

## Self Emulsifying Drug Delivery System: A Review

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### ABSTRACT

The oral route is the favourite route for chronic drug therapy, majority of drugs are frequently administered through oral route. Oral drug delivery systems being the most cost-effective to manufacture, have always lead the worldwide drug delivery market. This oral route may be a problem route for drug molecules which exhibit poor aqueous solubility. When a drug is administered by oral route the first step for it to get absorbed is its solubilisation followed by permeation. However, an increasing number of poorly soluble drug candidates with low, variable and food-dependent bioavailability are facing the pharmaceutical industry today. Approximately 40% of new chemical entities exhibit poor aqueous solubility and present a major challenge to modern drug delivery system. A rate limiting step for the absorption of these drugs is often their solubilisation in the gastrointestinal tract. These drugs are classified as class II drug by Biopharmaceutical classification system (BCS), drugs with poor aqueous solubility and high permeability. Thus for such drug substances to be effectively absorbed, there is a need to increase their dissolution rate. Oral delivery of such drugs is complicated for the reason that of their low bioavailability, high intra- and inter-subject variability, and not have dose linearity. To overcome these problems, a variety of strategies have been developed including the use of surfactants, lipids, permeation enhancers, micronization, salt formation, cyclodextrins, nanoparticles and solid dispersions, and self emulsifying drug delivery system.

**Keywords:** Self emulsifying drug delivery system, oral bioavailability, lipid based formulations.

### INTRODUCTION

Self-emulsifying drug delivery systems (SEDDS) have gain exposure to improve the bioavailability of hydrophobic drugs. SEDDSs are belongs to lipid formulations<sup>1</sup>. Lipid-based drug delivery systems have been demonstrated to be useful in enhancing the bioavailability of highly lipophilic compounds because they can keep the drug in the dissolved state until it is absorbed, thus overcoming the barrier of slow dissolution rates<sup>2</sup>.

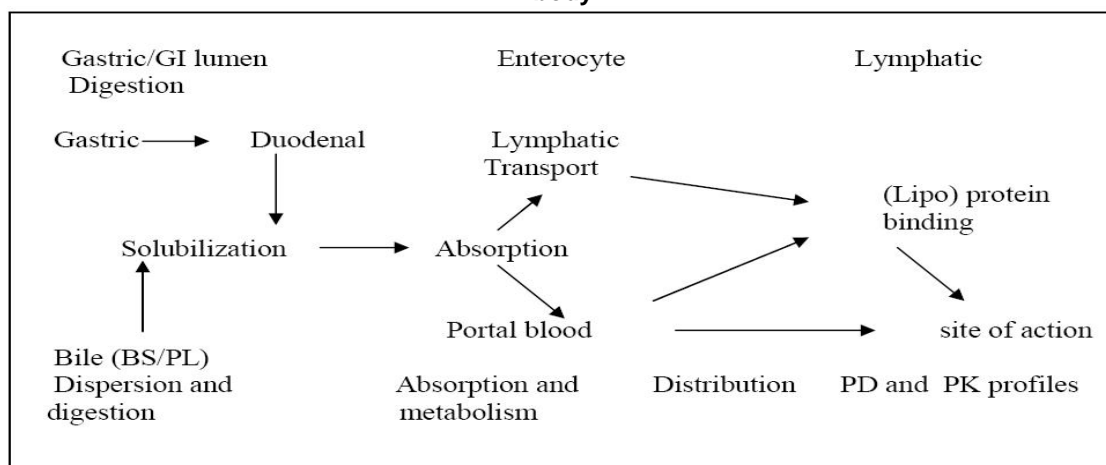
The theory behind dissolution rate improvement by means of SEDDS is the spontaneous development of the emulsion in the gastrointestinal tract with mild agitation provided by gastric mobility, which presents the drug in solubilised form, and the small size of the formed droplet provides a large interfacial surface area for drug absorption. Due to its small globule size, the micro/nanoemulsified drug can easily be absorbed through lymphatic pathways, thereby bypassing the hepatic first-pass effect<sup>1</sup>.

