A REVIEW ON FORMULATION APPROACH TO ENHANCE ORAL BIOAVAILABILITY OF POORLY SOLUBLE DRUGS BY SELF EMULSIFYING DRUG DELIVERY SYSTEM

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ABSTRACT
Most of the drugs which are recently discovered are poorly water soluble and the oral delivery of these drugs have become a major problem. Drugs of Class II or IV, as per biopharmaceutical classification system (BCS) exhibit poor aqueous solubility. The oral delivery of these drugs are affected by low bioavailability, erratic absorption, inter and intra subject variability and lack of dose solubility. Since last couple of years Self-emulsifying drug delivery systems are becoming important tool in novel drug delivery. It is very useful in solving problems such as low bioavailability issues associated with poorly water soluble drugs. The bioavailability of lipophilic drugs (BCS-II and IV) can be enhanced by these systems. SEDDS is released in the lumen of the gastrointestinal tract (GIT) after administration and with the aid of GI fluid a fine emulsion (micro-/nano-emulsion) is formed. The increased surface area and amphoteric nature of SEDDS lead to increase in bioavailability. In this review we present a report on the formulation, characterization and dosage forms and applications of self-emulsifying formulations, with examples of currently marketed preparations.

KEYWORDS: Self emulsifying drug delivery system, Solubility, Bioavailability, Absorption.
INTRODUCTION

The oral route is the preferred way of dosing, because this is the easiest and most convenient way of noninvasive administration. Most of drug substance that applied orally today is small molecule that can permeate the intestinal gut membrane by transcellular passive diffusion. This process is determined by physicochemical law and by the properties of the intestinal cells. In addition to its permeability through the gut wall, the availability of drug in the body depends on its ability to dissolve in the gastrointestinal fluid. \(^1\)

The solubility or dissolution of the drug substance can be mainly altered on two levels, through material engineering of the drug substance or through formulation approaches. Whatever route is taken to enhance or modify the solubility and/or dissolution of a lead substance. It needs to be scalable to a commercially viable process later on in the development. Besides the aqueous solubility of a drug substance, its permeability is a second critical aspect for oral bioavailability. The biopharmaceutical classification system (BCS) was introduced in the mid-1990s to classify the drug substances with respect to their aqueous solubility and membrane permeability. Drug substances, for which solubility enhancement can improve the oral bioavailability, are substances that are classified in class 2 (poor soluble/permeable) and class 4 (poor soluble/poor permeable). Especially for class 2 substances, solubility enhancement is part of the strategies to improve the oral bioavailability. \(^2\)

In recent years, much attention has focused on lipid-based formulations to improve the oral bioavailability of poorly water soluble drug compounds. In fact, the most popular approach is the incorporation of the drug compound into inert lipid vehicles such as oils, surfactant dispersions, self-emulsifying formulations, emulsions and liposomes with particular emphasis on self-emulsifying drug delivery systems (SEDDS). \(^3\)

Self-emulsifying drug delivery systems (SEDDS) are isotropic mixtures of oil and a non-ionic emulsifier. One feature of these mixtures is their ability to form fine oil-in-water emulsions with only gentle agitation when exposed to aqueous media. This property makes SEDDS good candidates for the oral delivery of hydrophobic drugs with adequate oil solubility. After oral administration of soft gelatin capsules containing SEDDS, readily disperse in the stomach to form a fine emulsion; in this case, the digestive motility of the stomach and the intestine can provide the agitation necessary for self emulsification. At a given temperature, 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
performance of SEDDS is dependent upon two main factors: (1) the ability of the self-
emulsifying mixture to form an emulsion of fine particles with a uniform size distribution and
(2) the polarity of the resulting oil droplets to promote a fast rate of release of the drug into
the aqueous phase. The efficiency of emulsifiers in SEDDS is commonly related to their
ability to form fine droplet size of the emulsion on exposure to water, having polarity
favoring faster rate of the drug release. For drugs subject to dissolution rate limited
absorption, SEDDS may offer improvement in the rate and extent of absorption, as well as in
the reproducibility of the blood level-time profile

