SELF-EMULSIFYING DRUG DELIVERY SYSTEM: AN APPROACH TO INCREASE THE SOLUBILITY OF POORLY WATER SOLUBLE DRUGS

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**ABSTRACT**

As a development of recent drug discovery techniques, there has been an increase in the number of novel pharmacologically active compounds that are lipophilic in nature. It is indeed challenging for pharmaceutical researcher to enhance the oral bioavailability of such molecules. One of the most well-known and commercially suitable formulation approach for resolving these problems is self-emulsifying drug delivery systems (SEDDS). SEDDS has given promising results in improving the oral bioavailability of poorly water-soluble and lipophilic drugs. Highly lipophilic drugs can be dissolved in these systems and administered as solid dosage form for oral administration. This system gets released in the gastrointestinal tract, where it disperses to form a fine emulsion with the help of GI fluid. This leads to in situ solubilization of drug that can subsequently be absorbed by lymphatic pathways. So, these are the additional advantage associated with this system. For lipophilic drug compounds that exhibit dissolution-rate-limited absorption, SEDDS can offer an improvement in rate and extent of absorption, resulting in reproducible drug concentration in blood. Possibility of the system to adsorb on the solid carrier has gained popularity because systems can be administered as a unit dosage form for oral administration. It was concluded that although a lot of work has been done, still there is scope for exploring this technique for enhancement of poorly soluble drug.

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INTRODUCTION

The oral route is the favourite route for chronic drug therapy, majority of drugs are frequently administered through oral route, but approximately 40% of new drug candidates have poor-water solubility and the oral delivery of such drugs is complicated for the reason that of their low bioavailability, high inter- and intra-subject variability, and not have dose linearity. Solubility is one of the most important parameter to achieve desired concentration of drug in systemic circulation for therapeutic activity. As a development of recent drug discovery techniques, there has been an increase in the number of novel pharmacologically active compounds that are lipophilic in nature. It is indeed challenging for pharmaceutical researcher to convert those molecules into orally administered formulation with sufficient bioavailability. [1]

To overcome these problems, various formulation strategies have been used, such as the use of permeation enhancers, micronization, surfactants, lipids, salt formulation, nanoparticles, solid dispersions and cyclodextrins. The amount of the drug for absorption can be enhanced by formulation of the drug as a solubilize within a colloidal dispersion. Although many solubility enhancement methods are available, but they have their own limitations like hygroscopicity (salt formation), Poor wettability (Size reduction), can’t be used for thermolabile compound (Solid Solution) and Solvent removal (Solid Dispersion).

Much emphasis has been given on emulsions, lipid solutions and emulsion preconcentrates which can be prepared as physically stable formulations suitable for encapsulation of such hydrophobic drugs. Emulsion systems are associated with their own set of limitations, including stability and manufacturing problems. [2]

One of the most popular and commercially suitable formulation approaches for solving these problems is self-emulsifying drug delivery systems (SEDDS). SEDDS is defined as “isotropic mixtures of natural or synthetic oils, surfactants and co solvents/surfactants” Also known as SEOF: Self emulsifying oil formulations. The process of self-emulsification may be spontaneous or requires less amount of shear whereas conventional emulsification requires high amount of shear. These system forms o/w emulsions or micro emulsions upon mild agitation followed by dilution in aqueous media. i.e: GI fluids. Drug therefore remains in solution form, avoiding dissolution that limits absorption of hydrophobic drugs when given in crystalline form.

Self-emulsifying drug delivery systems have achieved great success in improving the oral bioavailability of poorly water-soluble and lipophilic drugs. Preparation of SEDDS involves dissolution of drugs in oils and their blending with suitable solubilizing agents. Self-emulsifying drug delivery systems are good alternative for solving low bioavailability issues of lipophilic drugs. Such drugs can be dissolved in these systems and then can also be converted to solid unit dosage form for oral administration. When this reaches to the gastrointestinal tract, it disperses to form a fine emulsion in GI fluid with the assistance of slight agitation provided by peristaltic movements. This leads to in situ solubilization of drug that can subsequently be absorbed by lymphatic pathways. So, this is an additional advantage associated with the system. [3]

A lot of research has been done on SEDDS formulations and it has been proved that SEDDS is promising way to improve the solubility and hence bioavailability of poorly soluble drugs. The review article compiles the work done on SEDDS.

