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Solid Self Nano-Emulsifying Drug Delivery Sysytem: A Review

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ABSTRACT

Self nanoemulsifying drug delivery (SNEDDS) is used for drugs which exhibit low water solubility. Dissolution is the rate limiting factor for these drugs. SNEDDS are capable of improving the bioavailability substantially of such drugs. They are formulated by utilizing an oil phase, surfactant and a co-surfactant. This formulation forms nano emulsion (O/W type) on contact with aqueous body fluids i.e. gastric juices when administered orally. Solid SNEDDS (s-SNEDDS) can also be formulated in the form of tablet which shows greater advantages. With recent and potential future developments, this technology will continue to enable novel applications in drug delivery and overcome limitations associated with the delivery of poorly water soluble drugs, mainly those belonging to BCS class-II and class-IV.

Keywords: Self nanoemulsifying drug delivery system (SNEDDS), oil phase, surfactants, cosurfactants, Pseudo ternary phase diagrams.

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INTRODUCTION[1-4]

In recent years, the formulation of poorly soluble compounds presented interesting challenges for formulation scientists in the pharmaceutical industry. Up to 40% of new chemical entities discovered by the pharmaceutical industry are poorly soluble or lipophilic compounds, which lead to poor oral bioavailability, high intra and inter subject variability and lack of dose proportionality. Efforts are ongoing to enhance the oral bioavailability of lipophilic drugs in order to increase their clinical efficacy. Self-emulsifying drug delivery systems have been shown to be successful in improving the oral bioavailability of poorly water soluble and lipophilic drugs. Self emulsifying drug delivery systems (SEDDS) also called as self emulsifying oil formulation which is mixture of oils and surfactants, ideally isotropic, and sometimes containing cosolvants, which emulsify spontaneously to produce fine oil in water emulsion when introduced into aqueous phase under gentle agitation. Self-nanoemulsifying (SNEDDS), self micro emulsifying (SMEDDS) and self emulsifying drug delivery systems (SEDDS) to improve the oral bioavailability of poorly water-soluble drugs.

Self nano-emulsifying drug delivery systems [6]

These systems have a unique property, they are able to self-emulsify rapidly in gastro-intestinal fluids and under the gentle agitation provided by the motion of the gastro-intestinal tract and they form fine O/W emulsions. These fine O/W emulsions produce small droplets of oil dispersed in the gastro-intestinal fluids that provide large interfacial area increasing the activity of pancreatic lipase to hydrolyze triglycerides and, thereby, promote a faster release of the drug and/or formation of mixed micelles of the bile salts containing the drug. Furthermore, in most cases the surfactant used for such formulations increases the bioavailability of the drug by activation of different mechanisms, maintaining the drug in solution and, thus, avoiding the dissolution step from the crystalline state and enhancing intestinal epithelial permeability at the same time. Moreover, the oil droplets lead to a faster and more uniform distribution of the drug in the gastrointestinal tract, minimizing the irritation due to contact between the drug and the gut wall. In addition, lipids affect the oral bioavailability of drugs by exerting their effect through several mechanisms, including protection of the drug from enzymatic or chemical degradation in the oil droplets and activation of lipoproteins promoting the lymphatic transport of lipophilic drugs. These systems may then be incorporated into capsules directly, or transformed into granules, pellets, and powders for dry filled capsules as well as tablet preparations. The latter option is possible by innovative adaptations of conventional equipment with relative ease and process simplicity, using methods like melt

granulation, adsorption on a solid support, spray drying, spray cooling, melt-extrusion/spheronization, and supercritical fluid based methods.

In Self Nanoemulsifying drug delivery systems

Oil droplet size is: <100nm

Appearance is optically clear

Required HLB value is >12

Formulation components and considerations

Successful formulation of SNEDDS depends on the through understanding of the spontaneous nanoemulsification process and also on the physicochemical and biological properties of the components used for the fabrication of SNEDDS. The factors influencing the phenomenon of self nanoemulsification are the physicochemical nature and concentration of oily phase, surfactant and co-emulsifier or cosurfactant or solubilizer (if utilized); The ratio of the components, especially oil-to surfactant ratio; The temperature and pH of the aqueous phase where nanoemulsification would occur, Physicochemical properties of the drug, such as hydrophilicity/lipophilicity, pKa and polarity.These factors should receive attention while formulating SNEDDS. In addition, the acceptability of the SNEDDS components for the desired route of administration is also very important while formulating SNEDDS.

