Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2016, 8(7):149-157

Review Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Self-emulsifying drug delivery systems for solubility and bioavailability enhancement of poorly water soluble drugs

Ashish Kumar and Arun Nanda

Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, Haryana, India

---

ABSTRACT

Oral delivery of lipophilic drugs having low aqueous solubility presents a major challenge in pharmaceutical product development because these drugs have limited solubility in gastrointestinal fluids and hence have poor absorption and bioavailability. Various pharmaceutical techniques involving chemical modification (e.g. pro-drug, salt formation etc.) or formulation modification (e.g. size reduction, solid dispersion, lipid based drug delivery systems etc.) are available for solubility enhancement of poorly aqueous soluble drugs. The formulation approach is better option than chemical modification approach which may lead to the change in chemical structure which in turn may influence pharmacological activity of drug. Out of various formulation approaches Lipid based drug delivery systems have taken much attention due to their excellent ability to improve the solubility and bioavailability of poorly water soluble drugs and higher degree of biocompatibility. Lipid based drug delivery systems may include emulsions (self emulsifying drug delivery systems), vesicular systems (Liposomes, Neosomes) and particulate system (solid lipid particle). Self emulsifying drug delivery systems are isotropic mixture of natural or synthetic oils, surfactants and/or one or more hydrophilic co-surfactants which upon mild agitation followed by dilution in aqueous media, such as GI fluids, can form fine oil−in−water (o/w) emulsions or microemulsions. Self emulsifying drug delivery systems are gaining popularity in pharmaceutical research and development because of many advantages like reduction in intra-subject and inter-subject variability and food effect, capability to deliver peptides that are prone to enzymatic hydrolysis in GIT, suitable for formulating both liquid and solid dosage form and ease of manufacture and scale-up.

Keywords: Lipophilic, Absorption, Bioavailability, Self emulsifying drug delivery systems

---

INTRODUCTION

Oral route is most acceptable for drug delivery because of ease of administration and good patient compliance. Between 40 - 70 % of new chemical entities inflowing drug development programs have poor water solubility and oral bioavailability of these drugs exhibit inadequate magnitude with high intra- and inter-subject variability [1].

Self-emulsifying formulations have excellent ability to improve the solubility and bioavailability of poorly water soluble drugs. Self-emulsifying formulations are isotropic mixtures of drug, lipids and emulsifiers, usually with one or more of hydrophilic co-solvents/co-emulsifiers. After oral administration, Self-emulsifying formulations spread readily in the GI tract and motility of digestive tract provide the agitation necessary for self-emulsification. Emulsified oil droplets contain the drug in dissolved form and provide increase in specific surface area for absorption and increased bioavailability. Self emulsifying drug delivery system with dispersed oil droplet size

between 100 and 250 nm are termed as microemulsions (SMEDDS) and with oil droplet size less than 100nm is termed as nanoemulsions (SNEDDS) [2]**.**

ADVANTAGES OF SEDDS [3]
Self emulsifying drug delivery system offers following advantages:

- **Improvement of oral bioavailability and reduction in intersubject/intrasubject variability-** Micro or Nano emulsified oil droplets provide drug in dissolved form, increase in specific surface area for absorption, enable more efficient drug transport through intestinal aqueous boundary layer, increase the extent of its transportation via intestinal lymphatic system and avoid pre-systemic first pass effect leading to improved bioavailability and reduction in intersubject/intrasubject variability of severely poorly water soluble drugs.
- **Ease of manufacture and scale-up-**Manufacturing of SEDDS does not require special equipments and manufacturing process is very simple. Hence scale-up from R&D to commercial stage does not pose any difficulty.
- **Ability to deliver macromolecules-** SEDDS can be formulated for macromolecules like peptides, hormones, enzyme substrate/inhibitors and offer protection from enzymatic hydrolysis in GIT.
- **Increased drug loading capacity-** Different types of lipids, surfactants and co-surfactants available offer high solubility for drug and hence high drug loading capacity.
- **Ease of formulation-** SEDDS can be formulated easily as liquid, semisolid and solid dosage forms.

