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Review on: Self Micro-Emulsifying Drug Delivery System

Gade Abhishek V[1*], K.S. Salunkhe[1], S.R. Chaudhari [1], Gadge P.B[1], Dighe G.S[1], Amit Asati[2]
1. Department of pharmaceutics Amrutvahini College of Pharmacy, Sangamner, Ahemednagar.
2. Dr. Reddy laboratories limited, Hydrabad.

ABSTRACT

The oral delivery of lipophilic drugs has a major challenge because of low aqueous solubility of such drugs. Self-microemulsifying drug delivery systems (SMEDDS) have ability to increase solubility and bioavailability of poorly soluble drugs. Self-micro emulsifying drug delivery systems are isotropic mixtures of oil, surfactant, co-surfactant of co-solvents can be used for the design of formulations in order to improve the oral absorption of highly lipophilic drugs. Self micro-emulsifying drug delivery system can be orally administered in hard or soft gelatin capsule and form fine stable emulsion (oil-in-water emulsion) aqueous dilution owing to the gentle agitation of gastrointestinal fluid. Efficiency of oral absorption of the drug from the SMEDDS depends on formulation elated parameters such as concentration of surfactant, co-surfactant, ratio of oil and surfactant, charge and droplet size. Thus, there are few drug products of the pharmaceutical market formulated as SMEDDS confirming the difficulty of formulating hydrophobic drug compounds in to such formulations. The fact that almost 40% of the new drugs are hydrophobic in nature which are studies with SMEDDS will continue and more drug compounds formulated as SMEDDS will reach pharmaceutical market.

Keywords: Lipophilic, Self micro-emulsifying drug delivery system (SMEDDS), oral absorption, stable in water.

*Corresponding Author Email: abhishekgade777@gmail.com
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INTRODUCTION

In recent years, the formulation of poorly aqueous soluble drugs is a challenging job to scientist. Owing to poor aqueous solubility , these drug lead to low absorption following low absorption following oral administration portion of the administered dose is absorbed which shows therapeutic effect and remaining causes untoward action due to improper distribution. With the concept of novel dug delivery system, emphasis has been has been placed on reduced the toxicity of the drugs, to broaden their mode of administration targeting and distribution profile of the drugs and enhancing the bioavailability of bioactive. Oral delivery of poorly aqueous soluble drugs is frequently associated with low bioavailability, high inter and intra–subject variability lack of dose proportionality. These class of Biopharmaceutical classification (BCS-II) II drugs. Here drug dissolution is the rate limiting step is the absorption process. To overcome these problem, different formulation approaches have been exploited including the use of surfactant ,lipids ,permeation enhancers and formation of salt ,solid dispersion and colloidal vesicles like liposome. The most popular and commercially viable lipid based formulation approach for solving these problem is Self micro-emulsifying drug delivery system (SMEDDS)[1]. In modern drug discovery techniques, there has been a consistent increase in the number of poor water soluble drug candidate compounds, and currently more than 50% of new pharmacologically active chemical entities are lipophilic and exhibit poor water solubility. Various techniques are used to improve the bioavailability of those drugs like salt formation, pH change, β-cyclodextrines complex, micro-emulsion etc. Self micro-emulsifying drug delivery (SMEDDS) is one of the methods for the improvement of oral bioavailability. SMEDDS are class of emulsion that has received particular attention as a means of enhancing oral bioavailability of poorly absorbed drugs. These systems are essentially mixes of oil and surfactant (sometimes with added co-surfactant) that form emulsion on mixing with water with little or no energy input.[2]

Types of Self Dispersing Lipid Formulations

Lipid based formulations have been classified on the basis of particle size of oil droplets of the system. Figure 1 shows different self dispersing lipid formulations.

