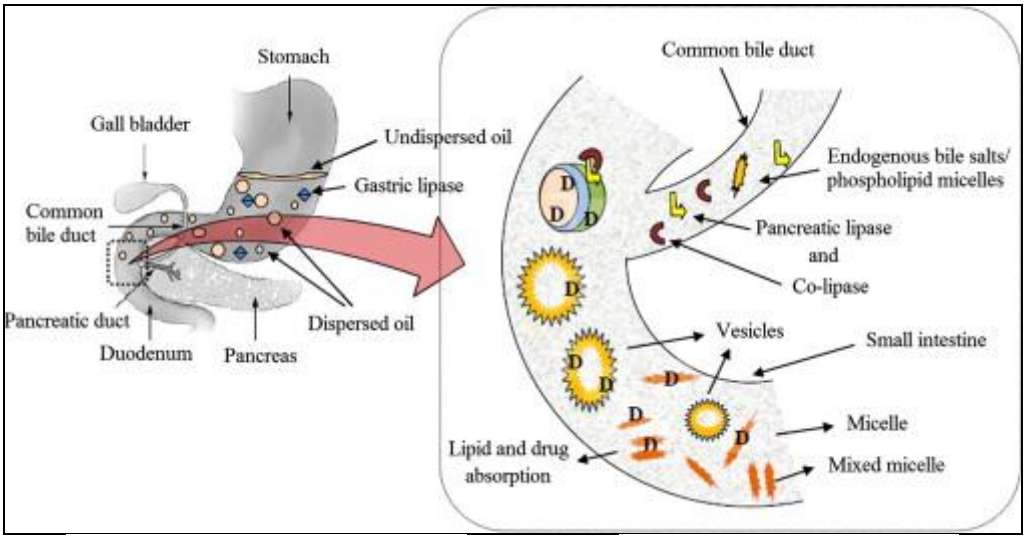

Figure 1: Lipid digestion and drug solubilization process in the small intestine.

Table 2: Various formulations depending on their HLB values as depicted.

Various formulations depending on their HLB values as depicted	
Common name/type	Examples
Low HLB (<10) emulsifier	
Phosphatidylcholine and phosphatidylcholine/solvent mixtures	Phosphatidylcholine, phosphatidylcholine in propylene glycol, phosphatidylcholine in medium chain triglycerides, and phosphatidylcholine in safflower oil/ethanol
Unsaturated polyglycolized glycerides	Oleoyl macrogolglycerides, linoleoyl macrogolglycerides
Sorbitan esters	Sorbitan monooleate, sorbitan monostearate, sorbitan monolaurate, and sorbitan monopalmitate
High HLB (>10) emulsifier	
Polyoxyethylene sorbitan esters	Polysorbate 20, polysorbate 40, polysorbate 60, and polysorbate 80
Polyoxyl castor oil derivatives	Polyoxyl 35 castor oil, polyoxyl 40 hydrogenated castor oil
Polyoxyethylene polyoxypropylene block copolymer	Poloxamer 188, poloxamer 407
Saturated polyglycolized glycerides	Lauroyl macrogolglycerides, stearoyl macrogolglycerides
PEG-8 caprylic/capric glycerides	Caprylocaproyl macrogolglycerides
Vitamin E derivative	Tocopherol PEG succinate

2. Dispersion - Formulations that exhibit adequate solubility of the drug candidate ought to be examined for emulsification and dispersion properties in binary compound vehicles. A preliminary screening ar typically administered by microscopic observation of the formulation once mixed with water. Vigorous combining, amid diffusion and stranding mechanisms, occurring at the water/formulation interface is indicative of associate economical emulsification. Absence of drug precipitate when complete combining of the formulation with binary compound medium is another demand. Particle size measuring of emulsion droplets by optical device light-weight scattering or alternative techniques is useful to select promising formulations. Construction of ternary part diagrams could also be a way often used to confirm the types of structures ensuing from emulsification and to characterize behavior of a formulation on a dilution path. associate example is shown in Figure 1; the road from A to B represents dilution of a formulation consisting at first of thirty fifth wetter, 65% oil, passing through regions of a water-in-oil microemulsion and a lamellar liquid till reaching a stable bicontinuous oil-in-water microemulsion when dilution. it's typically excess to construct the complete part diagram, however associate understanding of the structures arising on a dilution path of a given formulation is important to assure formation of stable spread structures upon dilution. acceptable mixtures of low HLB and high HLB surfactants often cause smaller emulsion driblet size than single surfactants. These a lot of advanced mixtures ar typically examined by pseudoternary part diagrams.[13]