Theoretical Considerations

The efficiency of SEDDS depends on two main factors: (1) uniform fine particle size of oil
droplets on exposure to aqueous media; and (2) the polarity of the resulting oil droplets. Both
Properties control the rate of release of the drug from the oil to the aqueous phase. Once
exposed to the aqueous phase, SEDDS form oil-in-water (o/w) emulsions. The resulting o/w
emulsions produced spontaneously because SEDDS are thermodynamically stable, as
opposed to the regular emulsions, which are thermodynamically unstable. There are two
factors that favor emulsion stability in the case of SEDDS: (1) relatively small volume of the
dispersed oil phase; and (2) narrow range of droplet size distribution. For a given
combination of components, emulsions with small, uniform droplet size will take longer to
break. Larger droplets are less stable than smaller droplets due to their larger area to volume
ratio, and so will tend to grow at the expense of the smaller droplets. The smaller droplets
will have a larger interfacial surface area per unit volume. The diffusion path for a drug will
decrease with the reduction of the radius of the droplets. Another important factor for the
performance of SEDDS is the polarity of the oil droplets. The polarity of the oil droplets is
governed by the hydrophile-lipophile balance (HLB), the chain length and degree of
unsaturation of the fatty acid, the molecular weight of the hydrophilic portion and the
concentration of the emulsifier. The combination of small droplets together with the
appropriate polarity (lower PC. of the drug) of the droplets will permit an acceptable rate of
release of the drug. Polarity of the oil droplets is also estimated by the oil/ water partition
coefficient (PC,) of the lipophilic drug. \cite{4}

Mechanism of self emulsification

Self emulsifying process are related to the free energy, ΔG given by

\[ \Delta G = \Sigma N \pi r^2 \sigma \]
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 interface between the oil and water phase is energetically not favorable. The system commonly classified as SEDDS have not yet been shown to emulsify spontaneously in the thermodynamic sense. Pouton has argued 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. 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 a minimization of phase inversion temperature, thereby increasing the ease of emulsification. [5]

**Advantages associated with SEDDS**

1. Protection of drug from GIT environment.
2. Selective targeting of drug toward specific absorption window in GIT.
3. Enhanced oral bioavailability.
4. Consistent drug absorption profile.
6. Versatility of dosage form as can be used with liquids or solids.
7. Predictable therapy due to reduced variability including food effects.
8. Drug payloads are high.

**Components of SEDDS**

SEDDS formulation containing following components:

1. Oil phase
2. Primary surfactant
3. co-solvent

These systems are usually easier to formulate than ordinary emulsion. The type of associated structure formed from these components at particular temperature it is not depends only on the chemical nature of each component but also depends on their relative concentration.
Oil Phase
In the self-emulsifying formulations different oils have been used. Oils can solubilize the lipophilic drug in a specific amount. It is the very important excipient. Because it can be increase the fraction of lipophilic drug transported via the intestinal lymphatic system, therefore increasing absorption from the GI tract. Unmodified edible oils provide the ‘natural’ basis for lipid vehicles, but their poor ability to dissolve the large amounts of the hydrophobic drugs and difficulty in efficient self-emulsification so, reduce their use in SEDDS. In contrast, modified or hydrolyzed vegetable oils have been widely used. Because of the higher Fluidity, better solubility properties. Examples of commonly used oils are listed in Table 1.

Surfactant
Surfactants are formed by two parts with different affinities for the solvents. One of them has affinity toward the water (polar solvents) and the other has for oil phase (non-polar solvents). A little amount of surfactant a molecule is rest upon the water-air interface and decreases the water surface tension value (the force per unit area needed to make available surface). The surfactants used in self emulsifying formulations are known to improving the bioavailability by various mechanisms including increased intestinal epithelial permeability, improved dissolution increased tight junction permeability to GIT. Surfactants may be classified based on the nature of the hydrophilic group.

The four main groups of surfactants are defined as follows
1. Anionic Surfactants: in these hydrophilic group having a negative charge such as sulphonate (RSO₃⁻) or sulphate (ROSO₃⁻), carboxyl(RCOO⁻). Examples: sodium lauryl sulphate. Potassium laurate
2. Cationic surfactants: in these hydrophilic group having a positive charge. Examples: quaternary ammonium halide.
3. Ampholytic surfactants (also called zwitter ionic surfactants) having both a positive and a negative charge. Examples: sulfobetaines.
4. Nonionic surfactants, in these hydrophilic groups having no charge but derive its water solubility from highly polar groups such as polyoxyethylene (OCH₂CH₂O) or hydroxyl. Examples: Polysorbates (Tweens), Sorbitan esters (Spans).
Co-Solvents