Advantages of SNEDDS [7-10]

Improvement in oral bioavailability

The ability of SMEDDS to present the drug in GIT solubilized form (globule size between 1-100nm) and subsequent increase in specific surface area enable more efficient drug transport through the intestinal aqueous boundary layer and through the absorptive brush border membrane leading to improved bioavailability. E.g. In case of Halofantrine approximately fold increase in bioavailability of drug was reported in comparison to tablet formulation.

Ease of manufacture and scale-up

Ease of manufacture and scale-up is one of the most important advantages that makes SMEDDS unique when compared to other drug delivery systems like solid dispersions, liposomes, nanoparticles etc., dealing with improvement of bioavailability. SMEDDS requires very simple and economical manufacturing facilities like simple mixer, agitators and volumetric liquid filing equipment for large scale manufacturing. This explains the interest of industry in the SMEDDS.

Reduction in inter-subject and intra-subject variability and food effects

There are various drugs which show large in inter-subject and intra-subject variation in absorption leading to decreased performance of drug and patient non-compliance. Food is a major factor

affecting the therapeutic performance of the drug in the body. SMEDDS are a remedy for such a drug. Several research paper specifying that, the performance of SMEDDS is independent of food and, SMEDDS offer a reproducibility of plasma profile are available.

Ability to deliver peptides that are prone to enzymatic hydrolysis in GIT

One unique property that makes SMEDDS superior as compared to other drug delivery systems is their ability to deliver macromolecules like peptides, hormones, enzyme substrates and inhibitors and their ability to offer protection from enzymatic hydrolysis.

No influence of lipid digestion process

Unlike the other lipid-based drug delivery systems, the performance of SMEDDS is not influence by the lipolysis, emulsification by the bile salts, action of pancreatic lipases and mixed micelle formation. SMEDDS are not necessary digested before the drug is absorbed as they present the drug in micro-emulsified form which can easily penetrate the mucin and water unstirred layer.

Increased drug loading capacity

SMEDDS also provide the advantage of increased drug loading capacity when compared with conventional lipid solution as the solubility of poorly water soluble drugs with intermediate partition coefficient(2<log p>4) are typically low in natural lipids and much greater in amphilic surfactants, co surfactants and cosolvents.

Sterilizable

SNEDDS formulation can be sterilized; therefore they can be given parenterally with i.v. fluids.

Components in Self- Nanoemulsifying Drug Delivery System[11-16]

1. Active Pharmaceutical Ingredient
2. Oil Phase
3. Surfactant
4. Co-surfactant
5. Adsorbent

Oils

The oil represents one of the most important excipients in the SEDDS formulation not only because it can solubilize marked amounts of the lipophilic drug or facilitate self-emulsification but also and mainly because it can increase the fraction of lipophilic drug transported via the intestinal lymphatic system, thereby increasing absorption from the GI tract depending on them molecular nature of the triglyceride 20-23. Both long and medium chain triglyceride oils with different degrees of saturation have been used for the design of self-emulsifying formulations. Furthermore, edible oils which could represent the logical and preferred lipid excipients choice for the

development of SEDDS are not frequently selected due to their poor ability to dissolve large amounts of lipophilic drugs. Modified or hydrolyzed vegetable oils have been widely used since these excipients form good emulsification systems with a large number of surfactants approved for oral administration and exhibit better drug solubility properties. They offer formulative and physiological advantages and their degradation products resemble the natural end products of intestinal digestion. Novel semi-synthetic medium chain derivatives, which can be defined as amphiphilic compounds with surfactant properties, are progressively and effectively replacing the regular medium chain triglyceride oils in the SEDDS.