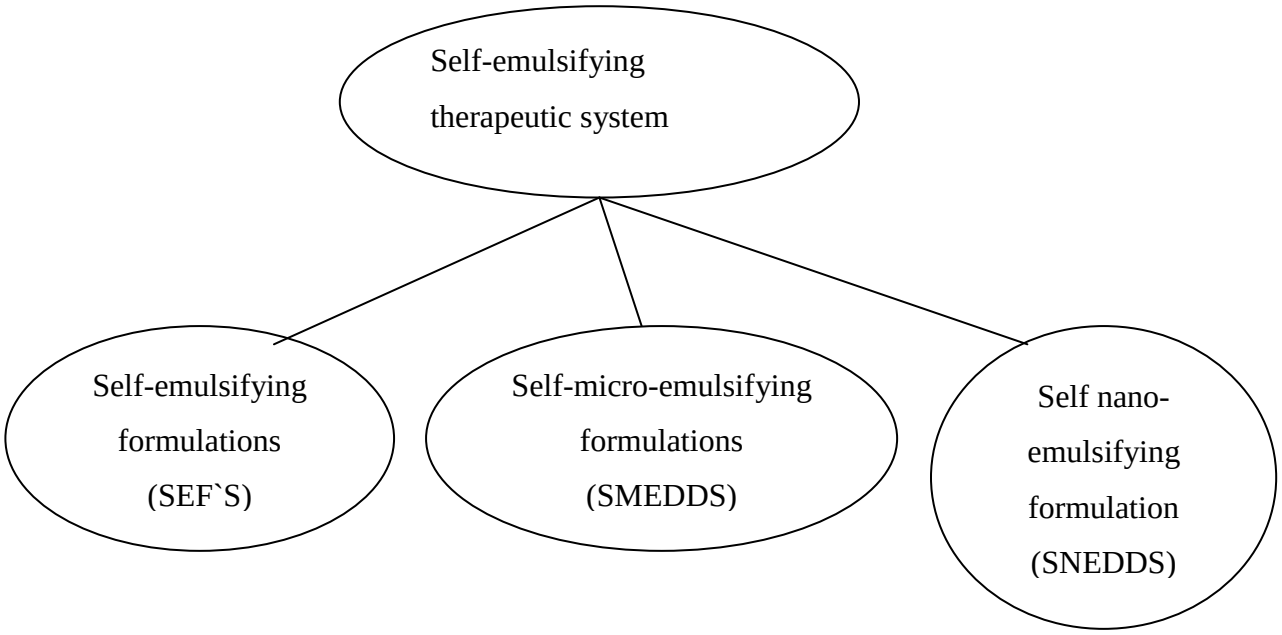

Figure 1: Different self-emulsifying lipid formulations [3]

Self Micro-Emulsifying Drug Delivery System

Self-micro emulsifying drug delivery system (SMEDDS) 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 that have a unique ability of forming fine oil-in-water (o/w) micro emulsions upon mild agitation followed by dilution in aqueous media, such as GI fluids. SMEDDS spread readily in the GI tract, and the digestive motility of the stomach and the intestine provide the agitation necessary for self-emulsification.[4]

Table 1: Difference and Similarities Between SEDDS And SMEDDS[5]

SEDDS	**SMEDDS**
Difference	
Can be a simple binary formulation with the drug and a lipidic excipient able to self-emulsify in Contact with GIF.	Are composed of the drug compound, surfactant, and oil.
Lipid droplet size in the dispersion ranges From 200nm-5µm providing large surface area absorption. The dispersion has a turbid appearance.	Lipid droplet size in the dispersion is <200nm.
SEDDS system is not thermodynamically stable in water or physiological condition	SMEDDS system is thermodynamically Stable.
Similarities	
Form fine oil-in-water dispersion in contact with GIF	

Benefits of SMEDDS

1. They led to enhanced oral bioavailability of drugs e.g. Ketoprofen
2. They decrease inter-subject and intra subject variability and food effects. E.g Cyclosporine.

3. SMEDDS are used to deliver peptides which are prone to enzymatic hydrolysis in GIT.
4. SMEDDS are used for both liquid and solid dosage forms. e.g. progesterone.
5. They can be produced at large scale.

Limitations of SMEDDS

1. They are not used for drugs which are chemically unstable and have high stability concentrations.
2. The large amount of surfactant in formulations (30-60%) causes irritation in GIT
3. Self emulsifying formulations which contain volatile co-solvents are incorporated in soft or hard gelatin capsules resulting in the precipitation of the lipophilic drug[3].

