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SELF EMULSIFYING DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

Self-emulsifying drug delivery systems (SEDDS) possess unparalleled potential in improving oral bioavailability of poorly water-soluble drugs. Following their oral administration, these systems rapidly disperse in gastrointestinal fluids, yielding micro- or nanoemulsions containing the solubilized drug. Owing to its miniscule globule size, the micro/nanoemulsified drug can easily be absorbed through lymphatic pathways, bypassing the hepatic first-pass effect. This Article gives the overview of SEDDS with emphasis on different types of self-emulsifying formulation, their formulation, characterization, biopharmaceuticals aspect, advantage and recent development. Finally the existing challenges and future aspects are pointed out.

INTRODUCTION

Defination: SEDDS or self-emulsifying oil formulations (SEOF) are defined as Isotropic mixtures of natural or synthetic oils, solid or liquid surfactants or, alternatively, one or more hydrophilic solvents and co-solvents/ surfactants

1.Self-emulsifying drug delivery systems (SEDDSs) have gained exposure for their ability to increase solubility and bioavailability of poorly soluble drugs.

2.SEDDSs are mixtures of oils and surfactants, sometimes containing cosolvents, and can be used for the design of formulations in order to improve the oral absorption of highly lipophilic compounds.

3.SEDDSs emulsify spontaneously to produce fine oil-in-water emulsions when introduced into an aqueous phase under gentle agitation.

Self-emulsifying drug delivery systems (SEDDS) are mixtures of oils and surfactants, ideally isotropic, and sometimes containing co-solvents, which emulsify spontaneously to produce fine oil-in-water emulsions when introduced into aqueous phase under gentleagitation 6, 7,39,40,41. Recently, SEDDS have been formulated using medium chain tri-glyceride oils and nonionic surfactants, the latter being less toxic. Upon peroral administration, these systems form fine emulsions (or micro-emulsions) in gastro-intestinal tract (GIT) with mild agitation provided by gastric mobility.42, 43 Potential advantages of these systems include enhanced oral bioavailability enabling reduction in dose, more consistent temporal profiles of drug absorption, selective targeting of drug(s) toward specific absorption window in GIT.

The self-emulsifying process depends on:

- The nature of the oil and surfactant
- The concentration of surfactant
- The temperature at which self-emulsification occurs.

OILS: Oils can solubilize the lipophilic drug in a specific amount. It is the most important excipient because it can facilitate self-emulsification and increase the fraction of lipophilic drug transported via the intestinal lymphatic system, thereby increasing absorption from the GI tract. e.g. mono- di -tri- glycerides, Fractionated triglyceride of coconut oil(medium-chain triglyceride), Corn oil, Hydrogenated soya bean oil, Soyabean oil, Peanut oil, Beeswax.

Surfactants: Surfactants will improve bioavailability by different mechanisms: Improved drug dissolution Increased intestinal epithelial permeability Increased tight junction permeability e.g.Tween , Span, Brij , Labrasol , Labrafac , Arlatone , Estatan , Arlasolve , Renex Non-ionic surfactants with high HLB values are used in formulation.

Co-Surfactants: They improve solvent capacity and emulsification Sorbitan fatty acid esters (spans) Sorbitan trioleate (Span 85) is more lipophilic Sorbitan monooleate (Span80) contains more number of hydroxyl groups Hence, they are most widely used in pharmaceuticals.

Co-Solvant: Co-solvents dissolve large amounts of hydrophilic surfactants or the hydrophobic drug in the lipid base They act also as Co-surfactant in some cases Transcutol(Diethylene glycol monoethyl ether), PEG 400, Glycerol, Propylene glycol, Ethanol, Polyoxyethylene , Propylene carbonate, Tetrahydrofurfuryl alcohol polyethylene glycol ether (Glycofurol)

Table: 1 Example of surfactants, co-surfactant, and co-solvent used in commercial formulations

