



## SELF EMULSIFYING DRUG DELIVERY SYSTEM: AN APPROACH TO IMPROVE ORAL BIOAVAILABILITY OF LIPOPHILIC DRUGS

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### ABSTRACT

Mostly about 35-40% molecules which are pharmaceutical active ingredients (API) having challenging issues regarding Solubility and found to be lipophilic in nature. Those kind of drugs (Lipophilic drugs) having no water solubility or poor solubility in water. Thus, to overcome this challenge now a day's various strategies have been investigated to improve the solubility and oral bioavailability. Among various approach self emulsifying drug delivery system gained more consideration due to enhanced oral bioavailability enabling reduction in dose, improved dissolution rate, temporal profile for absorption window, also discriminating targeting of drug(s) toward specific absorption window in GIT, and protection of drug(s) from the hostile environment in gut. Formulation face up to stability to overcome it in future SEDDS formulation should developed like Solid-SEDDS by converting emulsion to solid using carrier excipients, Developed Formulation should be applicable for large scale/industrial manufacturing because of economically simple technique of improvement of oral bioavailability.

**KEYWORDS:** Self emulsifying drug delivery system, Biopharmaceutical systems, Water insoluble drugs, Solubility enhancement.

### INTRODUCTION

The oral route is the ideal route for chronic drug therapy. Several potent lipophilic drugs reveal low oral bioavailability due to the poor aqueous solubility.<sup>[1]</sup>

Formulation may improve the bioavailability but they are likely to be compromised by their poor membrane permeability. If a class II drug can be maintained in a solubilized state in the lumen of the gut, one can achieve an absorption profile more like that of a class I drug.<sup>[2]</sup>

Self-emulsifying drug delivery systems (SEDDS) have gained disclosure for their ability to increase solubility and bioavailability of poorly water soluble drugs. Generally emulsions are distinguished as concentrated microemulsions, nanoemulsions, or preconcentrates as depends upon the size of globules.<sup>[3]</sup>

SEDDS or self-emulsifying oil formulations (SEOF) are isotropic mixtures of natural or synthetic oils, solid or liquid surfactants or, alternatively, one or more hydrophilic solvents and co-solvents/surfactants.<sup>[4]</sup> Formulation is fine oil-in-water emulsions immediately upon mild agitation, followed by dilution with aqueous solution (e.g. gastrointestinal fluid). SEDDs are called as Self microemulsifying drug delivery systems (SMEDDs)

when the formulation forms transparent microemulsions with oil droplets ranging between 100 to 250 nm.<sup>[5]</sup>

SEDDS has unique property for the lipid based formulation because of their ability to rapidly self-emulsify and form o/w emulsion hence oil dispersed in GI fluid that provide larger interfacial area for enhancing absorption, rate of dissolution and also increasing intestinal epithelial permeability as well as increasing permeability.<sup>[6]</sup>

### Components for SEDDS<sup>[7][8]</sup>

- (1) Natural product oils,
- (2) Semi-synthetic lipid excipients,
- (3) Co-solvents,
- (4) Surfactants/Co-surfactant.

The appropriate quantities of oil phase, surfactant and co-surfactant were selected based on the result of solubility study and Pseudo ternary phase diagram prepare self emulsifying drug delivery system.

### Preparation for SEDDS

Preliminary studies are performed for selection of oil, which is an important and critical requisite for formulation of SEDDS and prepare ternary phase

diagram. Here general processing steps for preparation of SEDDS describe below.

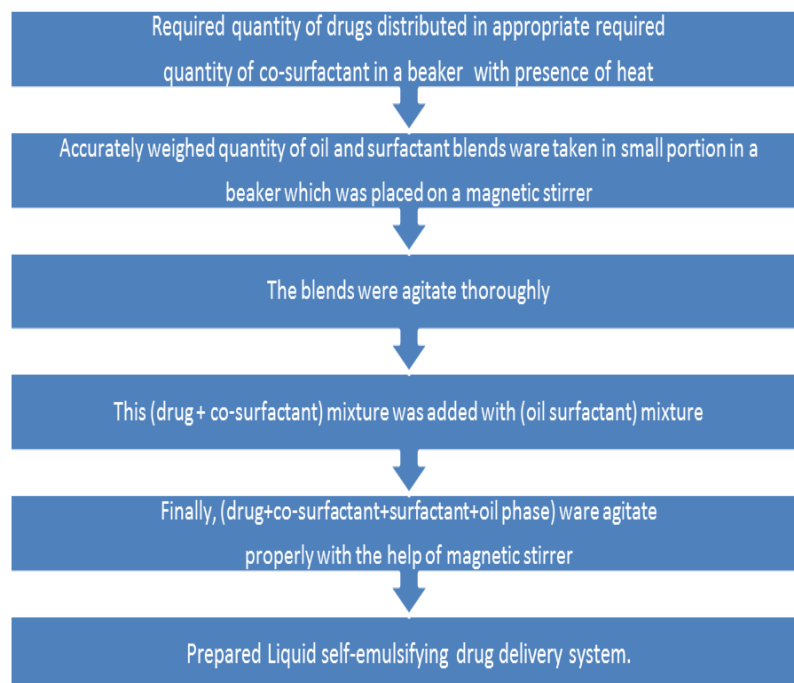


**Figure: 1 Steps for preparation of SEDDS**

## EVALUATION

### 1. Thermodynamic stability studies<sup>[9]</sup>

The physical stability 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, also affecting visual appearance, incompatibilities between the formulation and the gelatine capsules shell can lead to brittleness order formation, delayed disintegration, or incomplete release of drug.

#### Heating cooling cycle

Six cycles between refrigerator temperature (40°C) and 45°C with storage at each temperature of not less than 48 his studied. Those formulations, which are stable at these temperatures, are subjected to centrifugation test.