### Self Emulsifying Drug Delivery System (SEDDS)

#### Basic Concepts

The mixture of oil, surfactant, co-surfactant, and co-solvents (absence of external phase water) forms a transparent isotropic solution, which emulsify under gentle agitation similar to those which would be encountered in GI tract and is referred as the self-emulsifying formulation (SEF). It has been recognized that this formulation when administered orally undergo spontaneous emulsification in aqueous GI fluids. This emulsified oil (triglycerides) stimulates bile secretion and drug containing oil droplets are further emulsified by bile salts. Lipid droplets are then metabolized by lipases and co lipases, secreted from the salivary gland, gastric mucosa and pancreas, which also hydrolyze the triglycerides into di- and monoglycerides and free fatty acids. Further, solubilisation of these molecules occurs during the passage through the GI tract and eventually forms a range of emulsion droplets, vesicular structures and mixed micelles containing bile salts, phospholipids and cholesterol<sup>3</sup>.

**Fig. 1: shows the processing of lipid and co-administered drugs in human body**



**Fig.1: Processing of lipid and co-administered Drug<sup>4</sup>**

The chylomicron synthesis takes place into lymphatics which ensures the enhancement of drug absorption. The bioavailability enhancing property of self-emulsifying formulations has been mainly associated with a number of in vivo properties including

- The inhibition of cellular efflux mechanisms, which keep drugs out of the circulation.
- Reduction of first-pass drug metabolism in the liver due to association of certain lipidic excipients with selective drug uptake into the lymphatic transport system.
- The formation of fine dispersions and micellar suspensions to prevent precipitation and recrystallization of the drug compound.

- The ability of certain lipid compounds and their metabolites to initiate changes in the GI fluid in favour of improved drug absorption.

SEFs are prepared using surfactants of HLB < 12 while self-microemulsifying formulations (SMEFs) and self-nanoemulsifying formulations (SNEFs) with surfactants of HLB >12. These formulations possess high stability and improved dissolution (for poorly soluble drugs) due to enhancement in surface area on dispersion<sup>3</sup>. Therefore, their absorption is independent of bile secretion and ensures a rapid transport of poorly soluble drugs into the blood. Further, these preparations have few distinct features associated with improved drug delivery properties<sup>3</sup>.

## Types of SEDDS

**Table1: Types and comparative features of all self emulsifying formulations<sup>3,20</sup>**

Isotropic mixture of the drug compound, surfactant, co-surfactant and lipid phase which emulsify under conditions of gentle agitation, when come in contact with gastro-intestinal fluid.			
Type of SEDDS	Comparative features		
	Oil droplet size	Appearance	HLB value of Surfactants
Self-emulsifying formulations (SEFs)	200 nm to 5 µm	Turbid	< 12
Self-micro emulsifying formulations(SMEFs)	Less than 200 nm	Optically clear to translucent	> 12
Self-nanoemulsifying formulations (SNEFs)	Less than 100 nm	Optically clear	> 12

The types and comparative features of reported systems are illustrated in Table 1.



Fig. 2: Difference between Self-Emulsions and Self-Micron Emulsion<sup>5</sup>.

#### Advantages of SEDDS<sup>6,7</sup>

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

#### Disadvantages of SEDDS<sup>7,8,9</sup>

1. Lack of good predicative in vitro models for assessment of the formulations.
2. High surfactant concentration used in this formulation which irritates GIT.
3. Volatile co-solvent migrates into the shells of soft or hard gelatin capsule.
4. The precipitation tendency of drug on dilution may be higher due to dilution effect of hydrophilic solvent.
5. Formulations containing several components become more challenging to validate.

#### Mechanism of Self Emulsification

According to "Reiss" self emulsification occurs when the entropy changes that favour dispersion is greater than the energy required to increase the surface area of the dispersion. The free energy of the conventional emulsion is a direct function of the energy required to create a new surface between the oil and water phase and can be described by the equation-

$$DG = SNPr2s$$

DG – free energy associated with the process (ignoring free energy in mixing)  
 N – Number of droplets of radius r and s represent the interfacial energy<sup>10</sup>.

