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SELF-EMULSIFYING DRUG DELIVERY SYSTEM - A NOVEL APPROCH TO IMPROVE ORAL BIOAVAILABILITY

Swati Lade*, Umesh Telrandhe, Sushil Burle, Satish Kosalge

Hi-Tech College of Pharmacy, Chandrapur-442406.

***Correspondence for Author: Swati Lade**

Hi-Tech College of Pharmacy, Chandrapur-442406.

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ABSTRACT

The oral route is the most favorite route of drug delivery for cure of a number of diseases. It is estimated that 35-40% of active substances are poorly soluble in water. The major problem in oral drug formulations is low and erratic bioavailability, which mainly results from poor aqueous solubility. The improvement of bio-availability of drugs with such properties presents one of the greatest challenges in drug formulations. Various technological strategies are reported in the literature including Micronization, solid dispersions or cyclodextrines complex formation and different technologies of drug delivery systems. SEDDS are promising advance for oral delivery of poorly water-soluble compounds or lipophilic drugs. SEDDS are ideally isotropic mixtures of drug, oil, surfactant and/or co surfactant. Purpose of this review article is to provide brief outline of self emulsifying drug delivery system & it's possible to increase the bioavailability of poorly soluble drugs.

KEYWORDS: Self-emulsifying drug delivery systems (SEDDS), drug delivery, Surfactant; Co Surfactant; bioavailability.

INTRODUCTION

The oral route is the most preferred route of drug delivery for cure of a number of diseases. Nearly 35 to 40% of newly launched drugs possess low aqueous solubility which leads to their poor dissolution and thereby low bioavailability, resulting in high intra & inter subject variability & lack of dose proportionality.[11, 12] For these drugs absorption rate from gastrointestinal tract is mainly governed by dissolution and improvement in solubility may lead to enhanced bioavailability.[1] Self-emulsifying drug delivery systems (SEDDS) possess unparalleled potential in improving oral bioavailability of poorly water-soluble or lipophilic 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.[2] The main techniques for converting SEDDS to SSEDDS are spray cooling, spray drying, adsorption onto solid carriers, meltgranulation, melt extrusion, super-critical fluid based methods and high pressure homogenization. But adsorption process is simple and involves simply addition of the liquid formulation to solid carriers by mixing in a blender.[3,21,22,23] In the case of sparingly soluble drugs that exhibit dissolution rate limited absorption, the SEDDS system offers a way to improve the rate and extent of oral absorption and to produce more reproducible blood-time profiles. Self-emulsifying formulations reach readily in the gastrointestinal tract (GIT), and the GI motility of the stomach and the intestine provide the necessary agitation for self emulsification. These systems have the advantage that the drug in dissolved form and the small droplet size provides a large interfacial area for the drug absorption. SEDDSs are physically stable formulations that are easy to manufacture, but when compared with emulsions, which are sensitive and metastable dispersed forms.[4] [5] Oral absorption of several drugs has been enhanced by SEDDS with different mechanisms. In SEDDS, solubility is most important factor. There are several ways by which of solubility of the drug can be enhanced, many of the methods which aimed at increase in the surface area of the drugs such as - Micronization, salt form of drug, use of metastable polymorphs, solvent deposition, selective adsorption on insoluble carriers, Selective adsorption on insoluble carriers, solid dispersion, solute solvent complexation. But, there are practical limitations of these techniques.[6, 7, 13]

DEFINATION OF SEDDS: SEDDS are defined as isotropic mixtures of natural or synthetic oils, solid or liquid surfactants or alternatively, one or more hydrophilic solvents & co-solvents/co-surfactants.[1]

PROPERTIES OF SEDDS[1, 6, 24, 27]

- They are able to self emulsify quickly in gastro-intestinal fluids & under the influence of gentle agitation.

- Peristaltic and other movements of gastro intestinal tract, they form a fine o/w emulsion.
- They can efficiently include drug (hydrophobic or hydrophilic) within the oil surfactant mixture.
- They can be used for liquid as well as solid dosage forms.
- They require lower dose of drug with respect to conventional dosage forms.

EXCIPIENTS USED IN SEDDS[1, 15, 16]

A large number of excipients are used in the formulation of self emulsifying drug delivery systems. Use of other excipients in SEDDS is used by the type of dosage form.

❖ **Oils**

Oil along with surfactant is necessary components. Various types of oils (natural, synthetic or semi synthetic) have been used for the formulation of SEDDS of various drugs. Some examples of the oils used in the marketed preparations are cited in the table 1.

