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SELF-EMULSIFYING SYSTEMS: A REVIEW

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ABSTRACT: Effective delivery of drugs can be made through various routes of administration, and the oral route is considered to be the most convenient for the administration of drugs to patients. Poor aqueous solubility was acknowledged as the main reason for the poor oral absorption of chemical entities. Apart from the conventional solubilization approaches like co-solvency, salt formation, solid dispersion, more recently self-emulsifying drug delivery systems (SEDDS) have been studied in improving the solubility and dissolution rate of poorly water-soluble and lipophilic drugs. SEDDS can be administered orally in soft or hard gelatin capsules or by converting them into tablets using different techniques like adsorption, melt granulation/ extrusion and spray drying for improved stability and ease of administration.

INTRODUCTION: The techniques like solid lipid nanoparticles, nanocrystals, nanosuspensions, solid dispersions, emulsions, microemulsions, nano-emulsions, self-emulsifying system, and liposomes, reported to improve the rate and extent of absorption of BCS class II compounds [1]. Among them, self-emulsifying drug delivery systems (SEDDS) is relatively newer lipid-based technological innovations with immense promise to improve the rate and extent of absorption of poorly water-soluble drugs. SEDDS are anhydrous homo-geneous liquid mixtures, composed of lipids, surfactant, drug and/or co-surfactants/co-solvents, which form transparent and stable microemulsion spontaneously upon aqueous dilution with gentle agitation.

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These formulae owe their self-emulsifying properties to the low free energy requirement for microemulsion formation. Spontaneous formation of microemulsion presents the drug in a dissolved form, and the resultant small globule size provides a large interfacial surface area for drug release and absorption [2, 3, 4]. The oral bioavailability of 6-benzyl-1-benzyloxymethyl - 5 - iodouracil, a novel non-nucleoside reverse transcriptase inhibitor, was increased through the formulation of SNEDD [5]. Increased dissolution rate, bioavailability, and decreased potential side effects reported with SMEDDS formulation of the hydrophobic anti-hypertensive drug, Olmesartan medoxomil [6].

SEDDS are isotropic mixtures of drugs, lipids, and surfactants, usually with one or more hydrophilic co-solvents or co-emulsifiers. Upon mild agitation followed by dilution with aqueous media, these systems can form fine (oil in water) emulsion instantaneously. 'SEDDS' typically produce emulsions with droplet size ranging from a few nanometers to several microns [7, 8]. Self-Emulsifying formulations spread readily in the GI

tract, the digestive motility of the stomach and intestine provide the agitation necessary for self-emulsification [9]. Many excipient combinations are possible to prepare lipid-based formulations and self-emulsifying systems in particular. Pouton established Lipid Formulation Classification System (LFCS) to help stratify formulations. LFCS classifies lipid-based formulations into four types according to their composition and the possible effect of dilution and digestion on their ability to prevent drug precipitation [10]. "Self-micro-emulsifying drug delivery systems" (SMEDDS) indicate the formulations forming transparent microemulsions with oil droplets ranging between 100 and 250 nm providing large interfacial surface area for the drug absorption [11]. SNEDDS is a recent term with the globule size ranging less than 100 nm [3, 12]. Nanoemulsions are optically transparent with high stability against sedimentation and creaming. They possess low viscosity, very high interfacial area, long-term colloidal stability [13].

The self-emulsification process is specific to:

a) Nature of oil used.

b) Nature of surfactant and co-surfactant.

c) The nature of the oil/surfactant pair.

d) The surfactant concentration and oil / surfactant ratio.

e) The temperature at which self-emulsification occurs.

There are many ways to support the fact that only very specific combinations of pharmaceutical excipients and drugs lead to efficient self-emulsifying systems[14]. The composition of SEDDS is given in **Fig. 1** [15].