1. MECHANISM OF SELF EMULSIFICATION
Self-emulsification occurs when the entropy change favoring dispersion is greater than the energy required to increase the surface area of the dispersion [4]. The free energy of a conventional emulsion formulation is a direct function of the energy required to create a new surface between the oil and water phases. The thermodynamic relationship for the net free energy change is described by equation below.

$$\Delta G = \Sigma N_i 4\pi r_i^2 \sigma$$

Where, ΔG is the free energy associated with the process, r_i is the radius of droplets, N_i is the number of droplets, σ is the interfacial energy. The two phases of the emulsion tend to separate with time to reduce the interfacial area and thus, minimize the free energy of the system(s). Emulsifying agents stabilize the emulsions by forming a monolayer around the emulsion droplets, reducing the interfacial energy and forming a barrier to coalescence. On the other hand, emulsification occurs spontaneously with SEDDS, as the free energy required to form the emulsion is low, whether positive or negative [5]**.** The interface between the oil and aqueous continuous phases is formed upon addition of a binary mixture (oil/non-ionic surfactant) to water. This is followed by solubilization within the oil phase, as a result of aqueous penetration through the interface. Invariably, this tends to occur until the solubilization limit is attained close to the interphase. Further, aqueous penetration will lead to the formation of the dispersed liquid crystal phase. Ultimately, everything that is in close proximity with the interface will be liquid crystal, the actual amount of which depends upon the emulsifier concentration in the binary mixture. Hence, following gentle agitation of the self-emulsifying system, water rapidly penetrates into the aqueous cores leading to interface disruption and droplet formation.

2. CLASSIFICATION OF SEDDS
SEDDS can be classified on the basis of oil, surfactant, co-surfactant/co-solvent content and resulting droplet size of emulsion. Table 1 indicates the fundamental differences between types I, II, III and IV formulations [6].

Table 1: Types of SEDDS Formulations

Constituents/Attributes	Type I	Type II	Type-IIIA	Type-IIIB	Type-IV
Triglycerides or mixed glycerides	100%	40-80%	40-80%	<20%	-
Water insoluble emulsifier	-	20-60%	-	-	0-20%
Water soluble emulsifier	-	-	20-40%	20-50%	30-80%
Hydrophilic cosolvents	-	-	0-40%	20-50%	0-50%
Particle size of dispersion (nm)	Coarse	100-250	100-250	50-100	-

3. COMPONENTS OF SEDDS:
The SEDDS consist of following components:

- **OILS**

Oil is required to dissolve lipophilic drug, facilitate self emulsification and to improve fraction of lipophilic drug transported via intestinal lymphatic system, thereby increasing absorption from GI tract. Oils are generally obtained from natural sources and are thus prone to variability in composition such as fatty acid chain length and degree of unsaturation. Long chain triglycerides are derived from vegetable sources such as soyabean or safflower oil, where as medium chain triglycerides are obtained by re-esterificiation of fatty acids with glycerine. Many synthetic lipids are also available in which the glycerol backbone have been replaced by propylene glycol and/or polyethylene glycols. Additionally, the degree of esterification of the fatty acid moiety may vary, forming mono-, di- and tri-glyceride with esters of propylene glycol and polyethylene glycols [7,8,9]**.** Commonly used oils are listed in table 2.

Table 2: Commonly used Oil Constituents in the Formulations of SEDDS [10, 11, 12]

Excipient	Trade Name	Melting point(°C) / Physical State	HLB
Glyceryl mono- and dicaprylate	Capmul MCM C-8 (Abitec Co)	20-25	3-4
Glyceryl mono- and dicaprylate/caprate	Capmul MCM (Abitec Co)	25-30	3-4
Glyceryl tricaprylate/ caprate/ linoleate	Captex 810D (Abitec Co) Miglyol 818 (Sasol)	Liquid	-
Glyceryl monoleate	Capmul GMO (Abitec Co)	24	3
Glyceryl monostearate	Campul GMS-50K (Abitec Co)	57	3-4
PEG-6 glyceryl oleate	Labrafil M 1944 CS (Gattefosse)	Liquid	3-4
Polyglyceryl-3 dioleate	Plurol oleique CC497 (Gattefosse)	Liquid	6
Glyceryl mono- and dicaprate	Capmul MCM C-10 (Abitec Co)	40-41	-
Glyceryl tricaprylate/ caprate (medium chain triglycerides)	Neobee 1053 (Stepan),Captex 300 (Abitec Co)	-5	1
Glyceryl dilaurate	Stepan GDL (Stepan)	30	4
Polyglyceryl-6 octastearate	Caprol ET (Abitec Co)	38	2.5