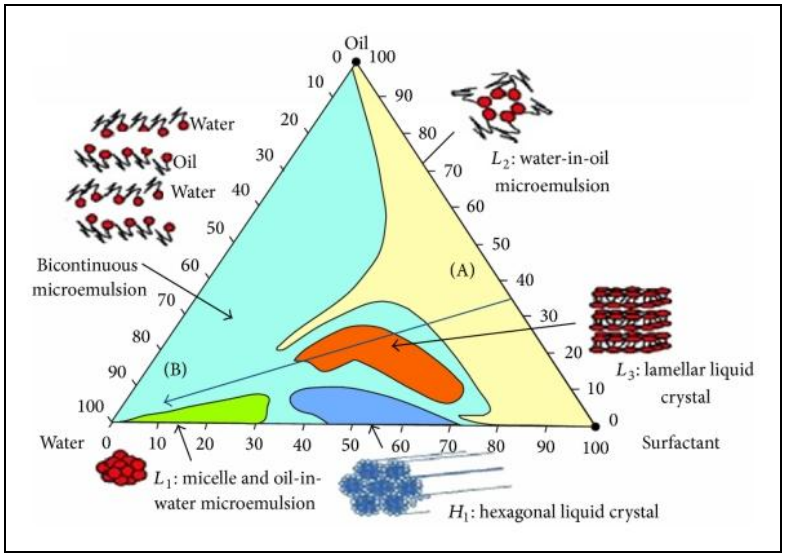

Figure 2:

3 Digestion - The activities of enteral lipases within the alimentary {canal|alimentary tract|digestive tube| digestive tract|GI tract|duct|epithelial duct|canal| channel} can have a profound impact on the behavior of lipid-based formulations and should be taken into consideration in their development. it's long been well-known that non-dispersible however easier to digest lipids like triglycerides are often absorbed by the body to mono-/diglycerides and fatty acids via lipases, that emulsify any remaining oil. Therefore, the presence of high concentrations of surfactants are often excess to confirm the acceptable tiny particle sizes and enormous surface aras are generated for drug unleash. In 2000, Pouton introduced a classification theme for lipid-dependent formulations supported the elements of the formulations and digestion dependence to push dispersion.[14] as shown in Table no.3.

Significance of binary compound dilution Limited importance Solvent capability unaffected Some loss of solvent capability Significant part changes and potential loss of solvent capacity.

Significance of digestibility Crucial requirement Not crucial, however probably to occur Not crucial, however could also be inhibited Not needed and unlikely to occur..

Table 3: Formulations based on the formulation components and the dependence on digestion to facilitate dispersion.

formulations based on the formulation components and the dependence on digestion to facilitate dispersion				
	Type I	**Type II**	**Type IIIA**	**Type IIIB**
% triglycerides or mix d glycerides	100	40–80	40–80	<20
% surfactants	—	20–60 (HLB < 12)	20–40 (HLB > 11)	2 –50 (HLB > 11)
% hydrophilic cosolvents	—	—	0–40	20–50
Particle size of dispersion (nm)	Coarse	100–250	1 0–250	50–100
Significance of aqueous dilution	Limited importance	Solvent capacity unaffected	Some loss of solvent capacity	Significant phase changes and potential loss of solvent capacity
Significance of digestibility	Crucial requirement	Not crucial, but likely to occur	Not crucial, but may be inhibited	Not required and not likely to occur

4 Absorption - Naturally, effective absorption of the drug by the stomachic membrane cells is that the final goal of any oral lipid-based formulation. Figure two shows the processes for lipid-based drug formulations that occur within the enteral milieu.[13] 1st the elements ar spread to create lipoid droplets (for formulations of kind I) or emulsion droplets (for sorts II-III), in the midst of lipolysis and steroid solubilization of the digestion materials, forming mixed mixture micelles. it's assumed that the medication then partitions the emulsion oil droplets and salt mixed micelles to be absorbed by the enteral wall's membrane cells.