Drug properties suitable for SMEDDS[6]

1. Dose should not be so high.
2. Drug should be oil soluble.
3. High melting point of drug is poorly suitable to SMEDDS.
4. Log P value should be high.

Appropriate drug candidates for SMEDDS[7]

Challenges faced by a formulator during formulation of an oral dosage form is to maintain drug solubility within the gastrointestinal tract and, particularly, maximizing its solubility within the principle absorptive site. SMEDDS improve rate and extent of absorption of lipophilic/ hydrophobic drugs that exhibit dissolution rate-limited absorption. This may ultimately result in reproducible time profiles. However, we can apply SMEDDS approach to all drugs under biopharmaceutical classification system (BCS). The table 1 shows the various problems that can be solved through SMEDDS.

Table 2: Problems of BCS class entities that can be solved through SMEDDS.

BCS class	Problems
Class I	Enzymatic degradation and gut wall efflux
Class II	Solubilization and bioavailability
Class III	Enzymatic degradation, gut wall efflux and bioavailability
Class IV	Solubilization, bioavailability, Enzymatic degradation and gut wall efflux

Properties of the drug such as aqueous solubility and/or log P alone may not be sufficient for identifying suitability of lipid-based formulation, because they may not be able to effectively predict potential in vivo effects.

Mechanism of Self-Emulsification[8]

According to remiss, self emulsification occurs when the entropy change that favors dispersion is

greater than the energy required to increase the surface area of the dispersion, The free energy of the convention all emulsion is a direct function of the energy required to create a new surface between the oil and water phases and can be described by the following equation:-

$$DG = sn_i\ pr_i2s$$

Where-

DG is the free energy associated with the process

N is the number of droplets of radius

R and S represent the interfacial energy.

Two phases of emulsion tend to separate with time to reduced the interfacial area and subsequently, the emulsion is stabilized by emulsifying agents, which form a monolayer of emulsion droplets, and hence reduces the interfacial energy, as well as providing a barrier to prevent coalescence.

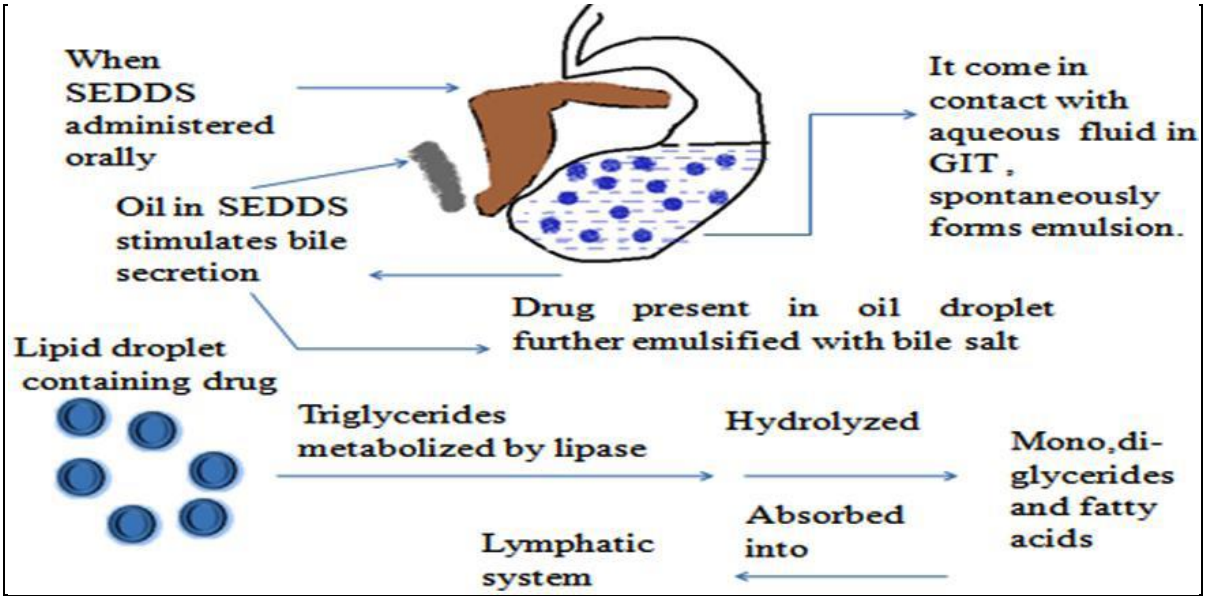

Figure 2: process of self emulsification [9]