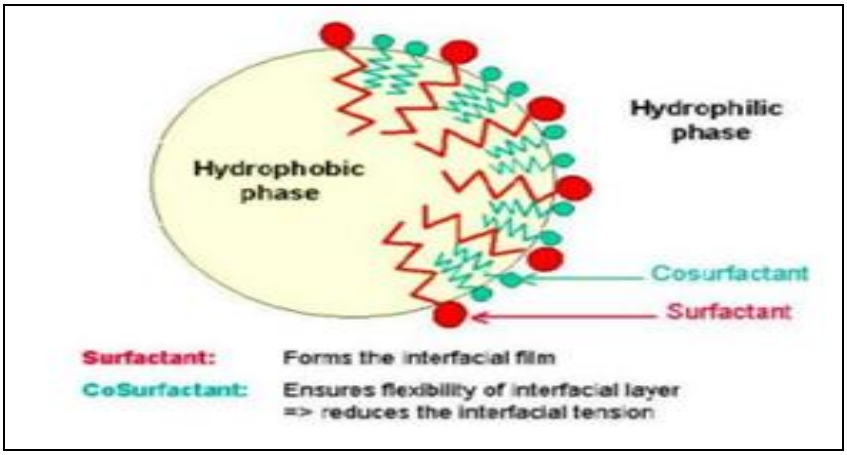

FIG. 1: SEDDS COMPOSITION

Lipids: Lipid is a vital ingredient of SEDDS formulation. It can not only solubilize large amounts of lipophilic drugs or facilitates self-emulsification but also enhance the fraction of lipophilic drugs, which are transported *via* the intestinal lymphatic system, thereby increasing its absorption from the GIT [1, 16]. Novel semi-synthetic medium-chain triglyceride oils have surfactant properties and are widely used replacing the regular medium-chain triglyceride, which is approved for oral administration.

TABLE 1: OILS USED IN SEDDS FORMULATIONS

Category	Examples
Fixed oils (long chain triglycerides)	Soybean oil, sunflower oil, sesame oil, cottonseed oil, castor oil, palm oil, sunflower oil, palm oil
Medium-chain triglycerides and related esters	Miglyol 810, Captex 355, Miglyol 812, Captex 300, Labrafac cc, Triacetin
Medium-chain mono and di-glycerides	Capmul MCM and Imwitor
Long-chain mono glycerides	Paceol, Capmul GMO, Maisine-35
Propylene glycol fatty acid esters	Labrafac-PG, Sefsol-218, Miglyol 840
Fatty acids	Oleic acid, Caprylic acid
Fatty acid esters	Ethyl oleate, Ethyl butyrate, Isopropyl myristate
Vitamins	Vitamin-E
Mineral oil	Liquid paraffin

Long-chain triglyceride, medium-chain triglyceride and natural oils with different degrees of saturation have been used in the design of SEDDS. Modified or hydrolyzed vegetable oils have contributed widely to the success of SEDDS owing to their formulation and physiological advantages [17]. Novel semi-synthetic medium-chain triglyceride oils have surfactant properties and are widely used replacing the regular medium-chain triglyceride, which is approved for oral administration. Some of the oils widely used in SEDDS are given in **Table 1** [18].

Surfactant: Primarily function of a surfactant is to provide the essential emulsifying characteristics to SEDDS. Surfactants, being ampiphilic in nature, invariably dissolve high amounts of hydrophobic drug compounds [1]. Factors that govern the selection of a surfactant are hydrophilic-lipophilic balance (HLB) and safety. The HLB of a surfactant provides vital information on its potential utility in the formulation of SEDDS. SEDDS formulation should contain an emulsifier with high HLB value and high hydrophilicity for attaining high emulsifying performance, *i.e.,* the immediate formation of o/w droplets and rapid spreading of formulation in aqueous media. It would keep drug solubilized for a prolonged period of time at the site of absorption for effective absorption, so precipitation of drug compounds within GI lumen is prevented [19, 20].

Some of industrial nonionic surfactants were screened for their ability to form SEDDS with medium-chain and long-chain triglycerides by Pouton, Porter, and Werkley *et al.*, using subjective visual assessment. Polyoxyethylene surfactants, nonionic, are widely used in most formulations today. Commonly used surfactants with HLB (hydrophilic-lipophilic balance) are given in **Table 2** [19, 20].