Ex. Sunflower oil, Castor oil, corn oil, Olive oil, Peanut oil, Cotton seed oil, Canola oil, Repeseed oil, Coconut oil, Soyabean oil ,Paim oil, Palm Kernel oil, Cocoa butter, Lard, Tallow, Captex 500 P(Abitec Co), Capmul MCM C-10(Abitec CO), Capmul MCM (Abitec CO), etc.

Surfactants

Several compounds exhibiting surfactant properties may be employed for the design of self emulsifying systems, the most widely recommended ones being the non-ionic surfactants with are natively high hydrophilic-lipophilic balance (HLB). The commonly used emulsifiers are various solid or liquid ethoxylatedpolyglycolyzed glycerides and Polysorbate 80 (Tween 80). Safety is a major determining factor in choosing a surfactant. Emulsifiers of natural origin are preferred since they are considered to be safer than the synthetic surfactants. However, these excipients have a limited self-emulsification capacity.Non-ionic surfactants are less toxic than ionic surfactants but they may lead to reversible changesin the permeability of the intestinal lumen25. Usually the surfactant concentration ranges between30 and 60% w/w in order to form stable SEDDS. It is very important to determine the surfactant concentration properly as large amounts of surfactants may cause GI irritation. The surfactant involved in the formulation of SEDDS should have a relatively high HLB and hydrophilicity so that immediate formation of o/w droplets and/or rapid spreading of the formulation in the aqueous media (good self-emulsifying performance) can be achieved. For an effective absorption, the precipitation of the drug compound within the GI lumen should be prevented and the drug should be kept solubilized for a prolonged period of time at the site of absorption. Surfactants are amphiphilic in nature and they can dissolve or solubilize relatively high amounts of hydrophobic drug compounds. The lipid mixtures with higher surfactant and cosurfactant/ oil ratios lead to the formation of SNEDDS There is a relationship between the dropletsize and the concentration of the surfactant being used. In some cases, increasing the surfactant concentration could lead to droplets with smaller mean droplet size such as in the case of amixture of saturated C8-C10 polyglycolized glycerides (Labrafac CM-10). This could be

explained by the stabilization of the oil droplets as a result of the localization of the surfactant molecules at the oil-water interface. On the other hand, in some cases the mean droplet size may increase with increasing surfactant concentrations. This phenomenon could be attributed to the interfacial disruption elicited by enhanced water penetration into the oil droplets mediated by the increased surfactant concentration and leading to ejection of oil droplets into the aqueous phase.

Ex.- Labrasol, Labrafil WL 2609 BS, Tween 80, Tween 20,Pluronic F 127, Tween 85, Emulphor EI-620, Cremophor-EL, Cremophor RH 40, Span 80, Cerex ELS 250, Cremophor-ELP, etc.

Co-surfactants

The production of an optimum SEDDS requires relatively high concentrations (generally more than 30% w/w) of surfactants. Organic solvents such as, ethanol, propylene glycol, and polyethylene glycol are suitable for oral delivery, and they enable the dissolution of large quantities of either the hydrophilic surfactant or the drug in the lipid base. These solvents can even act as co-surfactants in microemulsion systems. On the other hand, alcohols and other volatile co-solvents have the disadvantage of evaporating into the shells of the soft gelatin, or hard, sealed gelatin capsules in conventional SEDDS leading to drug precipitation. Thus alcohol-free formulations have been designed, but their lipophilic drug dissolution ability may be limited. There are at least three reasons why cosolvents have been included in lipid-based formulations. More commonly it has been assumed that cosolvents could be included to increase the solvent capacity of the formulation for drugs which dissolve freely in cosolvents. However, to enhance the solvent capacity significantly the cosolvent must be present at high concentration and this is associated with the risk of drug precipitation when the formulation is dispersed in water cosolvents loose their solvent capacity quickly following dilution. A third reason for inclusion of cosolvents is to aid dispersion of systems which contain a high proportion of water soluble surfactants. There are practical limits on the concentrations of cosolvents which can be used, governed by issues of immiscibility with oil components and also possible incompatibilities of low molecular weight cosolvents with capsule shells.

