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A Review of Self Emulsifying Drug Delivery System

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ABSTRACT:
Around 40 - 60% of potential drugs in the pharmaceutical market are lipophilic in nature due to the low aqueous solubility and low permeability and thereby facing problems in their formulation. Their rate-limiting step is the dissolution-rate of the drug. For BCS class II drugs which have the therapeutic delivery of lipophilic active moieties receive more attention due to this reason. One of the formulation systems that deal with poor solubility, slow dissolution rate is selfmicro emulsifying drug delivery systems. The hypothesis behind dissolution rate enhancement with SEDDS is the spontaneous formation of the emulsion in the gastrointestinal tract which presents the drug in solubilized form and the small size of the formed droplet provides a large interfacial surface area for drug absorption. Due to its small globule size, the micro/nano-emulsifed drug can easily be absorbed through lymphatic pathways, thereby bypassing the hepatic first-pass effect. In practical use, the lipid formulations range from pure oils to blends which contain a strong proportion of hydrophilic surfactants or co-solvents. This review gives a complete summary of SEDDS which may be a promising approach to effectively overcome the problem of poorly soluble molecules

KEY WORDS : Classification of sedds,Adventages of sedds,Properties,Factros affecting of sedds,Method of preparation, Formulation, evulation of sedds.

I. INTRODUCTION:

Oral delivery of many proteins and medical peptides is limited. Due to the GI tract's enzymatic and absorption membrane limitation, technologies have been investigated to solve these obstacles. SEDDS from the last few years have acquired much interest as prospective carriers for oral peptide and protein administration. Emulsions serve as drug carriers in pharmaceutical preparations even though they can likely improve the medicine's oral bioavailability by having poor absorption profiles. The prominent strategies for enhancing the stability of orally administered APIs are to use delivery systems of drugs that are based on lipids. According to the literature, the terminology for lipid-based techniques is highly debated. The initial droplet size is not the primary factor determining micro and nano emulsions (SMEDDS and SNEDDS). If the droplet size of emulsion is in the nanoscale range, the SNEDDS term should be used. SEDDS are oil and surfactantbased preparations with the help of slow agitation that can be emulsified rapidly in water . The chemical structure and physical properties of SEDDS physical qualities were essential determinants of application and tolerance. As a result, these variables must be established at the stage of preformulation .

CLASSIFICATION OF SEDDS:

Single component lipid solutions: This is the simplest formulation that consists of the drug solubilized in a single excipient in plant oil or glyceride or a PEG. The evident advantage of this formulation approach is its congeneric simplicity. This formulation depend solvent on the gastrointestinal lipid handling pathways to promote emulsification which is essential for facile drug release and absorption with the exclusion of PEGs. In patients for whom lipid digestion has been determined by age or disease, the drug absorption is lower than the optimal. The single- component PEG solutions often have high solubilizing power for poorly water soluble drugs. So, the degree of bioavailability enhancement is dose- dependent, which renders PEG solution formulations poorly effective for high- dose drugs .

Self emulsifying formulations: Self- emulsifying drug delivery systems are physically stable isotropic mixtures of oil, surfactant, co- surfactant and solubilized drug substance that are suitable for oral delivery in soft and hard gelatin capsules. Depending on the excipient selection and relative composition of the formulation, aqueous dilution will result in spontaneous formation of lipid droplets ranging in size from approximately 100 nm (SEDDS) to less than 50 nm (SMEDDS). The optimum concentrations or concentration ranges of

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oil, surfactant and co- surfactant are necessary to promote self- emulsification. Since droplet surface area is inversely proportional to diameter, smaller lipid droplets with their associated, greater surface area are thought to facilitate digestion, resulting in more lipid and uniform drug release and absorption. The improved drug absorption provided by self- emulsifying for utilization is contingent upon the maintenance of the drug in the solubilized state until it canbe absorbed from the GIT. In some instances, SMEDDS formulations have proven useful in palliating the enhancing effect that food can have on the absorption of poorly water-soluble drugs .