Table 1: Type of oils used in marketed SEDDS

Type of oil	Marketed Product	Drug
Corn oil	Depakene capsule	Valproic acid
Olive oil	Sandimmune oral solution	Cyclosporine
Sesame oil	Marinol soft gelatin capsule	Dronabinol
Soya bean oil	Accutane soft gelatin capsule	Isotretinoin, Ibuprofen
Peanut oil	Prometrium soft gelatin capsule	Progesterone, Griseofulvin
Bees wax	Vesanoid soft gelatin capsule	Tretinoin
Hydrogenated soya bean oil	Accutane soft gelatin capsule	Isotretinoin

Generally oils with long & medium chain triglycerides with varying degrees of saturation are used for formulation of SEDDS. Edible oils without any modification provide the "Natural" base for lipid vehicles, but their poor ability to dissolve larger amount of drugs & their lower self emulsification efficiency restricts their use in SEDDS. Therefore, modified or hydrolyzed vegetable oils are preferred as compared to Natural edible oils for use in SEDDS formulation. [1, 15, 16]

❖ **Surfactants[1]**

Emulsifiers obtained from natural sources are expected to be safer than synthetic surfactants. As compared to cationic or anionic surfactants, nonionic surfactants are less toxic. Nonionic surfactants with higher HLB value are preferred for formulation of SEDDS. Ethoxylated polyglycolyzed glycerides & tween 80 are the most commonly used surfactants. The concentration of surfactant in self emulsifying systems varies from 30-60% w/w of the formulation in order to prepare & maintain emulsion state in the GIT but higher concentration of surfactant may cause local irritation in the GI tract as well as moderate reversible changes in intestinal wall affecting its permeability. The surfactants being amphiphilic in nature can solubilize higher quantities of hydrophobic drug. Some of the surfactants used in the marketed preparations are given in the table 2. Various surfactant used with drugs in SEDDS are shown in table 3.[1]

Table 2: Type of surfactants used in marketed SEDDS

Surfactant	Marketed Product	Drug
Span 80,Tween 80	Gengraf soft gelatin capsule	Cyclosporine
Tween 20	Targretin Hard gelatin Capsule	Bexarotene
Cremophor RH 40	BCNU self emulsifying implant	Carmustine
D-alpha Tocopheryl Poly ethylene Glycol 1000 Succinate (TPGS)	Agenerase Soft Gelatin capsule, Agenerase oral solution	Amprenavir
Labrafil M 1944 CS	Sandimmune oral solution.	Cyclosporine

Table 3: Type of surfactants used with different drugs in SEDDS

Surfactant	Drug
Tween 80	Ketoprofen, Carvedilol
TPGS	Tacrolimus
Labrafil M 1944 CS	Probucol
Tween 85	Indomethacin
Cremophor EL	Loratadine

❖ **Co solvents /Co-surfactants[1]**

Generally high surfactant concentrations (usually greater than 30% w/w) are required for formulation of SEDDS. Organic solvents such as ethanol, propylene glycol, glycerol, polyethylene glycol, aids in dissolving large amount of either the drug in hydrophilic surfactants or the lipid base. These solvents also act as co-surfactant in the micro emulsion systems. It has been observed that

drug release from the formulation improves with increasing amount of co-surfactant. Alcohol & other volatile solvents used in the conventional self emulsifying formulations migrate into shells of capsules resulting precipitation of lipophilic drug.

Table 4: Type of Co surfactants used in marketed SEDDS

Co surfactants	Marketed preparation
Poly Ethylene Glycol	Targretin soft gelatin Capsule, Gengraf hard gelatin capsule, Agenerase soft gelatin capsule
Glycerin	Sandimmune soft gelatin capsule
Propylene glycol	Neoral soft gelatin, Neoral oral solution, Gengraf hard gelatin, Lamprene soft gelatin capsule.
Ethanol	Neoral Soft gelatin & Neoral oral, sandimmune soft gelatin & oral sol, gengraf hard gelatin capsule

MECHANISM OF SELF-EMULSIFICATION

According to Reiss, the energy required to increase the surface area of the dispersion for self-emulsification process bear less importance when compared to the entropy change that favors dispersion. Self emulsifying process is related to the free energy. That is free energy of the conventional emulsion is a direct function of the energy essential to create a new surface between the oil and water phases and can be described by the equation:

$DG = S\ N_1 p\ r_1^2 s$

Where, DG is the free energy related to the process,
N is the number of droplets of radius r
s is the interfacial energy.

The emulsion is stabilized by emulsifying agents only after the two phases of emulsion is separated with respect to time to reduce the interfacial area. The emulsifying agent forms a monolayer of emulsion droplets, and hence reduces the interfacial energy, and providing a barrier to avoid coalescence. In the case of self-emulsifying systems, the free energy required to form the emulsion is either very low and positive, or negative. Emulsification requires very little input energy involves destabilization through contraction of local interfacial regions.[8]

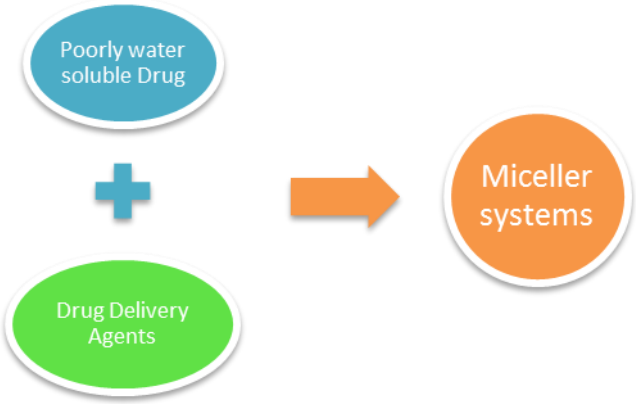

Figure 1: Self-Emulsifying Drug Delivery Systems.