- **SURFACTANTS**

Surfactants tend to accumulate at a surface or interface of oils. Surfactants are formed by two parts, one is hydrophobic and other is hydrophilic. They are categorized by their Hydrophilic-Lipophilic Balance (HLB) number, with a low value (≤10) corresponding to greater lipophilicity and a higher value (≥10) corresponding to higher hydrophilicity. The addition of surfactants improves ability of oil to accommodate a hydrophobic drug in solution and disperse the liquid vehicle on dilution in gastrointestinal fluid. Hence, the drug is present in fine droplets of the oil / surfactants mixture which spread readily in the gastro-intestinal tract [13, 14]**.**

Non-ionic surfactants are less toxic than ionic surfactants but non-ionic surfactant may lead to reversible changes in the permeability of the intestinal lumen. Usually the surfactant concentration ranges between 30-60% w/w in order to form stable SMEDDS. There is a relationship between the droplet size and the concentration of the surfactant, increasing the surfactant concentration could lead to droplets with smaller mean droplet size. Commonly used Surfactants are listed in table 3.

Table 3: Popular surfactants Employed in the SEDDS Formulations with their HLB Values [10,11,12]

Chemical Name	HLB	Commercial/ Brand Name	Manufacturer
PEG-6 apricot kernel oil	4	Labrafil M 1944 CS	Gattefosse
PEG-8 caprylic/capric glycerides	14	Labrasol	Gattefosse
Polyoxyethylene-polyoxypropylene copolymers	18-23	Pluronic F 127	BASF
PEG-20 sorbitan monooleate	15	Tween-80	Atlas/ ICI
PEG-20 sorbitan trioleate	11	Tween-85	Atlas/ ICI
PEG-20 sorbitan monolaurate	17	Tween20	Atlas/ ICI
PEG-25 trioleate	11	Tagat TO	Goldschmidt
PEG-35 castor oil	12-14	Cremophor-EL	BASF
PEG-40 hydrogenated castor oil	13	Cremophor RH40	BASF
Sorbitan monooleate	4.3	Span 80	Atlas/ ICI
Methyl-oxirane polymer with oxirane	12-18	Pluronic L-64	BASF
Ethoxylated castor oil	12-15	Emulphor El-620	Rhodia

- **CO-SURFACTANTS**

For manufacture of optimum SMEDDS, high concentration of surfactants is required in order to reduce interfacial tension sufficiently, which can be harmful, so co-surfactants are used to shrink the concentration of surfactants. Co-surfactants together with surfactants afford sufficient litheness to interfacial film to take up different curvature required to form microemulsion over a wide range of compositions. Organic solvents like ethanol, propylene glycol,

polyethylene glycol are able dissolve large amounts of either drug or hydrophilic surfactant in lipid base. Alternatively alcohol or other volatile co-surfactant have disadvantage that by evaporation they get entered in to soft/hard gelatin capsule shell resulting in precipitatation of drug [15].

Newer cosolvents like Transcutol™ and Glycofurol™ have several stellar advantages over the traditional ones, including better stability and less volatility [16]**.**

4. FORMULATION DEVELOPMENT OF SEDDS

Following steps should be considered for formulation of SEDDS [3, 17].

- To determine solubility of drug in different oils, surfactants and cosurfactants
- To select oil, surfactant and cosurfactant based on the solubility of drug
- To construct Pseudo ternary phase diagram for mapping optimal range for oil, surfactant and cosurfactant. Mix surfactant and co-surfactant in different weight ratio to prepare various Smix. For each phase diagram mix oil and specific Smix in different weight ratio. Develop Pseudo-ternary phase diagram for each Smix using aqueous titration method. Perform slow titration with aqueous phase for each weight ratio of oil and Smix and visual observation is carried out for transparent o/w micro emulsion. The physical state of the micro emulsion is marked on a pseudo-three-component phase diagram with one axis representing oil phase, the other representing surfactant and the third representing a co-surfactant.

- Formulation optimization and evaluation of SEDDS in selected range of oil, surfactant and cosurfactant.

5. EVALUATION OF SEDDS:

Following are general characterization methods used for evaluation of SEDDS.

