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THE SELF EMULSIFYING DRUG DELIVERY SYSTEM (SEDDS) IS A NEED OF MORDEN DRUG DELIVERY SYSTEM- A REVIEW

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ABSTRACT
The oral shipping of hydrophobic tablets gives the main task due to the low aqueous solubility of such compounds. Self-emulsifying drug shipping systems (SEDDS), which can be isotropic combinations of oils, surfactants, solvents, and co-solvents/surfactants, may be used for the layout of formulations so one can enhance the oral absorption of noticeably lipophilic drug compounds. The performance of oral absorption of the drug compound from the SEDDS relies upon many formulation−associated parameters, which include surfactant concentration, oil/surfactant ratio, the polarity of the emulsion, droplet length, and charge, all of which in essence decide the self-emulsification ability. The oral direction is the maximum famous direction for the scientific management of medicine to deal with diverse diseases. Before a drug is absorbed into the blood circulation, it needs to go through dissolution and permeation. However, maximum tablets show off poor aqueous solubility, and their constrained absorption ends in low oral bioavailability. The solubility of hydrophobic tablets can be advanced via way of means of diverse ways, which includes stable dispersion, salt formation, pH modification, and self-emulsifying drug shipping machine (SEDDS) use. Depending on the training procedure, drug-loaded SEDDS may be divided into micro- (SMEDDS) and nano- (SNEDDS) formulations. In this review, we summarize the type machine of lipid formulations, the mechanism underlying advanced oral drug absorption via way of means of SEDDS, and the latest advances withinside the SEDDS.

KEYWORDS: SEDDS, Permeability, Solubility, HLB, Emulsion.

INTRODUCTION
SEDDS is used to solve the problem of permeable compounds with low and high solute bioavailability. Hydrophobic drugs can be dissolved in these systems, allowing them to be delivered as a unit dose for oral administration. When SEDDS formula is released into the lumen of the gastrointestinal tract, it contacts the digestive juices and forms an emulsion (micro/nano). The so-called self-emulsifying emulsifiers or colours are added causing the drug to dissolve and then be absorbed through the lymphatic route, bypassing the first effect on the liver. Oral and intravenous (IV) routes are the two most common routes of administration. IV injection is the best route of administration for most drugs because 100% of the drug is delivered directly into the bloodstream.[1]

However, intravenous administration has certain limitations, including discomfort on admission, the need for a sterile needle, difficulty in inserting the needle, and the need for medical personnel trained in intravenous administration. Therefore, oral administration is now considered an attractive and therefore attractive route. Oral administration is safe, easy, and painless. Compared with the method of IV injection, orally, patients can easily use it at home without any discomfort. With oral administration, blood levels of the drug can be maintained longer than with intravenous administration.[2]

Alternatively, the medication can be taken by mouth as a liquid, capsule, solid tablet, or chewable tablet. For oral administration, the drug must be dissolved in the gastrointestinal (GI) fluid before being absorbed into the bloodstream. However, more than 40% of New Chemical Entities (NECs) are insoluble in water, resulting in poor absorption and low bioavailability (BA). In general, drug absorption is mainly influenced by two factors, namely solubility, and permeability. Amidon et al. introduced a biopharmaceutical classification system based on these two factors. The oral route is the main drug delivery route for the chronic treatment of many diseases.[3]

However, the oral administration of 50% of the drug's compounds is impeded due to the high lipophilicity of the drug itself. Nearly 40% of new drug candidates have low water solubility, resulting in low oral bioavailability, high intra- and inter-individual variability, and lack of

dose ratios. Thus, for such compounds, the rate of absorption from the gastrointestinal tract (GI) is controlled by dissolution. Altering the physicochemical properties, such as salt formation and reducing the particle size of a compound can be one of the approaches to improving drug dissolution rates.[4]

However, these methods have their limitations. For example, the formation of salts of neutral compounds is not feasible, and the synthesis of weak acids and weak base salts may not always be practical. In addition, the salts formed can be converted back to their original acidic or basic form and lead to agglomeration in the gastrointestinal tract. A reduction in particle size may not be desirable in situations where handling difficulties and poor wettability are present for very fine powders.[5]