TABLE 2: LIST OF COMMONLY USED SURFACTANTS WITH HLB VALUES

Chemical Name	Trade Name	HLB
POE Sorbitan monolaurate	Tween 20	17.0
POE Sorbitan monopalmitate	Tween 40	15.6
POE Sorbitan monostearate	Tween 60	15.0
POE Sorbitan monooleate	Tween 80	15.0
POE Sorbitan tristearate	Tween 65	10.5
POE Sorbitan trioleate	Tween 85	11.0
POE glycerol trioleate	Tagat TO	11.5
POE-40-Hydrogenated castor oil	Cremophor RH40	14.0-16.0

Co-surfactants / Co-solvents: The formulation of an effective SEDDS requires high concentrations of surfactant. Co solvents such as ethanol, propylene glycol, and polyethylene glycol are required to enable the dissolution of large quantities of hydrophilic surfactant. The lipid mixture with higher surfactant and co-surfactant: oil ratios lead to the formation of SMEDDS. Alcohol and other volatile co-solvents have the disadvantage of evaporating into the shell of soft or hard gelatin capsules, leading to precipitation of drugs. Excipients widely used in the SEDDS are given in **Table 3** [18, 19, 21]. Criteria for the design of lipidic system are, drug compound Log P >2 and <4, followed by dose, *i.e.,* low drug dose are the most suitable [22].

TABLE 3: EXCIPIENTS IN FORMULATION OF SEDDS

Lipids	Surfactants	Co-surfactants / Co-solvents
Oleic acid	Tween 80	Propylene glycol
Castor oil	Cremophor RH40	Capmul MCM L8
Capryol 90	Tween 20	Transcutol P
Lemon oil	Cremophor EL	Capmul MCM C8
Soybean oil	Cremophor EL	Capmul MCM C8
Palm oil	Tween 80	Solutol 80
Labrafac	Cremophor EL	Transcutol P

Factors Affecting SEDDS:

- **Nature and Dose of Drugs:** Drugs with high doses are not suitable unless they exhibit good solubility in any one of the components used in the formulation [23].
- **Polarity of the Lipophilic Phase:** Polarity is governed by HLB, the chain length and degree of unsaturation of the fatty acid. High polarity will promote a rapid release rate of the drug [24]. Sang-Cheol chi *et al.,* 2000 observed that the rate of release of idebenone from SEDDS is dependent upon the polarity of the oil phase used. The highest release was obtained with the formulation that had the oil phase with the highest polarity [25].

Mechanism of Self-Emulsification: Self-emulsifying process is related to the free energy, ΔG is given by

$$\Delta G = \Sigma N \pi r2 \sigma$$

Here, N is the number of droplets with radius r and σ the interfacial energy. It is apparent from the

equation that the spontaneous formation of the interface between the oil and water phase is energetically not favorable. The system commonly classified as SEDDS has not yet been shown to emulsify spontaneously in the thermodynamic sense. Mustafa and Groves developed a method of quantitatively assessing the ease of emulsification by monitoring the turbidity of the oil-surfactant system in a water stream, using phosphate nonylphenol ethoxylate (PNE) and phosphate fatty alcohol ethoxylate (PFE) 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, resulting in greater ease of emulsification [19, 20, 26].

