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A REVIEW ON DIFFERENT PROPERTIES AND TYPES OF A NOVEL PROMISING APPROACH FOR ENHANCING THE BIOAVAILABILITY OF POORLY WATER-SOLUBLE DRUGS

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Keywords:

lipid-based system, Self-micro-emulsifying drug delivery systems (SMEDDS), Micro-emulsions, Bioavailability, Lipophilic drug

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ABSTRACT: Poor aqueous solubility has been one of the major challenges in modern drug delivery as it hinders the absorption process leading in the decrease of bioavailability. As a consequence of low water solubility of drugs, low oral bioavailability is a growing challenge to the development of new pharmaceutical products. There has been a consistent increase in the number of new pharmacologically active lipophilic compounds that are poorly water-soluble. Approximately 40% of new drug candidates are lipophilic and exhibit poor water solubility. One of the popular approaches of oral bioavailability and solubility enhancement is the utilization of lipid-based drug delivery systems - self microemulsifying drug delivery system (SMEDDS). Self-micro emulsifying drug delivery system (SMEDDS) is one of the exclusive approaches to increase bioavailability by improving solubility for the poorly aqueous soluble drug and to increase the oral absorption of highly lipophilic drugs. These systems have unique property to form oil in water emulsion under gentle agitation provided by digestive motility of the stomach and intestine. A greatest advantages of incorporating poorly soluble drugs into such formulations is their spontaneous emulsification and formation of a microemulsion in aqueous media. This review gives an overview on SMEDDS focuses on properties, components and different types of the lipid-based drug delivery system for oral use with their characteristics thus enabling a broader perspective and understanding of their present role in medicine and drug delivery.

INTRODUCTION: Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been employed for the systemic delivery of drug via various pharmaceutical products of different dosage forms.

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The oral route has been the major route of drug delivery for chronic treatment of many diseases as it is the most cost-effective and leads the world wide drug delivery market.

In the present scenario, oral drug delivery is continuously looking into newer avenues as mostly 40% of new drug candidates have poor water solubility and absorption, high fluctuation in the drug plasma level and lack of dose proportionality which are playing major role in obtaining results leading to failure of conventional drug delivery system. 1, 2 Due to have low solubility of drugs, this leads to low dissolution and therefore limits the

absorption. To overcome this dilemma, some clinical formulations have been developed, but low oral bioavailability of most drugs is still a major obstacle leading to challenges for pharmaceutical manufacturers to design delivery systems that can be improved by increasing its gastrointestinal solubilization with modification of pharmaco-kinetic action and therapeutic responses. [3]

In Pharmaceutical industry continuous innovation is one of the most defining characteristics. Most of the newly discovered drug candidate limits the bioavailability of orally administered drugs [4]. The fact that 40% of new chemical entities discovered are lipophilic in nature with poor aqueous solubility, it hinders the absorption process leading in the decrease of bioavailability, which, signifies the need of suitable drug delivery approach for optimal benefit.

Various formulation techniques such as solid dispersion/amorphous formulation, micronization and lipid-based formulations such as of micro-emulsion are considered to deliver the drug in a more prominent way. Among these, micro-emulsion formulations, with a notable emphasis on self-micro-emulsifying drug delivery system (SMEDDS), have gained much more importance as a promising drug delivery system for both soluble as well as poorly water soluble drugs in recent times as these are advantageous in the aspect of their stability, self-dispersing nature, ease of preparation, and scale-up. [5, 6]

Self-micro Emulsifying Drug Delivery Systems (SMEDDS): Self-micro emulsifying drug delivery systems (SMEDDS) are defined as isotropic mixtures of natural or synthetic oils, solid or liquid surfactants and co-solvents/co-surfactants that have a unique ability of forming fine oil-in-water (o/w) or micro emulsions upon mild agitation followed by dilution in aqueous media, such as GI fluids.

The emulsification process requires little entropy change which is obtained from the peristaltic motion of gut. SMEDDS form transparent micro emulsions with a droplet size below 100 nm upon dilution is a promising alternative for conventional oral emulsions because of its ability to be delivered specifically with greater efficacy and relatively high stability [7].