- **Phase separation and clarity studies** [18, 19, 20]: The emulsions are centrifuged (usually between 13000 and 15000 rpm) for a specified time period and subsequently stored at different temperatures (like 5, 15, 25 and 37°C). Phase separation and turbidity are observed.
- **Self emulsification characterization** [6, 21, 22]: One milliliter of each formulation is added to 500 mL of water at 37 ± 0.5°C. A standard stainless steel dissolution paddle rotating at 50 rpm tends to provide gentle agitation. The *in-vitro* performance of the formulations is visually assessed from such dispersion, using a suitable grading system. A grading system has been reported to be based upon the formation of a microemulsion (o/w or w/o), microemulsion gel, emulsion or emulgel.
- **Globule Size and Zeta Potential:** The value of zeta potential, as well as the size of the droplets/globules of the SEDDS formulation, can be measured using diverse techniques like Dynamic Light Scattering (DLS), Static Light Scattering Multi-Angle Light Scattering, Electron Microscopic Studies etc. [12].
- **Turbidity measurement:** It is a relatively crude parameter for estimation of droplet size as well as emulsification time. It is used to determine the rapid equilibrium reached by the dispersion and the reproducibility of this process [23]. Turbidity measurements are carried out on turbidity meters, with the instrument connected to a dissolution apparatus. The optical density of the formulation is recorded periodically (say every 15 sec) to determine the clarity of microemulsion formed as well as the emulsification time, i.e., time required by the formulation to emulsify completely.
- **Drug loading capacity:** Drug from pre-weighed SEDDS is extracted by dissolving in suitable solvent. Analyze Drug content in the solvent extract by suitable analytical method against the standard solvent solution of drug [15].
- ***In-vitro* drug release study:** *In-vitro* dissolution studies are carried out to study the drug release behavior of formulation and to predict the *in-vitro* assessment of bioavailability. Place the SEDDS in dialysis bag during the release period. Withdraw sample solution at predetermined time intervals. Replace equal amount of fresh dissolution medium immediately after withdrawal of the test sample. Filter test sample through suitable membrane filter, dilute suitably if required and analyze by suitable analytical method. Calculate Percent drug dissolved at different time intervals [15].
- ***Digestion Assay***. Lipids and lipid base excipients are subject to digestive process occurring in GIT. Gastric and pancreatic lipase can lipolyze glycerides as well as PEG esters of fatty acids. Lipase may also have an effect on emulsification/dispersion properties of fatty acid esters, altering their solubilization capacity in vivo. Thus digestibility of lipid excipients by lipase should take in to account during development of lipid based formulation. The principle of *in-vitro* digestion assay is to measure the amount of fatty acid released when the formulation is digested in a lipolysis medium.

Ideally test involves two steps:
Gastric phase: 1.5 ml of formulation is introduced in to 36 ml of lipolysis medium at 37°C, pH is fixed at 5.5. The dispersion should be maintained under stirring for 30 min.

Intestinal phase: After 30 min, add 22 ml of lipolysis medium. The pH should be adjusted to 6.25 and maintained constant by addition of NaoH during experiment. Three different conditions are tested:

without enzyme, with the addition of PPL and with addition of inactivated PPL. The agitation should remain for next 60 minutes.

Sample are collected at t=0, 15, 30, 35, 40, 45, 60 and 90 minutes.

Samples are centrifuged and micellar phase is sampled. Drug is then assayed. The amount of solubilized drug is plotted against time. A comparison can be done to see how lipolysis impacts the drug solubilization.

- **Viscosity determination:** The rheological properties of the micro emulsion are evaluated by Brookfield viscometer. Techniques like the diffusing wave spectroscopy (DWS) is particularly interesting. DWS investigates micro rheological properties of a fluid based on the mean square displacement of the particles [15].
- **Robustness to dilution:** Formulations to be subjected to 50,100,250 fold dilution with enzyme free simulated gastric fluid pH 1.2; enzyme free simulated intestinal fluid pH 6.8 and distilled water. The resultant diluted emulsions were observed for any physical changes like coalescence of droplets, precipitation or phase separation after 24 hrs [24].
- **Electron Microscopic Studies:** Freeze-fracture electron microscopy has been used to study the surface characteristics of the SEDDS. Transmission Electron Microscopy (TEM), Cryo-Transmission Electron Microscopy (Cryo-TEM Studies) techniques are used to perform electron microscopic studies [12].
- **Permeation studies:** ***In Situ Single Pass Perfusion Technique (SPIP)*** In this technique, the proximal part of the jejnum, 2-5 cm below the ligament of Trietz is cannulated with a glass cannula and connected to the reservoir [25]. The intestine segment is perfused with blank phosphate buffer (37± 1°C) until perfusate is clear. The intestine is subsequently perfused with drug solution maintained at 37± 1°C at a perfusion rate of 0.2-0.3 ml/min. During the experiment, the animal is kept under a heating lamp, and the exposed abdomen is covered with a cotton pad to minimize dehydration. Steady state is usually achieved within 30 min, following which 4-5 samples are obtained at regular intervals of around 15 minutes. During the experiment, the amount of water entering into the system and water leaving the system is carefully recorded to calculate water flux [26]. Effective permeability (Peff) is calculated after correcting the outlet concentration for water flux on the basis of ratio of weight of perfusion solution collected and infused for each sampling points as mentioned in Equation below.