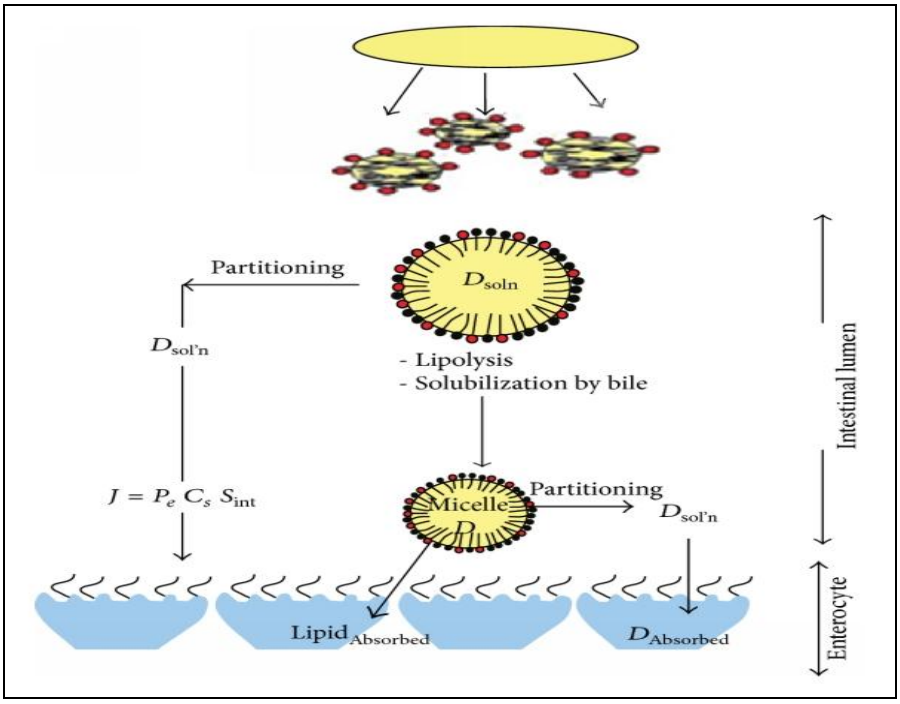

Figure 3:

Merits (15)

- Controlled and controlled unleash of medicine.
- Pharmaceutical stability.
- High and improved drug quality (compared to alternative carriers).
- Feasibility of carrying each lipotropic and deliquescent medicine.
- Biodegradable and biocompatible.
- Skillfulness of the excipients.
- Skillfulness of the formulation.
- Low risk profile.

Types of Lipid-Based Drug Delivery Systems

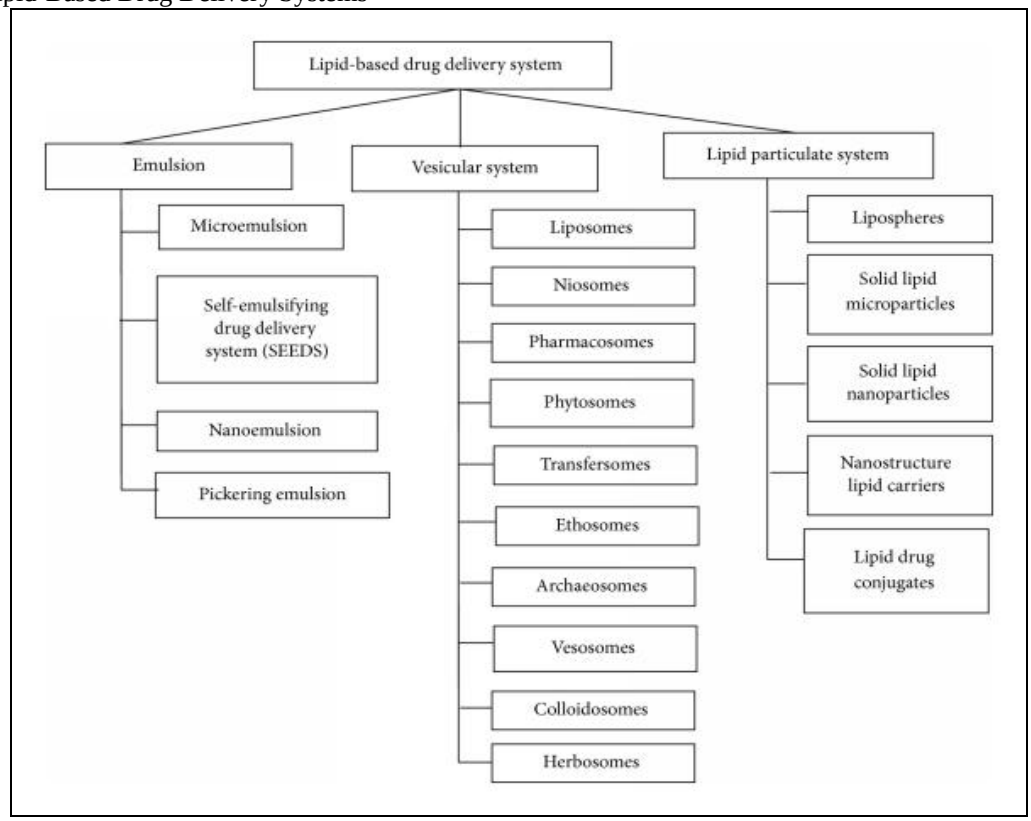

Figure 4:

Guidelines for Design of Lipid-Based Formulations[16,17]