Ex.- SLS, Pluronic L 64, Lutrol F 68, Pluronic L44, Transcutol P, PlurolOleique, Akoline MCM, etc.

Pseudo Ternary Phase Diagram [26]

Pseudo ternary phase diagram is used to map optimum concentration range of excipients according to the resulting droplet size following self emulsification, in vitro cell toxicity, stability upon dilution and viscosity. It is a good tool for optimizing SNEDDS composition. The phase behavior of simple microemulsion system consisting of oil, water and surfactant/cosurfactant mixture can be

studied with the aid of pseudo ternary phase diagram in which each corner of diagram represents 100% of that particular component. Phase diagram are useful tool to determine the number and types of phased, the % wt. of each phase and the composition of each phase at a given temperature and composition of the system these diagram are three dimensional but are illustrated in two dimensions for ease of drawing and interpretation. Constructing phase diagram is time consuming, particularly when the aim is to accurately delineate a phase boundary, as the phase boundary is approached. The procedure most often employed is to prepare a series of (pseudo) binary compositions and titrate with the third component, evaluating the mixture after each addition.

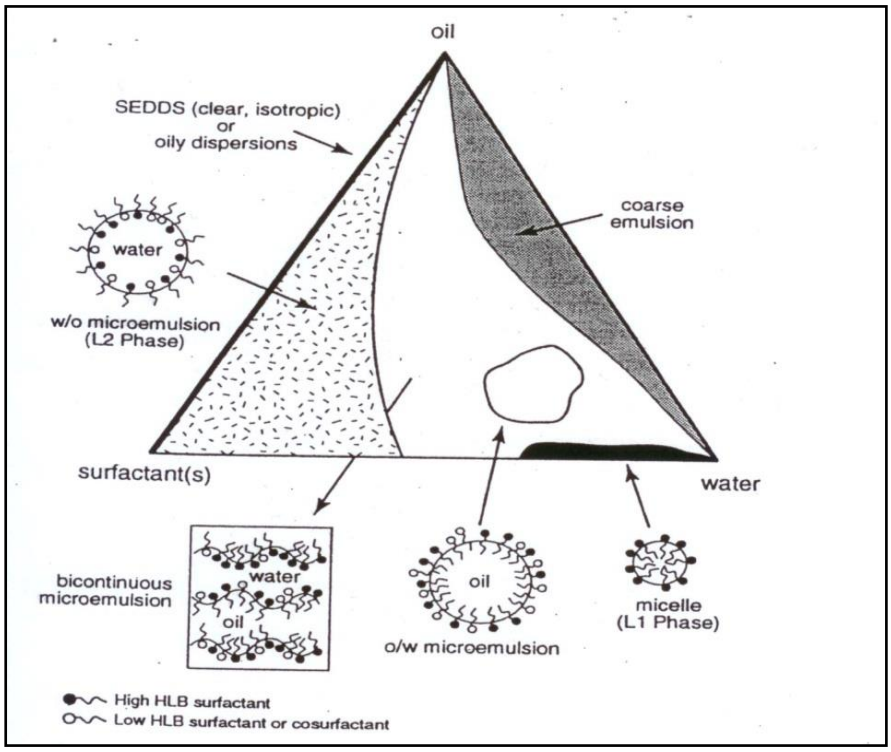

Figure 1:.Pseudoternary phase diagram.

Interpretation of Pseudo ternary phase diagram [26]

These diagrams are three-dimensional but are illustrated in two-dimensions for ease of drawing and interpretation. In a ternary diagram the relative percentage (normally weight %) of three components are represented by **A, B** and **C**. The only requirement is that the three components have to sum to 100%. If they don't, you have to normalize them to 100%.

Techniques for solid formulations [17-19]

Techniques are chosen on the basis of properties of lipid excipient. The techniques reviewed here under facilitate the transformation of liquid or semi-solid formulations into solid particles (powders, granules or pellets) which could subsequently be filled into capsules, sachets or compressed into tablets.