EXCIPIENT USED IN SMEDDS

The self emulsifying process depends on:

•The nature of the oil–surfactant pair

•The surfactant concentration

•The temperature at which self-emulsification occurs.[10]

1) Oil

2) Surfactant

3) Co solvent / Co surfactant

Oil

The oil represents the most important excipient in the SMEDDS formulation. Indeed it can solubilize relevant amount of the poorly water soluble drug. Both long-chain triglyceride (LCT) and medium chain triglyceride (MCT) oils with different degrees of saturation have been used in the design of SMEDDS.[11] It can not only solubilize large amount of lipophilic drugs or facilitate self-emulsification but also enhance the fraction of lipophilic drug transported via intestinal lymphatic system, thereby increase its absorption from GIT. Natural edible oils, comprising medium chain triglycerides, are not frequently preferred in this regard owing to there poor ability to dissolve large amount of lipophilic drugs.[8]

E.g. - Corn oil, olive oil, soybean oil, hydrolyzed corn oil.

Surfactant

Several compounds exhibiting surfactant properties may be employed for the design of self-emulsifying systems, but the choice is limited as very few surfactants are orally acceptable. The most widely recommended ones being the non-ionic surfactants with a relatively high hydrophilic-lipophilic balance (HLB). The commonly used emulsifiers are various solid or liquid ethoxylated polyglycolyzed glycerides and polyoxyethlene 20 oleate. Safety is a major determining factor in choosing a surfactant. Emulsifiers of natural origin are preferred since they are considered to be safer than the synthetic surfactants. However, these surfactants have a limited self-emulsification capacity. Non-ionic surfactants are less toxic than ionic surfactants but they may lead to reversible changes in the permeability of the intestinal lumen. The lipid mixtures with higher surfactant and co-surfactant/oil ratios lead to the formation of SMEDDS. There is a relationship between the droplet size and the concentration of the surfactant being used. In some cases, increasing the surfactant concentration could lead to droplets with smaller mean droplet size, this could be explained by the stabilization of the oil droplets as a result of the localization of the surfactant molecules at the oil-water interface. On the other hand, in some cases the mean droplet size may increase with increasing surfactant concentrations[4]. Surfactant molecules may be classified based on the nature of the hydrophilic Group within the molecule.

The four main groups of surfactants are defined as follows,

1. Anionic surfactants
2. Cationic surfactants
3. Ampholytic surfactants
4. Nonionic surfactants

1. Anionic Surfactants: where the hydrophilic group carries a negative charge such as carboxyl (RCOO-), sulphonate (RSO3 -) or sulphate (ROSO3 -).

Examples: Potassium laurate, sodium lauryl sulphate.

2. Cationic surfactants: where the hydrophilic group carries a positive charge. Example: quaternary ammonium halide.

3. **Ampholytic surfactants** (also called zwitter ionic surfactants) contain both a negative and a positive charge.

Example: sulfobetaines.

4. Nonionic surfactants- where the hydrophilic group carries no charge but derives its water solubility from highly polar groups such as hydroxyl or polyoxyethylene (OCH2CH2O).

