

SELF EMULSIFYING DRUG DELIVERY SYSTEM: A CONVENTIONAL AND ALTERNATIVE APPROACH TO IMPROVE ORAL BIOAVAILABILITY OF LIPOPHILIC DRUGS

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ABSTRACT

Out of newly discovered drugs most of the drugs are found to be lipophilic and out of which up to 40 % of pharmacologically active new molecules failed to reach to market only due to little or no water solubility; a serious challenge for the successful development and commercialization of new drugs in the pharmaceutical industry. Therefore various formulation strategies have been investigated to improve the solubility and the rate of dissolution to enhance the oral bioavailability of lipophilic drugs. Amongst various approaches self emulsifying drug delivery system has gained more attention due to enhanced oral bio-availability enabling reduction in dose, more consistent temporal profiles of drug absorption, selective targeting of drug(s) toward specific absorption window in GIT, and protection of drug(s) from the hostile environment in gut. The present review discussed the mechanism of self emulsification, composition, formulation approaches, different techniques, evaluation, factors affecting SEDDS, advantages, drawbacks, applications and future trends in SEDDS.

Key Words: Self emulsifying drug delivery system, Biopharmaceutical systems, Insoluble drug delivery system, Drug delivery system for lipophilic drugs

Introduction:

The oral route is the preferred route for chronic drug therapy. Numerous potent lipophilic drugs exhibit low oral bioavailability due to their poor aqueous solubility properties. For this class of compounds dissolution in the environmental lumen is the rate controlling step in the absorption process.^[1] Efforts are ongoing to enhance the oral bioavailability of lipophilic drugs in order to increase their clinical efficacy. The most popular approach is the incorporation of the active lipophilic component into inert lipid vehicles ^[2], such as oils ^[3], surfactant dispersions ^[4,5], self-emulsifying

formulations ^[6,7], emulsions ^[8,9] and liposomes ^[10], with every formulation approach having its special advantages and limitations. From these one of the most popular and commercially viable formulation approaches for solving these problems is self-emulsifying drug delivery systems (SEDDS). SEDDS have been shown to be reasonably successful in improving the oral bioavailability of poorly water-soluble and lipophilic drugs.^[11] SEDDS or self-emulsifying oil formulations (SEOF) are defined as isotropic mixtures of natural or synthetic oils, solid or liquid surfactants or, alternatively, one or more hydrophilic solvents and co-solvents/ surfactants.^[12-16]

Upon mild agitation followed by dilution in aqueous

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media, such as gastrointestinal (GI) fluids, these systems can form fine oil-in-water (o/w) emulsions or micro emulsions (SMEDDS). Fine oil droplets would pass rapidly from the stomach and promote wide distribution of the drug throughout the GI tract, thereby minimizing the irritation frequently encountered during extended contact between bulk drug substances and the gut wall. When compared with emulsions, which are sensitive and metastable dispersed forms, SEDDS are physically stable formulations that are and extent of absorption and more reproducible plasma concentration profiles easy to manufacture. An additional advantage of SEDDS over simple oily solutions is that they provide a large interfacial area for partitioning of the drug between oil and water. Thus, SEDDS can be an efficient vehicle for class II to Class IV molecules of biopharmaceutical classification system drugs.^[17]

2. Mechanism of self emulsification:

According to Reiss, 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 conventional 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 equation: In emulsification process the free energy (ΔG) associated is given by the equation:

$$\Delta G = \Sigma N \pi r^2 \sigma \quad [18,19]$$

Where, ΔG is the free energy associated with the process (ignoring the free energy of mixing), N is the number of droplets of radius r and σ represents the interfacial energy. The two phases of emulsion tend to separate with time to reduce 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.^[18,19]

The specificity of surfactant combination required to allow spontaneous emulsification may be associated with a minimization of the phase inversion temperature, there by increasing the ease of emulsion. Phase studies are also necessary for liquid crystal formation in self-emulsification. These indicate that good formulations are usually operating close to a phase inversion region and in a region of enhanced close to a phase inversion region and in a region of enhanced aqueous solubilization.^[18,19]