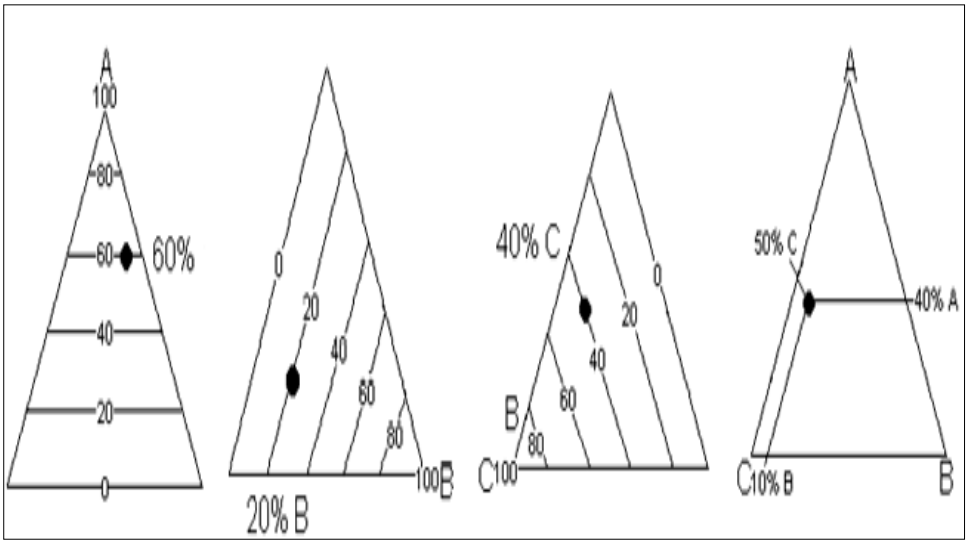

Figure2. Interpretation of Pseudo ternary phase diagram

1. Spray Cooling

The molten droplets are sprayed into cooling chamber, which will congeal and re-crystallize into spherical solid particles and subsequently collected as fine powder. The fine powder may be used for development of solid dosage forms tablets or direct filling into hard shell capsules. Many types of equipment area vailable to atomize the liquid mixture and to generate droplets rotary, pressure, two-fluid or ultrasonic atomizers.

2. Spray Drying

Spray drying is defined as a process by which a liquid solution is sprayed into a hot air chamber to evaporate the volatile fraction. Polyoxylglycerides (lauroyl or stearoyl) have been used alone or in combination with a solid carrier (silicon dioxide) to form micro particles of etoricoxib and glibenclamide. Technology solves the stability problems associated with classic emulsions during storage and helps also avoid using harmful or toxic organic solvents. Dry emulsions may be redispersed into water before use. Medium chain triglycerides are commonly used as oil phase for these emulsions.

3. Adsorption on Solid Carriers

Solid carriers are used for the adsorption of liquid formulation to get final solid product and it will be free flowing so that it can be compressed or directly filled in hard gelatine capsules. A significant benefit of the adsorption technique is good content uniformity as well as the possibility for high lipid exposure. The adsorption technique has been successfully applied to gentamicin and erythropoietin with (Labrasol®) formulations that maintained their bioavailability enhancing effect after adsorption on carriers.

4. Melt Granulation

Melt granulation or pelletization is a transformation of a powder mix containing the drug into granules or spheronized pellets. The melted binder forms liquid bridges with the powder particles that shape into small granules which can, by further mixing under controlled conditions transform to spheronised pellets. The main parameters that control the granulation process are impeller speed, mixing time, binder particle size, and the viscosity of the binder during melt granulation. Nucleation is largely affected by binder viscosity at high impeller speed and binder particle size at low speed.

5. Melt Extrusion/ Spheronisaton

Extrusion is a process of converting a raw material with plastic properties into a product of uniform shape and density by forcing it through a die under controlled temperature, product flow and pressure conditions. This approach has been successfully tried for 17-estradiol and two model drugs with surfactants such assucrose monopalmitate, lauroyl polyoxyl glycerides and polysorbate 80 (Tween® 80) Gelucire® 44/14 to be used directly in the core of the formulation matrix. An innovative "system-in cylinder" moulding technique was recently for dual purpose enhanced bioavailability and controlled release.