Kohli K., et al., reviewed that Self-emulsifying drug delivery systems are promising way to solve the low bioavailability problems of hydrophobic drugs. Lipophilic drugs can be dissolved in these systems and administered as a unit dosage form for oral administration. As the drug can be absorbed by lymphatic pathways, hence these systems can bypass the hepatic first-pass metabolism as well. Although the potential utility of SEDDS has been known for some time, it is only in recent years that a mechanistic understanding of their impact on drug disposition has emerged. To this end, the use of a combination of in vitro dispersion and digestion methodologies has enabled a much improved understanding of the role of intestinal lipid processing on the solubilization behaviour of lipid based formulations. This SEDDS can be taken as an emulsion premix with high stability as such in the formulation. With future developments in this novel technology, SEDDS will remove deficiencies associated with delivery of hydrophobic drugs. Thus, this field requires further exploration and research to bring out a wide range of commercially available self-emulsifying formulations. It was concluded that this system is not only about lipids and surfactants but also about their selection and the ratio in which they are used [1].

Tang B., et al., reviewed that SEDDS are generally prepared in a liquid form, which can produce some drawbacks. So, it is preferred to use Solid self-emulsifying drug delivery system (S-SEDDS), which is prepared by solidification of liquid self-emulsifying ingredients into solid. As improvements of conventional liquid SEDDS, S-SEDDS are superior in reducing production cost, improving stability and simplifying industrial manufacture, as well as patient compliance. S-SEDDS are very flexible to develop various solid dosage forms for oral and parenteral administration. This article summarized the recent advances in the study of S-SEDDS, techniques for solidification and the development of solid self-emulsifying dosage forms [2].

Sunitha R., et al., reviewed that Self-emulsifying drug delivery systems (SEDDS) have gain exposure to improve the bioavailability of poorly water soluble drugs. SEDDSs are belongs to lipid formulations, and size range is from 100nm to less than 50nm and contains an isotropic mixtures of oils, co-surfactants, and surfactants, which are emulsified in aqueous media under conditions of gentle stirring. Several studies had showed that SEDDS provides significantly improved solubility/dissolution, bioavailability and absorption of hydrophobic drugs. S-SEDDS are superior in simplifying industrial manufacture, reducing production cost and improving stability as well as patient compliance. Most importantly, S-SEDDS are very convenient to develop various solid dosage forms for oral and parenteral administration. Also GI irritation is avoidable and controlled/sustained release of drug is achievable. Here also some disadvantages are there, like higher concentrations of surfactant to be used may causes some allergic reactions and lack of good predicative in vitro models for assessment of the formulations [3].
Sudheer P., et al., reviewed, Self-micron emulsifying drug delivery system (SMEDDS) and reported that they are an effective approaches to improve the bioavailability of poorly soluble drugs. Conventional SMEDDS are mostly prepared in a liquid form, which can have many disadvantages. Hence, solid SMEDDS (S-SMEDDS) prepared by solidification of liquid/semisolid self-micron emulsifying (SME) ingredients into solid, have extended popularity. This article briefs about the recent advancements in S-SMEDDS such as development methods and the future research directions [4].

Rajesh B. V et al., reviewed that use of a lipid based system is one of the most popular methods to enhance the oral bioavailability of poorly water soluble molecules is the Self emulsifying drug delivery systems (SEDDS) are a class of lipid based delivery systems. SEDDS are normally prepared in a liquid dosage form that can be administered in Soft gelatine capsules. But they have some disadvantages especially in the manufacturing process. That is why, Solid-Self emulsifying drug delivery systems (Solid-SEDDS), prepared by solidification of liquid self-emulsifying ingredients into powders in order to create solid dosage forms. This article provides information on SEDDS and solidification techniques of Solid-SEDDS [5].