Mustafa and Groves developed a method of quantitatively assessing the emulsification by monitoring the turbidity of the oil surfactant system in a water stream using phosphated nonylphenoxylate and phosphate fatty alcohol ethoxylate in n hexane and suggested that the 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 the interface, thereby resulting in greater ease of emulsification.^[20] Consequently, the authors were able to relate the phase behavior to the spontaneity of emulsification, with liquid crystals formation, tending to form emulsion more readily, as indicated by the lower equilibration times.^[21] Poton has argued that the emulsification properties of the surfactant may be related to phase inversion behavior of the system.^[22] For example, if one increases the temperature of the oil in the water system stabilized by using non ionic surfactants, the cloud point of the surfactant will be reached followed by phase inversion.^[23] The surfactant is highly mobile at the phase inversion temperature; hence the o/w interfacial energy is minimized, leading to a reduction in energy required to bring about emulsification.^[23]

3. Composition of SEDDSS

The self-emulsifying process is depends on:^[24]

- ❖ The nature of the oil–surfactant pair
- ❖ The surfactant concentration

- ❖ The temperature at which self-emulsification occurs.

3.1 Oils: Oils can solubilize the lipophilic drug in a specific amount. It is the most important excipient because it can facilitate self-emulsification and increase the fraction of lipophilic drug transported via the intestinal lymphatic system, thereby increasing absorption from the GI tract.^[25] Long-chain triglyceride and medium-chain triglyceride oils with different degrees of saturation have been used in the design of SEDDSs. Modified or hydrolyzed vegetable oils have contributed widely to the success of SEDDSs owing to their formulation and physiological advantages.^[26] Novel semisynthetic medium-chain triglyceride oils have surfactant properties and are widely replacing the regular medium-chain triglyceride.^[27]

3.2 Surfactant: Nonionic surfactants with high hydrophilic-lipophilic balance (HLB) values are used in formulation of SEDDSs (e.g., Tween, Labrasol, Labrafac CM 10, Cremophore, etc.). The usual surfactant strength ranges between 30–60% w/w of the formulation in order to form a stable SEDDS. Surfactants have a high HLB and hydrophilicity, which assists the immediate formation of o/w droplets and/or rapid spreading of the formulation in the aqueous media. Surfactants are amphiphilic in nature and they can dissolve or solubilize relatively high amounts of hydrophobic drug compounds. This can prevent precipitation of the drug within the GI lumen and for prolonged existence of drug molecules.^[27]

3.3 Cosolvents: Cosolvents like diethylene glycol monoethyle ether (transcutol), propylene glycol, polyethylene glycol, polyoxyethylene, propylene carbonate, tetrahydrofurfuryl alcohol polyethylene glycol ether (Glycofurol), etc., may help to dissolve large amounts of hydrophilic surfactants or the hydrophobic drug in the lipid base. These solvents

sometimes play the role of the cosurfactant in the microemulsion systems.^[25-27]

4. General formulation approach:

Preliminary studies are performed for selection of oil, which is an important and critical requisite for formulation of SEDDS. SEDDS consisted of oil, a surfactant and a co-surfactant. Solubility of drug is determined in various oils and surfactants. Prepare a series of SEDDS system containing drug in various oil and surfactant. Then, in vitro self-emulsification properties and droplet size analysis of these formulations upon their addition to water under mild agitation conditions is studied. Pseudo-ternary phase diagram is constructed, identifying the efficient self-emulsification region. From these studies, an optimized formulation is selected and its bio-availability is compared with a reference formulation.^[22,28]

SMEDDS are distinguished from SEDDS by the much smaller emulsion droplets produced on dilution, resulting in a transparent or translucent solution. SMEDDS generally contain relatively high concentrations of surfactant (typically 40-60% w/w), and regularly contain hydrophilic co-solvents (e.g. propylene glycol, polyethylene glycols). They are often described as microemulsion pre-concentrates, as the micro-emulsion is formed on dilution in aqueous media^[28]. When developing lipid based formulations the following parameters are believed to be important; The solubility of drug in the formulation as such and upon dispersion (for SEDDS),

- ❖ The rate of digestion (for formulations susceptible to digestion) and possibly.
- ❖ The solubilization capacity of the digested formulation.