6. 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. In freeze-drying, a slow cooling rate and the addition of amorphous cryoprotectants have the best stabilizing effects, hile heat treatment before thawing decreases the stabilizing effects. The technique of spray drying is more frequently used in preparation of dry emulsions. The O/W emulsion was formulated and then spray-dried to remove the aqueous phase. The most exciting finding in this field ought to be the newly developed enteric-coated dry emulsion formulation, which is potentially applicable for the oral delivery of peptide and protein drugs. This formulation consisted of a surfactant, a vegetable oil, and a pH-responsive polymer, with lyophilisation used.

7. Self-Emulsifying Beads

In an attempt to transform SES into a solid form with minimum amounts of solidifying excipients, investigated loading SE S into the micro channels of porous polystyrene beads (PPB) using the solvent evaporation method. PPB with complex internal void structures is typically produced by copolymerizing styrene and divinyl benzene. They are inert, stable over a wide Ph range and to

extreme conditions of temperature and humidity.

8. Self-Emulsifying Suppositories

Some investigators proved that S-SEDDS could increase not only GI adsorption but also rectal/vaginal adsorption. Glycyrrhizin, which, by the oral route, barely achieves therapeutic plasma concentrations, can obtain satisfactory therapeutic levels for chronic hepatic diseases by either vaginal or rectal SE suppositories. The formulation included glycyrrhizin and a mixture of a C6–C18 fatty acid glycerol ester and a C6–C18 fatty acid macrogolester.

9. Self-Emulsifying Implants

Research into SE implants has greatly enhanced the utility and application of S-SEDDS. As an example, 1, 3-bis (2-chloroethyl)-1-nitrosourea (carmustine, BCNU) is achemo therapeutic agent used to treat malignant brain tumors. However, its effectiveness wash indered by its short half-life. In order to enhance its stability compared with that released from poly (d,l-lactide-co glycolide) (PLGA) waferim plants, SES was formulated with tributyrin Cremophor RH 40 (polyoxyl40hydrogenated castor oil) and Labrafil1944(polyglycolyzed glyceride). Then self-emulsified BCNU was fabricated into wafers with flat and smooth surface by compression moulding. Ultimately, SES increased in vitro half-life of BCNU up to 130 min contrasted with 45 min of intact BCNU.

Characterization of Snedds [20-25]

1. **Thermodynamic stability studies**

The physical stability of a lipid –based formulation is also crucial to its performance, which can be adversely affected by precipitation of the drug in the excipient matrix. In addition, poor formulation physical stability can lead to phase separation of the excipient, affecting not only formulation performance, but visual appearance as well. In addition, incompatibilities between the formulation and the gelatin capsules shell can lead to brittleness or deformation, delayed disintegration, or incomplete release of drug.

i. Heating cooling cycle:

Six cycles between refrigerator temperature (4°C) and 45°C with storage at each temperature of not less than 48 h is studied. Those formulations, which are stable at these temperatures, are subjected to centrifugation test.

ii. Centrifugation:

Passed formulations are centrifuged thaw cycles between 21°C and +25°C with storage at each temperature for not less than 48 h is done at 3500 rpm for 30 min. Those formulations that does not show any phase separation are taken for the freeze thaw stress test.

iii. Freeze thaw cycle:

Those formulations pass this test show good stability with no phase separation, creaming, or cracking.

2. Self-Emulsification Time

The efficiency of self-emulsification is assessed using dissolution apparatus. 1ml SEDDS was dissolved in 250ml of water at 37±0.5◦C. Gentle agitation was provided by paddle rotating at 60RPM. SEDDS was assessed visually according the rate of emulsification and the final appearance of the emulsion. Time was noted in triplicates standard. Also any precipitation was observed visually.

3. Dispersibility test

The efficiency of self-emulsification of oral nano emulsion is assessed using a standard USP dissolution apparatus II. One milliliter of each formulation was added to 500 ml of water at 37 ± 0.5^0C. A standard stainless steel dissolution paddle rotating at 50 rpm provided gentle agitation. The in vitro performance of the formulations is visually assessed using the following grading system.