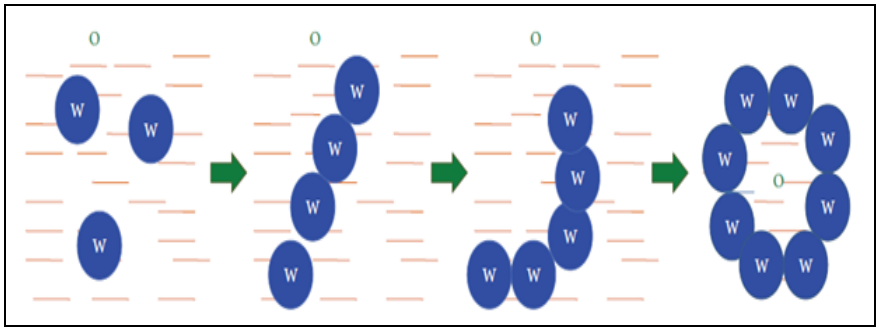

FIG. 2: MECHANISM OF SEDDS FORMULATION AFTER ADDITION OF WATER

Mechanism of SEDDS formulation is given in **Fig. 2** [27]. Pouton has opined that the emulsification properties of the surfactant may be related to phase inversion behavior of the system. 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 [15]. 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. Pouton has suggested that the specificity of surfactant combination required to allow spontaneous emulsification is associated with minimization of phase inversion temperature, thereby increasing the ease of emulsification. Comparative properties of SEDDS, SMEDDS and SNEDDS are given in **Table 4** [28, 29,3 0].

TABLE 4: PROPERTIES OF SEDDS, SMEDDS, AND SNEDDS

Properties	SEDDS	SMEDDS	SNEDDS
Size	>300nm	<250nm	<100nm
Appearance	Turbid	Optically clear	Optically clear
HLB value of surfactant	<12	>12	>12
Classification as per lipid formulation classification system	Type II	Type IIIB	Type IIIB
Concentration of oil	40-80%	>20%	>20%
Concentration of surfactant	30-40%	40-80%	40-80%

Solidification Techniques: Self-emulsifying formulations are usually prepared as liquids. The disadvantages of liquids are high production cost, low stability, difficulty in portability and precipitation of irreversible drugs/excipients. Such systems require the solidification of liquid self-emulsifying (SE) ingredients into powders/ nanoparticles to create various solid dosage forms as SE tablets and SE pellets. S-SEDDS are combinations of SEDDS and solid dosage forms, so many properties of S-SEDDS (*e.g.* excipients selection, specificity and characterization) are the sum of the corresponding properties of both SEDDS and solid dosage forms. Thus, S-SEDDS combines with the advantages of SEDDS (*i.e.* enhanced solubility and bioavailability) and solid dosage forms (*e.g.*, low production cost, convenience of process control, high stability, reproducibility, and better patient compliance). S-SEDDS means solid dosage forms with self-emulsification properties. S-SEDDS focuses on the incorporation of liquid/semisolid SE ingredients into powders/nanoparticles by different solidification techniques (*e.g.* adsorptions to solid carriers, spray drying, melt extrusion, nanoparticles technology. Such powders/nanoparticles, which

refer to SE nanoparticles /dry emulsions/solid dispersions, are usually further processed into other solid SE dosage forms, or, filled into capsules (*i.e.* SE capsules). A detailed account of the techniques used to convert liquid SEDDS into solid SEDDS is given below [2, 14].

Spray Drying: In this technique the formulation is prepared by mixing lipids, surfactants, drug, solid carriers and solubilizing all ingredients before spray drying. The solubilized liquid 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 [19].

Adsorption to Solid Carriers: Free flowing powders may be obtained from liquid SE formulations by adsorption to solid carriers. The adsorption process is simple and involves adding the liquid formulation onto carriers by mixing in a suitable blender. The resulting powder may then be filled directly into capsules or, combined 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)] on to suitable carriers [19].

Melt granulation: It is a process in which powder agglomeration is obtained through a binder that melts or softens at relatively low temperatures. As a 'one-step' operation, melt granulation offers several advantages compared to conventional wet granulation since the liquid addition and the subsequent drying phase are excluded. It is also an excellent 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 is usually used for adsorbing SES (lipids, surfactants and drugs) onto solid neutral carriers (mainly silica and magnesium-aluminum Meta silicate [31].

Melt Extrusion: Melt extrusion is a solvent-free process that allows high drug loading (60 %) as well as content uniformity.

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 [31].

Method of Preparation:

Solubility Studies of Drugs in Various Oils, Surfactants and Co-surfactants / Co-solvents: Solubility of drug measured in various oils, surfactants, co-surfactant, water and buffers (different pH media) [32, 33]. An excess amount of the drug is added to each of the selected vehicle (2 ml), and the mixture is stirred for 5 min in Cyclomixer and further in Water bath shaker for 72 h at 37 ºC followed by centrifugation for 15 min at 3000 rpm. From supernatant 1 ml is diluted with methanol to 10 ml, and its absorption measured by UV Spectrophotometer [34, 35, 36].