To overcome these disadvantages, many other formulation strategies have been applied, including the use of cyclodextrin, nanoparticles, solid dispersants, and permeability enhancers. Indeed, in a select few cases, these approaches have been successful. In recent years, much attention has been focused on lipid-based formulations to improve the oral bioavailability of poorly water-soluble medicinal compounds. The most common approach is to introduce the drug compound into inert lipid media such as oils, and surfactant dispersants.[6]

Excipients used in SEDDS

Oils

Oil is one of the most important excipients in the SEDDS formula not only because it is soluble in large amounts of lipophilic drugs or facilitates self-emulsification but also and above all because it can increase. The lipophilic fraction is transported through the intestinal lymphatic system, thereby increasing absorption Sugar depends on the molecular nature of the triglycerides. Long and medium-chain triglyceride oils with Different saturation levels were used for the design self-emulsifying formula. In addition, cooking oil which may represent the rational and preferred choice of lipid carrier for the development of infrequent SEDDS was chosen because of its poor solubility in large quantities of lipophilic drugs.[7]

Modified or hydrolyzed vegetable oils are widely used because these excipients form a good emulsification system with a large number of approved surfactants. For oral administration and showed improved drug solubility Characteristics. They provide the same formulation and physiological benefits and degradation products as natural end products of intestinal digestion. New medium-chain semisynthetic derivatives, which can be defined as amphiphilic compounds with surfactant properties, gradually and effectively replace conventional media triglyceride oil chains in SEOFs.[8]

Surfactants

Some compounds with surfactant properties can be used to design self-emulsifying systems, The most widely recommended is a non-ionic surfactant with a relatively high hydrophilic-lipophilic balance (HLB). Commonly used emulsifiers are various solids or liquid glycerol ethoxylated polyglycolysis and polyoxyethylene 20 oleate (Tween 80). Safety is a major deciding factor in the selection of surfactants. Emulsifiers of natural origin are preferred because they are considered safer synthetic surfactants. However, these excipients have limited self-emulsification ability.[9]

Non-ionic Surfactants are less toxic than ionic surfactants, but they can lead to reversible changes in intestinal permeability lumens. Usually, different concentrations of surfactants from 30 to 60% w/w form stable SEDDS. Here very important in determining surfactant concentration properly, as large amounts of surfactants can irritate the gastrointestinal tract. Surfactants involved in the formulation of SEDDS must have a relatively high HLB and hydrophilicity for immediate and/or rapid droplet formation Spread the formula in the aquatic environment (good self-emulsifying performance) can be achieved. For effective absorption, the precipitation of the drug compound in the gastrointestinal tract should be avoided and the drug should be aged for a long time at the site of absorption. Surfactants are amphiphilic and can dissolve or dissolve in relatively of high amounts hydrophobic drug compounds. Mixture of lipids with A higher ratio of surfactants and co-surfactants/oils leads to the formation of SMEDDS.[10]

There is a relationship between the size of the droplets and the concentration of surfactant used. In some cases, surfactant increases concentration can lead to smaller average size droplets, as in the case of a saturated C8–C10 mixture of polyglycolized glycerol (Labrafac CM–10). It may bs explained by the stability of the oil droplets as a result of the localization of surfactant molecules in oil mựcwater display. On the other hand, in some cases, on average Droplet size may increase with increasing surfactant concentration.[11]

This phenomenon can be caused by the surface disturbance caused by better penetration of water into oil droplets mediated by an increase in surfactant concentration and cause the ejection of oil droplets in stirred water. A very detailed in vitro study was performed using a Caco2 cell culture model that evaluated the effects of a novel SEDDS containing paclitaxel and no Cremophor EL to drink. The authors mainly focused on the influence of the ratio of nonionic surfactant/tyloxapol ion/sodium deoxycholate, corresponding.[12]

It has been proven that effective drug combination is increased about five times compared to market formulations and excipients with little or no toxicity up to a certain dilution range. In the same study, The cytotoxicity of tyloxapol which can form lyotropic liquid crystal (LC) structures upon contact with water has emerged. masked by sodium deoxycholate. It has been

suggested that the localization of two surfactants at the oil droplet interface of the SEDDS and Caco2 cell membranes may be the reason for this observation.[13]

