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***Review Article** (Open Access)*

LIPIDS AS CARRIERS OF LIPID BASED DRUG DELIVERY SYSTEM (LBDDS) AND TYPES OF LBBDS: A REVIEW

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ABSTRACT
In Pharmaceutical industry the constituents obtained through natural sources are used basically as excipients and secondary metabolites are used as therapeutic constituents. Development of novel drug delivery systems with natural polymers gained much importance in the recent years. Lipids are used as an integral part to formulate lipid based drug delivery system. With the advent of drug design, various molecules have been created that have a potential for therapeutic action. But most of the newly discovered chemical entities are of high molecular weight and belong to biopharmaceutical classification system (BCS) – II, with poor aqueous solubility and high membrane permeability. Hence these two characteristics limit the bioavailability of orally- administered drugs. Lipids as carriers in lipid based drug delivery system improves the solubility and bioavailability of drugs with poor water solubility.

***Keywords**: Lipids; Triglycerides; Emulsions, Vesicular system, Lipid particulate system*

INTRODUCTION

Because of their ability to improve the solubility and bioavailability of drugs with poor water solubility, lipid-based drug delivery (LBDD) systems have gained a lot of attention in recent years (Jannin *et al.,* 2008). Drug design has resulted in the development of a variety of compounds with medicinal promise. However, the majority of recently discovered chemical entities have a large molecular weight and are classified as biopharmaceutical classification system (BCS) – II, which means they have low water solubility and high membrane permeability. As a result, these two properties reduce the bioavailability of medications taken orally Amidon *et al.,* 1995).

Many substantial attempts have been made in recent years to harness the potential of lipid-based drug delivery systems, as they provide a good way of site-specific and time-controlled distribution of medicines of various molecular weights, small and big, as well as bioactive chemicals (Brigger *et al.,* 2002; Panyam and Labhasetwar, 2003). In terms of solubility and bioavailability, poorly water-soluble medicines pose a challenge to formulation experts. Lipid-based drug delivery systems (LBDDS) have gained a lot of attention due to their effective size dependant features. LBBDS has also grabbed the lead due to the obvious benefits of greater biocompatibility and adaptability. These systems can be used to make medications for topical, oral, pulmonary, or parenteral administration. Lipid formulations can be altered in a variety of ways to fulfil a variety of product needs, including disease state, method of administration, cost, toxicity, and efficacy. Lipid-based carriers have been shown to be promising alternatives for the formulation of medicines, vaccines, diagnostics, and neutraceuticals because they are safe and efficient (Muller *et al.,* 2002).

ROLE OF LIPID EXCIPIENTS

The lipid-based drug delivery system (LBDDS) is a drug delivery method that has gotten a lot of interest in recent years for improving the solubility, dissolution, and bioavailability of medicines that are poorly water-soluble (Kalepu *et al.,* 2013). There is a growing need to develop acceptable lipid drug carriers in order to better regulate, localize, and target drugs. They have size-dependent features as well as evident benefits including biocompatibility and biodegradability (Shrestha *et al.,* 2014). LBDDS may also improve oral bioavailability of medication (Shrestha *et al.,* 2014) by reducing the intrinsic constraint of

delayed and incomplete dissolution of poorly soluble pharmaceuticals and facilitating the formation of the solubilized structure after digestion in the gastrointestinal tract (GIT), from which absorption improves[8].
The lipid-based formulation may shield active chemicals from biological and enzymatic degradation, resulting in increased therapeutic potency. The bio distribution of drug 5 has been proven to minimize the toxicity of several medications using a lipid-based formulation technology. The majority of lipid drug delivery systems employed as drug carriers have high drug stability, drug carrier capacity, and the ability to incorporate both hydrophilic and lipophilic molecules, as well as the ability to provide via oral, topical, parenteral, and pulmonary routes. An LBDDS is typically composed of lipids, and a surfactant may also contain a hydrophilic co-solvents (Čerpnjak *et al.*, 2013). In practice, lipid formulations are a diverse group of formulations, which have a wide range of properties.