Examples: Sorbitan esters (Spans), polysorbates (Tweens).[12]

Co-surfactant

In SMEDDS, generally co-surfactant of HLB value [10-14] is used. Hydrophilic co-surfactants preferably alcohols of intermediate chain length such as hexanol, pentanol and octanol which are known to reduce the oil water interface and allow the spontaneous formulation of micro emulsion, are used in formulation of SMEDDS.[13]

Co-solvents

The production of an optimum SMEDDS requires relatively high concentrations (generally more than 30% w/w) of surfactants. Organic solvents such as, ethanol, propylene glycol (PG), and polyethylene glycol (PEG) are suitable for oral delivery, and they enable the dissolution of large quantities of either the hydrophilic surfactant or the drug in the lipid base. These solvents can even act as co-surfactants in micro-emulsion systems. On the other hand, alcohols and other volatile co-solvents have the disadvantage of evaporating into the shells of the soft gelatin, or hard, sealed gelatin capsules in conventional SEDDS leading to drug precipitation. Thus, alcohol−free formulations have been designed, but their lipophilic drug dissolution ability may be limited[14]

Table 3: Example of surfactant, co-surfactant ,oil and co-solvent used in commercial formulations.[6]

Sr.no	Excipient name	Example of commercial product in which has commercial used
	Surfactant /co-surfactants	
1	Polysorbate 20(tween 20)	Target in soft gelatin capsule
	Cremophor RH 40	Retanavir soft gelatin capsule
	Labrafil M 2125 cs	Sandimmune soft gelatin capsule
	Labrafil M 1944 cs	Sandimmune oral solution
2	**Co-solvents**	

Ethanol,glcerine,PEG	Neoral soft gelatin capsule
PEG,ethanol	Neural oral solution
Polyethyline glycol	Gengraf hard gelatin capsule
Ethanol,glycerine	Sandimmune soft gelatin capsule
Ethanol	Sandimmune oral solution
Propylene glycol	Lamprene soft gelatin capsule

Phase diagrams

Pseudo ternary phase diagram is used to map the optimal composition range for three key excipients according to the resulting droplet size following self emulsification, stability upon dilution and viscosity. Phase diagrams are useful tools to determine the number and types of phases, the wt % of each phase and the composition of each phase at a given temperature and composition of the system. These diagrams are three-dimensional but are illustrated in two-dimensions for ease of drawing and interpretation. On the basis of the solubility study of drug, oil, surfactants, co-surfactants and aqueous phase were used for construction of phase diagram. Oil, surfactant, and co-surfactant are grouped in four different combinations for phase studies. Surfactant and co-surfactant (Smix) in each group were mixed in different weight ratio. These Smix ratios are chosen in increasing concentration of surfactant with respect to co-surfactant and in increasing concentration of co surfactant with respect to surfactant for detail study of the phase diagram for formulation of micro emulsion. For each phase diagram, oil, and specific Smix ratio are mixed thoroughly in different weight ratio in different glass vials. Different combination of oils and Smix were made so those maximum ratios were covered for the study to delineate the boundaries of phase precisely formed in the phase diagrams. Pseudo-ternary phase diagram was developed using aqueous titration method. Slow titration with aqueous phase is done to each weight ratio of oil and Smix and visual observation is carried out for transparent and easily flowable o/w micro emulsion. The physical state of the micro emulsion was marked on a pseudo-three-component phase diagram with one axis representing aqueous phase, the other representing oil and the third representing a mixture of surfactant and co-surfactant at fixed weight ratios (Smix ratio)[15]

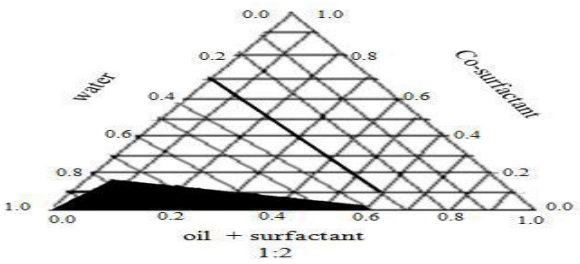

Figure 3: Ternary phase diagram[9]

Preparation formulation

Briefly accurately weighted drug is placed in glass vial and oil, surfactant and co-surfactant added. Then the components are mixed gentle stirring and vortex mixing and are at heated 40 ^{o}c on magnetic stirrer, until drug is perfectly dissolved[16]

Biopharmaceutical Aspects

The ability of lipids and/or food to enhance the bioavailability of poorly water soluble drugs is well known. Although incompletely understood, the currently accepted view is that lipids may enhance bioavailability via a number of potential mechanisms, including.