#### Formulation of SEDDS<sup>1, 11, 12, 13, 15, 16, 21</sup>

Self-emulsification process is highly specific to the nature of the oil/surfactant pair used; oil/surfactant ratio, surfactant concentration, and temperature at which self-emulsification occur. These important discoveries were further supported by the fact that only very specific combinations of pharmaceutical excipients led to efficient self-emulsifying therapeutic systems. Various major components used in the SEDDS are discussed below

1. Oils
2. Surfactants / Co-surfactants
3. Solvents / Co-solvents

#### 1. Oils

The oily/lipid component is generally a fatty acid ester or a medium/long chain saturated, partially unsaturated

hydrocarbon, in liquid, semisolid or solid form at room temperature. Examples include mineral oil, vegetable oil, silicon oil, lanolin, refined animal oil, fatty acids, fatty alcohols, and mono-/di-/triglycerides. Unmodified edible oils provide the most 'natural' basis for lipid vehicles, but their poor ability to dissolve large amounts of hydrophobic drugs and their relative difficulty in efficient self-emulsification markedly reduce their use in SEDDS. In contrast, modified or hydrolyzed vegetable oils exhibit formulative and physiological advantages. These excipients form good emulsification systems, with a large number of non-ionic surfactants approved for oral administration, while their degradation products resemble the end products of intestinal digestion. Eg. Cotton seed oil, Soybean oil, Corn oil, Sunflower oil, Sesame oil, Peanut oil, Castor oil, Labrafil, Labrafac, Captex 200, Captex 300, Captex 350, Captex 500, Ethyl oleate, etc.

## 2. Surfactants / Co-surfactants

The most widely recommended surfactants are non-ionic surfactants with a relatively high hydrophilic-lipophilic balance (HLB) value. Various liquid or solid ethoxylated polyglycolized glycerides and polyoxyethylene 20 oleate (Tween 80) are the most frequently used excipients. Emulsifiers derived from natural sources are expected to be safer than synthetic ones and are recommended for SDLF (self dispersed lipid formulation) use. Non-ionic surfactants are known to be less toxic compared to ionic surface-active agents, but they may cause moderate reversible changes in intestinal wall permeability. The surfactant concentration ranges between 30% and 60% (w/w) in order to form stable SEDDS. A large quantity of surfactant may irritate the GI tract. The high HLB and subsequent hydrophilicity of surfactants is necessary for the immediate formation of o/w droplets and/or rapid spreading of the formulation in the aqueous environment, providing a good dispersing/self emulsifying performance. The surface active agents are amphiphilic by nature, and they are therefore usually able to dissolve and even solubilize

relatively high quantities of the hydrophobic drug. The latter is of prime importance for preventing precipitation within the GI lumen and for the prolonged existence of the drug molecules in soluble form, which is important for effective absorption. The lipid mixtures with higher surfactant and co-surfactant/oil ratios lead to the formation of self-micro emulsifying formulations (SMEDDS).

Eg. Polysorbate 20 (Tween 20), Polysorbate 80 (Tween 80), D-alpha Tocopheryl polyethylene glycol 1000 succinate (TPGS), Polyoxy-35-castor oil (Cremophor RH40), Polyoxy-40-hydrogenated castor oil (Cremophor RH40), Labrasol, etc.

## 3. Solvents / Co-solvents

Organic solvents, suitable for oral administration (ethanol, propylene glycol (PG), polyethylene glycol (PEG), etc.) may help to dissolve large amounts of either the hydrophilic surfactant or the drug in the lipid base. These solvents sometimes play the role of the co-surfactant in the micro emulsion systems. Indeed, such systems may exhibit some advantages over the previous formulations when incorporated in capsule dosage forms, since alcohol and other volatile cosolvents comprised in the conventional self-emulsifying formulations are known to migrate into the shells of soft gelatin, or hard, sealed gelatin capsules, resulting in the precipitation of the lipophilic drug. On the other hand, the lipophilic drug dissolution ability of the alcohol free formulation may be limited. Drug release from the formulation increases with increasing amount of cosurfactant.