(1) Maintaining drug solubility within the formulation, when dispersion and when digestion is crucial.
(2) Properties of the mixture species created when GI process ar presumably a lot of vital than the properties of the formulations themselves in up absorption.
(3) In general, higher lipoid proportions (>60 percent) and lower wetter (<30 percent) and cosolvent proportions (<10 percent) result in simpler drug solubilization when dilution.
(4) Medium-chain triglycerides could offer larger drug solubility and formulation stability, however long-chain triglycerides could enhance potency formation of mixture salt lipoid species and will so afford larger absorption rate.
(5) Formulations of kind IIIB SMEDDS offer lower driblet sizes when spreading. These are, however, a lot of dependent on the wetter properties used and indigestible surfactants usually offer larger bioavailability.
(6) Dispersion of kind IV formulations (surfactant / cosolvent) is probably going to be simpler if 2 surfactants ar used instead of one.
(7) Type IV formulations could offer higher drug solubility however should be designed rigorously to assure that drug doesn't precipitate when dispersion.

Formulation Approaches for LBDDS

Spray Congealing

This is conjointly remarked as spray cooling. during this technique, melted lipoid is sprayed into a cooling chamber and, on contact with the cool air, congeals into spherical solid particles. The solid particles ar collected from all-time low of the chamber, which might be stuffed into exhausting gelatin capsules or compressed into tablets. inaudible atomizers ar oftentimes accustomed turn out solid particles during this spray cooling method. The parameters to be thought of ar the freezing point of the excipient, the body of the formulation, and also the cooling air temperature within the chamber to permit instant action of the droplets.

Spray Drying

This technique is somewhat just like preceding one however differs within the temperature of the air within the atomizing chamber. during this technique, the drug resolution (drug in organic solution/water) is sprayed into a hot air chamber, wherever the organic solvent or water evaporates giving rise to solid microparticles of drug. throughout this method, beside the lipoid excipients, solid carriers like silicon oxide are often used. Gelucire (lipid excipient) enhances the drug unleash method by forming atomic number 1 bonds with the active substance, resulting in the formation of stable solids of amorphous drug in microparticles.[17,18]

Surface assimilation onto Solid Carrier

This is a straightforward and economical method (in the context of kit investment) during which a liquid-lipid formulation is adsorbable onto solid carrier like silicon oxide, Ca salt, or metallic element aluminometasilicate. The liquid-lipid formulation is adscititious to the carrier by admixture in a very liquidiser. The carrier should be hand-picked specified it should have larger ability to sorb the liquid formulation and should have smart flow property when surface assimilation. antibiotic and glycoprotein with caprylocaproyl polyoxylglycerides (Labrasols) formulations were with success regenerate into solid intermediates whose bioavailability was maintained even when surface assimilation on carriers. blessings of this technique embrace smart content uniformity and high lipoid exposure.[19–21] Ito et al. have developed a solid formulation of antibiotic victimisation surface-active agent and adsorbent. victimisation solid adsorbents like Ca salt, metallic element aluminometasilicate, and silicon oxide, the liquid mixture (drug and surface-active agent like Labrasols) was regenerate to solid by a kneading method.[21]

Soften Granulation

This is conjointly remarked as pelletization, that transforms a powder combine (with drug) into granules or pellets.[22,24] during this technique a soften in a position binder (molten state) is sprayed onto the powder combine in presence of high-shear admixture. This method are often remarked as a "pump on" technique. as an alternative, the soften in a position binder {is blended|is combineed} with powder mix and, thanks to the friction of particles (solid/semisolid) throughout the high-shear admixture, the binder melts. The liquefied binder forms liquid bridges between powder particles and forms little granules that rework into spheronized pellets beneath controlled conditions. betting on the fineness of the powder, 15%–25% of the lipid-based binder are often used. The parameters to be thought of throughout the method ar binder particle size, admixture time, vane speed, and body of the binder on melting.[25] The dissolution rate of benzodiazepine was increased by formulating soften agglomerates containing solid dispersions of benzodiazepine.[26] disaccharide hydrate was soften-agglomerated with a melt in a position binder like PEG 3000 of Gelucires 50/13 in a very high-shear mixer. Polyoxylglycerides, partial glycerides or polysorbates, and phospholipid ar a number of the lipoid excipients utilized in the soften granulation technique to make self-microemulsifying systems.[26,27]

Critical Fluid-Based technique

This technique uses lipids for coating drug particles to provide solid dispersions. during this technique, the drug associated lipid-based excipients ar dissolved in an organic solvent and critical fluid (carbon dioxide) by elevating the temperature and pressure.[28,29] The coating method is expedited by a gradual reduction in pressure and temperature so as to cut back the solubility of the coating material within the fluid and thus precipitate onto the drug particles to make a coating.[30,31] The solubility of the formulation elements within the critical fluid and

stability of the substance throughout {the process|the technique} ar vital concerns of this method.