Self emulsifying processes are related to the free energy, ΔG given by[1, 14]

$$\Delta G = \Sigma N \pi r^2 \sigma$$

Where, N = Number of droplets with radius r
σ = Interfacial energy

It is apparent from the above equation that spontaneous formation of interface between oil & water phase is not favorable due to higher energy level.

Groves & Mustafa developed a method of quantitatively assessing the ease of emulsification by monitoring the turbidity of oil-surfactant system in aqueous system, using phosphate nonylphenoxylate (PNE) and phosphate fatty alcohol ethoxylate (PFE) and suggested that emulsification process may be associated with the ease with which water penetrates the oil-water interface, with formation of liquid crystalline phase resulting in swelling at interface, thereby resulting in greater ease of emulsification.

Pouton has said that the emulsification capacities of surfactant may be related to phase inversion behavior of the system. If one increases the temperature of the oil in water system which is stabilized by using non-ionic surfactants, the cloud point of the surfactant will be reached followed by phase inversion. The surfactant is highly mobile at phase inversion temperature due to

which o/w interfacial energy is minimized leading to a reduction in energy required for emulsification.[1]

As a result of the liquid crystal interface formation surrounding the oil droplets, the SEDDS become quite stable to coalescence.[2]

TYPES OF SEDDS[1]

On the basis of the water solubility of components, SEDDS can be classified as shown in Figure 2.

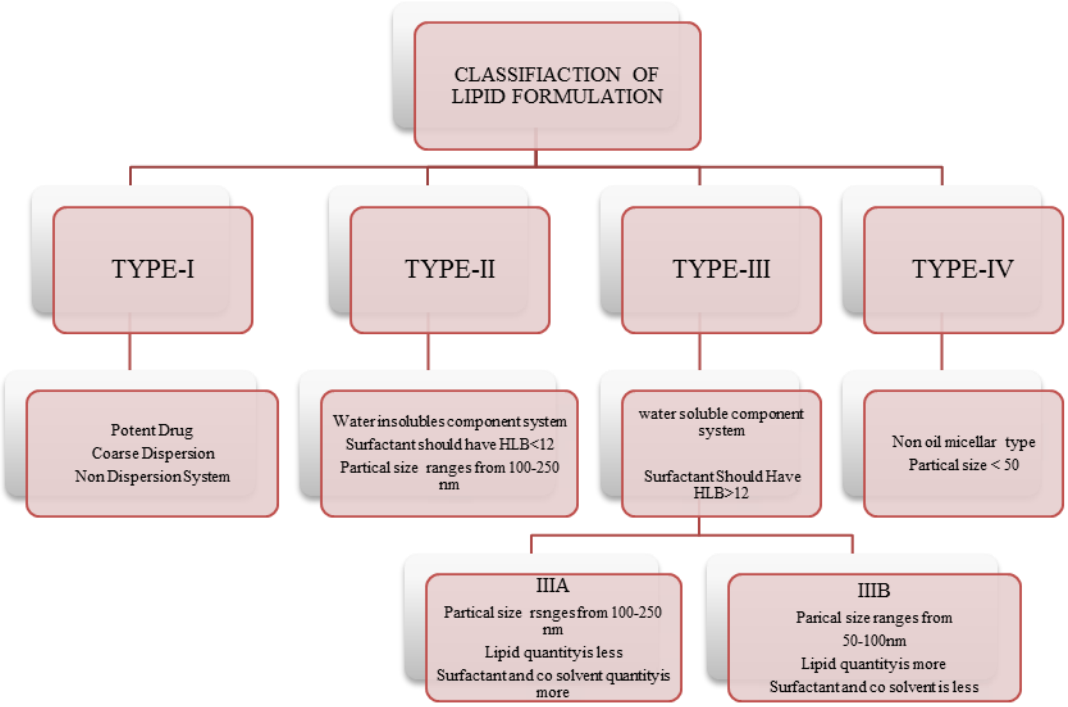

Figure2: Lipid formulation classification system (LFCS)

(A) Non-water soluble Component Systems[1]

These systems are isotropic mixtures of lipids & lipophilic surfactants having HLB value less than 12 that self emulsify to form fine oil in water emulsion in aqueous medium. Self emulsification is generally obtained at a surfactant level above 25% w/w. But at a surfactant level of 50-60% w/w the emulsification process may be compromised by formation of viscous liquid crystalline gels at the oil/water interface. This system is also known as Type-II SEDDS according to lipid formulation classification System (LFCS).Poorly water soluble drugs can be incorporated in SEDDS & encapsulated in capsules (hard or soft gelatin) to produce convenient single unit dosage forms. They are able to generate large interfacial areas which cause efficient partitioning of drug between oil droplets and the aqueous phase. They can overcome the slow dissolution step observed with solid dosage forms.