$$P_{eff} = \frac{Q\left[\frac{C_{in}}{C_{out}} - 1\right]}{2\pi rl}$$

6. SEDDS DOSAGE FORMS [27]

- **Dry emulsions:** Dry emulsions are powders from which emulsion spontaneously occurs in vivo or when exposed to an aqueous solution. Dry emulsions can be useful for further preparation of tablets and capsules. Dry emulsion formulations are typically prepared from oil/ water (O/W) emulsions containing a solid carrier (lactose, malto dextrin, and so on) in the aqueous phase by rotary evaporation, freeze-drying or spray drying
- **Self-emulsifying Capsules:** After administration of capsules containing conventional liquid SE formulations, micro emulsion droplets form and subsequently disperse in the GI tract to reach sites of absorption
- **Self-emulsifying controlled release gel:** In order to reduce significantly the amount of solidifying excipients required for transformation of SMEDDS into solid dosage forms, a gelled SEDDS has been developed. Colloidal silicon dioxide was selected as a gelling agent for the oil based systems, which served the dual purpose of reducing the amount of required solidifying excipients and aiding in slowing down of the drug release
- **Self-emulsifying sustained/controlled release pellets:** Self-emulsifying controlled release pellets incorporates drugs into Self-emulsifying system that enhance their rate of release and then by coating pellets with a water insoluble polymer, the rate of drug release is reduced.

- **Self-emulsifying nanoparticles:** Nanoparticles techniques have been useful in the production of Self emulsifying nanoparticles. Solvent injections are one of these techniques. In this method, the lipid, surfactant, and drugs are melted together, and injected drop wise into a stirred nonsolvent. The resulting Self emulsifying nanoparticles are there after filtered out and dried.

7. APPLICATION OF SEDDS: various researchers have worked on Self emulsifying drug delivery system and work done has been summarized in table 4. Some marketed formulation based on SEDDS have been summarized in table 5.

Table 4 Research work on Self emulsifying drug delivery systems

Drugs	Composition			References
	Lipid	Emulsifier	Co Emulsifier	
Progesterone	Ethyl oleate	Tween 80 and oleylamine	Benzyl alcohol	[28]
Simvastatin	Capryol 90	C-EL	Carbitol, PEG 400	[29]
Flurbiprofen	Capmul PG8	Tween 20 or Cremophore EL	-	[30]
Itraconazole	Transcutol acetate	Pluronic L-64	Transcutol	[31]
Fenofibrate	PEG-8-caprylic/capric glyceride	PEG-4 lauryl ether	PEG-400	[32]
Piroxicam	Labrafil M 1944CS	C-EL	Transcutol P	[33]
Tamoxifen citrate	Maisine 35-1, Caproyl 90	C-RH 40	Propylene glycol	[34]
Zedoary turmeric oil	Ethyl oleate	Tween 80	Transcutol P	[35]
Valsartan	Capmul MCM	Tween 80	PEG 400	[36]
Curcumin	Isopropyl myristate	Cremophor RH40	Ethanol	[37]
Persimmon leaf extract	Labrafil M1944 CS	Cremophore EL	Transcutol P	[38]
Gemfibrozil	lemon oil	Cremophore® EL	capmul MCM C8	[39]
Lovastatin	Capryol 90	Cremophore RH 40	Transcutol P	[40]
Flubiprofen	Labrafil M1944 CS	Labrasol	Transcutol HP	[41]
Carbamazepine	Mygliol	Polysorbate 80	Cremophore RH40	[42]
Puerarin	Castor oil	Cremophore EL	1,2-propanediol	[43]
β-arteether	Ground nut or sesame oil	Tween 80 or cremophore EL	Absolute ethanol	[44]
Amiodarone HCL	Campul C8	Tween 80	Propylene glycol	[45]
Amphotericin B	Capryol 90/capryol PGMC/Lauroglycol 90/Labrafac/Pecol	Tween 20/Tween 80/Tween 85	Span 20/Span 80/Span 85	[46]
Valsartan	Capmul MCM	Cremophore RH 40	1,2-propylene glycol	[47]
Rosuvastatin calcium	Cinnamon oil	Labrasol	Capmul MCM C8	[48]
Rosuvastatin calcium	Capmul MCM,	Cremophor EL	propylene glycol	[49]
Lovastatin	Peceol	Cremophor RH 40	Transcutol P	[50]
AJS (Novel medicative compound against depression)	Castor oil	Labrasol/Cremophore EL	Transcutol HP	[51]
Atorvastatin calcium	Capmul MCM	Tween 20	Tetraglycol	[52]
Rosuvastatin calcium	Capryol 90 and maisine	Tween 20	Lutrol E400	[53]
Acyclovir	Oleic acid	Tween 80	Transcutol P	[54]
Telmisartan	CapmulMCM	Tween 80	Propylene glycol	[55]