Following are the some examples of the oils, surfactants, cosurfactants, and some cosolvents.

Eg. Span 20, Span 80, Capryol 90, Lauroglycol, Transcutol, Capmul, Ethanol, Polypylene glycol, Polyethylene glycol, etc.

## Different dosage forms of SEDDS<sup>3,4,11,13,14,15</sup>

1. Dry emulsions
2. Self-emulsifying capsules

3. Self-emulsifying sustained/controlled-release tablets
4. Self-emulsifying sustained/controlled-release pellets
5. Self-emulsifying solid dispersions
6. Self-emulsifying beads
7. Self-emulsifying sustained-release microspheres
8. Self-emulsifying nanoparticles
9. Self-emulsifying suppositories
10. Self-emulsifying implant

### 1. Dry emulsions

Dry emulsions are powders outside the body. Emulsion spontaneously occurs in vivo or when exposed to an aqueous solution. Dry emulsions can be used for further preparation of tablets and capsules. Dry emulsion formulations are typically prepared from oil/water (O/W) emulsions containing a solid carrier (lactose, maltodextrin, and so on) in the aqueous phase by rotary evaporation, freeze-drying or spray drying. Myers and Shively obtained solid state glass emulsions in the form of dry 'foam' by rotary evaporation, with heavy mineral oil and sucrose. Such emulsifiable glasses have the advantage of not requiring surfactant.

In freeze-drying, a slow cooling rate and the addition of amorphous cryoprotectants have the best stabilizing effects, while heat treatment before thawing decreases the stabilizing effects. The technique of spray drying is more frequently used in preparation of dry emulsions. The O/W emulsion was formulated and then spray dried to remove the aqueous phase. The most exciting finding in this field ought to be the newly developed enteric-coated dry emulsion formulation, which is potentially applicable for the oral delivery of peptide and protein drugs. This formulation consisted of a surfactant, a vegetable oil, and a pH-responsive polymer, with lyophilization used. Recently, Cui et al. prepared dry emulsions by spreading liquid O/W emulsions on a flat glass, then dried and triturated to powders<sup>15,22</sup>.

### 2. Self emulsifying capsules

Administration of capsules containing conventional self emulsifying formulations, microemulsion droplets form and subsequently disperse in the GI tract to reach sites of absorption. Improvement of drug absorption cannot be expected, if irreversible phase separation of the microemulsion occurs. For handling this problem, sodium dodecyl sulfate was added into the SE formulation. With the similar purpose, the supersaturatable SEDDS was designed, using a small quantity of HPMC (or other polymers) in the formulation to prevent precipitation of the drug by generating and maintaining a supersaturated state in vivo. This system contains a reduced amount of a surfactant, thereby minimizing GI side effects. Besides liquid filling, liquid SE ingredients also can be filled into capsules in a solid or semisolid state obtained by adding solid carriers (adsorbents, polymers, and so on). As an example, a solid PEG matrix can be chosen. The presence of solid PEG neither interfered with the solubility of the drug, nor did it interfere with the process of self-microemulsification upon mixing with water<sup>15,22</sup>.

### 3. Self emulsifying sustained/controlled release tablets

Lipids and surfactants combination have present great potential of preparing SE tablets that have been widely researched. Nazzal and Khan evaluated the effect of some processing parameters (colloidal silicates—X1, magnesium stearate mixing time—X2, and compression force—X3) on hardness and coenzyme Q10 (CoQ10) dissolution from tablets of eutectic-based SMEDDS. The optimized conditions (X1 = 1.06%, X2 = 2 min, X3 = 1670 kg) were achieved by a face-centered cubic design. In order to reduce significantly the amount of solidifying excipients required for transformation of SEDDS into solid dosage forms, a gelled SEDDS has been developed by Patil et al. In their study, colloidal silicon dioxide (Aerosil 200) was selected as a gelling agent for the oil-based systems, which served the dual purpose of reducing the amount of required solidifying excipients and aiding



in slowing down of the drug release. SE tablets are of great utility in obviating adverse effect, as disclosed by Schwarz in a patent. Inclusion of indomethacin (or other hydrophobic NSAID), for example, into SE tablets may increase its penetration efficacy through the GI mucosal membranes, potentially reducing GI bleeding. In these studies, the SES was composed of glycerol monolaurate and Tyloxapol TM (a copolymer of alkyl phenol and formaldehyde)<sup>15,17,23</sup>.

