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Review on Lipid- Based Drug Delivery System to Enhance Bioavailability of Poorly Water Soluble Drugs

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Abstract: *The most popular and well acknowledged method of delivering drugs is oral administration. Poorly water soluble medications, however, are shown to have a difficult time achieving sufficient bioavailability when taken orally. Drugs that are poorly soluble in water are still an issue. Among the many creative methods for improving drug bioavailability, the lipid-based drug delivery system is one of the most unique and promising methods. The bioavailability of a lipophilic medicine can be enhanced by altering the makeup of lipid excipients and other additions. The unique mechanism of lipid digestion is involved in lipid-based drug delivery systems; hence, the lipid utilized in the formulation needs to be biodegradable. Furthermore, as compared to free medications, lipid nanoparticles may shield pharmaceuticals from chemical and enzymatic deterioration, improving their medicinal qualities. This review examines various novel delivery systems designed to improve the oral bioavailability of poorly water soluble medicines, with a particular emphasis on the lipid-based drug delivery system, its possible uses, and excipients.*

Keywords: lipid- Based Drug Delivery System, Lipid Excipients, Bioavailability, Formulation Techniques, Applications.

I. INTRODUCTION

Oral administration is the most commonly preferred route for drug delivery because of its simplicity, convenience and patient compliance, especially in the case of repeated dosing for chronic therapy. Additionally, it is a preferable choice for various threatening diseases such as antidiabetic, antihypertensive and antitumor categories of drugs. Poor aqueous solubility and intrinsic dissolution rate are the major factors that affect oral delivery of many existing drugs. However around 40% of the new chemical entities generated via drug delivery screens exhibit poor aqueous solubility. Biopharmaceutical classification system is an advanced tool used for classify medicines based on dissolution, water solubility and intestinal permeability into four classes, in which the class two drugs (low solubility and high permeability) and class four drugs (low solubility and low permeability) are considered as complicated for the formulation to enhance bioavailability. In recent few years there are various formulation techniques were discovered to conquer the barriers related to the bioavailability of drugs. Lipid based drug delivery system becomes more significant for promising drug delivery because of its biocompatibility, low toxicity, simplicity of formulation approaches and alternative option for various root of administration with significant bioavailability profile. In the last few decade lipid have gain much attention as a carriers for delivery of drugs with poor water solubility. The existing of novel lipid excipients with their acceptable regulatory and safety profiles combine with their efficiency to increase the oral bioavailability of poorly soluble drugs has play important role in the development of lipid base formulation for drug delivery. The excipients in lipid based formulation consists of water-insoluble triglycerides such as olive oil, corn oil, vegetable oil, peanut oil, hydrogenated soybean oil, coconut oil and palm seed oil, organic liquids/semisolids such as bees wax, oleic acid. Lipid excipients are mainly categorized as triglycerides (TG), mix glycerides, polar oils, water-soluble and insoluble surfactants, course solvents and other additives. In nanotechnology, efforts are ongoing to extend its application in various medical and pharmaceutical aspects and this nanoscale technologies generally classified into

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the lipid- based nanocarriers, polymeric nanocarriers, drug nanoparticles or nanosuspensions and inorganic nanocarriers. There are some of the drugs that are effectively marketed as lipid based drug formulations are include efavirenz (Sustiva®), saquinavir (Fortovase®), ritonavir (Norvir®), clofazamine (Lamprene®). Appropriate solvent selection is necessary for effective lipid based drug delivery system, when drug is an oil like substance (e.g. ethyl icosapentate, tocopherol, nicotinate, teprenone, idomethacin farnesil and dronabinol) in such cases water insoluble drugs can be formulated as a lipid- based formulations.

II. LIPID- BASED DRUG DELIVERY SYSTEM

In the last few years lipid- based drug delivery system achieve a great significance to improve the bioavailability of drug with poor water solubility. Routes like oral parenteral ocular intranasal, dermal or transdermal and vaginal routes used for the administration of lipid- based drug delivery system, but oral route is highly preferred because of its noninvasiveness, cost effectiveness and less susceptible to the side effects such as parenteral site reactions.