Construction of Ternary Phase Diagram: Based on the observations of solubility studies, a series of self-emulsifying systems with varying concentrations of oil (10-40%) and S-mix (a mixture of both surfactant and Co-surfactant 10-80%) were taken. S-mix was prepared in different ratios of (1:1, 2:1, 3:1, 4:1, 1:2) of surfactant and Co- surfactant respectively [37, 38]. Selected S-mix ratios then combined with oil in different ratios of Oil-S-mix such as 1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2 and 9:1 respectively [39]. The samples were vortexed until homogenous oily liquid mixtures are obtained. Each sample is then diluted with purified water. Samples that could easily spread in water and form a fine emulsion are considered in the microemulsion / nanoemulsion regions and kept for 2 h and the transmittance is determined at 638 nm using UV–visible spectrophotometer.

The self-emulsifying performance of the samples was visually observed for 24 h. Samples that showed drug precipitation or cracking are rejected. Ternary phase diagram can be plotted using Origin pro 8, Sigma plot, and Chemixschool. Finally, an appropriate percentage of oil and S-Mix are selected for preparation of SEDDS formulation [40, 41, 42]. Visual grades used to assess the clarity of the diluted solution are given in **Fig. 3** [43]. An example for a ternary phase diagram is given in **Fig. 4** [44].

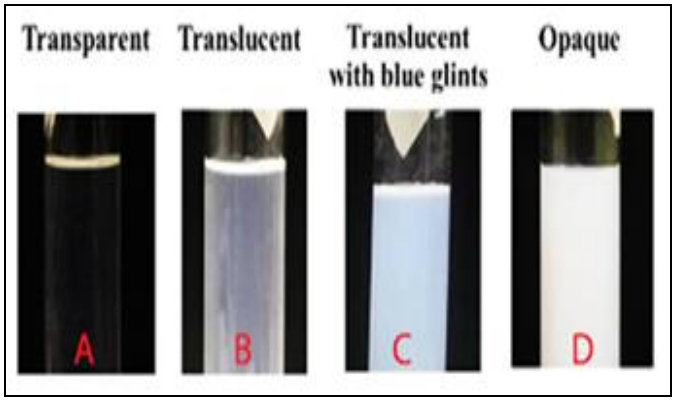

FIG. 3: VISUAL GRADES USED TO ASSESS THE CLARITY OF THE SOLUTION

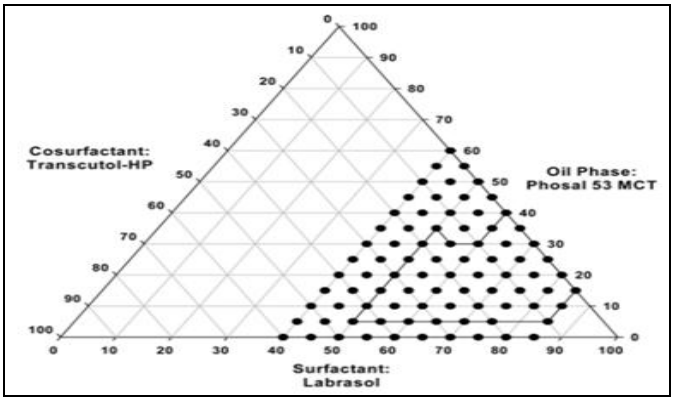

FIG. 4: TERNARY PHASE DIAGRAM WITH OIL, SURFACTANT AND CO-SURFACTANT AND EMULSIFYING REGION

Preparation of Self-Emulsifying Formulation with Drug: Once the Self-Emulsifying region was identified, the desired component ratios of Self-Emulsifying formulations were selected for drug incorporation and further optimization [43, 45].

Drug with required dose is added in an accurately weighed amount of oil into a screw-capped glass vial and heated in a water bath at 40 ºC [46, 47]. The Surfactant and Co-surfactant are added to the oily mix using pipette and stirred with a magnetic stirrer [48, 49].