Role of Lipids in Bioavailability

When some medications are taken with food, their bioavailability is improved Many pharmacological compounds, on the other hand, have little to no interaction with food. Food has no effect on the absorption of BCS class I medications, but it does impair the absorption of class II pharmaceuticals when they are co-administered with food. Solubility, permeability, and inhibition of efflux transporters in the presence of food may all have a role in increased bioavailability. Grifofulvin, halofantrine, danazol, troglitazone, and atovaquone are some of the medications that have improved bioavailability when given with food.
The FDA produced a guidance document titled "Food-Effect Bioavailability and Fed Bioequivalence" in December 2002. Because high fat meals (800–1000 calories, 50–65 percent fat, 25–30 percent carbohydrates, and 15%–20 percent proteins) influence GI physiology and maximize medication transport into the systemic circulation, the USFDA approved them for food-effect research.
The lipid component of food, in particular, plays a critical role in the absorption of lipophilic drugs, resulting in increased oral bioavailability. This can be explained by the ability of a high fat meal to stimulate biliary and pancreatic secretions, to decrease metabolism and efflux activity, to increase intestinal wall permeability, and to a prolongation of gastro intestinal tract (GIT) residence time and transport via lymphatic system.
Triglycerides and long-chain fatty acids are important in extending GIT residence duration. A high-fat meal also increases the levels of TG-rich lipoproteins, which interact with medication molecules. This interaction of lipoproteins with drug molecules improves intestinal lymphatic transport, modifies drug disposition, and, ultimately, changes the pharmacological action kinetics of poorly soluble drugs.
When co-administered without meals, this dietary effect on drug absorption raises major concerns regarding sub therapeutic plasma drug concentrations. Such food effect is also a serious problem ford rugs with a narrow therapeutic index, where increased bioavailability may lead to serious untoward effects. As a result, when administering such medications, food consumption must be controlled or monitored. However, by producing the medication as a lipid-based formulation, which can increase the solubility and dissolution of lipophilic medicines and facilitate the generation of solubilized species from which absorption occurs, food-dependent bioavailability can be greatly reduced. As a result, lipid-based formulations can be employed to minimize therapeutic doses while also increasing oral bioavailability[6].

LIPID EXCIPIENTS

Drugs must be mixed into a proper mixture of oil(s) and surfactant(s) for creating LBDDS; thus, excipient selection is often the first step in formulation development. Because there are so many lipid-based compounds that can be utilized to make LBDDS, some generic excipient selection criteria were developed to save time and money.
Miscibility, solvent capacity, self-dispersibility and ability to promote self-disperssion of the formulation; digestibility and fate of digested products; regulatory issues – irritancy, toxicity, purity, chemical stability; capsule compatibility; melting point, and cost.are all factors that influence the selection of excipients for lipid-based formulations (Pouton and Porter, 2008).

Triglycerides

In lipid-based formulations, tri-glycerides are the most often utilized excipients. Tri-glycerides are a type of lipid that has no known side effects because they are completely digested and absorbed by the body. Tri-glycerides are further classified into three groups, Long Chain Triglycerides (LCT), Medium Chain Triglycerides (MCT), and Short Chain Triglycerides (SCT) Table 1. The effective concentration of the ester group determines the solvent capacity of a medication. The solvent capacity of MCT is larger than that of LCT (Kalepu *et al.*, 2013).

Mixed Glycerides

Partial hydrolysis of vegetable oils yields mixed glycerides. The chemical makeup of the mixed glycerides produced is determined by the starting material (triglyceride) and the extent of hydrolysis. Medium chain mixed glycerides are resistant to oxidation, have a higher solvent capacity, and help to emulsify. These polar oily excipients also boost the formulation's solvent capacity and dispersibility. Polar oils include sorbitan trioleate (Span85), for example, aside from that, oleic acid can be found in a variety of commercial items (Strickley, 2004; Strickley, 2007).

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Table 1 Triglycerides used in formulation of Lipid based drug delivery system

Class	Examples	Characteristic
Long-chain tri glycerides (LCT)	Corn oil, soybean oil, olive oil, peanut oil, sesame oil, sunflower oil, castor oil, *etc.*	GRAS status, easily ingested, digested, and absorbed, poor self-dispersing properties of LCT and generally lower loading capacity for drugs with intermediate log P values. Their advantage is generally a higher solubilizing capacity after dispersion and digestion of the formulation
Medium-chain triglycerides (MCT)	Fractionated coconut oil, palm seed oil, triglycerides of Caprylic/ capric acid Miglyol® 812, Captex® 355	MCTs exhibit a good solubilizing capacity for less lipophilic drugs and good self-dispersing ability. Semi-synthetic MCT with hydrogenated double bonds are resistant to oxidation
Mixed mono-, di- and tri-glycerides	Imwitor® 988, Imwitor® 308, Maisine® 35-1,Peceol®, Plurol, Oleique®CC49, Capryol®, Myrj®	They possess surface-active properties because of their amphiphilic nature and are effective in replacing conventionally used oils owing to their better self-dispersing ability and higher solubilizing capacity for poorly water-soluble drugs