Generally high surfactant concentrations (more than 30% w/w) are used in order to produce an effective self-emulsifying formulation. Organic solvents are suitable for oral administration (propylene glycol (PG), ethanol, polyethylene glycol (PEG), etc.) may be help to dissolve large quantity of the hydrophilic surfactant in the drug which is the lipid base and can act as co-surfactant in the self emulsifying drug system. Co-solvent plays the role of the co-surfactant in the self emulsion systems. This systems may exhibit some advantages over the previous formulations that when incorporated in the capsule dosage forms, since alcohol and other volatile co-solvents composed in the recently self-emulsifying formulations are to migrate into the shells of soft gelatin, or hard gelatin capsules, resulting in the precipitation of the lipophilic drug. Drug release from the formulation increased with increasing amount of co-surfactant. Co-solvents may help to dissolve large quantity of hydrophilic surfactants or the hydrophobic drug in the lipid base. Examples of commonly used Co-solvents are listed in Table-1.

Table-1 List of Surfactants/Co Surfactants, Co-Solvents, Lipid Ingredients Used In SEEDDS

<table>
<thead>
<tr>
<th>S.N.</th>
<th>Component of SEEDDS</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Surfactants/co-surfactants</td>
<td>Polysorbate 20 (Tween 20),Polysorbate 80 (Twee 80), Sorbitan monooleate (Span 80), Polyoxy-35-caster oil (Cremophor RH40), Polyoxy-40- hydrogenated castor oil (Cremophor RH40), Polyoxyethylated glycerides (Labrafil M 2125 Cs), Polyoxyethylated oleic glycerides (Labrafil M1944 Cs), D-alpha Tocopheryl polyethylene glycol 1000 succinate (TPGS)</td>
</tr>
<tr>
<td>2.</td>
<td>Co-solvents</td>
<td>Ethanol, Glycerin, Polypylene glycol and Polyethylene glycol</td>
</tr>
<tr>
<td>3.</td>
<td>Lipid ingredients</td>
<td>Corn oil mono, 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 soyabean oil, Hydrogenated vegetable oils, Soyabean oil and Peanut oil</td>
</tr>
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Dosage Forms Self Emulsifying Drug Delivery System

Self Emulsifying Capsule

It is a capsules containing liquid or semisolid form of self emulsifying system. In the GIT, the capsules get dispersed to SES uniformly in the fluid to micron size, enhancing bioavailability. Second type of self emulsifying capsule is solid SES filled into capsule.
Self Emulsifying Tablets
S. Nazzal was developed self nanoemulsified tablet dosage form of Ubiquinone. The main objectives of this study were to study effect of formulation ingredients on the release rate of Ubiquinone and to evaluate an optimized self nanoemulsified tablets formulation. The first prepared self nanoemulsions system containing Ubiquinone was prepared as nanoemulsions. This nanoemulsion was absorbed by granular materials and then compressed to form tablets. The optimized formulation of coenzyme Q10 self nanoemulsified tablet dissolution profile showed that 80-90% drug release took place in 45 minute.

Self Emulsifying Pellets
C. Tuleu presented comparative bioavailability study in dogs of a self – emulsifying formulation of progesterone presented as in pellets and the liquid form was compared with an aqueous suspension of progesterone. The in vitro dissolution tests showed that nearly 100% of progesterone dissolved within 30 min and within 5 min from capsules containing the progesterone dissolved in self emulsifying system. From the aqueous suspension, 50% of the dose was released within 60 min. They also showed that pellets administered orally to dogs were tested versus the same dose of progesterone dissolved in liquid SES in capsules or a suspension of micronized progesterone. In that SES pellets and SES solution had higher plasma levels of progesterone at each time point as compared to the aqueous suspension of progesterone.

Self Emulsifying Beads
Self emulsifying system can be formulated as a solid dosage form by using less excipient. Patil and Paradkar discovered that deposition of SES into microporous polystyrene beads was done by solvent evaporation. Porous polystyrene beads with complex internal void structures were typically produced by co polymer styrene and divinyl benzene. It is inert and stable over a wide range of pH, temperature and humidity.