Excipient Name (commercial name)	**Examples of commercial products in which it has been used**
1.Surfactants/co-surfactants	
Polysorbate 20 (Tween 20)	Targretin soft gelatin capsule
Polysorbate 80 (Tween 80)	Gengraf hard gelatin capsule
Sorbitan monooleate (Span 80)	Gengraf hard gelatin capsule
Polyoxy-35-castor oil(Cremophor RH40)	Gengraf hard gelatin capsule, Ritonavir soft gelatin capsule
Polyoxy-40- hydrogenated castor oil (Cremophor RH40)	Nerol soft gelatin capsule, Ritonavir oral solution
Polyoxyethylated glycerides (Labrafil M 2125 Cs)	Sandimmune soft gelatin capsules
Polyoxyethlated oleic glycerides (Labrafil M1944 Cs)	Sandimmune oral solution
D-alpha Tocopheryl polyethylene glycol 1000 succinate (TPGS)	Agenerage Soft gelatin capsule, Agenarage oral solution

2. Co-solvents	
Ethanol	Nerol soft gelatin Capsule, Nerol Oral Solution, Gengraf hard gelatin Capsule, Sandimmune soft gelatin Capsule, Sandimmune oral solution
Glycerin	Nerol soft gelatin Capsule, Sandimmune soft gelatin Capsules
Polypylene glycol	Nerol soft gelatin Capsule, Nerol Oral Solution, Lamprene soft gelatin capsule, Agenerage Oral solution , Gengraf hard gelatin capsule
Polyethylene glycol	Targretin soft gelatin capsule, Gengraf hard gelatin capsule, Agenerase soft capsule, Agenerase oral solution
3.Lipid ingredients	
Corn oilmono,di,,tri-glycerides	Nerol soft gelatin Capsule, Nerol Oral Solution
DL-alpha-Tocopherol	Nerol Oral Solution, Fortavase soft gelatin capsule
Fractionated triglyceride of coconut oil (medium-chain triglyceride)e	Rocaltrol soft gelatin capsule, Hectrol soft gelatin capsule
Fractionated triglyceride of palm seed oil (medium-chain triglyceride)	Rocatrol oral solution
Mixture of mono-and di-glycerides of caprylic/capric acid	Avodat soft gelatin capsule
Medium chain mono-and di-glycerides	Fortavase soft gelatin capsule
Corn oil	Sandimmune soft gelatin capsule, Depakene capsule
Olive oil	Sandimmune oral solution
Oleic acid	Ritonavir soft gelatin capsule, Norvir soft gelatin capsule
Seasame oil	Marinol soft gelatin capsule
Hydrogenated soyabean oil	Accutane soft gelatin capsule
Hydrogenated vegetable oils	Accutane soft gelatin capsule
Soyabean oil	Accutane soft gelatin capsule
Peanut oil	Prometrium soft gelatin capsule
Beeswax	Vesanoid soft gelatin capsule

Formulation:

The method for preparing SEDDS involves various steps:

1) Preparation of phase diagram.

2) Solubilizing the drug and/or pharmaceutical ingredient, in a mixture of surfactant, co-surfactant and solvent. Now mix the oil phase suitably prepared, if necessary, by heating or other preparatory means, to the solubilized drug formulation and thoroughly mixed.

3)The emulsion can then be added to a suitable dosage form such as soft or hard-filled gelatin capsules and allowed to cool.se They act also as Co-surfactant in some cases Transcutol (Diethylene glycol monoethyl ether), PEG 400, Glycerol, Propylene glycol, Ethanol, Polyoxyethylene , Propylene carbonate, Tetrahydrofurfuryl alcohol polyethylene glycol ether (Glycofurol)

Potential advantages of these systems include;

1. Enhanced oral bioavailability enabling reduction in dose,
2. More consistent temporal profiles of drug absorption,
3. Selective targeting of drug(s) toward specific absorption window in GIT,
4. Protection of drug(s) from the hostile environment in gut.
5. Control of delivery profiles
6. Reduced variability including food effects
7. Protective of sensitive drug substances
8. High drug payloads
9. Liquid or solid dosage forms.