A) Alterations (reduction) in gastric transit, thereby slowing delivery to the absorption site and increasing the time available for dissolution.

B) Increases in effective luminal drug solubility. The presence of lipids in the GI tract stimulates an increase in the secretion of bile salts (BS) and endogenous biliary lipids including phospholipids (PL) and cholesterol (CH), leading to the formation of BS/PL/CH intestinal mixed micelles and an increase in the solubilization capacity of the GI tract. However, intercalation of administered (exogenous) lipids into these BS structures either directly (if sufficiently polar), or secondary to digestion, leads to swelling of the micellar structures and a further increase in solubilization capacity.

C) Stimulation of intestinal lymphatic transport. For highly lipophilic drugs, lipids may enhance the extent of lymphatic transport and increase bioavailability directly or indirectly via a reduction in first-pass metabolism. A hydrophilic drug is less likely to be absorbed through the lymphatic (chylomicron) and instead may diffuse directly in to the portal supply. Hence in this case, increased dissolution from the large surface area afforded by emulsion may be a contributing factor to enhanced absorption of drugs.

D) Changes in the biochemical barrier function of the GI tract. It is clear that certain lipids and surfactants may attenuate the activity of intestinal efflux transporters, as indicated by the p glycoprotein efflux pump, and thus reduce the extent of enterocyte based metabolism.

E) Changes in the physical barrier function of the GI tract. Various combinations of

Lipids, lipid digestion products and surfactants have been shown to have permeability enhancing properties. For the most part, however, passive intestinal permeability is not thought to be a major barrier to the bioavailability of the majority of poorly water-soluble, and in particular, lipophilic drugs.[12]

FACTOR AFFECTING SMEDDS [17]

Drug dose:

Usually drugs having high dose are not preferred for developing SMEDDS. However, such drug if extremely soluble in any components of SMEDDS particularly in lipid phase. The drug which are not well soluble both in Water and oil, and also posses low log p value (around 2) are not suitable Candidates for SMEDDS.

Drug solubility in oil phase:

Solubility of the drug in oil phase greatly influenced the ability of SMEDDS in maintaining the drug in solution state. When the drug is solubilized by the use of surfactant and co surfactant the dilution of SMEDDS can lead to lowering the solvent capacity of surfactant or co surfactant, Their by resulting precipitation.

Equilibrium solubility:

For assessment of possibilities of precipitation in the gut Equilibrium solubility measurement can be employed. Such formulation can take Up to 5 days to reach equilibrium and that the drug can remain in a super saturated State up to 24 h after the initial emulsification event.

Recent Advancements and Future Prospects [18]

- Dry emulsions
- Self-emulsifying Capsules
- Self-emulsifying sustained/controlled release tablets
- Self-emulsifying sustained/controlled release pellets
- Self-emulsifying solid dispersions
- Self-emulsifying beads
- Self-emulsifying sustained release microspheres
- Self–emulsifying suppositories
- Self-emulsifying implants
- Self-emulsifying fast dissolving tablets

Table 4: Various Solidification Techniques For Transforming Liquid Or Semisolid[9]

Technique	Benefits	Description
Capsule filling	Simple manufacturing suitable for low-dose drugs	Liquids and semisolid elf-emulsifying system are filled in to the capsules
Spray drying	Simple	Spray drying of mixture containing lipids, solid carriers, surfactants and drug
Spray cooling	Simple	The molten formulation is sprayed in to a cooling chamber

Direct adsorption on carrier	Provide good drug content uniformity and simpler approach	Liquid SEDDS adsorb in to solid carrier

Recent Patents[3]