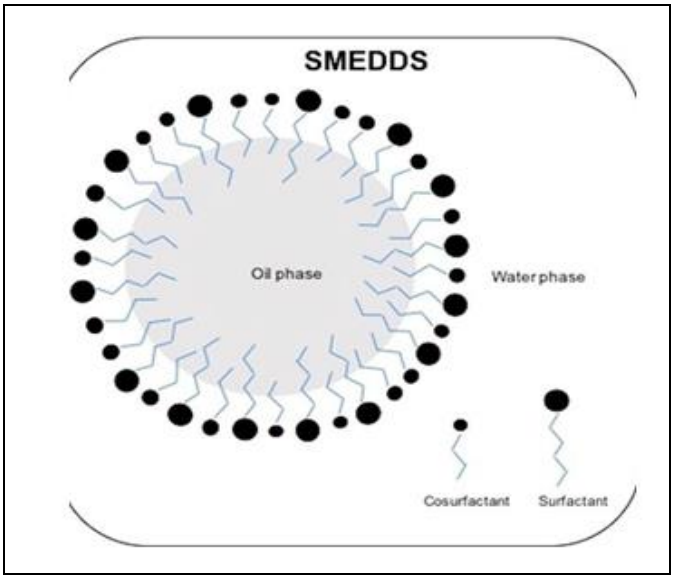

FIG. 1: MICELLE OF SELF-MICRO EMULSIFYING DRUG DELIVERY SYSTEM

Rational for Self-micro Emulsifying Drug Delivery System:

1. Salt formation of neutral compounds is not feasible and the synthesis of weak acid and weak base salts may not always be practical. Moreover, aggregation in the gastrointestinal tract may occur as the salts that are formed may convert may back to their original acid or base forms [8].

2. Particle size reduction may not be desirable in situations where handling difficulties and poor wettability are experienced for very fine powders. Problem with micronization is chemical / thermal stability, many drug may degrade and lose bioactivity when they are micronized by conventional method [9].

3. For solid dispersion the amount of carriers used is often large, and thus if the dose of active ingredient is high, swallowing the tablets or capsules will be difficult as the formation will be large in volume. Moreover, since the carriers used are usually expensive and freeze-drying or spray drying method requires particular facilities and processes, leading to high production cost [10]. The oral bioavailability of poor water soluble drugs may be enhanced when co-administered with meal rich in fat and this realization has led to increasing recent interest in the formulation of poorly water soluble drugs in lipids. SMEDDS is a novel and versatile approach to improve water solubility and ultimate bioavailability of lipophilic drugs.

Need of SMEDDS:

1. Normal motility of the GIT provides energy for emulsification. Prolonged contact between the drug and the wall of the GIT can cause irritation which can be surmounted by the formulation of SMEDDS as the microscopic droplets formed help in the transportation of drug quickly from the stomach by distributing the drug widely along the GIT [11].

2. Upon dispersion in water, these formulations produce fine droplets with enormous interfacial area and enhance permeation across the intestinal membrane, and facilitates transcellular and paracellular absorption with the use of surfactants. They dramatically improve the bioavailability of lipophilic molecules and essential oils by increasing drug solubilization and surface area due to small droplet size [12].

3. Formulation of SMEDDS with consequent stable plasma-time profile can help in the efficient absorbption of poorly water soluble drugs which have dissolution rate limited absorption. Presentation of the poorly soluble drug in dissolved form might cause constant plasma levels of drug that bypasses the critical step in drug absorption, *i.e,* dissolution [13].

4. Food effects which are usually observed with lipophillic drug molecules are significantly reduced by their incorporation into SMEDDS. Formulation of SMEDDS can protect the drugs which have propensity to be degraded by the chemical and enzymatic means in GIT as the drug will be in the form of oil droplets in the body [14].

Advantages: SMEDDS being a novel and versatile approach to improve water solubility and ultimately bioavailability of lipophilic drugs has numerous advantages:

1. In terms of the stability SMEDDS are advantageous over emulsions because of the low energy consumption and the manufacturing process does not include critical steps. To formulate SMEDDS simple mixing equipment is enough and time required for preparation is also less compared to emulsions [15].

2. In the formulation of SMEDDS along with the lipids, surfactants that are commonly used like Tween 80, Spans, Cremophors (EL and RH40), and Pluronics are reported to have inhibitory action on efflux transporters which help in improving bioavailability of the drugs which are substrates to the efflux pumps. Surfactants of high HLB like Tween 80 are reported to increase the permeability of the drug when administered along with the formulation due to the loosening effect of these on tight junctions [16].

3. Protection of sensitive drug substances with selective targeting of drugs toward specific absorption window in GIT and giving high drug payloads and stability as it belongs to a thermodynamics stable system [17].