The formulation is sonicated for 15 min and stored at room temperature for subsequent studies [47, 50].

Characterization of Sedds:

Self- Emulsification Time / Visual Assessment: Self-Emulsification time of SEDDS is estimated by type II USP dissolution apparatus [51, 52]. From each formulation, 500 mg is added dropwise into 500 ml distilled water maintained at 37 ± 0.5 ºC and at 50 rpm. The resulting mixture is evaluated for precipitation and phase separation for 12, 24, 48 h) are given in **Table 5** [53].

TABLE 5: GRADING BY VISUAL ASSESSMENT OF SELF-EMULSIFYING FORMULATIONS

Grade	Dispersibility	Appearance	Self-Emulsification time
A	Rapid emulsification	Clear or slightly bluish	<1min
B	Rapid emulsification	Slightly less clear and bluish-white	<2min
C	Slow emulsification	Bright white emulsion	>3min
D	Slow emulsification	Dull, grayish-white emulsion slightly oily	>3min
E	Poor or minimal emulsification	Large oil droplets present on the surface	>3min

Grade A and Grade B formulations will remain as nanoemulsions when dispersed in the GIT, while formulations falling in grade C could be recommend for SEDDS formulation

Phase Separation & Drug Precipitation Study: Drug loaded SEDDS are exposed to 10, 100, and 1000 times with dissolution media like distilled water, 0.1N HCl, and pH 6.8 phosphate buffer solution.

These dilutions are kept for 24 h and observed visually for turbidity, phase separation, and drug precipitation [35, 54, 55].

Centrifugation Test: The liquid SEDDS preparation is diluted 1:100 ratio with distilled water and centrifuged (5000 rpm for 30 min) for observing the changes in the homogeneity of nanoemulsion. In this method, formulations are diluted with distilled water and centrifuged [35, 55].

Cloud Point Measurement: The formulation is diluted 100 folds with distilled water and kept in a water bath maintained at a temperature of 25 ºC with a gradual increase of temperature at a rate of 5 ºC/ min, and the corresponding cloud point temperatures are read at the first sign of turbidity by visual observation [35, 56].

Freeze-Thaw Cycle: Three freeze-thaw cycles between -21 ºC and + 25 ºC with storage at each temperature for not less than 48 h carried out for the formulations [57].

Percentage Transmission Measurement: The formulation (100 mg) is diluted into 100 ml of distilled water, 0.1 N HCl and pH 6.8 phosphate

buffer solutions. Percent transmission measured by UV spectrophotometer at 628 nm in triplicate [36, 55].

Drug Content Determination: SEDDS equivalent to formulation drug dose is dissolved in the buffer. Drug content is analyzed by UV-spectrophotometer after suitable dilution [36, 58].

Droplet size and PDI Determination: The droplet size of Micro/Nanoemulsion is determined by photo correlation spectroscopy, which analyses the fluctuations in light scattering due to the Brownian motion of particles using a Zetasizer. The formulation is diluted 100 fold with distilled water and stirred for 5 min [59, 60, 61].

Zeta Potential: Zeta potential is used to identify the charge on the droplets. The value of zeta potential indicates the degree of electrostatic repulsion between particles in the dispersion. The higher the zeta potential the more stable is the dispersion preventing aggregation. Zeta potential is determined on zeta meter by diluting the formulation 100 folds with distilled water [62, 63].

Turbidity Measurement: The extent of emulsification is measured at 510 nm using a colorimeter. From SEDDS formulation, 0.5 ml is taken into 250 ml of distilled water in 500 ml flask using magnetic stirrer rotating at a constant speed. The emulsification is done at room temperature [64].

Electro Conductivity Study: SEDDS contain ionic or non-ionic surfactant, oil, and water. This test is used to measure the electroconductive nature of system, and electroconductivity is measured by electro conductometer [65].

Viscosity Determination: The viscosity of the liquid SEDDS determined using Brookfield viscometer at a speed of 15 rpm for 10 min [66].

Refractive Index: The SEDDS formulations diluted 100 folds with distilled water and the refractive index is measured. The formulation is said to be transparent when the refractive index of the system is similar to the refractive index of the water (1.333) [67, 68, 69, 70].