Excipient Name	Example of commercial products in which it has been used
Surfactant/Cosurfactant Polysorbate 20 (Tween 20) Poly sorbate 80 (Tween 80) Sorbitan Mono oleate (Span 80) Polyoxy-35-castor oil(Cremophor RH40) Polyoxy-40- hydrogenated castor oil (Cremophor RH40) Polyoxyethylated glycerides (Labrafil M 2125 Cs) D-alpha Tocopheryl polyethylene glycol 1000 succinate	Targretin soft gelatin capsule Gengraf hard gelatin capsule Gengraf hard gelatin capsule Gengraf hard gelatin capsule, Ritonavir soft gelatin capsule Nerol soft gelatin capsule, Ritonavir oral solution Sandimmune soft gelatin capsules AAgenerage Soft gelatin capsule, Agenerage oral solution
Co-solvents Ethanol Glycerin Polypylene glycol Polyethylene glycol	Nerol soft gelatin Capsule, Nerol Oral Solution, Gengraf Hard gelatin Capsule, Sandimmune soft gelatin Capsule, Sandimmune oral solution\ Nerol soft gelatin Capsule, Sandimmune soft gelatin Capsules Nerol soft gelatin Capsule, Nerol Oral Solution, Lamprene soft gelatin capsule, Agenerage Oral solution, Gengraf hard gelatin capsule Targretin soft gelatin capsule, Gengraf hard gelatin capsule, Agenerase soft capsule, Agenerase oral solution
Lipid ingredients Corn oilmono,di.,tri-glycerides DL-alpha-Tocopherol Fractionated triglyceride of coconut oil (medium-chain triglyceride) Fractionated triglyceride of palm seed oil (medium-chain triglyceride) Mixture of mono-and di-glycerides of caprylic/capric acid Medium chain mono-and di-glycerides Corn oil Olive oil Oleic acid Sesame oil Hydrogenated soybean oil Hydrogenated vegetable oils Soyabean oil Peanut oil Beeswax	Nerol soft gelatin Capsule, Nerol Oral Solution Nerol Oral Solution, Fortavase soft gelatin capsule Rocaltrol soft gelatin capsule, Hectrol soft gelatin capsule Rocatrol oral solution Avodat soft gelatin capsule Fortavase soft gelatin capsule Sandimmune soft gelatin capsule, Depakene capsule Sandimmune oral solution Ritonavir soft gelatin capsule, Norvir soft gelatin capsule Marinol soft gelatin capsule Accutane soft gelatin capsule, Vesanoïd soft gelatin capsule Accutane soft gelatin capsule, Vesanoïd soft gelatin capsule Accutane soft gelatin capsule Prometrium soft gelatin capsule Vesanoïd soft gelatin capsule

Table: 1 Example of surfactants, co-surfactant, and co-solvent used in commercial formulations [22,28]

5. Technique of solid SEDDS development:

5.1 Spray drying:[29]

Essentially, this technique involves the preparation of a formulation by mixing lipids, surfactants, drug, solid carriers, and solubilization of the mixture before spray drying. The solubilizedliquid formulation is then atomized into a spray of droplets. The droplets are introduced into a drying chamber, where the volatile phase (e.g. the water contained in an emulsion) evaporates, forming dry particles under controlled temperature and airflow conditions. Such particles can be further prepared into tablets or capsules. The

atomizer, the temperature, the most suitable airflow pattern and the drying chamber design are selected according to the drying characteristics of the product and powder specification.

5.2 Adsorption to solid carriers:[29-32]

Free flowing powders may be obtained from liquid SE formulations by adsorption to solid carriers. The adsorption process is simple and just involves addition of the liquid formulation onto carriers by mixing in a blender. The resulting powder may then be filled directly into capsules or, alternatively, mixed with suitable excipients before compression into tablets. A

significant benefit of the adsorption technique is good content uniformity. SEDDS can be adsorbed at high levels (up to 70% (w/w)) onto suitable carriers. Solid carriers can be microporous inorganic substances, high surface-area colloidal inorganic adsorbent substances, cross-linked polymers or nanoparticle adsorbents, for example, silica, silicates, magnesium trisilicate, magnesium hydroxide, talcum, crospovidone, cross-linked sodium carboxymethyl cellulose and crosslinked polymethyl methacrylate. Cross-linked polymers create a favorable environment to sustain drug dissolution and also assist in slowing down drug reprecipitation. Nanoparticle adsorbents comprise porous silicon dioxide (Sylysia 550), carbon nanotubes, carbon nanohorns, fullerene, charcoal and bamboo charcoal.

5.3 Melt granulation:^[29]

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.

5.4 Melt extrusion/extrusion spheronization:^[33]

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: dry mixing of the active ingredients and excipients to achieve a homogeneous powder; wet massing with binder; extrusion into a spaghetti-like extrudate; spheronization from the extrudate to spheroids of uniform size; drying; sifting to achieve the desired size distribution and coating (optional).