Self emulsifying solid dispersion formulations : Liquid self- emulsifying formulations rely on micelle or solvent to fully solubilize the drug dose, which helps to ensure optimal absorption. However, the utility of these formulations can be limited by their inability to solubilize the entire drug dose in the volume of a single oral capsule. In these instances solid dispersion formulations, which may not fully solubilize the drug in the excipient matrix, can provide a viable, alternative oral formulation. These formulations consist of a dispersion of the drug in an inert excipient matrix, where the drug could exist in either the finely divided crystalline, solubilized or amorphous states or a mixture thereof. This can increase the dissolution rate of the drug and subsequent absorption from, the GI tract relative to the stable crystalline drug substance. These excipient have the potential to further increase the absorption of poorly water- soluble drugs relative to previously used PEG solid dispersions and may also be filled directly into hard gelatin capsules in the molten state, thus obviating the former requirement for milling and blending prior to filling.

ADVENTAGES OF SEDDS:

o Enhanced oral bioavailability.
o Uniform temporal profiles of drug absorption.
o Exclusive drug targeting toward a particular absorption window in GI tract.
o Easyof manufacture and scale up.
o No influence of lipid digestion process.
o Increased drug loading capacity.
o Reduction in inter-subject and intra-subject variability and food effects.
o Ability to delivery peptides that is prone to enzymatic hydrolysis in GI tract.
o Protection of sensitive drug substances.
o Protection of drugs from the gut environment.
o Liquid or solid dosage forms.

Properties of SEDDS

They form o/w emulsion by gentle agitation by peris-taltic movement in the G.I. tract.

Hydrophobic and hydrophilic drugs can be used with an oil surfactant mixture.

A lower dose of drugs can be used for liquid as wellas a solid dosage form.

Clear dispersion of SEDDS should be formed instan-taneously in the G.I. tract that remains stable on dilu-tion. Such distributions are either micro (100-250n-m) or nanoemulsions (less than 100 nm) depending upon

PROPERTIES OF SEDDS:

- They form o/w emulsion by gentle agitation by peristaltic movement in the G.I.tract.
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- A lower dose of drugs can be used for lipid as well as solid dosage form.
- Clear dispersion of sedds should be formed instantaneously in the G.i tract that remains stable on dilution.such distribution are either micro or nanoemulsion (100-250nm)or nanoemulsions (less than 100nm)depending upon the globule size of the sedds formulation .
- Dose should not be so high,
- drug should be oil soluble,
- high melting point drug is poorly suited to SMEDDS and Log P value should be high.

FACTORS AFFECTING ON SEDDS:

1.Dose and nature of drug
2.polarity of lipophilic phase

METHOD OF PREPARATION OF SEDDS:

1. Spray Cooling:

The molten droplets are sprayed into cooling chamber, which will set and re-crystallize in to spherical solid particles that fall to the bottom of the chamber and it is subsequently collected as fine powder. The fine powder is then be used for developing solid dosage forms or direct filling into hard shell capsules. Many types of equipments are available to atomize the liquid mixture and to generate droplets: rotary, pressure, two-fluid or ultrasonic atomizers.

2. Spray Drying:

Spray drying is defined as a process in which a liquid solution is sprayed into a hot air chamber to evaporate the volatile fraction. Polyoxylglycerides have been used alone or in combination with a solid carrier to form

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microparticles of etoricoxib and glibenclamide. Dry emulsion technology solves the stability problems associated with classicemulsions during storage and helps also avoid using harmful or toxic organic solvents. Dry emulsions may be re-dispersed into water before use. Medium chain triglycerides are commonly used as oil phase for these emulsions.

3. Adsorption on Solid Carriers:

Solid carriers are used for the adsorption of liquid formulation to get final solid product and it will be free flowing so that it can be compressed or directly filled in hard gelatin capsules. A significant benefit of the adsorption technique is good content uniformity, as well as the possibility for high lipid exposure. The adsorption technique has been successfully applied to gentamicin and erythropoietin with caprylocaproylpolyoxylglycerides formulations that maintained their bioavailability enhancing effect after adsorption on carriers.