(B) Water soluble component system[1]

These systems are formulated by using hydrophilic surfactants with HLB more than 12 & co solvents such as Ethanol, Propylene Glycol & Polyethylene glycols. Type III SEDDS are commonly known as self micro-emulsifying drug delivery systems (SMEDDS). Type III formulations can be further divided into type III A & Type III B formulations in order to identify more hydrophilic forms. In Type III B, the content of hydrophilic surfactants and co solvents is increased and lipid content is reduced.[1]

FACTOR WHICH AFFECT SEDDS[4]

❖ Polarity of the Lipophilic Phase

The polarity of the lipid phase is one of the main factors that govern the drug release from the micro-emulsions. The polarity of the droplet is governed by the HLB, the chain length and degree of unsaturation of the fatty acid, the molecular weight of the hydrophilic portion and the concentration of the emulsifier. In fact, the polarity reflects the affinity of the drug for oil and /or water, and the type of forces formed. The high polarity will promote a rapid rate of release of the drug into the aqueous phase. The highest release was obtained with the formulation that had oil phase with highest polarity.

❖ Nature and Dose of the Drug

Drugs which are administered at very high dose are not suitable for SEDDS unless they have extremely good solubility in at least one of the components of SEDDS, preferably lipophilic phase. The drugs which have limited or less solubility in water and lipids are most difficult to deliver by SEDDS. The ability of SEDDS to maintain the drug in solubilised form is greatly influenced by the solubility of the drug in oil phase. As mentioned above if surfactant or co-surfactant is contributing to the greater extent in drug solubilization

then there could be a risk of precipitation, as dilution of SEDDS will lead to lowering of solvent capacity of the surfactant or co-surfactant.[4]

METHOD OF SOLIDIFICATION

There are number of techniques for transformation of liquid & semi-solid SE formulations into solid SEDDS. These techniques are spray drying, spray cooling, melt extrusion and melt granulation, adsorption on to solid carriers and super critical fluid based method.

❖ **Spray Drying**

In this technique, first all formulation having oil, surfactant, drug and solid carrier are sprayed into a drying chamber through a nozzle. The volatile vehicles evaporate leaving behind small solid particles which may be compressed into tablets or filled into capsules. This technique has been used to prepare dry emulsions by removing water from an ordinary emulsion.