6. Evaluation:

6.1 Thermodynamic stability studies:^[34]

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 (4°C) and 45°C 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°C and +25°C with storage at each temperature for not less than 48 h is done at 3500 rpm for 30 min. Those formulations that do 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.

6.2 Dispersibility test:^[34]

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 ± 0.5

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

6.3 Turbidimetric Evaluation:^[35,36]

Nepheloturbidimetric evaluation is done to monitor the growth of emulsification. Fixed quantity of Selfemulsifying 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).

6.4 Viscosity Determination:^[35,36]

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 viscosities then it is w/o type of the system.

6.5 Droplet Size Analysis Particle Size Measurements:^[35,36]

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.

6.6 Refractive Index and Percent Transmittance:^[35,36]

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.

6.7 Electro conductivity Study:^[35,36]

The SEDD system contains ionoc 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.

6.8 In Vitro Diffusion Study:^[35]

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

6.9 Drug content:^[35,36]

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.

7. Factors Affecting SMEDDS^[37]

7.1 Drugs which are administered at very high dose are not suitable for SMEDDS, unless they exhibit extremely good solubility in at least one of the components of SMEDDS, preferably lipophilic phase. The drugs exhibit limited solubility in water and lipids (typically with log P values of approximately 2) are most difficult to deliver by SMEDDS.

7.2 The ability of SMEDDS to maintain the drug in solubilized form is greatly influenced by the solubility of the drug in oily phase. If the surfactant or cosurfactant is contributing to a greater extent for drug solubilization, then there could be a risk of precipitation, as dilution of SMEDDS will lead to lowering of solvent capacity of surfactant or cosurfactant.

7.3 Equilibrium solubility measurement can be carried out to anticipate potential cases of precipitation in the gut. However, crystallization could be slow in solubilizing and colloidal stabilizing environment of the gut.

7.4 The polarity of lipid phase is one of the factors that govern the release from the micro-emulsion. HLB, chain length and degree of unsaturation of the fatty acid, molecular weight of the hydrophilic portion and concentration of the emulsifier govern polarity of the droplets. In fact, the polarity reflects the affinity of the drug for oil and/or water, and the type of forces involved. The high polarity will promote rapid rate of release of the drug into the aqueous phase.

8. Advantages:^[38,39]

8.1 Enhanced oral bioavailability enabling reduction in dose.

8.2 More consistent temporal profiles of drug absorption.

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

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

8.5 Control of delivery profiles.

8.6 Reduced variability including food effects.

8.7 Protective of sensitive drug substances.

8.8 High drug payloads.

8.9 Liquid or solid dosage forms.

8.10 Poor water soluble drugs give poor dissolution and bioavailability. SEDDS is novel approach to improve water solubility and ultimate bioavailability of lipophilic drugs. The ability of SEDDS to present the drug to GIT in globule size between 1-100 nm and subsequent increase in specific area enables more efficient drug transport through the intestinal aqueous boundary layer leading to improvement in bioavailability.

8.11 Many drugs show large inter-subject and intrasubject variation in absorption leading to fluctuation in plasma profile. Food is major factor affecting therapeutic performance of the drug in the body. SEDDS produce reproducible plasma profile.

8.12 Fine oil droplets empty rapidly from the stomach and promote wide distribution of the drug through out the intestinal tract and thereby minimizing irritation frequently encountered with extended contact of drugs and gut wall.

8.13 Ease of manufacture and scale up is one of the most important advantages that make SEDDS unique, when compared to other drug delivery system like solid dispersion, liposomes, nanoparticles etc., dealing with improved bioavailability. SEDDS require very simple and economical manufacturing facility like simple mixture with agitator and volumetric.

9. Drawback Of SEDDS:^[38,39]

9.1 Lack of good predicative *in vitro* models for assessment of the formulations bcoz Traditional dissolution methods do not work, because these formulations potentially are dependent on digestion prior to release of the drug.

9.2 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.

9.3 Need of different prototype lipid based formulations to be developed and tested *in vivo* in a suitable animal model.

9.4 The large quantity of surfactant in self-emulsifying formulations (30-60%) irritates.

9.5 Volatile cosolvents in the conventional self-emulsifying formulations are known to migrate into the shells of soft or hard gelatin capsules, resulting in the precipitation of the lipophilic drugs.