Apart from various lipid components as discussed above various other excipients plays important role in designing LBDDS are-

Co solvents

Co solvents are used in most marketed medicinal formulations to improve the solubilization process[10, 11]. Ethanol, glycerol, propylene glycol, and poly ethylene glycols (PEG)-400 are some of the most often used chemical solvents. The reason for their employment is to improve the solvent capacity of medication formulations and to aid in the dispersion of systems containing a high proportion of water soluble surfactants.

However, there are various practical limitations to these co solvents, including precipitation of the solubilized drug from the solvent due to loss of solvent capacity after dilution 11, and precipitation of the solubilized drug from the solvent due to loss of solvent capacity following dilution, immiscibility of some co solvents with oils, and incompatibilities of low molecular weight solvents with capsuleshells[12].

Surfactants

The most significant component in the proper design of LBDDS is the selection of appropriate surfactants. The kind and concentration of emulsifier utilized determines how stable a lipid dispersion or lipid-based formulation is to various environmental stresses such as pH, ionic strength, and temperature. The formation of most stable emulsions in the presence of surfactant combinations, in which one works as an emulsifier and the other as a co-emulsifier, is generally accepted, depending on their HLB values (Pandey and Kohli 2018; Maurya *et al.*, 2017).

When co-surfactants with an HLB value of 10-14 are combined with surfactant to reduce interfacial tension, the interface expands to generate finely distributed droplets. The inclusion of a co-surfactant creates a fluid interfacial film. The use of a co-surfactant will improve the fluidity of the interface, enhancing the system's entropy (Tejeswari 2014). Table 2 demonstrates the types of surfactants with their HLB values.

Table 2 Types of surfactant and their HLB values

HLB value	Types of surfactant
Low HLB (< 10)	Phosphatidyl choline and Phosphatidyl choline mixtures Phosphatidyl choline, mixtures in propylene glycol / MCT, ethanol glycerides Unsaturated polyglycolized (macrogol glycerides): Labrafil® M1944 CS, Labrafil® M2125CS. Sorbitan esters: Capmul®, Capmul® S, Span® 20, Span® 40. Polyethoxylated alkyl ethers: Brijs®
High HLB (> 10)	Polyoxyethylene Sorbitan esters (Polysorbate): Tweens® 20, 40, 60, 80. Polyethoxylated fatty acid ester - Myrj® 52, Solutol® HS15. Polyethoxylated alkyl ethers - Brijs® 35, 56, 78 Polyethoxylated glycerides Caprylo/caproil macrogolglycerides: Labrasol® Polyoxyl castor oil derivatives. Polyoxyl 35 castor oil: Cremophor® EL, Polyoxyl 40 hydrogenated castor oil: Cremophor® RH40. Polyoxyethylene polyoxypropylene block copolymer: Poloxamer® 188, Poloxamer® 407. Saturated polyglycolized glycerides: Lauroyl macrogolglycerides: Gelucire® 44/14, Stearoyl macrogolglycerides: Gelucire® 50/13

TYPES OF LIPID BASED DRUG DELIVERY SYSTEM

This section illustrates the use of lipids as a carrier molecule for the formulation of the dosage forms which can be termed as Lipid based drug delivery system types and subtypes (Fig.1).