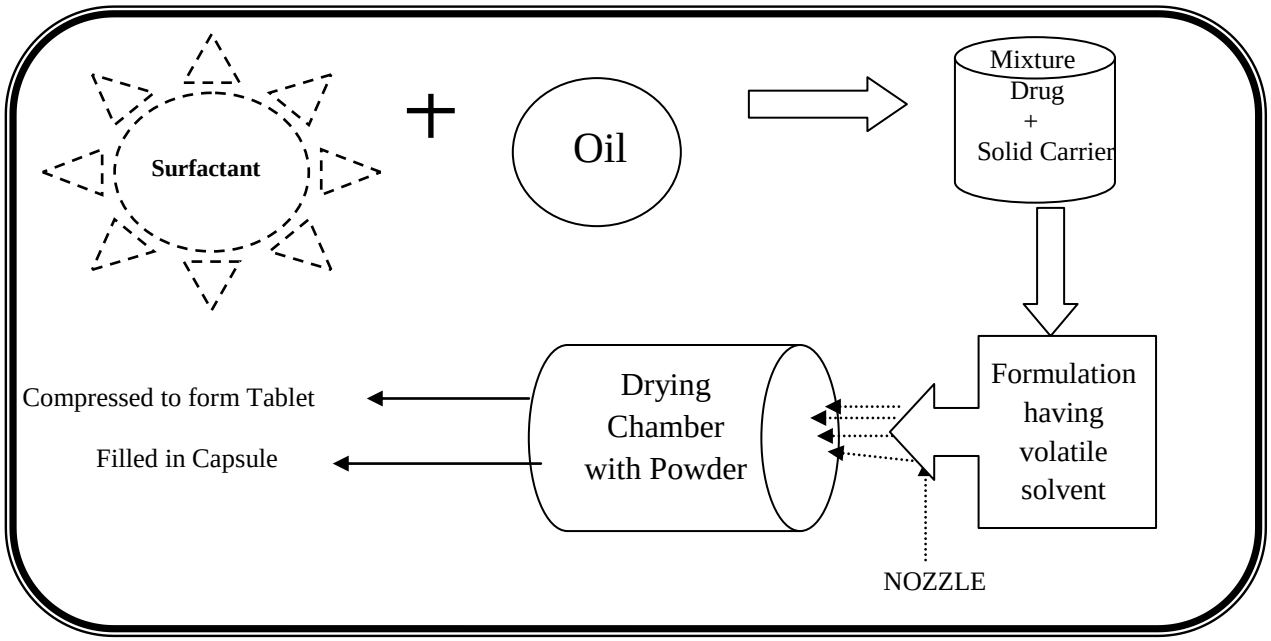

Figure 3: Spray drying technique

❖ **Spray cooling**

The technique spray cooling is also known as spray congealing, where, the molten formulation is sprayed into a cooling chamber. When this molten mixture comes in contact with cooling air, the molten droplets congeal & recrystallize into spherical solid particles which collect into the bottom of the chamber as fine powder. The fine powder may then be used for development of solid dosage from such as capsules, tablets etc. To atomize the liquid mixture & to generate droplets, different atomizers can be used but ultrasonic atomizer is most preferred. The excipients used with this technique are polyoxyl glycerides specially steroyl polyoxyl glycerides, gelucire 50/13. Praziquantel & diclofenac SEDDS have been prepared by using spray cooling technique.

❖ **Melt extrusion/extrusion spheronization**[5]

Melt extrusion is a solvent-free process that allows high drug loading (60%), as well as content uniformity. Extrusion is a procedure of converting a raw material with plastic properties into a product of uniform shape and density, by forcing it through a die under controlled temperature, product flow, and pressure conditions. The size of the extruder aperture will determine the approximate size of the resulting spheroids. The extrusion–spheronization process is commonly used in the Pharmaceutical industry to make uniformly sized spheroids (pellets). The extrusion–spheronization process requires the following steps:

a) Dry mixing of the active ingredients and excipients to achieve a homogeneous powder; wet massing with binder.

b) Extrusion into a spaghetti-like extrudate.

c) Spheronization from the extrudate to spheroids of uniform size.

d) Drying Sifting to achieve the desired size distribution and coating (optional).

❖ **Melt granulation**[5]

Melt granulation is a process in which powder agglomeration is obtained through the addition of a binder that melts or softens at relatively low temperatures. As a ‘one-step’ operation, melt granulation offers several advantages compared with conventional wet granulation, since the liquid addition and the subsequent drying phase are omitted. Moreover, it is also a good alternative to the use of solvent. The main parameters that control the granulation process are impeller speed, mixing time, binder particle size, and the viscosity of the binder. The melt granulation process was usually used for adsorbing SES (lipids, surfactants, and

drugs) onto solid neutral carriers (mainly silica and magnesium aluminometa silicate)

Advantages associated with SEDDS[1, 4, 24, 25, 26]

- Protection of drug from GIT environment.
- Selective targeting of drug toward specific absorption window in GIT.
- Enhanced oral bioavailability.
- Consistent drug absorption profile.
- Better control of drug delivery profiles.
- Versatility of dosage form as can be used with liquids or solids.
- Predictable therapy due to reduced variability including food effects.
- Drug payloads are high.
- Protection of sensitive drug substances.
- Selective targeting of drug(s) toward specific absorption window in GIT.
- Protection of drug(s) from the gut environment.
- Reduced variability including food effects.
- High drug loading efficiency.
- For both liquid and solid dosage forms.

EVALUATION OF SEDDS [1, 28, 29, 30, 32, 33, 34, 35]

A number of tests are carried out for characterization and evaluation of SEDDS.

1. Dispersibility Test

The dispersibility test of SEDDS is carried out to assess its capability to disperse into emulsion and the size of resulting globules to categorize them as SNEDDS. It is carried by using a standard USP dissolution apparatus 2 (Paddle Type). 1 ml of each formulation is added to 500 ml of water at 37 + 0.5 ^{o}C and the paddle is rotated at 50 rpm/ min. On titration with water the SEDDS formulation forms a mixture or gel which is of different type (given in table 5) depending upon which the *in vitro* performance of formulation can be assessed.

Table 5: Type of formulation depending upon visual observation

Mixture/Gel	Type of formulation
Transparent mixture	Micro emulsion
Transparent Gel	Micro emulsion gel
Milky or cloudy mixture	Emulsion
Milky Gel	Emulgel

2. Rheological Properties Determination

The SEDDS system can also be administered in soft gelatin capsules, where, it should have appreciable flow properties for processing. The rheological properties (viscosity, flow, thixotropy, static yield, creep value) of formulation (diluted to 5 % v/v water) are determined by rotational viscometers, digital instruments coupled with either cup and bob or coaxial measuring device. A type of rotational viscometer has also been used for determination of viscosity of fresh as well as other SEDDS formulations which has been stored for longer duration of time. Viscosity determination of liquid SEDDS also indicates whether the system is o/w or w/o, as low viscosity systems are o/w and high viscosity systems are usually w/o in nature. Viscosity of formulation is inversely proportional to dilution.