Other Formulation Tools

Analysis of drug solubilization in digestive juice salt-lecithin mixed micelles is associate uncomplicated and effectual assay. Drug solubilization are often analyzed directly by spectrophotometry in some cases or as an alternative by HPLC. this system offers a speedy indication of whether or not a drug is probably going to be solubilised within the gut lumen. The solubility sweetening quantitative relation of steroids could be a smart illustration that solubilization can not be expected just by octanol-water partition constant. Molecular dynamics modeling could become a helpful formulation tool as accessible computing power will increase. The structure of lipoid formulations may well be examined victimisation similar techniques and studies of the partitioning.[32]

Characterization of Lipid-Based Drug Delivery Systems

1. Appearance - the looks are often checked in graduated glass cylinder or transparent glass container for its uniformity and colour at equilibrium.[33]
2. 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.[34]
3. Density - relative density or density of the formulation is a crucial parameter. A decrease in density often indicates the entrapment air within the structure of the formulation. Density measurements at a given temperature are often made using high precision hydrometers.[34]
4. 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 attenuate "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 suspension.[34]
5. 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. The particle size measurement are often performed by optical microscope employing a lightweight microscope for the particles with measurement within microns. Particle size analyzer are often used for the measurement of the particle size.
6. Droplet Size and Surface Charge (Zeta Potential) - The droplet size distribution of microemulsion vesicles are often determined by either microscopy or light-scattering technique. The dynamic light-scattering measurements are taken at 90° during a dynamic light-scattering spectrophotometer which uses a neon laser of wavelength 632 nm. the data processing is completed within the built-in computer with the instrument. Recently, with relation to the importance of particle size distribution in terms of particle characterization and merchandise physical stability testing, there has been interest in newer light-scattering methods for particle detection called photon correlation spectroscopy (PCS). The surface charge is determined employing a zeta potential analyzer 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. to induce stable nanoemulsions by preventing flocculation and coalescence of the Nano droplets, ZP should typically reach a worth above 30 mV.[34]
7. Viscosity Measurement - Brookfield type rotary viscometer are often 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 so the sample temperature must be maintained at 37 ± 0.2°C by a thermo bath. The viscometer should be properly calibrated to measure the apparent viscosity of the suspension at equilibrium at a given temperature to see suspension reproducibility. Apparent viscosity, like pH, is an exponential term, and thus the log-apparent viscosity is also an appropriate way of reporting the results.[34]
8. In Vitro Studies - In vitro evaluation of lipid-based drug delivery systems are often through with the employment of lipid digestion models. so on assess the performance of an excipient during formulation development and to predict in vivo performance, it's a necessity to style an in vitro dissolution testing method. this may be termed as "simulated lipolysis release testing".[35] the essential principle on which this method works requires maintaining a unbroken pH during a reaction which releases or consumes hydrogen ions. If any deviation is found, it's compensated by the reagent addition. The model consists of a temperature-controlled vessel (37 ± 1°C), which contains a model intestinal fluid, composed of digestion buffer, salt (BS), and phospholipid (PL). Into this model a fluid lipid-based formulation is added and to initiate the digestion process pancreatic lipase and colipase were added. because the digestion process starts it results in the liberation of fatty acids, causing a transient come by pH. This come by pH is quantified by a pH electrode. The pH electrode is including a pH-stat meter controller and auto burette. An equimolar quantity of hydroxide is added to titrate the liberated fatty acids by the auto burette, so on prevent a change in pH of the digestion medium from a preset pH value. By quantifying the speed of

hydroxide addition and considering the stoichiometric relationship between fatty acids and hydroxide, the extent of digestion are often quantized. During the digestion process, samples are often withdrawn and separated into a poorly dispersed oil phase, highly dispersed aqueous phase, and precipitated pellet phase by centrifugation. Quantification of drug within the highly dispersed aqueous phase indicates that drug has not precipitated, from which an assumption are often made with relation to in vivo performance of the lipid-based formulation.