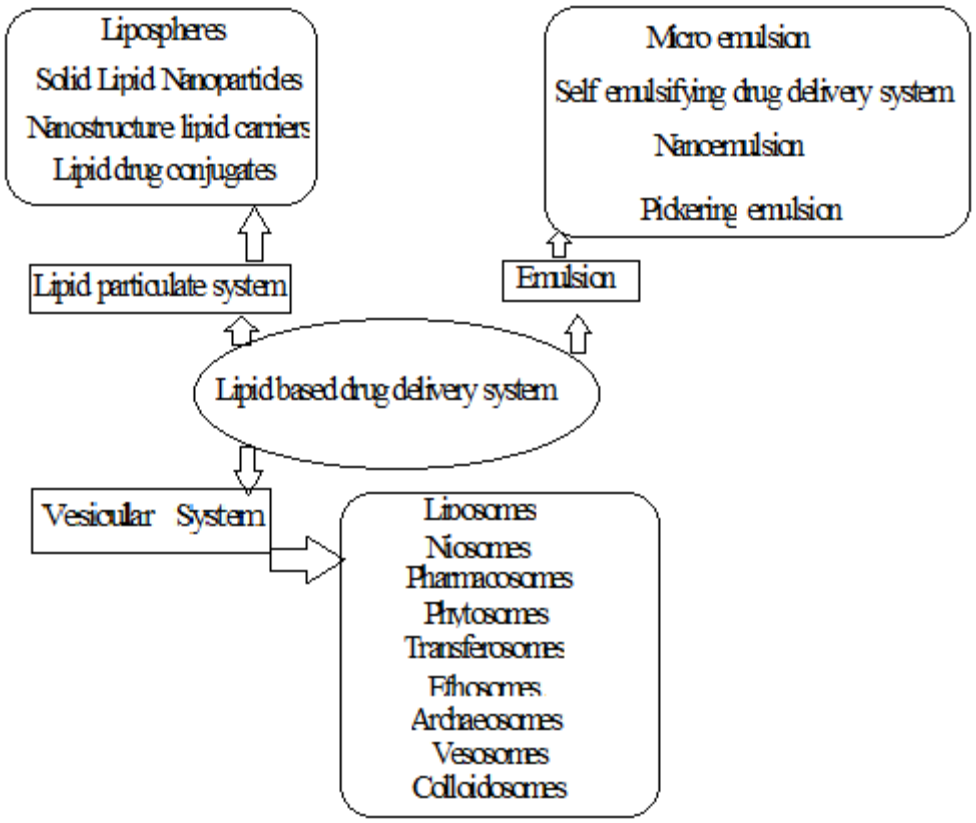

Fig. 1 Types and Subtypes of Lipid based drug delivery system

EMULSION

Micro-Emulsion

In 1940, Hoar and Schulman were the first to introduce the concept of micro-emulsion. They created a single-phase clear solution by titrating a milky emulsion with hexanol. Schulman and his colleagues created the term "micro emulsion" in 1959. Water, oil, and surfactant/ Co-surfactant make up a clear, thermodynamically stable micro-emulsion (Lade *et al.*, 2015; Asadujjaman and Mishuk, 2013).

Unlike a traditional emulsion, this micro-emulsion is created by simply mixing the materials together, with caution given to avoid a high shear environment that might promote phase separation. Micro-emulsion droplets have a smaller particle size (10-200 nm) than regular emulsion droplets, which have a particle size of (1-20 m). The emulsion is made up of droplets that are usually spherical in shape, whereas the micro-emulsion is made up of micelles or continuous bilayer structures[18]. Because distinct polarity micro domains exist inside the same single-phase solution, both water-soluble and oil-soluble molecules can be solubilized at the same time if required. Amphiphilic medicines can also be included into the micro-emulsion (Strickley, 2007).

Self-Emulsifying Drug Delivery System (SEDDS)

Pouton disclosed for the first time a self-emulsifying drug delivery system that uses Miglyol 812 (M812, medium-chain triglyceride, MCT) and Tween 85 (T85, polyoxyethylene-20-sorbitan trioleate) to improve

both solubility and bioavailability of poorly water-soluble medicines (Singh, 2015). The thermodynamically stable isotropic mixes of oil, surfactant, and co-surfactant that spontaneously form an emulsion when in contact with aqueous fluid in the GI tract are known as self-emulsifying drug delivery systems (SEDDS).

The particle size of an emulsion droplet determines whether it is categorized as a self-micro emulsifying drug delivery system (SMEDDS) or a self-nano-emulsifying drug delivery system (SNEDDS), with particle sizes ranging from 100 to 250 nm. SMEDDS is a commonly utilized technique for solubilizing hydrophobic medicines by partitioning them into two phases (oil and aqueous), resulting in increased bioavailability (Rani, 2019; Singh, 2015). The benefits of this method include increased oral bioavailability, reduced dose and frequency, the most consistent plasma level profile curve, specific drug targeting, and drug protection from the hostile GIT and gut environment (Asadujjaman and Mishuk, 2013).