Diana Shu-Lian Chow (Houston, TX, US) Pranav Gupta (Short Hills, NJ, US) Yulan Qi (Houston, TX, US) Dong Liang (Pearland, TX, US) published a patent (US20090048322, 19 JAN, 2009) entitled Parenteral and oral formulations of benzimidazoles. The Present invention comprises a benzimidazole derivative (mebendazole), oil, surfactant, co-surfactant and a dipolar aprotic solvent in a micro-emulsion formulation. Also provided are methods for improving the bioavailability of a benzimidazoles derivative during treatment of a pathophysiological condition by using a formulation combining a particular emulsion droplet diameter and ratio of the surfactant: cosurfactant. Sure Chem published a patent (US20101362, JAN 12, 2010) entitled. Self-microemulsifying mitotane composition. The invention provides a mitotane oily formulation which comprises mitotane in a matrix comprising propylene glycol monocaprylate; from 10 to 30% of the total weight of the mitotane oily formulation (w/w)propylene glycol di-caprate; from 20 to 60% of the total weight of the mitotane oily formulation(w/w) & polyoxyethylene sorbitan from 10 to 30% of the total weight of the mitotane oily formulation (w/w). Christina Holmberg published a patent (USOO7815933132, OCT 19, 2010) entitled Self emulsifying drug delivery system. The present invention include pharmaceutical composition comprising one or more NSAIDS, surfactants of which at least one is phospholipid forming oil in water emulsions upon contact with GI fluids.

Evaluation of Smedds

The efficiency of self micro emulsification could be estimated by determining the evaluation parameter

1. Droplet Size:

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 or a coulter nanosizer are mainly used for the determination of the emulsion droplet size. The reduction of droplet size values below 200 nm lead to the formation of SMEDDS, which are stable, isotropic and clear o/w dispersions[19]

2. Zeta potential measurement

This is used to identify the charge of the droplets. In conventional SEDDS, the charge on an oil droplet is negative due to presence of free fatty acids.[19]

3. Refractive index and percent transmission:

Refractive index and percent transmittance proves the clearness of formulation. The refractive index of the SMEDDS is measured by refractometer and compared with that of water. The percent transmittance of the system is measured at particular wavelength using UV-vis spectrophotometer keeping distilled water as blank. If refractive index of system should be similar to that of water. Formulation showing transmittance >99 percent is transparent in nature[17]

3. Thermodynamic stability studies

I) Heating cooling cycle:

Six cycles between refrigerator temperature (40C) and 450C with storage at each temperature of not less than 48 h is studied. Those formulations, which are stable at these temperatures, are subjected to centrifugation test

II) Centrifugation:

Passed formulations are centrifuged thaw cycles between 21 C and +25 0C with storage at each temperature for not less than 48 h is done at 3500 rpm for 30 min. Those formulations that does not show any phase separation are taken for the freeze thaw stress test.

III) Freeze thaw cycle:

Three freeze for the formulations. Those formulations passed this test showed good stability with no phase separation, creaming, or cracking.(10)

4. Dispersibility test

The efficiency of self-emulsification of oral nano or micro emulsion is assessed using a standard USP XXII dissolution apparatus 2. One millilitre of each formulation was added to 500 ml of water at 37 ± 0.5 0C. A standard stainless steel dissolution paddle rotating at 50 rpm provided gentle agitation. The in vitro performance of the formulations is visually assessed using the following grading system:

Grade A: Rapidly forming (within 1 min) nanoemulsion, having a clear or bluish appearance.

Grade B: Rapidly forming, slightly less clear emulsion, having a bluish white appearance.

Grade C: Fine milky emulsion that formed within 2 min.

Grade D: Dull, grayish white emulsion having slightly oily appearance that is slow to emulsify (longer than 2 min).

Grade E: Formulation, exhibiting either poor or minimal emulsification with large oil globules present on the surface.

Grade A and Grade B formulation will remain as nano-emulsion when dispersed in GIT. While formulation falling in Grade C could be recommend for SEDDS formulation[10]

5. Determination of emulsification time.

Quantified the efficiency of emulsification of various compositions of the Tween85 and medium-chain triglyceride systems using a rotating paddle to promote emulsification in a crude nephelometer. This enabled an estimation of the time taken for emulsification. Once emulsification was complete, samples were taken for particle sizing by photon correlation spectroscopy, and self-emulsified systems were compared with homogenized systems. The process of self-emulsification was observed using light microscopy. It was clear that the mechanism of emulsification involved erosion of a fine cloud of small particles from the surface of large droplets, rather than a progressive reduction in droplet size.