***In-vitro* Drug Dissolution Studies from Liquid SEDDS:** The *in-vitro* dissolution test is performed in 900 ml dissolution medium maintained at 37 ± ºC using USP Dissolution test apparatus II rotating at 50 rpm. The SEDDS formulation (containing an amount equivalent to dose of the drug) is filled in a capsule and drug release studies compared with the pure drug. Samples of 5 ml are withdrawn and replaced with fresh media after 5, 10, 15, 20, 30, 45 and 60 min. Samples are analyzed spectro-photometrically for the drug. Triple measurements are taken for each formulationand data presented as mean ± SD. A graph is plotted with percentage of cumulative drug dissolution at different time intervals versus time [71, 72].

Advantages of SEDDS over Conventional Emulsions:

- **Ease of Formulation:** SEDDS formed by mixing of oils, non-ionic surfactants and co-surfactants/co-solvents. Whereas, conventional emulsions are mixed using two immiscible liquid phases with mechanical shear and surfactant [27, 73].
- **Physical Stability:** SEDDS are physically stable systems. SEDDS before use are clear, isotropic (forming emulsion only *in-situ*) solutions posing no problem of physical stability. Whereas, emulsions are often prone to physical instability when exposed to environmental stress [27, 73].
- **Storage Conditions:** All emulsions need to be stored at specific temperature as emulsion configuration may change at phase-inversion temperature. SEDDS are not very sensitive to small temperature change [27].
- **Packaging:** SEDDS can be filled and sealed in a small soft or hard gelatin capsules as compared to conventional oral emulsions, which need to be packed in larger containers [74, 75].
- **Uniformity in Dose:** Uniformity in dose with emulsion is a factor of discussion and is a challenge to maintain the drug content in droplets and dispersion media. Since SEDDS are presented as soft/hard gelatin capsules or tablets as a unit dosage form, a high level of dose uniformity is assured [74, 75].

- **Convenience in Administration:** The patient can handle a tablet or a capsule easily than teaspoonful or tablespoonful of emulsion, enhancing patient compliance [47].

- **Scale-up:** The manufacturing process for emulsion and suspension need to be monitored, process controls like rate, intensity, and duration of agitation /mixing can be varied.

  One of the advantages of SEDDS over emulsions is in relation to scale up and to manufacture. SEDDS can be manufactured by the most basic mixing equipment as they form spontaneously upon mixing their components under mild agitation and they are thermodynamically stable [74, 75].

CONCLUSION: SEDDS is a promising approach for the formulation of drugs with poor water solubility. The oral delivery of hydrophobic drugs can be made possible by SEDDSs, which have been shown to substantially improve oral bioavailability. This approach has the advantage of pre dissolving the compound, which overcomes the rate-limiting step of particulate dissolution within the GIT. The present review highlighted the development steps *viz.*, solubility study, construction of ternary phase diagram, loading of drug into SEDDS, solidification techniques, and characterization of the liquid-SEDDS. Some of the marketed lipid-based dosage forms are given in **Table 6** [1, 30,] and the recent publications given in **Table 7** [76, 77, 78, 79, 80, 81, 82, 83, 84].

TABLE 6: MARKETED ORAL LIPID-BASED DOSAGE FORMS

Drug	Dosage form	Trade Name
Tretinoin	Soft gelatin capsule, 10 mg	Vasanoid (Roche)
Isotretinoin	Soft gelatin capsule, 10, 20 and 40 mg	Accunate (Roche)
Cyclosporine	Capsule, 50 and 100 mg	Panimumbioral (panacea biotec)
Cyclosporine A	Hard gelatin capsule, 25 and 100 mg	Gengraf (Abbott)
Cyclosporine A	Soft gelatin capsule, 25, 50 and 100 mg	Sandimmune (Novartis)
Lopinavir and Ritonavir	Soft gelatin capsule, Lopinavir 133.33mg and Ritonavir 33.3 mg	Kaletra (Abbott)
Saquinavir	Soft gelatin capsule, 200 mg	Fortovase (Roche)
Tipranavir	Soft gelatin capsule, 250 mg	Aptivus (Borhringeringelheim)
Amprenavir	Soft gelatin capsule	Agenerase (GSK)