Co-solvents

Producing an optimal SEDDS is a relatively demanding high concentration (usually more than 30% w/w) of surfactant. Organic solvents such as ethanol, propylene glycol (PG), and polyethylene glycol (PEG) are suitable for oral administration and permit the dissolution of large quantities. amount of hydrophilic surfactant or drug in lipid base.[14]

These solvents can even act as co-surfactants in microemulsions. On the other hand, alcohol and other volatile solvents have the disadvantage of evaporating in the shell of soft gelatin or hermetically sealed hard gelatin capsules in a conventional SEDDS leading to drug precipitation. Therefore, alcohol-free formulations have been designed, but their ability to solubilize lipophilic drugs can limit.[15]

Mechanism of SEDDS

Several factors can affect the absorption of oral drugs, such as dissolution, gastric emptying, intestinal transit, and lymphatic transport. drug Absorption is limited due to the low solubility of the drug. high first-pass metabolism or high-flow drug delivery. Therefore, SEDDS is designed to overcome these Levels. SEDDS is defined as an isotropic mixture that contains several main ingredients such as drugs, oils, surfactants, and surfactants/cosolvents. SEDDS has a small particle size and large surface area, which not only improves drug solubility and hydrophobicity drug dissolution but also improves drug absorption and BA SEDDS may affect drug absorption by increasing the solubility, permeability, and absorption of drugs in the lymphatic system. The process of oral absorption of SEDDS is that SEDDS can transport hydrophobic drugs through the intestinal lymphatic system into complete body circulation, avoid first-time metabolism in the liver, and increase oral BA. The lymphatic system is an extensive network throughout the body.[16,17]

Lymphatic transport plays an important role in the oral absorption of some drugs such as paclitaxel. cyclosporin A, moxidectin, puerarin, saquinavir, docetaxel, lycopene, probucol, huperzine, and halofantrine. When a SEDDS is taken orally, it is released into the lap of the HOLD and in contact with digestive juices to form micro- or nano-emulsions. Oil droplets can pass through the quickly stomach and promote the wide distribution of the drug in the gastrointestinal tract and absorbed through the lymphatic system allowing the drug to avoid first-pass metabolism.[18]

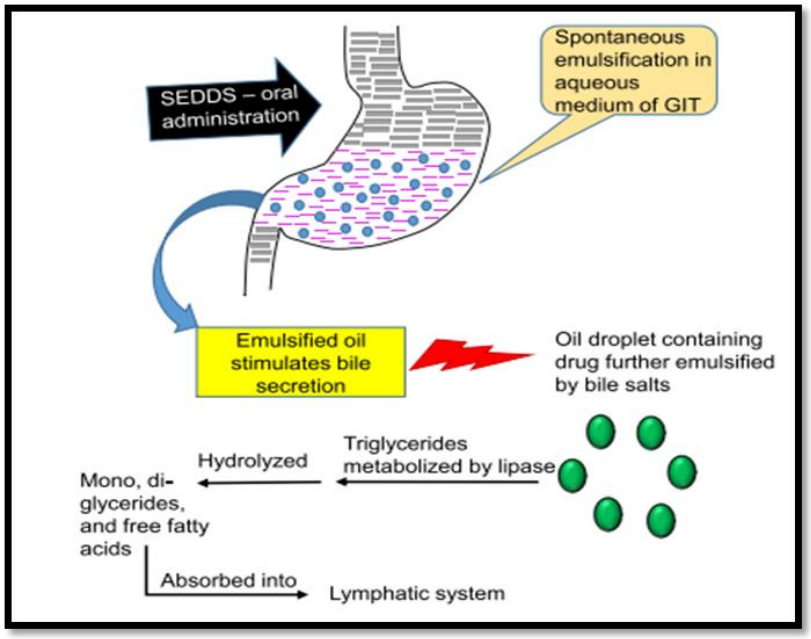

Fig no 1: Oral absorption process of SEDDS.