9. In vivo Studies - The impact of excipients on the bioavailability and pharmacokinetic profile of medication are often estimated by designing appropriate in vivo studies. an comprehensive study of intestinal lymphatic absorption is required, since lipid-based formulations enhance bioavailability by improving the intestinal uptake of drug. because of insufficient clinical data and differences in methods and animal models used, studies related to the drug transport by lymphatic system became difficult.[36] In Vitro-In Vivo Correlation (IVIVC) In vitro-in vivo correlation will help to maximise the event potential and commercialization of lipid-based formulations. A shortened drug development period and improved product quality may well 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 tissue and cell culture models) are various in vitro techniques which can be used to assess lipid-based formulations.[37] Such techniques provide information about specific aspects of the formulation only. But it is vital to grasp the in vivo interaction and performance of these systems. almost like that of in vivo enterocytes, Caco-2 cells produce and secrete chylomicrons on exposure to lipids. Next »

Applications

- So far, the planning of successful lipid-based delivery systems has been based largely upon empirical experiences. Systematic physicochemical investigations of structure and stability don't only help to hurry up the event of latest and improved formulations, but may additionally aid within the understanding of the complex mechanisms governing the interaction between the lipid carriers and thus the living cells. Hence they sought to be safe, efficient, and specific carriers for gene and drug delivery.
- LBDDS could also be accustomed deliver various kinds of drugs from new chemical entities to newer new developments for proteins and peptides, nucleic acids (DNA, siRNA), and cellular site specific delivery.[38–40]
- The utility of lipid-based formulations to bolster the absorption of poorly water-soluble, lipophilic drugs has been recognized for several years. Lipids are perhaps one in all the foremost 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, emulsions, microemulsions, mixed micelles, SEDDS, SMEDDS, thixotropic vehicles, thermo softening matrices, and liposomes.
- Lipid-based formulations, which are by no means a recent technological innovation, haven't only proven their utility for mitigating the poor and variable gastrointestinal absorption of poorly soluble, lipophilic drugs, but also, in many cases, have shown the flexibleness to chop back or eliminate the influence of food on the absorption of these drugs.[41]
- Some of the commercially available lipid-based formulations are depicted in Table 4

Table 4: Some of the commercially available lipid-based formulations are depicted.

Molecules/trade name	Indication	Dose	Type of formulation	Lipid excipients and surfactants
Calcitriol/Rocaltrol	Calcium regulator	Adult: 0.25–0.5 g q.d.	Soft gelatin capsule	Fractionated triglyceride of coconut oil
Cyclosporin/Nerol	Immunosuppressant	2–10 mg/kg/day b.i.d.	Soft gelatin capsule	Cremophor RH 40
Tretinoin/Vesanoid	Antineoplastic	45 mg/m^2 subdivided	Soft gelatin capsule	Bees wax, hydrogenated soybean oil
Valporic acid/Depakene	Antiepileptic	10–60 mg/kg/day	Soft gelatin capsule	Corn oil
Fenofibrate/Fenogal	Antihyperlipoproteinemic	200 mg q.d	Hard gelatin capsule	Gelucire
Testosterone/Restandol	Hormone replacement therapy	40–160 mg q.d.	Soft gelatin capsule	Oleic acid

Future Prospects

More consideration must be paid to the characteristics of varied lipid formulations available, in order that guidelines and experimental methods are often established that allow identification of candidate formulations at an early stage. Methods got to be looked for tracking the solubilization state of the drug in vivo, and there's a requirement for in vitro methods for predicting the dynamic changes, which are expected to require place within the gut. Attention to the physical and chemical stability of medicine within lipid systems and therefore the interactions of lipid systems with the components of capsule shells also will be required. Whilst these present challenges there's an excellent potential within the use of lipid formulations. The priority for future research should be to conduct human bioavailability studies and to conduct more basic studies on the mechanisms of action of this fascinating and diverse group of formulations.[42-45]

CONCLUSION

Lipid-based drug delivery systems provide the vast array of possibilities to formulations as they potentially increase the bioavailability of number of poorly soluble drugs along side the formulations of physiologically well tolerated class. the event of those systems requires proper understanding of the physicochemical nature of the compound also because the lipid excipients and gastrointestinal digestion. one among the main challenges of lipid excipients and delivery systems is that the varying range of compounds they contain. Proper characterization and evaluation of those delivery systems, their stability, classification, and regulatory issues consequently affect the amount of those formulations. On the way of conclusion, the prospect of those delivery systems looks promising.