Kumar A. et al., reviewed about the developments of SEDDS and biopharmaceutical aspects of SEDDS. The application and characterization of SEDDS is also introduced, with importance being placed on the developments of Solid self-emulsifying delivery system and dosage form of SEDDS. Self-emulsifying drug delivery systems are a promising approach for the formulation of drug compounds with poor water solubility. The oral delivery of such drugs can be made possible by SEDDSs, which improves oral bioavailability. In future, SEDDSs will continue to enable applications in drug delivery and solve problems associated with the delivery of poorly soluble drugs. There are some fields of SEDDS which should be further exploited, such as studies about correlation of in vitro/in vivo and human bioavailability. SE implants/suppositories/microspheres have not been as extensively studied as SE tablets/pellets/capsules. It has also pointed out some issues to which much attention should be paid, for example oxidation of vegetable oil, physical aging phenomenon associated with glyceride and interaction between drugs and excipients. It is very tough to select the appropriate excipients for developing S-SEDDS. Thus, these aspects should represent the major future working directions for S-SEDDS. Thus major breakthroughs are still required for proper development of S-SEDDS [6].

Sapra K. et al., reviewed that aqueous solubility of drugs can be increased by different methods such as salt formation, complex formation, solid dispersion, but Self Emulsifying Drug Delivery System (SEDDS) is gaining more attention for improving the solubility of hydrophobic drugs. SEDDS are prepared using triglycerides and non ionic surfactants. These provides an updated account of the advancements in SEDDS with regard to the selection of lipid systems for current formulations, solidification techniques, dosage forms for SEDDS, characterization and their applications. The SEDDS should be suitably exploited to develop platform technologies for improving bioavailability of BCS class II and IV drugs as well as for therapeutic application of various herbal drugs [7].

Attama A.A., et al., used Goat fat and Tween 65 admixtures to formulate self-emulsifying tablets containing diclofenac. The dissolution profile of diclofenac from the self-emulsifying tablets was determined in simulated gastric fluid without pepsin and it was found that batches with higher Tween 65: goat fat content ratios gave better release rates. Under mild agitation the release rates may be comparable to those of conventional tablets. Results obtained showed that diclofenac could be easily administered in the form of self-emulsifying tablets and this delivery system is best suited for lipophilic drugs where the resulting emulsification gives faster dissolution rates and absorption [8].

Wang Z., et al., prepared and evaluated the new solid self-emulsifying pellets of poorly soluble nitrendipine by extrusion/spheronization technique, using liquid SEDDS, adsorbents like crosspovidone, lactose, silicon dioxide and Microcrystalline cellulose. The prepared SE pellets had a uniform size, a spherical shape, appropriate hardness, perfect droplet size distribution and its self-emulsification was nearly same to the liquid SEDDS. The oral bioavailability of nitrendipine from the SE pellets, evaluated in beagle dogs, was much greater than the conventional tablets and there was no significant difference when compared with the liquid SEDDS. These studies illustrated that extrusion/spheronization technique could be useful in producing solid SE pellets from liquid SEDDS during large-scale production [9].

For enhancing the oral bioavailability of dexibuprofen, poorly water-soluble drug, a solid form of lipid-based self-emulsifying drug delivery system (SEDDS) was prepared by Balakrishnan P., et al., using spray drying technique of liquid SEDDS with Aerosil 200, an inert solid carrier. The particle size analysis proved that there was no difference in the average particle diameter of the reconstituted emulsion between liquid and solid SEDDS. The solid SEDDS was characterized by DSC, SEM and XRD studies. In vivo studies of prepared S-SEDDS and dexibuprofen powder were performed in rats and the results revealed the significant increase of AUC and Cmax of solid SEDDS than dexibuprofen powder. In particular, the AUC of solid SEDDS was about two-fold higher than that of dexibuprofen powder. Results proved that this solid SEDDS could be used as an effective oral solid dosage form to improve the bioavailability of poorly water-soluble drug dexibuprofen [10].