#### **4. Self emulsifying sustained/controlled release pellets**

Pellets are multiple unit dosage form which possess many advantages over conventional solid dosage forms, such as flexibility of manufacture, reducing intrasubject and intersubject variability of plasma profiles and minimizing GI irritation without lowering drug bioavailability. Thus, it is very appealing to combine the advantages of pellets with those of SEDDS by SE pellets. Serratori et al. prepared SE controlled release pellets by incorporating drugs into SES that enhanced their rate of release, and then by coating pellets with a water-insoluble polymer that reduced the rate of drug release. Pellets were prepared by extrusion/ spheronization and contained two water-insoluble model drugs (methyl and propyl parabens); SES contained monodiglycerides and Polysorbate 80. There is another report that SE sustained-release matrix pellets could be successfully formulated with glyceryl palmito-stearate (Gelucire 54/02) and glyceryl behenate (Gelucire 70/02)<sup>15</sup>.

#### **5. Self emulsifying solid dispersions**

Dispersions of solids could increase the dissolution rate and bioavailability of poorly water-soluble drugs, some manufacturing difficulties and stability problems existed. Serajuddin pointed out that these difficulties could be surmounted by the use of SE excipients. These excipients have the potential to increase further 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 before fillings. SE excipients like Gelucire1 44/14, Gelucire1 50/02, Labrasol, Transcutol and TPGS (tocopheryl polyethylene glycol 1000 succinate) have been widely used in this field<sup>15,22</sup>.

#### **6. Self emulsifying beads**

To transform SES into a solid form with minimum amounts of solidifying excipients, Patil and Paradkar investigated loading SES into the micro-channels of porous polystyrene beads (PPB) using the solvent evaporation method. PPB with complex internal void structures is typically produced by copolymerizing styrene and divinyl benzene. They are inert, stable over a wide pH range and to extreme conditions of temperature and humidity. This research concluded that PPB was potential carriers for solidification of SES, with sufficiently high SES to PPB ratios required to obtain solid form. Geometrical features, such as bead size and pore architecture of PPB, were found to govern the loading efficiency and in vitro drug release from SES loaded PPB<sup>15,19</sup>.

#### **7. Self emulsifying sustained release microspheres**

Zedoary turmeric oil (ZTO; a traditional Chinese medicine) exhibits potent pharmacological actions including tumor suppressive, antibacterial, and antithrombotic activity. With ZTO as the oil phase, You et al. prepared solid SE sustained-release microspheres using the quasiemulsion- solvent-diffusion method of the spherical crystallization technique. ZTO release behavior could be controlled by the ratio of hydroxypropyl methylcellulose acetate succinate to Aerosil 200 in the formulation. The plasma concentration- time profiles were achieved after oral administration of such microspheres to rabbits, with a bioavailability of 135.6% with respect to the conventional liquid SEDDS<sup>15</sup>.

#### **8. Self emulsifying Nanoparticles**

Nanoparticle techniques have been useful in the production of SE nanoparticles.

Solvent injection is one of these techniques. In this method, the lipid, surfactant, and drugs were melted together, and injected drop wise into a stirred non-solvent. The resulting SE nanoparticles were thereafter filtered out and dried. These approach yielded nanoparticles (about 100 nm) with a high drug loading efficiency of 74%<sup>15</sup>.

### 9. Self emulsifying suppositories

S-SEDDS could increase not only GI adsorption but also rectal/vaginal adsorption. Glycyrrhizin, which, by the oral route, barely achieves therapeutic plasma concentrations, can obtain satisfactory therapeutic levels for chronic hepatic diseases by either vaginal or rectal SE suppositories. The formulation included glycyrrhizin and a mixture of a C6–C18 fatty acid glycerol ester and a C6–C18 fatty acid macrogol ester<sup>15</sup>.