#### Centrifugation

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

#### Freeze Thaw Cycle

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

### 2. Dispensability test<sup>[9]</sup>

The efficiency of self-emulsification of oral poor microemulsion is assessed using a standard USP XXII dissolution apparatus

2. One millilitre of each formulation was added to 500mL of water at 37±0.50C. 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: Nanoemulsion (Rapidly forming), clear or bluish

Grade B: less clear emulsion (Rapidly forming), bluish white

Grade C: Emulsion (formed within 2 min) Fine milky

Grade D: Emulsion having slightly oily appearance (longer than 2 min) Dull, grayish white

Grade E: Formulation, exhibiting poor or minimal emulsification with large oil globules

Thus, Grade A and Grade B formulation will linger as nanoemulsion when dispersed in GIT. While formulation deteriorating in Grade C could be recommend for SEDDS formulation.

### 3. Turbidimetric Evaluation<sup>[10][11]</sup>

Nepheloturbidimetric evaluation is done to monitor the growth of emulsification. With continuous stirring at ambient temperature fixed quantity of Self emulsifying system is added to fixed quantity of suitable medium (0.1N hydrochloric acid).

#### 4. Droplet Size Analysis Particle Size Measurements<sup>[10][11]</sup>

The photon correlation spectroscopy is useful to measure the droplet size of the emulsions using a Zeta sizer able to measure sizes between 10 and 5000 nm. Lights cattering is monitored at 25=Cata90=angle, after external standardization with spherical polystyrene beads.

#### 5. Viscosity Determination<sup>[10][11]</sup>

By using Brookfield viscometer Viscosity is determined that are rheological properties can be evaluated by the same. Viscosities determination gives conformation regarding system like, If viscosity is low then it is o/w type of the system; If high viscosities then it is w/o type of the system.

#### 6. Electro conductivity Study<sup>[10][11]</sup>

To measure the electroconductive nature of system this test is used. The SEDDS system contains ionic or non-ionic surfactant, oil, and water. so, electroconductometer is used to measure the electroconductivity.

#### 7. Refractive Index and Percent Transmittance<sup>[10][11]</sup>

Transparency of formulation is measured through Refractive index and percent transmittance. By placing drop of solution on slide as well compare with water (1.333) the refractive index is measured by using refractometer. The percent transmittance of the system is measure wavelength using UV-spectrophotometer observance distilled water as blank. If Formulation have percent transmittance >99 percent evidence that refractive index of system is similar to the refractive index of water (1.333). It proved that formulation have transparent in nature.

#### 8. Drug content<sup>[10][11]</sup>

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

#### 9. InVitro Diffusion Study<sup>[10]</sup>

To study the release behaviour of formulation In vitro diffusion studies are performed.

#### Advantages<sup>[12][13]</sup>

- Enhanced oral bioavailability enabling to Reducing the dose of drugs
- Enhance solubility properties as well as dissolution rate profile increase.
- By use of this formulation prepare liquisolid dosage form
- Consistency temporal in absorption of drug, its having selective targeted drug(s) towards the absorption window in GI trac.
- Drug should be protected from hostile environmental condition in gut, also reducing variability including food effects etc.

- SEDDS produce reproducible plasma profile because many of drugs show large inter-subject and intra subject variation in absorption leading to fluctuation in plasma profile.
- High drug pay loads.
- Fine oil droplets empty rapidly from the stomach and promote wide distribution of the drug throughout the intestinal tract and thereby minimizing irritation frequently encountered with extended contact of drugs and gut wall.
- Simple, economical and Effective technique for large scale production having poor soluble drugs for improve bioavailability as comparing to other drug delivery system like solid dispersion, liposomes, nanoparticles etc.

#### Drawbacks<sup>[12][13]</sup>

- Chemical instabilities of drugs can be shown.
- Need of different prototype lipid based formulations to be developed and tested *in vivo* in a suitable animal model.
- The large quantity of surfactant in self-emulsifying formulations (30-60%) irritates.
- Lack of good predicative *in vitro* models for assessment of the formulations these formulations potentially are dependent on digestion prior to release of the drug because Traditional dissolution methods do not work.
- To mimic this, an *in vitro* model simulating the digestive processes of the duodenum has been developed. This *in vitro* model needs further development and validation before its strength can be evaluated.
- Volatile cosolvents in the conventional self-emulsifying formulations are known to migrate into the shell so soft or hard gelatine capsules, resulting in the precipitation of the lipophilic drugs.

#### Future Trend<sup>[14]</sup>

In next of kin to formulation development of poorly soluble drugs, there are 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. By using adsorbents, such as the Neusilin (Fuji Chemicals) and Zeopharm (Huber) products are for converting liquids into powders which can then be processed into powder fill capsules or tablets. For this formulation there is the ratio of SEDDS to solidifying excipients must be very high to obtain solidification as well achieve suitable processing properties which seems to be practically non- feasible for drugs having limited solubility in oil phase. Also an amount of excipients required for transformation in solid dosage forms will be significantly reduced if SEDDS is gelled. Generally Colloidal silicon dioxide (Aerosil200) is selected as a gelling agent which may provide the dual intention of

tumbling the amount of solidifying excipients required and aiding in slowing drug release.

## CONCLUSION

SEDDS is giving a promising approach for improve bioavailability of poorly soluble drugs which are generally BCS class II and IV having poor water solubility. As well also improved dissolution rate, absorption of drugs through absorption window due to developed formulation having fine oil droplet. Technique mostly useful for lipophilic drugs. Now a day's solid self emulsifying drug delivery system is favoured because of also this method is economical and simple in production cost, simplifying industrial manufactures and improving stability as well as patient better compliance.

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