3. Thermodynamic stability studies

The physical stability of a formulation is very important for its performance as it can be adversely affected by precipitation of the drug in excipients matrix. Poor physical stability of formulation can lead to phase separation of excipients which affects bioavailability as well as therapeutic efficacy. Also the incompatibilities between formulation & gelatin shell of capsule (if formulation filled in capsule) may cause brittleness, softness and delayed disintegration or incomplete release of drug. The following cycles are carried out for these studies).

i) Heating cooling cycle: - Six cycles of cooling and heating between refrigerator temperature (4°C) and elevated temperature (45°C) with exposure at each temperature for not less than 48 hours are carried. Those formulations, which are stable, are then subjected to centrifugation test.

ii) Centrifugation: - Formulations which pass the heating cooling cycle are centrifuged at 3500 r/ min for 30 min. Those formulations that doesn't show any phase separation are taken for the freeze thaw stress test.

iii) Freeze thaw stress cycle:- Three freeze thaw cycles b/w -21° C & 25° C with storage at each temperature for not less than 48 hours. Those formulations which pass this test show good stability with no phase separation, cracking or creaming. The formulations that pass this test are then further taken for dispersibility test for assessment of self emulsification efficiency.

4. Dilution

Emulsions upon dilution with various dissolution media should not show any phase separations or precipitation of drug even after 12 hrs of storage, that formulation is considered as robust to dilution.

5. Turbidimetric Evaluation

Turbidity is a parameter for determination of droplet size and self emulsification time. Fixed quantity of SEDDS is added to fixed quantity of suitable medium (0.1 N HCL or Phosphate Buffer) under continuous stirring at 50 r/ min on magnetic stirrer at optimum temperature and the turbidity is measured using a turbidimeter. Since the time required for complete emulsification is too short, it is not possible to monitor the rate of change of turbidity i.e. rate of emulsification. Turbidimetric evaluation is carried out to monitor the growth of droplet after emulsification.

6. Droplet size Analysis & Particle size Measurements

Photon correlation Spectroscopy (PCS) or dynamic light scattering (DLS) or Laser Diffraction Techniques are used to determine droplet size of emulsion. A number of equipments are available for measurement of particle

size viz. Particle Size Analyzer, Mastersizer, Zetasizer etc which are able to measure sizes between 10 and 5000 nm. In many instances nanometric size range of particle is retained even after 100 times dilution with water which indicates the system's compatibility with excess water.

7. Self Emulsification Time

The self emulsification time is determined by using USP dissolution apparatus II at 50 r/ min, where 0.5 g of SEDDS formulations is introduced into 250 ml of 0.1N HCL or 0.5% SLS solution. The time for emulsification at room temperature is indicated as self emulsification time for the formulation.[31]

8. Zeta Potential Determination

The stability of emulsion is directly related to the charge present on mobile surface, which is termed as zeta potential. Zetasizer, Mastersizer etc are often used to determine zeta potential. The Zetasizer uses light scattering techniques to determine globule size, zeta potential and molecular weight of nanoparticulate systems. The instrument determines size and zeta potential for optimization of stability and shelf life and speeding up the formulation development The SEDDS formulation is generally diluted in a ratio of 1: 2500 (v/v) with distilled water with constant stirring for determination of zeta potential. Zeta potential is calculated according to Helmholtz-Smoluchowski equation-

$U=\varepsilon \xi Ex/\mu$

U =Electrophoretic velocity

ε = permittivity

ξ = Zeta potential

μ = Viscosity

Ex = Axial electric field

9. In vitro Diffusion Study

This study is done to determine release behavior of formulation using dialysis method where phosphate buffer (pH 6.8) is generally used as dialysing medium. One end of the dialysis membrane is tied with a thread and 1 ml of the SEDDS formulation along with 0.5 ml of dialysing medium are filled in the membrane. The other end of membrane is also tied with thread and then allowed to rotate in dialyzing medium at 100 r/ min using magnetic stirrer or dissolution apparatus. Samples are withdrawn at different time intervals and then after suitable dilution are analyzed. Volume of samples withdrawn is replaced with fresh dialysing medium.

10. In vitro Dissolution Technique

The quantitative *in vitro* dissolution studies are carried out to assess drug release from oil phase into aqueous phase by USP type II dissolution apparatus using 500 ml of simulated gastric fluid containing 0.5% w/v of SLS (Sodium Lauryl Sulphate) at 50 r/ min and maintaining the temperature at 37 + 0.5°C. Aliquots of samples are withdrawn at regular intervals of time and volume withdrawn is replaced with fresh medium. Samples taken are then analyzed by using UV spectrophotometer or any other appropriate technique.