Table 5: Marketed Pharmaceutical self emulsifying drug delivery system [12]

Brand name/company	Active ingredient	Dosage form	Excipients
Neoral (Novartis)	Cyclosporine A	Soft gelatin capsule (10, 25, 50, 100 mg)	*dl-α*-tocopherol, corn oil-mono-di-triglycerides, polyoxyl 40 hydrogenated castor oil (Cremophore RH 40)
		Oral solution (100 mg/ml)	*dl-α*-tocopherol, corn oil-mono-di-triglycerides, polyoxyl 40 hydrogenated castor oil (Cremophore RH 40)
Kaletra (Abbott)	Lopinavir & Ritonavir	Soft gelatin capsule lopinavir (133.3 mg) & ritonavir (33.3 mg)	Oleic acid, polyoxyl 35 castor oil (Cremophor EL)
		Oral solution lopinavir (80 mg/ml) & ritonavir (20 mg/ml)	Polyoxoy hydrogenated castor oil (Cremophor RH 40), peppermint oil
Norvir (Abbott)	Ritonavir	Soft gelatin capsule (100 mg)	Oleic acid, polyoxyl 35 castor oil (Cremophor EL)
Fortovase (Roche)	Saquinavir	Soft gelatin capsule(200mg)	Medium-chain mono- and diglycerides,dl-α-tocopherol
Aptivus (Boehringer Ingelheim)	Tipranavir	Soft gelatin capsule (200 mg)	Polyoxyl 35 castor oil (Cremophor EL), medium-chain mono- and di-glycerides
Fenogal (Genus)	Fenofibrate	Hard gelatin capsule (200 mg)	Lauryl macrogol-glycerides (Gelucire 44/14)
Infree (Eisai Co.)	Indomethacin	Soft gelatin capsule (200 mg)	Polyoxoy 60 hydrogenated castor oil (Cremophor RH 60), hydrogenated oil, glyceryl monooleate
Agenerase (GaxoSmithKline)	Amprenavir	Soft gelatin capsule	TPGS (12%), PEG 400 (17%), Propylene glycol (55%), Sodium chloride
Solufen (Sanofi-Aventis)	Ibuprofen	Hard gelatin capsule	Lauryl macrogol-glycerides (Gelucire 44/14)
Accutane (Roche)	Isotretinoin	Soft gelatin capsule (10, 20, 40 mg)	Beeswax, BHA, EDTA, hydrogenated soybean oil flakes, hydrogenated vegetable oils, soybean oil

CONCLUSION

Self emulsifying drug delivery systems is a promising approach for the formulation of drug compounds with poor aqueous solubility, having high molecular weight, pre systematic first pass effect, enzymatic degradation, gastric irritation, having limited dissolution rate and low bioavailability. This is the method suited for all BCS class drugs where resulting emulsification gives faster dissolution and absorption rates. In future development SEDDS will continue to novel applications in drug delivery and solve the problems associated with the delivery of poor water soluble drug, pre-systemic first pass effect, enzymatic degradation and having limited dissolution and low bioavailability.