Nano-emulsion

The oil and water phases of a nano-emulsion are stabilized by a surfactant or alcohol. Nano-emulsions are oil-in-water (O/W) emulsions with droplet sizes ranging from 100 to 500 nano meters. Oil-in-water (O/W) and water-in-oil (W/O) particles occur, with the center of the particle being either oil or water, respectively. These nano-emulsions are meta-stable, meaning they can be diluted with water without affecting the droplet size. Temperature and pH are two parameters that affect the stability of nano emulsions (Shamant, 2016). Nano-emulsions are biodegradable and biocompatible, easy to scale up, and can be employed for lipophilic medicines. Surfactants and chemicals utilized in the formation of nano-emulsions that have been authorized by regulatory bodies as generally recognized as safe (GRAS) (Abhinav, 2016). They provide superior drug release patterns due to their enormous surface area. Nano-emulsions can be administered via parenteral, ocular, oral, pulmonary, and cutaneous channels[22].

Pickering Emulsion

Pickering emulsion is a form of O/W emulsion in which solid particles present at the interface of two phases provide stability, lowering the surface energy of system (McMullen *et al.*, 2013). Silica, calcium carbonate, titanium dioxide, latex, and a variety of other solid particles are used. In comparison to conventional emulsion, the added solid particles will adhere to the surface of the interface and prevent droplets from coalescing, resulting in a more stable emulsion Lade *et al.*, 2015). The stability of the Pickering emulsion can be affected by a variety of factors such as hydrophobicity, particle shape, and particle size (Asadujjaman and Mishuk, 2013)..

VESICULAR SYSTEM

Liposomes

Bangham and colleagues were the first to discover liposomes in the early 1960s (Asadujjaman and Mishuk, 2013). Liposomes are synthetic vesicles made up of a lipid bilayer of phospholipids and cholesterol with particle diameters ranging from 0.01 to 100 micro meters. Liposomes are made up of a variety of substances, the most important of which being phospholipids and cholesterol. Phospholipids' amphiphilic properties allow them to contain both lipophilic and hydrophilic pharmaceuticals in the structure of liposome (Chime and Onyishi 2013). It has downsides such as a proclivity for being taken up by the body's reticular endothelial system (RES), physical instability, and low cost (Lade *et al.*, 2015).

Liposomes are divided into three categories based on their size and quantity of bilayers: (1) multilamellar vesicles, (2) multilamellar vesicles, and (3) multilamellar vesicles (MLVs) (2) unilamellar vesicles, tiny (SUVs) (3) unilamellar vesicles of a large size (LUVs). Liposomes can be utilized to deliver medications via oral, ophthalmic, pulmonary, and transdermal routes. The aqueous and lipid phases of liposomes have been integrated with anti-tumor and antibacterial drugs, chelating agents, peptide hormones, enzymes, other proteins, vaccinations, and genetic materials (McMullen *et al.*, 2013; Kumar and Rao, 2012).

Niosomes

Niosomes, also known as anionic surfactant vesicles, are being investigated as a possible replacement for liposomes. Niosomes are non-ionic bilayer-based vesicles with surfactant sizes ranging from 10 to 100 nm. They are physically similar to liposomes, but instead of natural phospholipids, they contain a synthetic non-ionic surfactant. Cholesterol, which gives the structure integrity, rigidity, and form, and non-ionic surfactants such as Span 60, Span 40, Span 20, Span 80, Tween 20, Tween 40, Tween 60, and Tween 80 are the two main components of Niosomes (Chime and Onyishi 2013)..

In comparison to phospholipids, non-ionic surfactants are less expensive and chemically stable. Niosomes, which are comparable to liposomes in terms of functioning and drug bioavailability, are also utilized to target drugs to certain organs. However, Niosomes are chosen over liposomes due of their chemical stability and cost (Oliveira, 2017).

Niosomes have a number of drawbacks. Hydrolysis of encapsulated pharmaceuticals can occur as a result of physical instability during storage, fusion, or leaking, reducing the drug's shelf life. Niosomes, primarily enclose antigen and tiny compounds[22]. Both hydrophilic and hydrophobic medicines can be encapsulated in niosome vesicles and niosomes have been successfully employed for oral administration of protein and peptides (Abhinav, 2016; Oliveira, 2017).