### 10. Self emulsifying implants

Research into SE implants has greatly enhanced the utility and application of S-SEDDS. As an example, 1, 3-bis (2-chloroethyl)-1- nitrosourea (carmustine, BCNU) is a chemotherapeutic agent used to treat malignant brain tumors. However, its effectiveness was hindered by its short half-life. Loomis invented copolymers having a bio-resorbable region, a hydrophilic region and at least two cross-linkable functional groups per polymer chain. Such copolymers show SE property without the requirement of an emulsifying agent. These copolymers can be used as good sealants for implantable prostheses<sup>15</sup>.

### Applications of SEDDS<sup>11,13</sup>

#### Improvement in Solubility and bioavailability

Incorporation of drug in SEDDS increases the solubility because it circumvents the dissolution step in case of Class-II drug (Low solubility/high permeability), benidipine, gefitinib, ketoprofen etc. A moderately hydrophobic (log P 0.979) non steroidal anti-inflammatory drug (NSAID), is a drug of choice for sustained release formulation has high potential for gastric irritation during chronic therapy. Also because of its low solubility, ketoprofen

shows incomplete release from sustained release formulations. Vergote et al. (2001) reported complete drug release from sustained release formulations containing ketoprofen in nanocrystalline form. Different formulation approaches that have been sought to achieve sustained release, increase the bioavailability, and decrease the gastric irritation of ketoprofen include preparation of matrix pellets of nano-crystalline ketoprofen, sustained release ketoprofen microparticles and formulations, floating oral ketoprofen systems, and transdermal systems of ketoprofen. Preparation and stabilization of nano-crystalline or improved solubility forms of drug may pose processing, stability, and economic problems. This problem can be successfully overcome when Ketoprofen is presented in SEDDS formulation. This formulation enhanced bioavailability due to increase the solubility of drug and minimizes the gastric irritation. Increase in AUC i.e. bioavailability and C<sub>max</sub> is observed with many drugs when presented in SEDDS.

#### 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 degrading environment and the drug. Acetylsalicylic acid (Log P = 1.2, Mw=180), a drug that degrades in the GI tract because it is readily hydrolyzed to salicylic acid in an acid environment. When the drug was formulated in a Galacticles™ Oral Lipid Matrix System (SEDDS formulation) and compare with a commercial formulation, it showed the good plasma profile as compare to reference formulation. . The oral bioavailability of undegraded

acetylsalicylic acid is improved by 73% by the Galacticles™ Oral Lipid Matrix System formulation compared to the reference formulation. This suggests that the

SEDSS formulation has a capacity to protect drugs from degradation in the GI tract.

**Table 2: List of selected commercially available lipid-based formulations for oral administration<sup>3</sup>**

Drug	Excipients	Indication	Type of Formulation	Tradename/ Company
Ritonavir	Oleic acid, BHT, ethanol, polyoxyl 35, castor oil	HIV antiviral	Soft gelatin capsule	Norvir (Abbott)
Sanquinavir	Medium-chain povidone, mono-diglycerides, dl- $\alpha$ -tocopherol	HIV antiviral	Soft gelatin capsule	Fortovase (Roche)
Lopinavir and Ritonavir	Acesulfame potassium, alcohol, citric acid, glycerin, high fructose corn syrup, peppermint oil, polyoxyl 40 hydrogenated castor oil, povidone, propylene glycol	HIV-1 antiviral	Soft gelatin capsule	Kaletra (Abbott)
Bexarotene	Polyethylene glycol 400, NF, polysorbate 20, NF, povidone, USP, and butylated hydroxyanisole, NF	Antineoplastic	Soft gelatin capsule	Targretin (Ligand)
Tretinoin	soybean oil, butylated hydroxyanisole, edetate disodium, methylparaben, propylparaben	Acute promyelocytic leukemia	Soft gelatin capsule	Vesanoid (Roche)

### Evaluation of SEDSS<sup>1,6,11,12</sup>

#### 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.

#### 1. 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.

#### 2. Centrifugation

Passed formulations are centrifuged thaw cycles between 21 0C 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.