Self Emulsifying Microsphere
Self emulsifying can be formulated solid SE sustained-release microspheres using the quasi emulsion solvent diffusion method for the spherical crystallization technique. Zedoary turmeric oil release behavior could be controlled by the ratio of hydroxypropyl methylcellulose acetate succinate to Aerosil 200 in the formulation. The plasma concentration time profiles were achieved after oral administration of such microspheres into rabbits, with a bioavailability of 135.6% with respect to the conventional liquid SEDDS.
**Self Emulsifying Nanoparticle**

Nanoparticle technology can be applied to the formulation of self emulsifying nanoparticle. One of the solvent was injection, in this method the prepared molten lipid mass contained lipid, surfactant and drug. This lipid molten mass was injected drop wise into a non solvent system. This is filtered and dried to get nanoparticles. By this method 100 nm size particle with 70-75% drug loading efficiency was obtained second technique is sonication emulsion diffusion evaporation; by this method. [10]

**Characterization and Optimization of Sedds** [11]

SMEDDS forms fine o/w microemulsions with only gentle agitation, upon its introduction into aqueous media. Since the Gibbs energy required to form microemulsion is very low, the formation is thermodynamically spontaneous. Surfactants (emulsifiers) form a layer around the emulsion droplets and reduce the interfacial energy as well as provide a mechanical barrier to coalescence. For selecting a suitable self-emulsifying vehicle, it is important to assess (a) the drug solubility in various components, (b) the area of self emulsifying region in the phase diagram, and (c) droplet size distribution following self-emulsification.

**1. Solubility Studies**

The solubility of drug in various oils, surfactants and co surfactants is determined by using shake flask method. An excess amount of drug is added to each vial containing 1 ml of the selected vehicle i.e. oil, surfactant or solubilizer. After sealing, the mixture is vortex using a cyclo mixer for 10 min in order to facilitate proper mixing of drug with the vehicles. Mixtures are then shaken for 72 h in an isothermal shaker maintained at 37°C for equilibration. Equilibrated samples are centrifuged at 5,000 rpm for 15 min, followed by filtration through membrane filter (0.22 μm). The concentrations of drug are then determined by high-performance liquid chromatography (HPLC) method.

**2. Construction of Pseudoternary Phase Diagrams**

Pseudo-ternary phase diagrams are constructed to identify the self-emulsifying regions and to optimize emulsifier to co emulsifier ratio and the concentration of oil. The microemulsion regions in the diagrams are plotted, and the wider region indicated the better self-emulsification efficiency. Pseudo-ternary phase diagrams of oil, surfactant/ co surfactant, and water are developed using the water titration method. The mixtures of oil and S/coS at certain weight ratios are diluted with water in a drop wise manner. For each phase diagram at a specific ratio of S/CoS, transparent and homogenous mixture of oil and S/CoS is formed by
vortexing for 5 minutes. Then each mixture is titrated with water and visually observed for phase clarity and flowability. The concentration of water at which turbidity-to-transparency and transparency-to-turbidity transitions occurred is derived from the weight measurements. These values are then used to determine the boundaries of the self emulsifying domain corresponding to the chosen values of oils, as well as the S/CoS mixing ratio. It is visually the equilibrated samples after titration with saline under magnetic stirring or vortexing. The phase state was classified into three, that is, clear one-phase with low viscosity, clear one-phase with high viscosity, and multiple phases. The one-phase with low viscosity was separated further into water-in oil (w/o) or o/w microemulsion phase by simply considering the composition, that is, whether it was oil-rich or water-rich. The clear one-phase with high viscosity was separated further into gel or liquid crystalline by using polarized light microscope and multiple phases were considered as crude emulsion.

3. **Droplet Size Measurement**

Properly diluted samples of self-emulsifying systems are used for droplet size analysis using Photon Correlation Spectroscopy. Average droplet size and poly dispersity index are determined and the data obtained are further treated with regression analysis. Measurements are obtained in duplicate at an angle of 90°. The diluted emulsions are also allowed to stand for 12 h at room temperature to assess dilution stability.

4. **Transmission Electron Microscopy**

Transmission electron microscope is used as a visualizing aid for the observation of morphology of droplets. SMEDDS is diluted with water (1/100). A drop of the diluted emulsion is directly deposited on the holey film grid to observe the morphology of formulations. Xinru Li observed the morphology of microemulsion by transmission electron microscopy. To improve the contrast, the samples were treated with a 1 wt % phosphor tungstic acid solution for 2 h, deposited on copper grids, and allowed to dry for 48 h before TEM examination. The homogeneous and spherical droplets in microemulsion were observed. Singh examined the morphology of microemulsion with a transmission electron microscope. The droplet on the microemulsion appeared dark with the bright surroundings. TEM photographs further conformed that the globules were spherical in shape.