Also lipid based drug delivery system have taken the lead because of its greater advantages of higher degree of bio compatibility and versatility.

Lipid based drug delivery was introduce when it was recognized that the bioavailability of low aqueous soluble drugs like cyclosporine A (Sandimune neural®), Saquinavir (Fortovase®) and Ritonavir (Norvir®) enhance when co-administered with a fat- rich meal.

Lipid based formulations may contain different dosage forms like suspension or oil solution to coarse multiple and dry emulsion and more complex self- emulsifying, micro emulsifying and nanoemulsifying drug delivery system (SEDDS/SMEDDS/SNEDDS).

EXCIPIENTSUSEDIN LIPID- BASED ORAL FORMULATIONS:-

Water Insoluble Excipients	Water Soluble Excipients	Triglycerides	Surfactants
Bees wax Oleic acid Medium chain (C8/C10) mono and diglycerides Soy fatty acids Propylene glycol esters of fatty acids	Ethanol Glycerin Propylene glycol Poloxamer407 Dimethyl sulfoxide Hydroxypropyl-B-cyclodextrin Phospholipids PEG 300 PEG 400	Long- chain triglycerides Hydrogenated soybean oil Sesame oil Hydrogenated vegetable oil Medium- chain triglycerides Triglycerides derived from Caprylic/capric Coconut oil or palm seed oil	Polysorbate 20 (tween 20) Polysorbate 80 (tween 80) Polyoxyl 35 castor oil (cremophor EL) Sorbitan mono laurate (Span 20) Polyoxyl 40 hydrogenated castor oil cremophor PEG 300 oleic glycerides (Labrafil® M- 1944CS) Polyoxyl 60 hydrogenated castor oil (cremophor RH60) PEG 300 linoleic

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			glycerides (Labrafil® M-2125CS) PEG 1500 lauric glycerides (Gelucire® 44/14) PEG 400 caprylic/capric glycerides (Labrasol®)

TYPES OF LIPID EXCIPIENTS:-

1. Triglycerides: Triglycerides are the most commonly used excipients in the lipid- based formulations. These are naturally divided into long chain triglycerides (LCT), medium chain triglycerides (MCT), and short chain triglycerides (SCT).

2. Cosolvents:Cosolvents are design to increase the water solubility of drugs that do not contain ionic group. Cosolvents having a specific range of concentrations that do not exceed without causing biological damage. The low molecular weight excipients like glycerol, ethanol, polyethylene glycol (PEG)- 400, propylene glycol are used as a cosolvents.

3. Mixed glycerides and polar oils:Mixed glycerides are obtained from the vegetable oils by partial hydrolysis. The polar oil excipients improved solvent capacity and dispersibility of the formulations. Sorbitan trioleate (Span 85) act as a polar oil and oleic acid is used in a number of commercial products.

4. Water- soluble surfactants:These surfactants are most commonly used surfactants in a self- emulsifying drug delivery system. These materials can be prepared by combining polyethylene glycol (PEG) along with hydrolyzed vegetable oils. Alcohol can be used to react with ethylene oxide to synthesized alkyl ether ethoxylate, which is used as a surfactant (e.g. cetostearyl alcohol ethoxylate 'cetomacrogol')

5. Water- insoluble surfactants:The lipid excipients with HLB values in between 8 and 12 (intermediate hydrophilic-lipophilic balance) that comes under this category.These substances can form micelles but because of their insufficient hydrophilic nature they do not undergoes self-emulsification.Oleate esters like polyoxyethylene (20) sorbitan trioleate (Tween 85) and polyoxyethylene (20) glyceryl trioleate are used as a water- insoluble surfactants.

6. Additives:Lipid- soluble antioxidants such as propyl gallate, butylated hydroxyl toluene (BHT), butylated hydroxyanisole (BHA) are used to protect the formulation from oxidation.