Disadvantages: [17]

1. Lack of good predicative in-vitro models for assessment.

2. High surfactant concentrations (=30-60%) irritates.

3. In the conventional formulations volatile co-solvents may migrate into the shells of soft or hard gelatine capsules resulting in precipitation of lipophilic drugs.

4. Lack of good IVIVC correlation and suitable animal model for *in-vivo* studies.

Factors Affecting SMEDDS Formulation:

1. Solubility of Drug: It is preferable that drug solubilizes in all components used in the formulation. Solubility must be higher at least in oil so higher drug proportion can be administered with predicted bioavailability. The drug must be soluble in the excipients used and all the excipients should be compatible with drug and each other, thus no interaction with drug and within the components will be seen [18].

2. Dose of Drug: Some drugs are not suitable for SMEDDS which are administered at very high dose unless they exhibit extremely good solubility in at least one of the components of SMEDDS, preferably lipophillic phase [19].

3. Polarity of Lipid Phase: The polarity of the lipid phase is another factor that influences the drug release from the Microemulsion. Polarity indicates the affinity of drug towards solvent, oil or water.

Higher the polarity of lipid base, higher drug release profile is seen. Use of cationic surfactant may give a positive charge to the droplets which can lead to higher membrane penetration with increased bioavailability [20].

Drug Transport Mechanism of SMEDDS: SMEDDS partially avoids the additional drug dissolution step prior to absorption in the GI tract. They increase the amount of solubilized drug in the intestinal fluids resulting in good drug absorption. Absorption of the drug may also be enhanced by using lipid based excipients in the formulation. Once they reach the GIT, they undergo three processes; *i.e*,

1. Digestive
2. Absorptive
3. Circulatory

During digestion, SMEDDS form a coarse emulsion, which undergoes enzymatic hydrolysis at oil water interphase and thereby gets ready for absorption phase. After formation of mixed micelles, due to interaction of fatty acid with bile, digestion process stops. The next phase of drug absorption then starts.

These colloids are taken up by passive diffusion or active transport through enterocyte membrane. Some drugs may get absorbed *via* lymphatic circulation through chylomicrons. In circulatory phase, drug is released from chylomicrons and the residual lipid is used in body [21].

Self-micro Emulsifying Drug Delivery Systems (SMEDDS):

- Diluted in GIT with gastric fluid
- Micro-emulsion containing drug (swollen miscelles)
- Contraction, retropulsion and gastric emptying- coarse emulsion. Digestion by gastric acid pancreatic lipase and colipase
- Transport of drug through passive or facilitated diffusion. Absorption of free drug may merge with chlyomicrons.
- Lymphatic circulation of drug
- Chylomicrons enter systemic circulation where it releases the drug