#### 3. Freeze thaw cycle

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

#### Dispersibility test

The efficiency of self-emulsification of oral nano or micro emulsion is assessed using a standard USP XXII dissolution apparatus 2. One milliliter of each formulation was added to 500 mL of water at  $37 \pm 0.5$  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**

Fines 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 nanoemulsion when dispersed in GIT. While formulation falling in Grade C could be recommend for SEDDS formulation.

**Turbidimetric Evaluation**

Nepheloturbidimetric evaluation is done to monitor the growth of emulsification. Fixed quantity of Self emulsifying system is added to fixed quantity of suitable medium (0.1N hydrochloric acid) under continuous stirring (50 rpm) on magnetic plate at ambient temperature, and the increase in turbidity is measured using a turbidimeter. However, since the time required for complete emulsification is too short, it is not possible to monitor the rate of change of turbidity (rate of emulsification).

**Viscosity Determination**

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 to create a problem. The rheological properties of the micro emulsion are evaluated by Brookfield viscometer. This viscosities determination conform 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.

**Droplet Size Analysis Particle Size Measurements**

The droplet size of the emulsions is determined by photon correlation spectroscopy (which analyses the

fluctuations in light scattering due to Brownian motion of the particles) using a Zetasizer able to measure sizes between 10 and 5000 nm. Light scattering is monitored at 25°C at a 90° angle, after external standardization with spherical polystyrene beads. The nanometric size range of the particle is retained even after 100 times dilution with water which proves the system's compatibility with excess water.

**Refractive Index and Percent Transmittance**

Refractive index and percent transmittance proved the transparency of formulation. The refractive index of the system is measured by refractometer by placing drop of solution on slide and it compare with water (1.333). The percent transmittance of the system is measured at particular wavelength using UV-spectrophotometer keeping distilled water as blank. If refractive index of system is similar to the refractive index of water (1.333) and formulation have percent transmittance > 99 percent, then formulation have transparent nature.

**Electro conductivity Study**

The SEDD system contains ionic or non-ionic surfactant, oil, and water. So, this test is used to measure the electroconductive nature of system. The electro conductivity of resultant system is measured by electroconductometer.

**In Vitro Diffusion Study**

In vitro diffusion study is performed to study the release behaviour of formulation from liquid crystalline phase around the droplet using dialysis technique.

**Drug content**

Drug from pre-weighed SEDDS 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.

**CONCLUSION**

Self-emulsifying drug delivery systems are a promising approach for the formulation of drug compounds with poor aqueous solubility. The oral delivery of hydrophobic

drugs can be made possible by SEDDSs, which have been shown to substantially improve oral bioavailability. As improvements or alternatives of conventional liquid SEDDS, S-SEDDS are superior in reducing production cost, simplifying industrial manufacture, and improving stability as well as patient compliance. Most importantly, S-SEDDS are very flexible to develop various solid dosage forms for oral and parenteral administration. Moreover, GI irritation is avoidable and controlled/sustained release of drug is achievable.

In relation to formulation development of poorly soluble drugs, there are new techniques being used to convert liquid/semi-solid SEDDS and SMEDDS formulations into powders and granules, which can then be further processed into conventional 'powder-fill' capsules or even compressed into tablets. Hot melt granulation is a technique for producing granules or pellets, and by using a waxy solubilising agent as a binding agent, up to 25% solubilising agent can be incorporated in a formulation. There is also increasing interest in using inert adsorbents, such as the Neusilin (Fuji Chemicals) and Zeopharm (Huber) products for converting liquids into powders – which can then be processed into powder fill capsules or tablets. But to obtain solids with suitable processing properties, the ratio of SEDDS to solidifying excipients must be very high, which seems to be practically non-feasible for drugs having limited solubility in oil phase. In this regard, it was hypothesized that the amount of solidifying excipients required for transformation of SEDDS in solid dosage forms will be significantly reduced if SEDDS is gelled. Colloidal silicon dioxide (Aerosil 200) is selected as a gelling agent for the oil based systems, which may serve the dual purpose of reducing the amount of solidifying excipients required and aiding in slowing drug release.

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