9.6 Chemical instabilities of drugs.

10 Application:

10.1 Improvement in Solubility and bioavailability:

If drug is incorporated in SEDDS, it increases the solubility because it circumvents the dissolution step in

case of Class-II drug (Low solubility/high permeability). Ketoprofen, a moderately hydrophobic (log P 0.979) nonsteroidal 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 reported complete drug release from sustained release formulations containing ketoprofen in nanocrystalline form. 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.^[40]

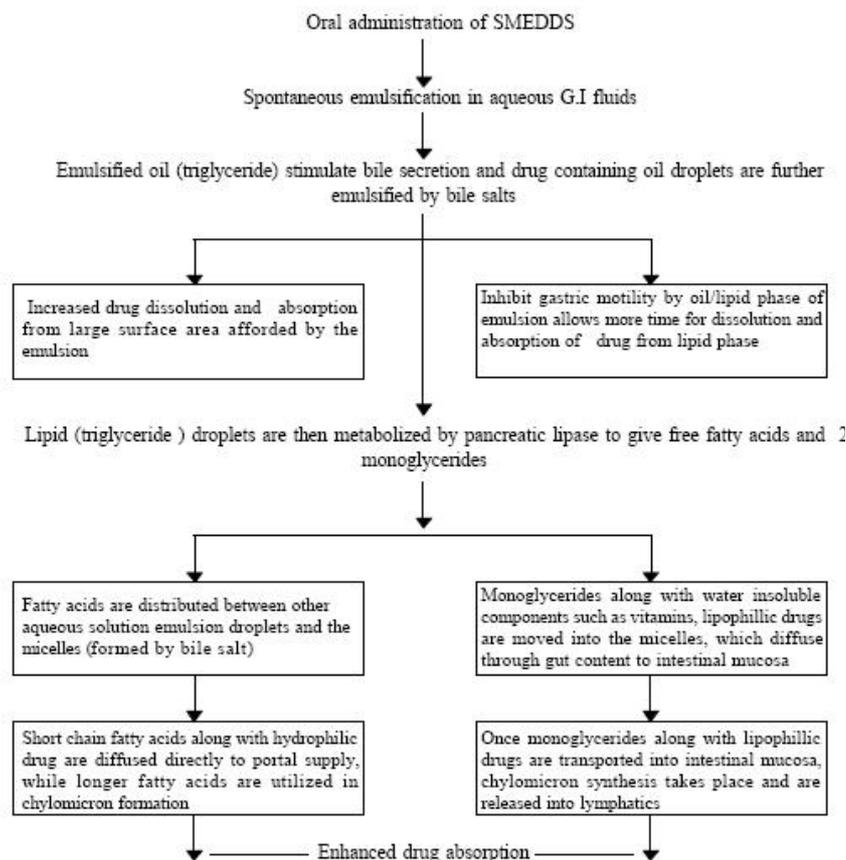


Figure 1: Fate of SMEDDS following oral administration and mechanisms proposed for bioavailability enhancement of drugs^[37]

10.2 Controlling the release of drug:

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^[39] and floating oral ketoprofen systems^[40], and transdermal systems of ketoprofen.^[41]

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. Also incorporation of gelling agent in SEDDS sustained the release of Ketoprofen.^[40-42]

10.3 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 SEDDS formulation has a capacity to protect drugs from degradation in the GI tract.^[42]

Supersaturable SEDDS contain a reduced amount of a surfactant and a water-soluble cellulosic polymer (or other polymers) to prevent precipitation of the drug by generating and maintaining a supersaturated state in vivo. The S-SEDDS formulations can result in enhanced oral absorption as compared with the related self-emulsifying drug delivery systems (SEDDS) formulation and the reduced surfactant levels may minimize gastrointestinal surfactant side effects.^[42]

11. Future Trend^[37]

In relation to formulation development of poorly soluble drugs in the future, there are now 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.

12. Conclusion:

Self emulsifying drug delivery system is promising approach for BCS class II to Class IV drugs. These drug delivery system having a advantages of improved solubility/dissolution, absorption and bioavailability for poorly soluble drugs. This is the method suited for lipophilic drugs where resulting emulsification gives faster dissolution rates and absorption. Recently solid self emulsifying drug delivery system is favoured because of reduction in production cost, simplifying industrial manufactures, and improving stability as well as patient compliance.

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