5. **Turbidimetric Evaluation**

Nepheloturbidimetric evaluation is done to monitor the growth of emulsification. Patil worked on Loratadine SES which was added to 0.1N hydrochloric acid (150 ml) under
continuous stirring (50 rpm) on magnetic plate at ambient temperature, and the increase turbidity was measured using a turbidimeter. Time required to disperse the system completely and uniformly was determined by observing change in turbidity as a function of time.

6. Zeta Potential Measurement
In disperse systems, electrical charges are developed by several mechanisms at the interface between the dispersed phase and the aqueous medium. The two most common mechanisms are the ionization of surface functional groups and the specific adsorption of ions. These electrical charges play an important role in determining the interaction between the particles of the dispersed phase and the resultant physical stability of the system, particularly for those in the colloidal size range. The potential between the tightly bound surface liquid layer (shear plane) of the particle and the bulk phase of the solution is called as zeta potential. The measurement of the zeta potential tells about the stability. For o/w emulsions with low electrolyte content in the aqueous phase, a zeta potential of 30 mV is found to be sufficient to establish an energy maximum to ensure emulsion stability.

7. Refractive Index and Percent Transmittance
The refractive index of the system was measured by an Abbe refractometer by placing 1 drop of solution on the slide. The percent transmittance of the system was measured at 650 nm using UV Spectrophotometer keeping distilled water as a blank. Ghosh measured the refractive index of acyclovir system and it was found similar to the water (1.333). In addition, the developed system showed percent transmittance > 99%. The refractive index and percent transmittance data prove the transparency of the system.

8. Thermodynamic Stability Study
In thermodynamic stability studies, formulations selected are subjected to different stress tests like centrifugation and freeze–thaw test. In Freeze thawing, the formulations are subjected to 3 to 4 freeze thaw cycles, which included freezing at –4°C for 24 hours followed by thawing at 40°C for 24 hours. Centrifugation is performed at 3000 rpm for 5 minutes. The formulations are then observed for phase separation. Only formulations that are stable to phase separation are selected for further studies. Samples of SMEDDS are also charged on accelerated and long term stability conditions.
9. In Vitro Intestinal Permeability Studies

Male Sprague-Dawley rats (250-300 g) are killed by overdose with pentobarbitone administered by intravenous injection. To check the in trudodenal permeability, the duodenal part of the small intestine is isolated and taken for the in vitro diffusion study. Then this tissue is thoroughly washed with cold Ringer’s solution to remove the mucous and lumen contents. The SEDDS sample is diluted with 1 ml of distilled water (outside mixing for 1 minute by vortex mixer). The resultant sample (2 mg/ml) is injected into the lumen of the duodenum using a syringe, and the 2 sides of the intestine are tightly closed. Then the tissue is placed in a chamber of organ bath with continuous aeration and a constant temperature of 37°C. The receiver compartment is filled with 30 ml of phosphate-buffered saline (pH 5.5). The absorbance is measured using a UV-VIS spectrophotometer at the specific wavelength, keeping the respective blank. The percent diffusion of drug is calculated against time and plotted on a graph.

10. Absorption Studies

The animals are divided into 3 groups, the first group is fasted for 12h before drug administration; the second and third groups are continuously fed with normal diet and lipid diet for 12 h before drug administration, respectively. After anesthesia, the femoral artery is cannulated and cannula is flushed with heparin saline solution to prevent blood clotting. After rats recovered from anesthesia, SEDDS after dilution with distilled water is administered orally to rats using oral. Blood samples are withdrawn at regular time intervals and frozen until analysis. The pharmacokinetic parameters like AUC, T max and C max are calculated from the plasma data. \(^{[11]}\)

APPLICATIONS OF SEDDS

Improvement in Solubility and Bioavailability

If SEDDS is used to incorporate the drug, the solubility increases because it circumvents the dissolution step in of BCS Class-II drug (Low solubility/high permeability). Ketoprofen a non steroidal anti-inflammatory drug (NSAID) is moderately hydrophobic (log P 0.979). For sustained release formulation it is a drug of choice and during chronic therapy it has high potential for gastric irritation. Ketoprofen shows incomplete release from sustained release formulations because of its low solubility. The SEDDS formulation of this drug enhanced bioavailability due to increase in the solubility and it also minimizes the gastric irritation. The release of Ketoprofen in SEDDS is sustained due to incorporation of gelling agent. The lipid
matrix interacts readily with water in SEDDS, leading to the formation of a fine particulate oil in-water (o/w) emulsion.