11. Refractive Index (R.I.) & Percent transmittance

Refractive Index & percent transmittance are determined to ensure the transparency of formulation. Refractive Index of the formulation is measured by refractometer by placing drop of solution on slide & then compare it with water (R.I=1.333). The percent transmittance of the formulation is measured at a particular wavelength using UV spectrophotometer by using distilled water as blank. If R.I. of formulation is similar to that of water & formulation having percent transmittance is greater than 99%, then the formulation are transparent in nature.

APPLICATION OF SEDDS[4, 17, 18, 19, 20]

- **Improvement in Solubility and Bioavailability**

If drug is formulated in SEDDS, then it increases the solubility because it circumvents the dissolution step in case of Class-II drug (Low solubility/ high permeability). SEDDS formulation enhanced bioavailability due to increase the solubility of drug and minimizes the gastric irritation. In SEDDS, the lipid matrix interacts readily with water, forming a fine particulate oil-in-water (o/w) emulsion. The emulsion droplets will deliver the drug to the gastrointestinal mucosa in the dissolved state readily accessible for absorption. Therefore, increase in AUC i.e. bioavailability and Cmax 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, hydrolytic degradation, or enzymatic 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 degradating environment and the drug.

NOVEL APPROCHES OF SEDDS[1, 6, 8]

In recent years, self-emulsifying and self-micro emulsifying drug delivery systems (SEDDS and SMEDDS) have shown a rational success in improving oral bioavailability of poorly water soluble and Either as liquids or encapsulated in soft gelatin capsules, which have some shortcomings especially in the manufacturing process, leading to high production costs.[6,8]

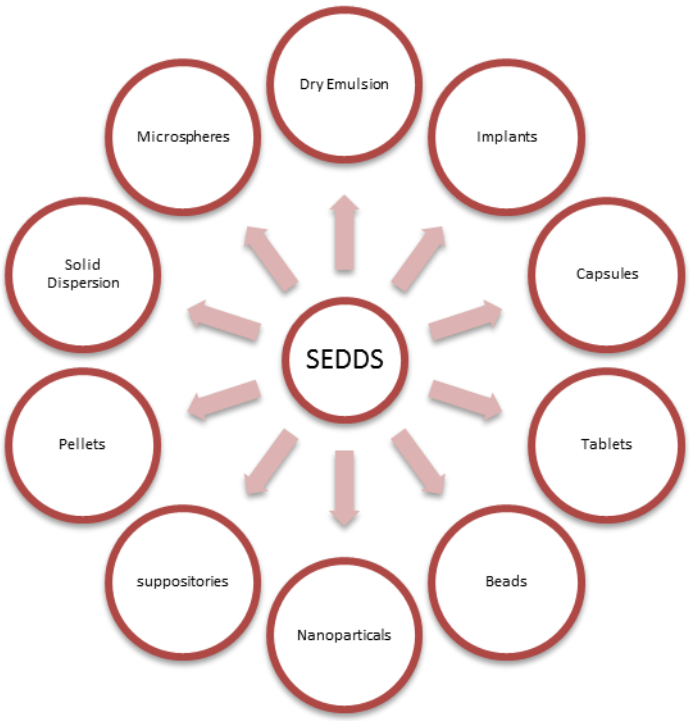

Figure 4: Types of solid SEDDS

❖ **Self Emulsifying Capsules**

Capsule having conventional liquid self emulsifying formulation, upon administration form droplets of micro emulsion spontaneously & then disperse in gastro intestinal tract and yield improved absorption. They however have certain limitations as if irreversible phase separation of micro emulsion takes place, then drug absorption decreases. In such cases, to improve the absorption, sodium dodecyl sulphate is added to SE formulations & super-saturable. SEDDS is formulated by using a small quantity of polymer in the formulation to prevent drug precipitation by generating & maintaining supersaturated state *in vivo*. These formulations contain a reduced amount of surfactant & minimize any gastrointestinal side effects. In the gastrointestinal tract, capsules dissolve to form SES uniformly dispersed to form very fine droplets (in microns) & enhances bioavailability. Another type of SE capsules is solid SES filled into capsule.

❖ **Dry Emulsion**[1]

It is mainly oil in water emulsion, converted into solid by using various techniques such as spray drying, using solid carrier adsorption or freeze drying technique. Dry emulsion may be re dispersed in water before use. These are actually powders in which emulsification spontaneously occurs *in vivo* or after exposure to an aqueous solution. Dry emulsion technology not only avoids the use of harmful or toxic organic solvents but effectively removes the stability problems (such as phase separation, creaming & contamination by micro-organism during storage) related with classic emulsion. MCT (Medium Chain Triglycerides) are generally used as oil phase for these formulations. A new interesting development in this field is newly developed enteric coated dry emulsion formulations which are more appropriate for peptide & protein drugs oral delivery.