TABLE 7: LIST OF RECENT PUBLICATION OF SEDDS

S. no.	Drug	Category	Oil/Surfactant/Co-Surfactant	Author
1	Darifinacin Hydrobromide	SEDDS	Peanut oil, Labrafil M 1944CS, PEG 400	SreeHarsha N *et al.,* (2019)
2	Atorvastatin calcium	SEDDS	Ethyl oleate, Span 80, Tween 80, Transcutol P	Snela A *et al.,* (2019)
3	Sylimarin	S-SEDDS	Cinnamon oil, Tween 20, PEG 200	Mantry S *et al.,* (2019)
4	Gliclazide	SEDDS	Olive oil, Tween 80, Propylene glycol	Balata GF *et al.,* (2018)
5	Rivaroxaban	SNEDDS	Isopropyl myristate, Tween 80, 1,2-propanediol	Xue X *et al.,* (2018)
6	Furosemide	S-SEDDS	Oleic acid, Cremophor RH 40, Ethanol	Renuka J *et al.,* (2018)
7	Rosuvastatin	SNEDDS	Labrafac, Cremophor RH 40, Propylene glycol	Salem HF *et al.,* (2018)
8	Carvedilol	SMEDDS	Velasan, Plurol, Transcutol HP	Silva LA *et al.,* (2018)
9	Olmesartanmedoxomil	S-SNEDDS	Labrafil M 1944CS, Tween 80, PEG 400	Reddy MS, *et al.,* (2018)
10	Docetaxel	SSMEDDS	Oliec acid, Tween 80, PEG400	Bhattacharya S, *et al*., (2018)
11	Budesonide	SEDDS	Capmul MCM L8, Tween 80, PEG 400	Gaikwad NM, et al., (2017)
12	Nimidopine	SMEDDS	Capryol 90, Kolliphor EL, PEG 400	Prajapat MD, *et al.* (2017)
13	Atorvastatin calcium	SNEDDS	Capryol PGMC, cremophor EL, Transcutol HP	Kassem AM, *et al.,(*2017)
14	Atorvastatin calcium	SEDDS	Sunflower oil, Labrasol, Transcutol HP	Akiladevi D, *et al*., (2017)
15	Prednisolone	SMEDDS	Capmul MCM C8, Tween 20, Propylene glycol	Bansode ST, *et al.,* (2016)
16	Lovastatin	S-	Labrafil M 1944CS, Acrysol EL 135,	Bakhle SS, *et al*., (2016)

		SMEDDS	Lauroglycol	
17	Olmesartan Medoxil	S-SNEDDS	Capryol 90, Cremophor RH40, Transcutol HP	Nasr A, *et al.,* (2016)
18	Satranidazole	SEDDS	Oliec acid, Tween 20, PEG 400	Gurav NP, *et al.,* (2015)
19	Glipizide	SEDDS	Phosal 53 MCT, Tween 80, Transcutol P	Agrawal AG, *et al.,*(2015)
20	Darunavir	S-SNEDDS	Capmul MCM C8, Tween 80, Transcutol P	Inugala S, *et al.,* (2015)
21	Valsartan	S-SEDDS	Capmul MCM, Kolliphor HS 15, PEG 400	Sri BU, *et al.,* (2015)
22	Rosuvastatin calcium	SNEDDS	Cinnamon oil, Labrasol, Capmul MCM C8	Balakumar K, *et al.,* (2013)
23	Atorvastatin Clacium	SNEDDS	Sefsol , Cremophor RH 40, Propylene glycol	Belhadj Z, *et al.,* (2013)
24	Lercanidipine HCL	SE Powder	Capryol 90, Tween 80, Capmul MCM C8	Kallakunta VR, *et al*. (2012)
25	Nitrendipine	SSE Pellets	Migliyol 812, Cremophor RH 40, Transcutol P	Wang Z, *et al.,* (2010)

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