Recently advanced formulations based on the SEDDS

In addition to the advantages of SEDDS, such as particle size, large surface area, improved solubility, and Increasing BA, SEDDS formulations have some disadvantages such as chemical instability of the drug, and high concentration of surfactants causing gastrointestinal irritation, or poor quality. in vitro model to evaluate SEDDS formulations.[19]

Now some new formulas like self-double emulsifying drug delivery system (SDEDDS), self-emulsifying/controlled-release sustained-release tablets, ultra-stable SEDDS, solid SEDDS, self-emulsifying granules, self-emulsifying solid dispersion, self-emulsifying capsules, self-emulsifying/controlled-release lozenges, self-emulsifying implants, self-emulsifying suppositories, and self-emulsifying agent for traditional

botanical therapy, has been was developed to overcome these problems.[20]

Factors affecting SMEDDS

1. Nature and dose of the drug

Medicine is okay It is not appropriate to use very high doses for SMEDDS unless they show good solubility in at least one of the SMEDDS ingredients, preferably lipophilic stage. Medicines have solubility in water and lipids are usually in log p-values around 2 are the hardest will be distributed by SMEDDS3. The ability of SMEDDS to maintain the drug in soluble form is strongly influenced by the solubility of the drug in the oil phase.[21,22]

2. The concentration of Surfactant or Cosurfactant

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3. Polarity of the Lipophilic phase

The polarity of the lipid phase is one of the factors governing the release of drugs from microemulsion. The pole of the drop is adjusted by HLB, chain length, and unsaturated levels of fatty acids, The molecular weight of the drug is micronized.[24]

Table 1: Studies carried out on different dosage forms.

Sr No	Dosage forms	Studies carried out	Refrence
1	Dry Emulsion:	Poorly water-soluble drug- amlodipine Enteric-coateded dry emulsion formulations which are more appropriate for peptide & protein drugs oral delivery. These formulations are prepared by using surfactant, vegetable oil pH-responsive polymer followed by lyophilization	[2]
2	Self-Emulsifying Solid Dispersion:	SE solid dispersion granules of seven drugs are prepared which includes using four carboxyl acid-containing drugs, an amide containing drug (Phenacetin), a hydroxyl-containing drug & a drug having no proton donating groups (Progesterone) in which Neusilin US2 was used as surface adsorbent and gel cure 50/13 was used an as dispersion carrier	[2]
3	Self-Emulsifying Tablets	To study the effect of formulation ingredients on the release rate of drug & to evaluate an optimized self-nano emulsifying tablet formulation- ubiquinone Self-emulsifying tablet using goat fat and Tween- diclofenac	[27]
4	Self-Emulsifying Nanoparticles	Biodegradable homo-lipid with a particle size of approximately 100nm are obtained with a loading efficiency of the 70-75%27-Solvent injection method. 5 Fluorouracil (5–FU) and antisense Epidermal Growth Factor Receptor (EGFR) plasmid in biodegradable PLGA/o-CMC nanoparticles. This combination i.e., PLGA & o carboxymethyl chitosan shows a self-emulsifying effect without any surfactant stabilizer. It was found that the release rate of 5-FU from self-emulsifying nanoparticles was sustained for as long as three weeks- sonication emulsion-diffusion-evaporation used multiple emulsions (o/w/o) for preparation of self-emulsifying nanoparticle system with chitosan and glyceryl monooleate (GMO) for the delivery of paclitaxel. These nanoparticles possessed bio-adhesive properties & increased cellular association of the drug-solvent evaporation method	[28]

Dosage forms in SEDDS

Self-Emulsifying Capsules

Capsules have Classic self-emulsifying liquid formula, on the management form microemulsion droplets and then dispersed in the gastrointestinal tract and allow for better absorption. However, they have certain restrictions as if they cannot be changed phase separation of the microemulsion takes place where then the absorption of the drug decreases. In such a case, to improve absorption, sodium dodecyl sulfate is added to the SE. formula & the ultra-durable SEDDS built by using a small amount of polymer in formulation to prevent drug precipitation by creating and maintaining a state of supersaturation alive. These formulas contain a reduced amount of surfactant and minimize any side effects on the gastrointestinal tract.[29]