REFERENCES

1. Brigger, C. Dubernet, and P. Couvreur, "Nanoparticles in cancer therapy and diagnosis," Advanced Drug Delivery Reviews, 2002; 54(5): 631–651.
2. J. Panyam and V. Labhasetwar, "Biodegradable nanoparticles for drug and gene delivery to cells and tissue," Advanced Drug Delivery Reviews, 2003; 55(3): 329–347.
3. R. H. Müller, M. Radtke, and S. A. Wissing, "Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations," Advanced Drug Delivery Reviews, 2002; 54(1): S131–S155.
4. P. Gershkovich, K. M. Wasan, and C. A. Barta, "A review of the application of lipid-based systems in systemic, dermal/transdermal, and ocular drug delivery," Critical Reviews in Therapeutic Drug Carrier Systems, 2008; 25(6): 545–584.
5. Ž. Pavelić, N. Škalko-Basnet, J. Filipović-Grčić, A. Martinac, and I. Jalšenjak, "Development and in vitro evaluation of a liposomal vaginal delivery system for acyclovir," Journal of Controlled Release, 2005; 106(1-2): 34–43.
6. H. Benameur, "Liquid and semi-solid formulations for enhancing oral absorption," Bulletin Technique Gattefossé, 2006; 99(1): 63–75.
7. C. W. Pouton and C. J. H. Porter, "Formulation of lipid-based delivery systems for oral administration: materials, methods and strategies," Advanced Drug Delivery Reviews, 2008; 60(6): 625–637.
8. C. J. H. Porter, N. L. Trevaskis, and W. N. Charman, "Lipids and lipid-based formulations: optimizing the oral delivery of lipophilic drugs," Nature Reviews Drug Discovery, 2007; 6(3): 231–248.
9. Dahan and A. Hoffman, "Rationalizing the selection of oral lipid based drug delivery systems by an in vitro dynamic lipolysis model for improved oral bioavailability of poorly water soluble drugs," Journal of Controlled Release, 2008; 129(1): 1–10.
10. W. Pouton, "Formulation of poorly water-soluble drugs for oral administration: physicochemical and physiological issues and the lipid formulation classification system," European Journal of Pharmaceutical Sciences, 2006; 29(3-4): 278–287.
11. P. P. Constantinides, "Lipid microemulsions for improving drug dissolution and oral absorption: physical and biopharmaceutical aspects," Pharmaceutical Research, 1995; 12(11): 1561–1572.
12. R. G. Strickley, "Solubilizing excipients in oral and injectable formulations," Pharmaceutical Research, 2004; 21(2): 201–230.
13. J. B. Cannon and M. A. Long, "Emulsions, microemulsions, and lipid-based drug delivery systems for drug solubilization and delivery, part II," in Oral Applications, 2008; 16: 227–254.
14. C. W. Pouton, "Lipid formulations for oral administration of drugs: non-emulsifying, self-emulsifying and 'self-microemulsifying' drug delivery systems," European Journal of Pharmaceutical Sciences, 2000; 11(2): S93–S98.
15. E. B. Souto and R. H. Muller, Nanoparticulate Drug Delivery Systems, vol. 166, Informa Healthcare, New York, NY, USA, 2007.
16. C. J. H. Porter, C. W. Pouton, J. F. Cuine, and W. N. Charman, "Enhancing intestinal drug solubilisation using lipid-based delivery systems," Advanced Drug Delivery Reviews, 2008; 60(6): 673–691.
17. B. Chauhan, S. Shimpi, and A. Paradkar, "Preparation and evaluation of glibenclamide-polyglycolized glycerides solid dispersions with silicon dioxide by spray drying technique," European Journal of Pharmaceutical Sciences, 2005; 26(2): 219–230.
18. B. Chauhan, S. Shimpi, and A. Paradkar, "Preparation and characterization of etoricoxib solid dispersions using lipid carriers by spray drying technique," AAPS PharmSciTech, 2005; 6(3): E405–E409.