Self-microemulsifying drug delivery system (SMEDDS) of carbamazepine, a low solubility drug, was prepared by Milovi M., et al. The formulation consisting of Polysorbate 80 (S)/Cremophor® RH40 (C)/Mygliol® 812 (O), was formulated, using, S/C (Km) ratio 1:1, as well as SC/O ratio 8:2. Four different adsorbents: Neusilin® UFL2, Neusilin® FL2, Sylysia® 320 and Sylysia® 350, with high specific surface area were used. Established SMEDDS showed high solubilization capacity for carbamazepine. Photon correlation spectroscopy proved the ability of CBZ-loaded SMEDDS to produce microemulsion droplet size. S-SMEDDS increases release rate of carbamazepine, but the type of adsorbent has significant affects over the release rate of S-SMEDDS. With porous silica adsorbents no difference in release rate was found in comparison to physical mixtures. It was concluded that further study on S-SMEDDSs should be performed in order to select appropriate solid carrier as well as to investigate stability of prepared solid formulations [11].
Onoue S., et al., developed a solid self-emulsifying drug delivery system of coenzyme Q10 (CoQ10/s-SEDDS) with high photostability and oral bioavailability. The CoQ10/s-SEDDS was prepared by spray-drying an emulsion preconcentrate containing CoQ10, sucrose ester of fatty acid, medium-chain triglyceride and hydroxypropyl cellulose, and its photochemical, physicochemical and pharmacokinetic properties were evaluated. In vitro dissolution testing demonstrated a clear improvement in dissolution behavior of CoQ10/s-SEDDS through self-emulsification in aqueous media. Both XRD and thermal analyses suggested that CoQ10 might be amorphized and dispersed molecularly in the CoQ10/s-SEDDS, which perhaps lead to enhanced wettability. The amorphization of CoQ10 increased the photodegradation of the CoQ10/s-SEDDS up to 8-fold higher when compared to crystalline CoQ10. The CoQ10/s-SEDDS provided 5-fold increase in oral bioavailability compared with crystalline CoQ10 in rats. From these findings, the present investigation illustrated the potential use of the s-SEDDS approach for CoQ10 for improving solubility and pharmacokinetic behavior, and thereby increasing the nutraceutical and pharmaceutical potential of CoQ10 [12].

Oha D. H. et al., prepared two solid SMEDDS formulations by spray-drying the solutions containing liquid SMEDDS and solid carriers, in order to compare the effects of hydrophilic and hydrophobic solid carrier on the formation of solid self-emulsifying drug delivery system (SEDDS). Colloidal silica and dextran were used as a hydrophobic and a hydrophilic carrier, respectively. Colloidal silica produced an excellent conventional solid SMEDDS in which the liquid SMEDDS was absorbed onto its surfaces. It gave a droplet size similar to that of the liquid SMEDDS (about 100 nm) which was smaller than the other solid SMEDDS formulation. In the solid SMEDDS prepared using dextran, liquid SMEDDS was not adsorbed onto the surfaces of carrier but formed a kind of nano-sized microparticle with carrier. But, the drug was in the amorphous state in two solid SMEDDS formulations and both the carriers greatly improved the dissolution rate and oral bioavailability of flurbiprofen in rats due to the fast spontaneous emulsion formation and the decreased droplet size. Thus, in this study, the two carriers used had no significant effects on the formation of solid SMEDDS such as dissolution, crystalline properties and oral bioavailability of flurbiprofen [13].

Agarwal V., et al., studied the dynamics of powder flow of griseofulvin-self-emulsified drug delivery system (SEDDS) using Powder Rheometer. The effect of adsorbents like Silica and silicates, on drug release was investigated. It was found that the effect of SEDDS on the flow behaviour of the adsorbent, was similar to that observed in wet granulation process. Dissolution and release of the SEDDS from the adsorbent was found to be dependent on pore length and nucleation at the lipid/adsorbent interface. It was detected that dissolution rate was increased with an increase in surface area and was independent of the chemical nature of the adsorbents. It was concluded that to manufacture free flowing powder containing liquid SEDDS, care needs to be taken for specific surface area, particle size, type and amount of adsorbent [14].