Pharmacosomes

The colloidal dispersion of pharmaceuticals covalently bound to lipids is known as pharmacosomes. Pharmacosomes are defined as a system that consists of attaching a drug (Pharmakon) to a carrier (soma). They can be ultra-fine vesicular, micellar, or hexagonal aggregates, depending on the chemical composition of the drug and lipid complex. They are an effective vehicle for medication targeting and controlled release. Entrapped hydrophilic and hydrophobic medicines can also be found in pharmacosomes. Surface and bulk interaction of lipids with the medication are critical factors for the creation of vesicular pharmacosomes.

Any medicine having an active hydrogen atom (-COOH, -OH, -NH2, etc.) could be esterified to the lipid, with or without a spacer chain, resulting in a highly amphiphilic molecule that will aid membrane, tissue, and cell wall transfer in the organism. The entire system developed hydrophilic and lipophilic properties, gaining amphiphilic characteristics in the process, lowering interfacial tension and exhibiting mesomorphic behaviour (Chime and Onyishi 2013).

Phytosomes

Herbosomes are another name for phytosomes. The name phytosome comes from two words: phyto, which means "plant," and somes, which means "cell-like structure. These are lipidic vesicles made by reacting a stoichiometric quantity of phospholipids with standardized extract, or polyphenolic compounds such as flavonoids, tannins, and other polyphenolic compounds in an aprotic solvent (Lade *et al.*, 2015; Chime and Onyishi 2013; Singh *et al.*, 2016).

When water is added to phytosomes, they become micellar and create a liposome-like structure. Phytosomes absorb better than traditional herbal extracts. Drug bioavailability and penetration via cell membranes are also improved by phytosomes. The active components in herbal extracts defend against gut bacteria and digestive secretion degradation (Asadujjaman and Mishuk, 2013).

In the fields of pharmaceuticals, cosmeceuticals, and neutraceuticals, herbosomes have become overly important in the formulation of solution, creams, lotions, gels, and emulsions (Elmowafy, 2017).

Transferosome

The word transferosome is derived from the words ‘transfer’ meaning ‘to take across’ and ‘soma’ meaning ‘body’. Transfersomes are an artificial vesicle that mimics the structure of a cell vesicle, allowing them to manage and target drugs effectively. Transfersomes were created to take advantage of phospholipid vesicles to administer medication transdermally (Asadujjaman and Mishuk, 2013).

These systems, which are primarily made up of phospholipids, surfactant, and water, can penetrate deeper into the dermal layer of the skin than traditional liposomes. These artificial vesicles comprise phospholipids and an amphiphilic group, such as Tween 20, Tween 60, Tween 80, Sodium cholate,

sodium deoxycholate, Span 60, Span 63, Span 80, or di potassium glycyrrhizinate, which give the system vesicle flexibility and deformability. They can transport both hydrophilic and lipophilic medications. The diameter of transferosomes ranges from 10 to 100 nanometres. They can also permeate the skin membrane via trans-epidermal water gradient action, which produces outcomes in the presence of high water content in spontaneous migration of the drug-loaded vesicles through skin barrier (Rajabi and Mousa 2016; Priyanka and Singh, 2014).

Ethosomes

Ethosomes are soft, flexible vesicles used to transfer active substances transdermally. Ethosomes are vesicular systems made up primarily of phospholipids, with the active element in the system's center being a hydro alcoholic combination. In comparison to other vesicular delivery systems, hydro-alcoholic mixtures typically contain 20-30% alcohol, which acts as a permeability enhancer and permeates through skin membrane quickly. Ethosomes can encapsulate hydrophilic, lipophilic, or amphiphilic medicinal molecules. The medicine is delivered to the deep stratum corneum of the skin and the systemic circulation via ethosomes, which are non-invasive (Lade *et al.*, 2015; Asadujjaman and Mishuk, 2013; Pandey *et al.*, 2015).

Archaeosomes

Archaeosomes are lipids containing vesicular structures found in archaeobacteria. These are composed of one or more fully saturated bipolar tetra ether lipids that are resistant to oxidative damage, high temperatures, and alkaline pH. Archaeosomes, like liposomes, are made from ether lipids taken from diverse archaeobacteria and have a size range of 200 nm. The addition of polyethylene glycol and Coenzyme Q10 to archaeosomes has been shown to change the tissue distribution characteristics of intravenously given vesicles. It had also reported that intravenous and oral delivery of nanometric-sized archaeosomes to an animal model was well tolerated with no apparent toxicity (Asadujjaman and Mishuk, 2013; Chime and Onyishi 2013).