Grade A: Rapidly forming (within 1 min) nano emulsion, having a clear or bluish appearance.

Grade B: Rapidly forming, slightly less clear emulsion, having a bluish white appearance.

Grade C: Fine milky emulsion that formed within 2 minutes

Grade D: Dull, grayish white emulsion having slightly oily appearance that is slow to emulsify(longer than 2 min).

Grade E: Formulation, exhibiting either poor or minimal emulsification with large oil globules present on the surface.

Grade A and Grade B formulation will remain as nano emulsion when dispersed in GIT. While formulation falling in Grade C could be recommend for SNEDDS formulation.

4. Robustness to dilution

Formulations were 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.

5. Droplet size analysis and Particle size measurements

The droplet size of the emulsions is determined by photon correlation spectroscopy (which analyses the fluctuations in light scattering due to Brownian motion of the particles) using a Zeta sizer able to measure sizes between 10 and 5000 nm. Light scattering is monitored at 25°C at a

90° angle, after external standardization with spherical polystyrene beads. The nano metric size range of the particle is retained even after 100 times dilution with water which proves the system's compatibility with excess water.

6. Zeta potential measurement

This is used to identify the charge of the droplets. In conventional SNEDDSs, the charge on an oil droplet is negative due to presence of free fatty acids.

7. Refractive index and Percentage Transmittance

Refractive index and percent transmittance proves the transparency of formulation. The refractive index of the system is measured by refractometer by placing drop of solution on slide and it compare with water (1.333). The percent transmittance of the system is measured at particular wavelength using UV-spectrophotometer keeping distilled water as blank. If refractive index of system is similar to the refractive index of water (1.333) and formulation have percent transmittance > 99 percent, then formulation have transparent nature.

8. Measurement of Polydispersity index

(PDI) is measure of droplet size homogeneity and it varies from 0.0 to 1.0. Polydispersity is the ratio of standard deviation to mean droplet size in the formulation. The higher the polydispersity, the lower the uniformity of the droplet size in the formulation. The closer to zero the polydispersity value the more homogenous are the droplets.

9. Cloud point measurement

The optimized SNEDDS formulations were diluted with distilled water in the ratio of 1:250. The diluted samples were placed in a water bath and its temperature was increased gradually. Cloud point was spectrophoto metrically determined as the temperature at which there was a sudden appearance of cloudiness.

10. Scanning Electron Microscope study

Morphological examination of surface of Neusilin US2 and formulation adsorbed on Neusilin US2 was carried out using a scanning electron microscope. Particles were vacuum dried and coated with thin gold-palladium layer and observed microscopically at an accelerating voltage of5.0 kV.

11. *In Vitro* Diffusion study

In vitro diffusion studies is performed for all the formulations developed, using a dialysis technique. The dialyzing medium is phosphate buffer pH 6.8. One end of pretreated cellulose dialysis tubing (7 cm in length) is tied with thread, and then 1 ml of self-nano emulsifying formulation is placed in it along with 0.5 ml of dialyzing medium. The other end of the tubing is also secured with thread and is allowed to rotate freely in 200 ml of dialyzing medium and stirred

continuously at 100 rpm with magnetic bead on magnetic plate at 37°C. Aliquots of 1 ml are removed at different time intervals and diluted further. Volume of aliquots is replaced with fresh dialyzing medium each time. These samples are analyzed quantitatively for drug dialyzed across the membrane at corresponding time by using UV-visible spectrophotometer.

12. Drug content determination

Drug from pre-weighed SNEDDS is extracted by dissolving in suitable solvent. Drug content in the solvent extract was analyzed by suitable analytical method against the standard solvent solution of drug.