19. N. Venkatesan, J. Yoshimitsu, Y. Ohashi et al., "Pharmacokinetic and pharmacodynamic studies following oral administration of erythropoietin mucoadhesive tablets to beagle dogs," International Journal of Pharmaceutics, 2006; 310(1-2): 46–52.
20. N. Venkatesan, J. Yoshimitsu, Y. Ito, N. Shibata, and K. Takada, "Liquid filled nanoparticles as a drug delivery tool for protein therapeutics," Biomaterials, 2005; 26(34): 7154–7163.
21. Y. Ito, T. Kusawake, M. Ishida, R. Tawa, N. Shibata, and K. Takada, "Oral solid gentamicin preparation using emulsifier and adsorbent," Journal of Controlled Release, 2005; 105(1): 23–31.
22. O. Chambin and V. Jannin, "Interest of multifunctional lipid excipients: case of Gelucire 44/14," Drug Development and Industrial Pharmacy, 2005; 31(6): 527–534.
23. B. Evrard, K. Amighi, D. Beten, L. Delattre, and A. J. Moës, "Influence of melting and rheological properties of fatty binders on the melt granulation process in a high-shear mixer," Drug Development and Industrial Pharmacy, 1999; 25(11): 1177–1184.
24. Royce, J. Suryawanshi, J. Shah, and K. Vishnupad, "Alternative granulation technique: melt granulation," Drug Development and Industrial Pharmacy, 1996; 22: 917–924.
25. Seo and T. Schæfer, "Melt agglomeration with polyethylene glycol beads at a low impeller speed in a high shear mixer," European Journal of Pharmaceutics and Biopharmaceutics, 2001; 52(3): 315–325.
26. J.N. Hunt, M.T. KnoxA relation between the chain length of fatty acids and the slowing of gastric emptying J Physiol, 194(1968): 327-336. CrossRefView Record in ScopusGoogle Scholar
27. D. Wagnera, H.S. Langguth, A. Hanafy, A. Koggela, P. LangguthIntestinal drug efflux: formulation and food effects Adv Drug Del Rev, 2001; 50 (Suppl. 1): Google Scholar 32
28. P. Gershkovich, A. HoffmanEffect of a high-fat meal on absorption and disposition of lipophilic compounds: the importance of degree of association with triglyceride-rich lipoproteins.
29. Eur J Pharm Sci, 2007; 32: 24-32. ArticleDownload PDFView Record in ScopusGoogle Scholar 33.
30. W.W. ChristieHigh-performance liquid chromatography and lipids: a practical guide Pergamon Press, Oxford 1-272 View Record in ScopusGoogle Scholar, 1987; 34.
31. Y. Cao, M. Marra, B.D. AndersonPredictive relationships for the effects of triglyceride ester concentration and water uptake on solubility and partitioning of small molecules into lipid vehicles.
32. J Pharm Sci, 93 2768-2779 ArticleDownload PDFView Record in ScopusGoogle Scholar, 2004; 35.
33. A.M. Kaukonen, B.J. Boyd, C.J. Porter, W.N. CharmanDrug solubilization behavior during in vitro digestion of simple triglyceride lipid solution formulations Pharm Res, 21 245-253 View Record in ScopusGoogle Scholar, 2004; 36.
34. F.B. Padley, F.D. Gunstone, J.L. HarwoodOccurrence and characteristics of oils and fats.
35. F.D. Gunstone, J.L. Harwood, F.B. Padley (Eds.), The lipid handbook, Chapman & Hall, London, 1994; 47-224.
36. E.M. Collnot, C. Baldes, M.F. Wempe, J. Hyatt, L. Navarro, et al.Influence of vitamin E TPGS poly(ethylene glycol) chain length on apical efflux transporters in Caco-2 cell monolayers J Control Release, 111 35-ArticleDownload PDFView Record in ScopusGoogle Scholar, 2006; 38.
37. E.M. Collnot, C. Baldes, M.F. Wempe, R. Kappl, J. Huttermann, J.A. Hyatt, et al.Mechanism of inhibition of p-glycoprotein mediated efflux by vitamin E TPGS: influence on ATPase activity and membrane fluidity Mol Pharm, 2007; 4: 465-474.
38. B.T. Griffin, C.M. O'DriscollA comparison of intestinal lymphatic transport and systemic bioavailability of saquinavir from three lipid based formulations in the anaesthetised rat model J Pharm Pharmacol, 2006; 58: 917-925. CrossRefView Record in ScopusGoogle Scholar 40
39. R.G. StrickleySolubilizing excipients in oral and injectable formulations Pharm Res, 21 201-230 View Record in ScopusGoogle Scholar, 2004.
40. R.G. StrickleyCurrently marketed oral lipid-based dosage forms: drugs products and excipients D.J. Hauss (Ed.), Oral lipid-based formulations: enhancing the bioavailability of poorly water soluble drugs, Informa Healthcare, New York 1-31 View Record in ScopusGoogle Scholar, 2007; 42.
41. S.H. YalkowskySolubility and solubilization in aqueous media (ACS Professional Reference Books) American Chemical Society, Washington, DC, 1999; 1-480. Google Scholar 43
42. E.T. Cole, D. Cade, H. BenameurChallenges and opportunities in the encapsulation of liquid and semi-solid formulations into capsules for oral administration Adv Drug Deliv Rev, 60 747-756 ArticleDownload PDFView Record in ScopusGoogle Scholar, 2008; 44.
43. M.G. Wakerly, C.W. Pouton, B.J. Meakin, F.S. MortonSelf-emulsification of vegetable oil-non-ionic surfactant mixture: a proposed mechanism of action ACS Symp Ser, 311 242-255 CrossRefView Record in ScopusGoogle Scholar, 1986; 45.
44. C.W. PoutonFormulation of self-emulsifying drug delivery systems Adv Drug Deliv Rev, 25 47-58 ArticleDownload PDFView Record in ScopusGoogle Scholar, 1997; 46.
45. D.J. Hauss (Ed.), Oral lipid-based formulations: enhancing the bioavailability of poorly water soluble drugs, Informa Healthcare, New York Google Scholar, 2007; 47.