Vesosomes

Vesosomes are vesicular structures that hold the medication and are made up of one or more bilayers encircling an aqueous core with unilamellar vesicles as an interior compartment. Vesosomes are multi-compartment structures with an interior compartment that is isolated from the outside membrane. Inside the core of unilamellar vesicles is a medication. Each vesosome compartment can encapsulate a variety of materials and have distinct bilayer compositions. Vesosomes could effectively entrap colloidal particles as well as biological macromolecules (Asadujjaman and Mishuk, 2013; Chime and Onyishi 2013).

Colloidosomes

Colloidosomes are microcapsules with densely packed colloidal particles as their shell. The physical properties of colloids, such as permeability, mechanical strength, and biocompatibility, can be accurately regulated using the right colloids and assembly circumstances.

Colloidosomes are appealing structures for encapsulation and controlled release of materials ranging from perfumes and active compounds to molecules produced by live cells due to their high degree of control over their physical properties. Colloidosomes are hollow, elastic shells with adjustable permeability and elasticity. It is a novel class of microcapsules whose shell consists of coagulated or fused colloidal particles at the interface of emulsion droplet.

To improve the viability of cells, colloidosomes can be made as hard porous superstructures.

They can also be utilized for a variety of therapeutic and pharmacological purposes, including:

Drug/protein delivery carrier, regulated and sustained drug release, for improved drug solubilization, in tumour therapy, antibacterial, antifungal, antiviral, cosmetics and dermatology, ocular drug delivery, brain delivery, DNA delivery, and enzyme immobilization

However, a key issue in the production of colloidosomes is the low yield of particles. If the shell locking is inefficient, the colloidosomes simply coalesce and fall apart on transfer into the water; a large

proportion of the colloidosomes are normally lost during the transfer from organic to water medium (Chime and Onyishi 2013).

LIPID PARTICULATE SYSTEM

Lipospheres

Lipospheres were first described as a particulate dispersion of solid spherical particles with diameters ranging from 0.2 to 100 m, made up of a solid lipophilic core such as triglycerides or fatty acid derivatives and supported by a phospholipid monolayer. The medicine is dissolved or disseminated in the inner core, which is hydrophobic. Liposphere, is a new type of fat-based encapsulated system designed for medication or bioactive administration via parenteral and topical routes. At room temperature, the lipospheres are micro droplets that are solid In microspheres and micro particles, as well as ordinary microspheres and micro particles including high dispersibility in an aqueous medium, and a release rate for the entrapped substance that is controlled by phospholipid coating and carrier.

There are also many advantages over the dispersion based delivery systems. Lipospheres are more stable than emulsion-based systems like vesicles and liposomes, and they disperse more effectively than most suspension-based systems. Furthermore, because the material to be supplied can be disseminated in the solid carrier, it does not need to be soluble in the vehicle.

Because the vehicle is a solid material, lipospheres have a lesser danger of the substance to be given reacting with the vehicle than an emulsion system. Furthermore, the inner solid vesicle or the outer phospholipid layer can be changed to control the rate of material release from the lipospheres. Lipospheres are also easier to prepare than vesicles such as liposomes and are inherently more stable (Chime and Onyishi 2013; Santamaria, 2017).

Solid-Lipid Micro particles

Although polymeric microspheres have been successfully evaluated as sustained release drug delivery systems, their safety is still unknown, prompting the creation of solid lipid micro particles (SLMs). Lipospheres are lipid microspheres with a solid hydrophobic fat core (triglycerides) and a layer of phospholipid molecules placed on their surface to stabilize them.

The bioactive component is dissolved or disseminated in the solid fat matrix in the interior core of these fat-based encapsulation devices.

Solid Lipid Nanoparticles (SLNs)

SLNs were first created in 1990 as a carrier for traditional lipid-based formulations such as liposomes, nanoemulsions, and polymeric particles 23. Particulate systems with particle sizes ranging from 50 to 1000 nm are known as SLNs. They are made by substituting solid lipids for liquid oil in a water emulsion (Shamant, 2016).