Biopharmaceutical Aspects [26]

Although incompletely understood, the currently accepted view is that lipids may enhance bioavailability via a number of potential mechanisms including:

- Alterations (reduction) in gastric transit, thereby slowing delivery to the absorption site and increasing the time available for dissolution.
- Increases effective lumenal drug solubility. The presence of lipids in the GI tract stimulates an increase in the secretion of bile salts (BS) and endogenous biliary lipids including phospho lipid (PL) and cholesterol (CH), leading to the formation of BS/PL/CH intestinal mixed micelles and an increase in the solubilization capacity of the GI tract. However, intercalation of administered (exogenous) lipids into these BS structures either directly (if sufficiently polar), or secondary to digestion, leads to swelling of the micellar structures and a further increase in solubilization capacity.
- Stimulation of intestinal lymphatic transport. For highly lipophilic drugs, lipids may enhance the extent of lymphatic transport and increase bioavailability directly or indirectly *via* a reduction in first-pass metabolism.
- Changes in the biochemical barrier function of the GI tract. It is clear that certain lipid and surfactants may attenuate the activity of intestinal efflux transporters, as indicated by the p-glycoprotein efflux pump, and may also reduce the extent of enterocyte-based metabolism.
- Changes in the physical barrier function of the GI tract. Various combinations of lipids, lipid digestion products and surfactants have been shown to have permeability enhancing properties. For the most part, however, passive intestinal permeability is not thought to be a major barrier to the bioavailability of the majority of poorly water-soluble, and in particular, lipophilic drugs.

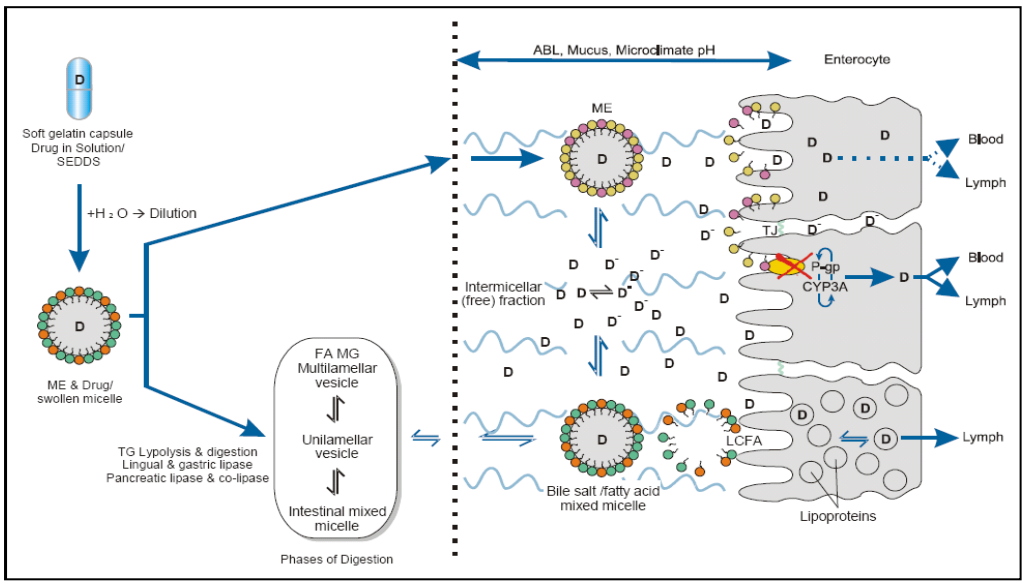

Figure 3: A graphical representation of in vivo fate of micro emulsion.

CONCLUSION

Solid-SNEDDS is a promising approach for BCS class II or IV drug compounds with poor aqueous solubility. Also chances of channelizing the API's through the lymphatic channels are possible, thereby limiting the hepatic first pass metabolism. 'Food Effect" of poorly water soluble drugs can also be minimized. This is the method suited for lipophilic drugs where resulting emulsification gives faster dissolution rates and absorption. The oral delivery of hydrophobic drugs can be made possible by solid-SNEDDS which have been shown to substantially improve oral bioavailability. With future development of this technology solid-SNEDDS will continue to enable novel applications in drug delivery and solve problems associated with the delivery of poorly soluble drugs, mainly BCS class-II and class-IV drugs.

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