**Protection against Biodegradation**

The self-emulsifying drug delivery system is able to reduce degradation as well as improve absorption may be especially useful for drugs which have both low solubility and degradation in the GI tract and low oral bioavailability. Because of acidic PH, enzymatic degradation or hydrolyte in stomach, many drugs are degraded in physiological system. These degradation processes can be well protected when drug is presented in the form of SEDDS, as liquid crystalline phase in SEDDS might act as barrier between degradation environment and the drug. [12]

**Supersaturable Sedds (S-Sedds)**

Most of the times high surfactant level cause GI irritation, So as to reduce the side effects associated with surfactants & to achieve rapid absorption of poorly soluble drug, S-SEDDS are developed. A better toxicity/safety profile than the conventional SEDDS formulation is significantly being achieved by reduced amount of surfactant to be used in the S-SEDDS formulation. HPMC is used as precipitation inhibitor in salicylic acid and docetaxel. SEDDS formulation. By replacing propylene glycol with HPMC as precipitation inhibitor, a fivefold increase in bioavailability was observed with PNU-91325.

**In delivery of Peptides**

Macromolecules like peptides, hormones, enzyme substrates and inhibitors can be protected from enzymatic hydrolysis and thus delivered efficiently by formulating them as SEDDS. These systems are suitable for thermolabile drugs such as peptides as these are spontaneously formed without aid of energy or heating e.g. if Polysorbate 20 is used as emulsifier in micro emulsion formulation, the intestinal hydrolysis of pro-drug by cholinesterase can be protected.

**Sedds for Herbal Drugs and Traditional Medicine**

Tremendous number of herbal drugs and traditional medicines are being used and exploited for formulation and development of SEDDS as most of them either contain volatile and fixed oils or are extracts. Silybin an active constituent from Carduus marianus has extremely low oral bioavailability because of its low aqueous solubility. By formulating silybin in SEDDS formulation, its oral bioavailability has increased by at least 4 folds. Chinese plant Fructus
Schisandral Chinensis (Wurenchun) is useful in lowering abnormal serum glutamic pyruvic transaminase (SGPT) level of patients suffering from acute or chronic hepatitis has also been formulated as SEDDS for improved solubility and bioavailability.\textsuperscript{[13]}

**Future Prospects**

SMEDDS are a promising approach for the formulation of drug candidates having poor aqueous solubility. The oral delivery of hydrophobic/lipophilic drugs is now possible by SMEDDs and further can be extended with consummate ease if certain factors can be solved out. However the efficiency of the SMEDDs formulation is case specific in most cases, so the composition of the SMEDDS formulation should be determined very carefully. Since a relatively high concentration of surfactants is generally employed in the SMEDDDs formulation, toxicity of the surfactant that is being used should be taken into account. In fact, a compromise must be done between the toxicity and self-emulsification ability of the surfactant that is considered for use. The reasons underlying the lack of application of these technologies is not clear, but the limited knowledge of the formulation parameters that are responsible for good in vivo performance and the fact that relatively few in vivo studies in human have been reported in literature when compared with conventional dosage forms have been reflected. Perhaps more importantly the lack of effective in vitro tests that are predictive of in vivo performance has significantly hindered successful development of the self-micro emulsifying drug delivery systems.

**CONCLUSION**

Several conventional methods such as micronization, chemical modification, use of surfactants and solubilises, solid dispersion and a few new emerging technologies such as cyclodextrin complexation, mucoadhesive microspheres, nanoparticles, nanosuspensions, micro emulsion and self emulsifying systems have been successfully developed for formulation development of BCS class II drugs. Though several studies are reported in this area, more intense research is needed to new and novel formulation techniques for BCS class II drugs. Self emulsifying drug delivery system in solid dosage form has improved solubility/dissolution, absorption and bioavailability for poorly water soluble drug. This is the method suited lipophilic drugs where resulting emulsification gives faster dissolution rates and absorption. Solid SEDDS is superior to SEDDS in reducing production cost, simplifying industrial manufacture, and improving stability as well as patient compliance. Solid SEDDS
has the flexibility to develop into different solid dosage form for oral and parenteral administrations.

REFERENCES