SLNs are sub-micron colloidal carriers made of physiological lipid that are distributed in water or an aqueous surfactant solution. The use of physiological lipids, the avoidance of chemical solvents, the potential for a broad application range (dermal, perioral, intravenous), and the use of high-pressure homogenization as a well-established production method are all advantages of SLN. Potential disadvantages such as poor drug loading capacity, particle growing, unpredictable gelation tendency, drug expulsion after polymeric transition during storage, and relatively high water content of the dispersions (70-99.9%) have been observed (Asadujjaman and Mishuk, 2013; Santamaria, 2017).

Nanostructured Lipid Carriers (NLCs)

Nanostructured lipid carriers (NLCs) were developed in 1999 to address difficulties with SLNs, such as poor drug loading capacity due to flawless crystalline structure, drug expulsion, system physical instability, undesired particle growth, and gelation propensity.

In the NLC system, solid lipid, liquid lipid, and surfactant are present. Additional liquid lipid is beneficial to the NLCs system because it improves drug loading capacity, system stability, and drug solubility in the lipidic matrix. The imperfect type, amorphous type, and numerous types are the three types of NLC (Chime and Onyishi, 2013; Elmowafy, 2017; Sucharitha *et al.*, 2019; Sharma and Baldi, 2018; Jaiswal *et al.*, 2016)

Lipid Drug Conjugates (LDC)

Lipid drug conjugates were created specifically for hydrophilic drug molecules, with an insoluble drug-lipid conjugate bulk synthesized either by salt formation (for example, using a fatty acid) or covalent bonding (for example, to the esters or ethers).

The majority of the lipid drug conjugates is next homogenized in water with a stabilizer utilizing high-pressure homogenization. Due to partitioning effects during the manufacturing process, SLNs have a limited capacity for loading hydrophilic medicines. LDC nanoparticles with drug loading capacities of up to 30% have been created to bypass this constraint. Such matrices may have potential applications in brain targeting of hydrophilic drugs in serious protozoal infections (Elmowafy, 2017).

ADVANTAGES

Followings are the advantages offered by the LBDDS-

- Drug release is controlled and in a targeted manner.
- Pharmaceutical stability.
- High drug content.
- Feasibility of carrying both lipophilic and hydrophilic drug.
- Lipids and developed formulation is bio-degradable and biocompatible in nature.
- Excipients versatility.
- Formulation versatility.
- Low-risk profile
- Passive, non-invasive formation of vesicular system which is available for immediate commercialization.
- Improved oral bioavailability.
- Reduces plasma profile variability.
- Increases permeation when used orally.
- The lipid-based dosage form is stable at a varying moisture content and pH.
- Lipids provide adequate protection of drugs that are sensitive to the gastric environment or undergo enzymatic degradation.
- They provide a hydrophobic environment to delay the release of the loaded drug
- They used in the design of sustained-release beads, tablets, microemulsion, implants, and microcapsule.
- Ability to improve physical stability of pharmaceuticals.
- Manufacturing and scale-up are easy.

CONCLUSION

Poor oral bioavailability is commonly attributed to the drug's low water solubility in BCS classes II and IV. A research scientist is primarily concerned with increasing the drug's oral bioavailability by putting it in a lipid-based formulation. To build any lipid-based formulation, however, you must have a thorough understanding of the medicine and excipients employed.

Lipids plays mainstay in the formulation of various lipid based drug delivery system. Lipid-based administration is the most promising because of the digestion of the system and direct absorption from the lymphatic system. The bioavailability of the drug is also improved. Various techniques used to improve the stability of lipid dispersion. Wide verities of carrier available for the encapsulation of the drug, drug may be hydrophilic, lipophilic, or both.

Because many medications are effectively marketed as lipid-based formulations, the lipid-based drug delivery system (LBDDS) has a wide range of potential applications in terms of improving solubility and bioavailability. The recent trends in the field of LBDDS in terms of formulation techniques and characterisation were the subject of this review. However, a few technological limitations, such as the

stability of lipid-based formulations, manufacturing methods, and the lack of a database that considers drug solubility in lipids, suggest that proper regulatory guidelines for lipid-based formulations must still be developed in depth to advance the technology. In this subject, more study is needed to create a proper in vivo model that can match the data collected in vitro studies to the actual in vivo experience.

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