4. Supercritical Fluid Based Method:

Lipids may be used in supercritical fluid based methods either for coating of drug particles, or for producing solid dispersions. For environmental reasons, the preferred supercritical fluid of choice is supercritical carbon dioxide. Examples include controlled releaseapplications using glyceryltrimyristate and stearoylpolyoxylglycerides.

FORMULATION OF SEDDS:

Drug

The most important parameter for SEDDS formulation is the lipophilicity and hydrophobicity of a drug. A drug's log P should preferably be 2. The drug is formulated at a modest dose and should not be subjected to substantial first-pass metabolism .

Oil

Oil is necessary for the lipophilic drugs solubilization. It improves the drug's availability for quick absorption in the GI tract via the intestinal lymphatic system. The degree of esterification and kind of fatty acids and with regard to glycerol to create mono or diglycerides determine the physical, melting, and hydrophilic–lipophilic balance (HLB) features of glycerides. Six to twelve carbon chains present in MCTs and are delivered into the systemic circulation via portal blood. The intestinal lymphatic system transports LCT with more than 12 carbon chains. MCT is the most extensively utilized lipid formulation because of its improved quality of solubility, fluidity, and ability to resist oxidation. By lowering the interfacial tension between the oil and water interface, as well as altering the interfacial film curvature and time, the self-emulsification feature boosts the solubility by minimizing precipitation.

Surfactant and co-surfactant

Surfactants lower the interfacial tension by forming an interfacial film, allowing for dispersion. During SEDDS formulation, the HLB value must be kept in mind. A surfactant with an HLB value greater than 12 is chosen to achieve better emulsification. It helps to disseminate the intended formulation quickly by forming small oil-in-water (o/w) droplets. Nonionic surfactants are commonly used in the formulation of SEDDS due to their nontoxic nature, despite the fact that they may produce a modest irreversible change in the permeability of the GIT wall. In GIT, a formulation of surface-active compounds that is 30–60% w/w results in improved self-emulsification. Surfactants in high amounts might irritate the wall of the GI tract.

EVALUATION OF SEDDS:

- **Dispersibility test**

The efficiency of self-emulsification of oral nano or microemulsion isassessed using a standard USP XXII dissolution apparatus 2. One milliliter of each formulation was added to 500 mL of water at 37 ± 0.5° C

- **Rheological property estimation**

The SEDDS system is generally administered in soft gelatin or hard gelatin capsules. So, it can be easily pourable into capsules and such system should not too thick. The rheological properties of the micro emulsion are evaluated by Brookfield viscometer.

- **Thermodynamic stability studies**

The physical stability of a lipid-based formulation is also crucial to its performance, which can be adversely affected by precipitation of the drug in the excipient matrix. In addition, poor formulation physical stability can lead to phase separation of the excipient, affecting not only formulation performance, but visual appearance as well. In addition, incompatibilities between the formulation and the gelatin capsules shell can lead to brittleness or deformation, delayed disintegration, or incomplete release of drug.

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- **Zeta potential measurement**:

This is used to identify the charge of the droplets. In conventional SEDDSs, the charge on an oil droplet is negative due to presence of free fatty acids

- **Droplet size analysis and particle size measurement**

This is a crucial factor in self- emulsification performance because it determines the rate and extent of drug release as well as the stability of the emulsion. Photon correlation spectroscopy, microscopic techniques are mainly used for the determination of the emulsion droplet size. The reduction of the droplet size to the values below 50 µm leads to the formation of SMEDDSs which are stable, isotropic and clear o/w dispersion

II. CONCLUSION:

SEDDS are a viable formulation method for medicinal molecules with low water solubility. SEDDS have been demonstrated to remarkably enhance oral bioavailability, and utilized to orally administer hydrophobic medicines. With future development of this technology, SEDDSs will continue to enable novel applications in drug delivery and solve problems associated with the delivery of poorly soluble drugs.

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