Abdalla A., et al., prepared pellet based self-emulsifying drug delivery system for the oral delivery of poorly soluble drugs by taking Progesterone as model drug. Furthermore, they wanted to investigate the influence of physiological dilution media and enzymatic digestion on the solubilization capacity of the formulation for the model drug Progesterone. In vitro dissolution and digestion experiments were carried out using physiological dissolution media. Stable isotropic SE mixtures have been formulated using a mixture of medium chain mono- and di-glycerides, medium chain triglycerides, and Solutol® HS 15 as a surfactant. The emulsion droplet size after dilution decreased with (i) increasing Solutol® HS 15 contents and (ii) for more polar lipid mixtures (e.g. increased ratio of partial glycerides compared to triglycerides). SE mixtures are able to solubilize Progesterone in buffer. Digestion of the lipid phase decreases the solubilisation capacity. Therefore, applying in vitro digestion experiments for lipid formulations is important to enable prediction of the possible fate of the co-administered drug. It was also shown that the solubilization capacity strongly depends on the concentration of endogenously secreted materials such as bile salts and phospholipids. The liquid lipid SE mixture was successfully transformed into solid pellets by means of extrusion/spheronization with a maximum load of 40%. The pellets had a uniform size, a spherical shape and low friability. SEM pictures show the adsorption of the liquid oil between the microcrystalline cellulose fibers. Moreover, the self-emulsifying properties are still preserved in the pellets. Therefore, extrusion/spheronization of SEDDS systems is an alternative to encapsulation in gelatin capsules [15].

Xiongwei Hua et al., Prepared Self-microemulsifying pellets of Sirolimus to enhance the dissolution and oral absorption. Sirolimus is a representative water insoluble drug with poor oral bioavailability. The market formulation Rapamune® tablets had overcome its problems of dissolution and erratic absorption to some extent due to the inherent advantages of nanomedicine, but the oral bioavailability was still low. Here, solubility test, ability for self-emulsification, ternary phase diagrams and factorial design were implemented for screening and optimization of the composition of liquid SEDDS. The optimized liquid Sirolimus -SEDDS formulations were converted into pellets by extrusion–spheronization method and the optimal formulation of Sirolimus -SEDDS pellets containing Sirolimus (1.0 mg), Labrafil M1944CS (22.4 mg), Cremophor EL (38.4 mg), Transcutol P (19.2 mg), Microcrystalline cellulose (121.6 mg), Lactose (30.4 mg) and CMS-Na (8.0 mg) was prepared. The optimized SRL-SEDDS pellets exhibited a significant faster redispersion rate than the dissolution rate of commercial SRL tablets Rapamune®. The property of reconstituted microemulsion was evaluated (polydispersity index, droplet size) which was almost unchanged after formulating it into Pellets. Size and friability of Pellets were also qualified. Scanning Electron Microscopic (SEM) analysis and Visual observation confirmed good appearance of the solid pellets. Absence of crystalline sirolimus in the pellets was confirmed by IR, XRD, and DSC analysis. In vivo study performed on beagle dogs showed the increase in oral relative bioavailability of Sirolimus -SEDDS pellets about 136.9%, as compared to the commercial Sirolimus tablets Rapamune®. Furthermore, the oil phase and surfactant used in this system might have some activity of facilitating the lymphatic transport and inhibiting the first-pass effect via intestinal and hepatic metabolism and efflux transporter P-glycoprotein, the solid pellets also might improve the stability of liquid Sirolimus -SEDDS. Based on above, it was concluded that solid SMEDDS pellets is a very good way to improve the oral absorption of Sirolimus and the extrusion–spheronization method is a viable technology for the solidification of liquid SEDDS [16].
Mahajan H D., et al., formulated a solid self-microemulsifying formulation of fenofibrate and evaluating its in vitro preparation. Fenofibrate was dispersed with a surfactant used for the self-microemulsifying drug delivery system (SMDDS), Tween 20, Cremophor, capmul and mixture was solidified with four kinds of adsorbents, microcrystalline cellulose, microporous calcium silicate (Florite TM RE), magnesium aluminometate silicate (Neusilin TM US2), silicon dioxide (Sylsysis TM 320). SMDDS formulations were evaluated for self-microemulsifying properties and the resultant microemulsions were evaluated for precipitation, clarity and particles size distribution. The SMDDS formulation showed faster release as compared with the plain drug and conventional marketed formulation. The optimized SEDDS was then subjected to stability studies and was found to be stable for more than three months. Dissolution profile of Fenofibrate from SMEDDS was much improved than Fenofibrate. So it was concluded that, SMEDDS can be considered as novel and commercially feasible alternative to current marketed Fenofibrate [17].