6. Viscosity Determination

The SMEDDS system is generally administered in soft gelatin or hard gelatin capsules. Therefore, it should be easily pourable into capsules and such system should not be too thick to create a problem. The rheological properties of the micro emulsion are evaluated by Brookfield Viscometer. This viscosity determination confirms whether the system is w/o or o/w. If system has low viscosity then it is o/w type of the system and if high viscosity then it is w/o type of the system[10]

7. Robustness to dilution

Formulations were subjected to 50,100,250 fold dilution with enzyme free simulated gastric fluid pH 1.2; enzyme free simulated intestinal fluid pH 6.8 and distilled water. The resultant diluted emulsions were observed for any physical changes like coalescence of droplets, precipitation or phase separation after 24 hrs.[20]

8.Cloud point measurement

The optimized SNEDDS formulations were diluted with distilled water in the ratio of 1:250. The diluted samples were placed in a water bath and its temperature was increased gradually cloud point was spectrophotmetrically determined as the temperature at which there was a sudden appearance of cloudiness.[20]

9. Drug content determination

Drug from pre-weighed SNEDDS is extracted by dissolving in suitable solvent. Drug content in the solvent extract was analyzed by suitable analytical method against the standard solvent solution of drug.[20]

10. Electron Microscopic Studies:

Freeze-fracture electron microscopy has been used to study the surface characteristics of the SEDDS. Transmission Electron Microscopy (TEM), Cryo-Transmission Electron Microscopy (Cryo-TEM Studies) techniques are used to perform electron microscopic studies[21]

11. Conductivity Measurement:

Conductivity Measurement based on the phase inversion phenomenon determines the point of aqueous phase addition where oil phase continuously changed in water continuous phase[22]

12.Polydispersibility Index

Polydispersity index (PDI) is measure of droplet size homogeneity and it varies from 0.0 to 1.0. Polydispersity is the ratio of standard deviation to mean droplet size in the formulation. The higher the Polydispersity, the lower the uniformity of the droplet size in the formulation. The closer to zero the Polydispersity value the more homogenous are the droplets[23]

13. % transmittance

The clarity of the formulations was observed by measuring % Transmittance of all formulations in UV spectrophotometer using double distilled water as blank.[24]

APPLICATIONS

Oral bioavailability enhancement poorly water soluble drugs

In case of poorly water soluble drugs dissolution rate dependent absorption is a major factor that limits the bioavailability. The ability of self-emulsification to release in the drug to GIT and disperses to micro emulsified form. As the globular size is so small subsequent increase in specific surface area enable more efficient drug transport through the intestinal aqueous boundary layer and through the absorptive brush border membrane leading to improved bioavailability[9]

Table 5: A Table of all the drugs whose bioavailability was increased by using SMEDDs

Drug	Bioavailability Enhancement
Simvastatin	1.5 folds
Ketoprofen	1.13 folds
Vitamin A	2 folds
Vinpocetin	17.3 folds

Protection against Biodegradation

The ability of self emulsifying drug delivery system to reduce degradation as well as improve absorption may be especially useful for drugs, for which both low solubility and degradation in the GI tract contribute to a low oral bioavailability. Many drugs are degraded in physiological system, may be because of acidic PH in stomach, enzymatic degradation or hydrolytic degradation etc. Such drugs when presented in the form of SEDDS can be well protected against these degradation processes as liquid crystalline phase in SEDDS might be an act as barrier between degradation environment and the drug[25]

CONCLUSION

Self micro-emulsifying drug delivery systems are a promising approach for the formulation of drug compounds with poor aqueous solubility, having high molecular weight , pre systematic first pass effect, enzymatic degradation, gastric irritation, having limited dissolution rate and low bioavailability. This is the method suited for all BCS class drugs where resulting emulsification is gives faster dissolution and absorption rates. In future development SMEDDS will continue to novel applications in drug delivery and solve the problems associated with the delivery of poor water soluble drug, pre-systematic first pass effect, enzymatic degradation and having limited dissolution and low bioavailability.

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