LIPID- BASED DRUG DELIVERYSYSTEM FORMULATION TECHNIQUES

A lipid-based drug delivery system can be designed successfully if formulation objectives are carefully taken into account. The table contains the names of lipid-based products that are commercially available and are intended for oral administration. Lipid-based drug delivery systems using a variety of formulation techniques, as listed below:

1.Oily liquids: Certain medications must be prepared as oily liquids since they are only soluble in oils due to their strong lipophilicity; for example, steroids are only soluble in triacyglycerols. Larsen et al. used castor oil and fractionated coconut oil (Viscoleo®) to create bupivacaine free base oily solution.

2.Blended micelles: Multiple molecular species are found in mixed micelles. These micelles have this leg shape and mimic lipid barriers quite a bit. The detergent created a shield around the lipid molecule in the detergent-lipid mixed micelle to keep it safe from water. When parthenolide and paclitaxel are co-encapsulated in a mixed micelle of PEG 2000, distearyl phosphatidylethanolamine (DSPE), and vitamin E, it has been observed that their effectiveness against taxol-resistant and sensitive lung cancer cell lines is enhanced.

3.System of self-emulsification: The presence of several surfactants in the oily phase can emulsify the system. Surfactants aid in dispersing the oily phase in GI fluid, while lipophilic drugs are soluble in the oily phase. The principal ingredients of a self-emulsifying formulation include drugs, oily carriers, surfactants, co-surfactants, and co-solvents. It was stated that 1,2-propanediol was employed as a co-emulsifier for oral administration and that SMEDDS sustained release pellets of puerarin and Cremophor® EL as an emulsifier were formulated using oil phase, castor oil.

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4.Liposomes: Liposomes are spherical bilayers with a structure that closely resembles the arrangement of a cell membrane. Because of liposomes' special complicated structure, hydrophilic materials can be incorporated into the globule's aqueous interior, whereas hydrophobic medications can dissolve in the inner fatty acid layer. To overcome the multidrug resistance associated with breast cancer, liposomes, such as those loaded with epirubicin in propylene glycol, are utilized to increase permeability through the membranes of both healthy and malignant cells.

5.Solid lipid nanoparticles: These spherical, lipid-based nanoparticles range in size from 10 to 1000 nm. They are stabilized by the use of surfactants, which also have the ability to solubilize lipophilic molecules.The lipids used In the solid lipid nanoparticles include triglycerides (such as tristearin), monoglycerides (such as glycerol monostearate), di-glycerides (such as glycerol behenate), fatty acids (such as stearic acid), and waxes (such as cetyl palmitate). It was possible to enhance the oral bioavailability of carvedilol by coating the formulation of solid lipid nanoparticles with N-carboxymethyl chitosan polymer.

APPLICATION

1. The intricate mechanism regulating the interactions between lipid carriers and living cells is precisely understood with the aid of lipid-based drug delivery systems. As a result, they are often reliable, effective, and specialized gene carriers.
2. Lipid-based drug delivery systems can be used to effectively deliver a wide range of medications, including more recently developed proteins, peptides, nucleic acids (DNA, SRNA), and cellular targeting.
3. Owing to the adaptability of lipid excipients, formulators have access to a wide range of formulation options for improving drug targeting, stability, and bioavailability, including lipid suspensions, emulsions, microemulsions, mixed micelles, SEDDS, and SMEDDS.
4. Recent advancements in lipid-based drug delivery technology not only lessen the impact of food on absorption, but also improve and stabilize gastrointestinal absorption.
5. The synthesis of multifunctional lipid-based nanoparticles using lipid-based nanotechnology can improve therapeutic outcomes.

III. CONCLUSION

The formulation of medications falling under BCS classes 2 and 4 presents a difficult task for formulation scientists as it limits the drugs aqueous solubility, thereby limiting their oral bioavailability. By incorporating different lipid excipients into the formulation, lipid-based drug delivery systems are thought to be the most innovative and promising way to improve drug bioavailability. An overview of lipid-based formulations is given in this review, which could aid in the development of this technology and lead to the creation of safer, more stable, and effective pharmaceutical products.

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