Suresh P K et al., develop and characterize SNEDDS of a BCS class II drug cinnarizine, for improved oral delivery. Tween 80, Oleic acid and Capmul MCM C-8 were selected as surfactants, oil and co-surfactant respectively. Droplet size and zeta potential of the formulations were investigated and found to be good. The SNEDDS showed good efficiency for self-emulsification. The in vitro dissolution was measured in 0.1 N HCl and phosphate buffer (pH 6.8). SNEDDS with δ(mix) surfactant : cosurfactant ratio (2:1) and δ(mix)-oil ratio (6:1) showed the highest drug release. it was concluded that SNEDDS is a promising approach to improve the dissolution rate solubility and bioavailability of cinnarizine [18].

Zadeh B S et al., formulated a SEDDS containing a lipophilic drug, loratadine. For optimization of formulation, full factorial design with three variables surfactant/co-surfactant, surfactant/oil and percentage of drug in two levels were used. The effects of various factors like: particle size, emulsifying efficiency, drug release and rat intestine permeability were checked. The results showed labrafil and liquid paraffin as oil with span 20 as surfactant and capryol as co-surfactant prepared stable emulsions with refractive index higher than acidic medium and water. The percentage of drug released after 6 hrs, for labrafil, was (30.87-54.26%) and for liquid paraffin (31.99-61.34%). Formulations showed good drug permeability through rat intestine compared to other. In was found that SEDDS prepared with liquid paraffin provided perfect solubility in acidic condition and increased intestinal permeability [19].

Khan F et al., prepared and characterized a self-emulsifying drug delivery system (SEDDS) of poorly water-soluble Atorvastatin for the improvement of dissolution and oral bioavailability. A high drug load (10% w/w) was achieved with a combination of Tween 80, oleic acid and polyethylene glycol 400. Effects of lipids and surfactants on physical properties of SEDDS like in vitro emulsification efficiency in terms of self-emulsification time, percent transmittance and emulsion droplet size were measured. Further evaluation revealed that a higher amount of surfactants significantly increased dissolution of Atorvastatin while decreasing emulsion droplet size and emulsification time. About 400% increase in dissolution was achieved by SEDDS compared to pure Atorvastatin powder. It can be concluded that dissolution of Atorvastatin can successfully be enhanced by incorporating it in SEDDS. And also the potential of these formulations for bioavailability enhancement and possible gastric irritation due to the use of large amount of surfactants needs to be evaluated by in vivo studies [20].

Chouksey R et al., formulated self-emulsified drug delivery systems (SEDDS) through the nanoemulsion for the effective delivery of Atorvastatin, a HMG-COA Inhibitor. The formulation was found to be the optimized formulation on the basis of results of ternary phase diagram, droplet size, in vitro drug release and other parameters. Study, clearly indicated that the usefulness of SEDDS in the improvement of the dissolution rate and there by oral bioavailability of poorly water soluble drugs like Atorvastatin without incompatibility between the ingredients [21].

Bok ki et al., formulated self-microemulsifying drug delivery system (SMEDDS) for enhancement of bioavailability of simvastatin, a poorly water soluble drug. Optimized formulation was selected based upon ternary phase diagram. The optimized formulation of SMEDDS containing simvastatin (high drug loading and small particle size) was as following: Carpryol 90 (37%), Cremophor EL (28%), and Carbitol (28%) due to high affinity for the continuous phase and forming the smallest particle size. The optimized SMEDDS of simvastatin was compared with the conventional tablet (Zocor®) and the dissolution rate from SMEDDS was higher than the conventional tablet. There was 1.5 fold increase in bioavailability of the drug as compared with conventional tablet, when given to fasted beagle dogs. It was concluded that SMEDDS can be used for the delivery of simvastatin by the oral route [22].