REFERENCES

[1] H Gupta; D Bhandari; A Sharma, *Recent Patents on Drug Delivery and Formulation*, **2009**, 3(2), 162-173.
[2] CW Pouton; CJ Porter, *Advanced Drug Delivery Reviews*, **2008**, 60(6), 625-637.
[3] K Sarpal; YB Pawar; AK Bansal, *Current Research and Information on Pharmaceutical Sciences*, **2010**, 11(3), 42-48.
[4] T Dabros; A Yeung; J Masliyah; J Czarnecki, *Journal of Colloid and Interface Science*, **1999**, 210(1), 222-224.
[5] PP Constantinides, *Pharmaceutical Research*, **1995**, 12(11), 1561-1572.
[6] CW Pouton, *International Journal of Pharmaceutics*, **1985**, 27(2-3), 335-348.
[7] YR Gonnade; K Niranjane; A Ambatkar, *World Journal of Pharmaceutical Sciences*, **2014**, 3(4), 572-589.
[8] CJH Porter; NL Trevaskis; WN Charman, *Drug Discovery*, **2007**, 6(1), 231-248.
[9] AU Kyatanwar; KR Jadhav; VJ Kadam, *Journal of Pharmacy Research*, **2010**, 3(1), 75-83.
[10] S Saxena; HN Singh; VK Agrawal, *Asian Journal of Biomedical and Pharmaceutical Sciences*, **2013**, 3(22), 16-22.
[11] S Kalepu; M Manthina; V Padavala, *Acta Pharmaceutica Sinica B.*, **2004**, 3(6), 361–372.
[12] B Singh; S Bandopadhyay; R Kapil; R Singh; OP Katare, *Critical Reviews in Therapeutic Drug Carrier Systems*, **2009**, 26(5), 427–521.
[13] R Asija; P Yadav; S Asija, I*nternational Journal of Research and Development in Pharmacy and Life Sciences*, **2014**, 3(2), 872-876.
[14] S Akula; AK Gurram; SR Devireddy, International *Scholarly Research Network*, **2014**, 1(1), 1-11.