❖ **Self Emulsifying Tablets**[1]

Ingredients on the release rate of drug & to evaluate an optimized self nano emulsifying tablet formulation. Prepared nano emulsion was adsorbed on granular materials and then compressed to form tablets. The dissolution profile of optimized self emulsifying tablet showed 80-90% drug release in 45 minutes. Some drug has also been formulated as Self emulsifying tablet using goat fat and Tween 65.

❖ **Self Emulsifying Implants**

The drug carmustine (BCNU) is a chemotherapeutic agent used to treat malignant brain tumours but has short biological half life. Self emulsifying implant was prepared by using tributyrin, cremophor RH 40 & Labrafil 1944 in order to increase the stability of drug and compared its release from PLGA (Poly d, l/lactate co-glycolide) water implants, fabricated into wafers with a flat & smooth surface by compression molding. It was observed that the in vitro half life of BCNU increased upto 130 minutes as compared to 45 minutes with intact BCNU.

❖ **Self Emulsifying Suppositories**

Some investigators have observed that solid SEDDS can not only increase GI adsorption but can also be used to improve rectal and vaginal absorption. Glycyrrhizin given by oral route does not achieve therapeutic plasma concentration but satisfactory therapeutic levels can be achieved by the use of either rectal or vaginal SE suppositories for the treatment of chronic hepatitis.

❖ **Self Emulsifying Beads**

In SE systems, solid dosage forms can be developed by using fewer amounts of excipients i.e. by formation of Beads. Solvent evaporation technique used for deposition of SE system into micro porous polystyrene beads. Porous polystyrene beads are having complex internal void structures. These beads are formed by copolymerization of monomers styrene and divinyl benzene. It is chemically inert, biocompatible and stable over a wide range of pH, temperature & humidity. Geometrical features of porous materials like bead size & pore architecture governs the loading efficiency and *in vitro* drug release from SES loaded porous poly styrene beads.

❖ **Self Emulsifying Nanoparticles**

Self emulsifying nanoparticles can be prepared by using various techniques. One of the techniques is solvent injection method in which molten lipid mass containing lipid, surfactant & drug is injected drop wise into a non-solvent system. Larger particles are removed by filtration and then filtrate is dried to get nanoparticles. By this method, self emulsifying nanoparticles using biodegradable homo lipid with particle size of approximately 100 nm are obtained with loading efficiency of 70-75%. These nanoparticles possessed bioadhesive properties & increased cellular association of the drug.[36]

❖ **Sustained Released Solid Self Emulsifying Drug Delivery System[1]**

(1) Self Emulsifying Microspheres

Formulated solid SE sustained release microspheres using Zedoary Turmeric oil (ZTO), a traditional Chinese Medicine (TCM), as oily phase. ZTO has potent pharmacological actions such as tumor suppression, antibacterial & antithrombotic activity. Quasi emulsion solvent diffusion method involving spherical crystallization was used for the preparation.[37]

(2) Self emulsifying sustained release tablets

A gelled SEDDS has been developed by using colloidal silicon dioxide as gelling agent in order to minimize the amount of solidifying excipients required for conversion of liquid SEDDS into solid SEDDS. Colloidal SiO2 reduces the amount of required solidifying excipients & aids in sustaining release rate of drug. Self Emulsifying (SE) tablet increase the penetration capacity of indomethacin through GI tract mucosal membrane.SE tablets were prepared by using glycerol monolaurate & tyloxapol (a copolymer of alkyl phenol & formaldehyde). A recent advance development in SE tablets is SE osmotic pump tablet of carvedilol.

(3) Self emulsifying controlled release pellet[1]

Pellets are the multiple unit dosage forms which possess a number of advantages over conventional solid dosage forms like ease of manufacturing, reduce the intra & inter subject variability of plasma profiles and also reduce GI irritation without lowering drug bioavailability. SE controlled release pellets were prepared using extrusion/ spheronization by incorporating drugs into SES for enhancing the release rate of drug and coating the pellets with a water insoluble polymer to control the release rate. It revealed that a combination of coating & self emulsification could effectively control *in vitro* release of drug and a range of release rates can be obtained.

SUMMARY AND CONCLUSION

The oral delivery of hydrophobic drugs can be made possible by SEDDSs, which have been shown to substantially improve oral bioavailability. Self emulsifying Drug Delivery Systems are actually mixtures of drug, lipid phase, emulsifier and/or co-solvent. SEDDS are a promising approach for drugs with poor aqueous solubility and hence can be more useful for BCS Class II and IV drugs as upon administration, when the dosage form reaches G.I.T, the SEDDS system take water from its surrounding environment and spontaneously form oil in water emulsion which disperse into fine droplets.

Most importantly SOLID-SEDDS are very flexible to develop various solid dosage forms for oral and parenteral administration. Self-emulsifying drug delivery systems are a hopeful approach for the formulation of lipophilic drugs.

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