DRAWBACK OF SEDDS

One of the obstacles for the development of selfemulsifying drug delivery systems (SEDDS) and other lipid-based formulations is the lack of good predicative *in vitro* models for assessment of the formulations.

Traditional dissolution methods do not work, because these formulations potentially are dependent on digestion prior to release of the drug. To mimic this, an *in vitro* model simulating the digestive processes of the duodenum has been developed. This *in vitro* model needs further development and validation before its strength can be evaluated. Further development will be based on *in vitro-in vivo* correlations and therefore different prototype lipid based formulations needs to be developed and tested *in vivo* in a suitable animal model. Future studies will address the development of the *in vitro* model.

APPLICATION:

1.The system has the ability to form an oil-in-water emulsion when dispersed by an aqueous phase under gentle agitation.

2.SEDDSs present drugs in a small droplet size and well-proportioned distribution, and increase the dissolution and permeability.

3.Selective targeting of drug(s) toward specific absorption window in GIT.

4. Protection of drug(s) from the hostile environment in gut

5. Control of delivery profiles

6. Reduced variability including food effects

7. Protective of sensitive drug substances

Review of Literature:

1.Hydrophobic drugs can often be dissolved in SEDDS allowing them to be encapsulated as unit dosage forms for peroral administration. When such a formulation is released into the lumen of the gut it disperses to form a fine emulsion, so that the drug remains in solution in the gut, avoiding the dissolution step which frequently limits the rate of absorption of hydrophobic drugs from the crystalline state. Generally this can lead to improved bioavailability.Ultra-low oil-water interfacial tension and/or substantial interfacial disruption are required to achieve self-emulsification **(Pouton, C.W., 1997)**.

2.Humberstone and Charman has shown the use of natural and synthetic lipids for the academic and commercial interest as a potential formulation strategy for improving the oral bioavailability of poorly water soluble drugs.

3.Patil et al had formulated a gelled self-emulsifying drug delivery system (SEDDS) containing ketoprofen as an intermediate in the development of sustained release solid dosage form. Captex 200 (an oil), Tween 80 (a surfactant), and Capmul MCM (a cosurfactant) were used to formulate SEDDS.

REFERENCES

1. G.L. Amidon, H et al., A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm. Res. 12

2. B.J. Aungst, Novel formulation strategies for improving oral bioavailability of drugs with poor membrane permeation or presystemic metabolism. J. Pharm. Sci. 1993; 82: 979-986.

3. D.L. Burcham, et al. Improved oral bioavailability of the hypocholesterolemic DMP 565 in dogs following oral dosing in oil and glycol solutions, Biopharm. Drug Dispos. 1997; 18: 737-742.

4. A.T.M. Serajuddin, et al. Effect of vehicle amphiphilicity on the dissolution and bioavailability of a poorly watersoluble drug from solid dispersion. J. Pharm. Sci. 1988; 77: 414-417.

5. B.J. Aungst, N. Nguyen, N.J. Rogers, S. Rowe, M. H Improved oral bioavailability of an HIV protease inhibitor using Gelucire 44/14 and Labrasol vehicles. B.T. Gattefosse 1994;87: 49-54.

6. M.G. Wakerly, C.W. Pouton, B.J. Meakin, F.S. Morton, Self-emulsification of vegetable oil-non-ionic surfactant mixtures. ACS Symp. Ser. 1986; 311: 242-255.

7. D.Q.M. Craig, et al. An investigation into the physicochemical properties of self-emulsifying systems using low frequency dielectric spectroscopy, surface tension measurements and particle size analysis. Int. J. Pharm.1993; 96: 147- 155.

8. D.L. Burcham, et al. Improved oral bioavailability of the hypocholesterolemic DMP 565 in dogs following oral dosing in oil and glycol solutions, Biopharm. Drug Dispos. 1997; 18: 737-742.

9. A.T.M. Serajuddin, et al. Effect of vehicle amphiphilicity on the dissolution and bioavailability of a poorly watersoluble drug from solid dispersion. J. Pharm. Sci. 1988; 77: 414-417.