[15] LM Ingle; VP Wankhade; TA Udasi; KK Tapar, *International Journal of Pharmacy and Pharmaceutical Science Research*, **2013**, *3*, 7–14.
[16] AA Kale; VB Patravale, *American Association of Pharmaceutical Scientist PharmSciTech*., **2008**, 9(1), 191-196.
[17] Bhavna; G Aggarwal; SL Harikumar, *Journal of Drug Delivery and Therapeutics*, **2013**,3,168-174.
[18] KC Ofokansi; KI Chukwu; SI Ugwuanyi, *Drug Development and Industrial Pharmacy*, **2009**, 35(2), 185-191.
[19] A Abdalla; K Mader, *European Journal of Pharmaceutics and Biopharmaceutics*, **2006**, 66(2), 220-226.
[20] S Cui; C Zhao; D Chen; Z He, *Drug Development and Industrial Pharmacy*, **2005**, 31(4-5), 349-356.
[21] C Tuleu; M Newton; J Rose; D Euler; R Saklatvala; A Clarke; S Booth, *Journal of Pharmaceutical Sciences*, **2004**, 93(6), 1495-1502.
[22] S Shafiq; F Shakeel; S Talegaonkar; FJ Ahmad; RK Khar; M Ali, *European Journal of Pharmaceutics and Biopharmaceutics*, **2007**, 66(2), 227-243.
[23] RN Gursoy; S Benita, *Biomed Pharmacother*, **2004**, 58(3), 173-182.
[24] A Chetan; KS Salunkhe; SR Chaudhari, *American Journal of Pharmatech Research*, **2014**, 4(3), 45 -57.
[25] YF Ho; MY Lai; HY Yu; DK Huang; WC Hsueh; TH Tsai; CC Lin, *Journal of the Formosan Medical Association*, **2008**, 107(1), 37-45.
[26] ME Lane; KA Levis; OI Corrigan, *International Journal of Pharmaceutics*, **2006**, *309*(1-2), 60-66.
[27] L Kaur; N Kanojia; R Bala; M Nagpal, *American Journal of Pharm Tech Research*, **2013**, 3(1), 261-288.
[28] T Gershanik; S Benita, *Pharmaceutical Development and Technology*, **1996**, 1(2), 147-157.
[29] BK Kang; JS Lee; SK Chon; SY Jeong; SH Yuk; G Khang; HB Lee; SH Cho, *International Journal of Pharmaceutics*, **2004**, 274(1-2), 65-73.
[30] P Li; A Ghosh; RF Wagner; S Krill; YM Joshi; AT Serajuddin, *International Journal of Pharmaceutics*, **2005**, 288(1), 27-34.
[31] JY Hong; JK Kim; YK Song; JS Park; CK Kim, *Journal of Control Release*, **2006**, 110(2), 332-338.
[32] AR Patel; PR Vavia, *American Association of Pharmaceutical Scientist Journal*, **2007**, 9(3), 344-352.
[33] XT Zhou; J Wang; Y Wang; JY Sun; SF Nie; WS Pan, *Yao Xue Xue Bao.*, **2008**, 43(4), 415-20
[34] YS Elnaggar; MA El-Massik; OY Abdallah, *International Journal of Pharmaceutics*, **2009**, 380(1-2), 133-141.
[35] Y Zhao; C Wang; AH Chow; K Ren; T Gong; Z Zhang; Y Zheng, *International Journal of Pharmaceutics*, **2010**, 383(1–2), 170–177.
[36] AR Dixit; SJ Rajput; SG Patel, *Association of Pharmaceutical Scientists PharmSci Tech*., **2010**, 11(1), 314-321.
[37] X Wu; J Xu; X Huang; C Wen, *Drug Development and Industrial Pharmacy*, **2011**, 37(1), 15–23.
[38] W Li; S Yi; Z Wang; S Chen; S Xin; J Xie; C Zhao, *International Journal of Pharmaceutics*, **2011**, 420(1), 161-171.
[39] AM Villar; BC Naveros; AC Campmany; MA Trenchs; CB Rocabert; LH Bellowa, *International Journal of Pharmaceutics*, **2012**, 431(1-2), 161-175.
[40] U Goyal; R Arora; G Aggarwal, *Acta Pharmaceutica Sciencia*, **2012**, 62, 357-370
[41] JH Kang; DH Oh; YK Oh; CS Yong; HG Choi, *European Journal of Pharmaceutics and Biopharmaceutics*, **2012**, 80(2), 289-297.
[42] M Milovic; J Djuris; L Djekic; D Vasiljevic; S DIbric, *International Journal of Pharmaceutics*, **2012**, 436(1), 58-65.
[43] Y Zhang; R Wang; J Wu; Q Shen, *International Journal of Pharmaceutics*, **2012**, 427(1), 337-344.
[44] PB Memvanga; V Préat, *European Journal of Pharmaceutics and Biopharmaceutics*, **2012**, 82(1), 112-119.
[45] D Pandya; J Patel; S, Patel, *Discovery Pharmacy*, **2013**, 5(14), 6-12.
[46] AE Silva; G Barratt; M Chéron; ES Egito, *International Journal of Pharmaceutics*, **2013**, 1(1), 1-8.
[47] BP Rao; B Baby; Y Durgaprasad; K Ramesh; S Rajarajan; B Keerthi; C Sreedhar, *Journal of Pharmaceutical Sciences*, **2013**, 3(2), 33-40.
[48] K Balakumar; CV Raghavan; NT Selvan, *Colloids and Surfaces B: Biointerfaces*, **2013**, 12(1), 337-343.
[49] V Rokad; C Nagda; D Nagda, *Journal of Young Pharmaceutics*, **2014**, 6(3), 37-46.
[50] MJ Qureshi; C Mallikarjun; WG Kian, *Asian Journal of Pharmaceutical Sciences*, **2014**, 1(1), 1-17
[51] W Lan; Q Yanli; W Lina; G Jiahua; W Guocheng; H Wei; Y Lifang; Z Jinhua, *American Association of Pharmaceutical Scientists PharmSci Tech.*, **2015**, 16 (5), 1051-1058.
[52] DW Yeom; YS Song; SR Kim; SG Lee; MH Kang; S Lee; YW Choi, *International Journal of Nanomedicine*, **2015**, 10(1), 3865-3878.
[53] NS Kulkarni; NS Ranipse; G Mohan, *Tropical Journal of Pharmaceutical Research*, **2015**, 14(4), 575-582
[54] V Peter; S Abraham, *International Journal of Innovative Pharmaceutical Sciences and Research*, **2015**, 3(8), 1021-1036.

[55] N Padia; AK Shukla; P Shelat, *Journal of Scientific and Innovative Research*, **2015**, 4(3), 153-164.