Dry Emulsion

It is mainly O/W emulsion, processed into a solid by spray drying, using solid carrier adsorption or lyophilization Skill. The dry emulsion can be reconstituted in water before use. This is powder in which emulsification occurs spontaneously in vivo or thereafter in contact with an aqueous solution. Dried Emulsion technology not only avoids using harmful or toxic organic solvents but effectively eliminates stability problems (such as mixing, whipping, and contamination by microorganisms in the process storage) bonded to the

classic emulsion. MCT (Medium Chain Triglyceride) is commonly used as the oil phase for these formulas. The dry emulsion can be used for Subsequent preparation of tablets and capsules.[30,31]

Self-Emulsifying Solid Dispersion-

Solid dispersions have been widely utilized to boost the rate of dissolution and bioavailability of drugs. Drugs that aren't very water-soluble, yet have a lot of stability are a key issue for them during their time there manufacturing. The term "hot-melt granulation" refers to the process of forming granules from melting a frequently used method for preparing food dispersion of solids.[32]

Self-Emulsifying Tablets

Prepare Self-emulsifying tablets involved in adsorption of nanoemulsions on granular materials and then compressed to form pellets. The Optimized self-emulsifying tablet dissolution profile shows 80-90% drug out after 45 minutes.[33,34]

Self-Emulsifying Beads

In the SE system, Solid dosage forms can be developed using fewer excipients, i.e., by forming Pearl. Solvent Used evaporation technique for SE. deposition microporous polystyrene particle system. Porous polystyrene beads with complex hollow inner structure. These pearls are produced by copolymerization of styrene and divinyl benzene monomers. He is Chemically inert, biocompatible, and stable over a wide range of pH, temperature & humidity. Geometrical characteristics of foam materials such as grain size and pore architecture govern loading and in vitro efficacy of drug release from porous poly containing SES styrene beads.[35]

Self-Emulsifying Nanoparticles

It can be prepared by solvent injection method. Sonication emulsion diffusion evaporation method. In the molten solvent injection method lipid mass containing lipids, surfactants and drugs are injected drop by drop in a solvent-free substance system. Larger particles are removed by filtered, then the filtrate was dried to obtain nanoparticles.[36]

Table 2: Application of self-emulsifying drug delivery systems.

Type of delivery system	Drug	Oil: Surfactant: Cosolvent	Improvement	Reference
SEDDS (gelled)	Ketoprofen	Capex 200: Tween80: Capmul MCM	Silicon dioxide was used as a gelling agent. As the Conc. of Silicon dioxide increases it causes an increase in the droplet size of emulsion and slows the drug diffusion	[37]
SEDDS	Carvedilol	Labrasol: Labrafil M: Transcutol P	It improves the oral bioavailability of Carvedilol up to 413% when compared to the conventional tablet.	[38]
SMEDDS	Simvastatin	Capro yl:Cremophor EL: Carbitol	The release rate was higher and oral bioavailability is about 1.5-fold higher than convectional tablet	[39]
Self-emulsifying tablet	Diclofenac sodium	Goat fat: Tween 65	SEDDS tablets were formulated by pouring molding using plastic mould the tablet containing a higher tween 65: goat fat ratio gives a better release rate	[40]
Self-emulsifying pellet	Methyl and propyl perabens	Mono and diglycerides of capric and caprylic acids: Tween 80	The self-emulsifying formulation improves the rate of drug release from the pellets by applying water in a soluble polymer containing a water-soluble plasticizer reducing the rate of drug release	[40]

CONCLUSION

Self-emulsifying drug administration the system is actually a mixture of drug, lipid phase, emulsifier, and/or co-solvent. SEDDS is a Promising approach to low carb drug solubility and thus may be more useful for BCS Group II and IV drugs when used. SEDDS is a promising approach to building medicinal compounds with low water solubility. Drinking hydrophobic drugs can be accomplished by SEDDS, and has been shown to significantly improve oral bioavailability. The effectiveness of the SEDDS formulation is case-by-case in most cases; therefore, the composition of SEDDS formulas must be defined very carefully. Because of the relatively high concentrations of surfactants commonly used in SEDDS formulations, the toxicity of the surfactant used must be taken into account. In fact, there

needs to be a trade-off between the toxicity and self-emulsification of the surfactant being considered for use. Size and charge of oil drop in emulsion formed are two other important factors affecting gastrointestinal absorption efficiency.

Conflicts of interest

There are no conflicts of interest and disclosures regarding the manuscript.

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