Villar A M et al., applied Quality by Design approach for improvement of dissolution and oral absorption of gemfibrozil by preparing Self-nanoemulsifying drug delivery systems. This study reports an approach on the use of a Box–Behnken design and response surface methodology in the optimization of self-nanoemulsifying drug delivery systems (SNEDDS) of Gemfibrozil for in vitro evaluation. Optimized gemfibrozil loaded SNEDDS composed of Gem (16.22%), lemon essential oil (21.62%), Cremophor® EL 300 (32.43%) and Capmul® MCM-C8 (29.73%) was selected. Visual characterizations, polydispersity index, mean droplet size, turbidity and Gem amount dissolved after 30 min assays showed differences at various pH media being the best results was for pH 7.5 medium. The quantity of co-surfactant and surfactant was found to significantly impact turbidity, dissolved amount of Gem and the droplet size of SNEDDS. In vitro release studies revealed a two-step release pattern (burst followed by a slower sustained release) with 100% release at 45 min, compared to conventional tablets which have slower release pattern, 90% drug was released within 15 min in comparison to 30% from conventional tablets. It is concluded that the SNEDDS of the gemfibrozil as a promising alternative to improve oral absorption [23].

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Parmar N et al., developed and characterized self-nanoemulsifying drug delivery system (SNEDDS) to improve the oral bioavailability of poorly soluble third generation calcium channel blocker lercanidipine. After constructing phase diagram of two different combinations NL-I and NL-II. It was confirmed that structure and chain length plays a vital role in the performance of second amphiphile (Cosurfactant). Results obtained indicated that apart from HLB value and type of surfactant, other factors such as structure and relative length of hydrophobic chains of co-surfactant had influence on micro-emulsification and therefore nanoemulsifying area. A SNEDDS formulation of lercanidipine containing Cremophor EL (45% wt/wt), Caproyl 90 (13.5% wt/wt) with Transcutol® HP (1.5% wt/wt) and Maisine oil (10% wt/wt) was successfully developed and optimized based on globule size in nanometer range, minimum polydispersity, lower viscosity, lower surfactant concentration thus minimizing toxicity issues, higher solubility and therefore increased dissolution rate. The mean droplet size was 20.01 nm. The in vitro dissolution of lercanidipine SNEDDS was found significant in comparison to the marketed lercanidipine (Zanidip) tablet and pure drug in pH 1.2, 4.5 and 6.8 buffers. The stability studies at 30 °C/65% RH, 40 °C/65%RH and 50 °C/75% indicated stability of the optimized formulation as there was no significant change in the observed physical parameters. The results indicate that SNEDDS of lercanidipine, owing to nano-sized, has potential to enhance the absorption of drug. It was confirmed that the developed SNEDDS formulation was superior to commercial formulation with respect to in vitro dissolution profile and could be used as a possible nanocarrier system to deal with poorly soluble calcium channel blocker lercanidipine and later on to enhance bioavailability because of droplet size in nanometers [24].

CONCLUSION

SEDDS is an emulsion system that works on the process of self-emulsification which may be spontaneous or requires less amount of stirring, provided by peristaltic movements, whereas conventional emulsification requires high amount of shear. The review highlighted that a lot of research has been done on SEDDS formulations and it has been proved that this technique is a promising way to enhance the bioavailability of poorly water soluble drugs. These system forms o/w emulsions or micro emulsions upon mild agitation followed by dilution in aqueous media. i.e: GI fluids. Drug therefore remains in solution form, avoiding dissolution that limits absorption of hydrophobic drugs when given in crystalline form. Moreover, the in situ solubilization of drug can subsequently be absorbed by lymphatic pathways, because of its lipid content. So, this is an additional advantage associated with the system. Possibility of the system to adsorb on the solid carrier has gained popularity because systems can be administered as a unit dosage form for oral administration. Although a lot of work has been done, still there is scope for exploring this technique for enhancement of poorly soluble drug. This review can prove to be helpful for the researcher who wish to work on the enhancement of poorly soluble drug by this technique.

ABBREVIATIONS


REFERENCES