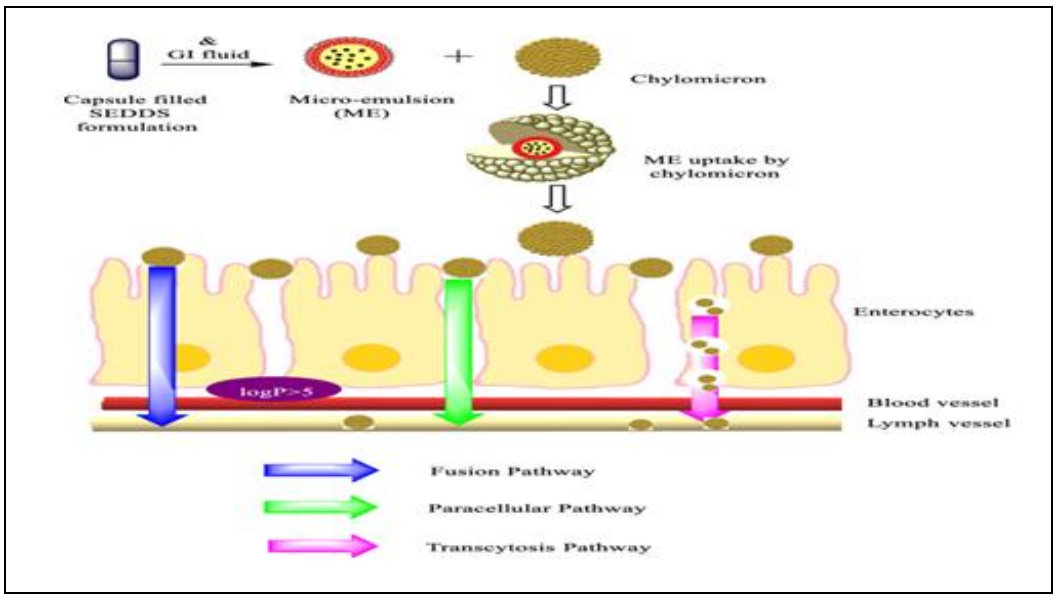

FIG. 2: DRUG TRANSPORT MECHANISM

Mechanism of Self-Emulsification: The self-emulsification process occurs due to the entropy change in the SMEDDS system which is provided by the peristaltic movement in the gut wall. At this point, the energy produced by the randomness of a molecule (entropy) is greater than the energy required to increase the dispersion surface area. Soon after gentle shaking of a self-emulsifying system within the GI medium, the water instantly penetrates to the aqueous core leading to interface disruption and micro-droplet formation. In conventional emulsion formulation, free energy is

directly proportional to the energy required to create new surface within two phases of the system. The equation can be given as:

$$\Delta G = \Sigma N \pi r 2 \sigma$$

Where ΔG is the associated free energy in the process, N is numbers of the droplet with radius "r", and "σ‟ is interfacial energy with time.

In order to decrease the interfacial area and simultaneously the free energy of the system, phases of emulsion will have a high affinity to separate. Here, in a self-emulsifying system, the free energy required to form the emulsion is very low, positive or negative thus the emulsion process occurs spontaneously. Very small amount of energy required for the emulsification involves the destabilization through concentration of local interfacial region [22].

Components of SMEDDS:

SMEDDS Formulation Contains the Following Components:

1. Drug: When poor solubility is the major reason for insufficient absorption of drug, lipid based formulations are preferred. Solubility of the drug in oil phase is important in the selection of suitable drug candidate for the formulation of lipid based delivery systems like SMEDDS. The drug should be sufficiently hydrophobic to be soluble in the lipid component of the formulation; that is, octanol: water partition coefficient should be high (log*P* > 5) to incorporate the whole required dose of the drug in one dosage unit [23]. Most of the hydrophobic drugs have good solubility in synthetic oils and surfactants compared to that in oils from natural source. The greater bioavailability from the SMEDDS can be achieved when the dose is very low especially for the drugs with high octanol: water partition coefficient. The absorption of the drug from SMEDDS is primarily dependent on its solubility in water and lipid phase [24]. Drugs that have poor bioavailability because of presystemic metabolism can be formulated as SMEDDS provided that the drug should have high solubility in long chain triglycerides (>50 mg/mL) and octanol: water partition coefficient of greater than five [25].

2. Oil: Oil is the most important component as it solubilizes the lipophilic drug and also results in increased absorption *via* intestinal mucosa in the area of emulsification [26]. Edible natural and synthetic oils are usually considered in the formulation of SMEDDS but as many natural oils are easily degraded by the microorganism and also by acidic environment in the stomach, hydrolyzed vegetable oils are used, which gives good emulsification system and are also compatible with larger number of surfactants approved for oral absorption [27].

Both long chain triglyceride and medium chain triglyceride are used having a varying degree of saturation. Example: cottonseed oil, soybean oil, palm oil, castor oil, hydrogenated specialty oil (hydrolyzed corn oil) *etc*.

3. Surfactant: Surfactant, also called surface active agent rest on the water-air interface and thus decrease the surface tension of water. Surfactant molecules consist of two parts, polar head group region and non-polar tail region. Surfactant molecules may be classified based on the nature of the hydrophilic group within the molecule. The four main groups of surfactants are defined as follows:

- Anionic surfactants
- Cationic surfactants
- Ampholytic surfactants
- Non-ionic surfactants [28]

Anionic Surfactants: where the hydrophilic group carries a negative charge such as carboxyl (RCOO), sulphonate (RSO3-) or sulphate (RO- SO3-). Examples: Potassium laurate, sodium lauryl sulphate.

Cationic surfactants: where the hydrophilic group carries a positive charge. Example: quaternary ammonium halide.

Ampholytic surfactants: (also called zwitterionic surfactants) contain both a negative and positive charge. Example: sulfobetaines.

Non-ionic Surfactants: where the hydrophilic group carries no charge but derives its water solubility from highly polar groups such as hydroxyl or polyoxyethylene (OCH_2CH_2O). Examples: Sorbitan Ester (Spans), Polysorbates (Tweens).

4. Co-surfactant: High concentration of surfactant is required for the production of an optimum SMEDDS, in order to reduce interfacial tension, which can be harmful, so co-surfactants are used to reduce the concentration of surfactants. Co-surfactants together with the surfactants provide the sufficient flexibility to interfacial film to take up different curvatures required to form micro-emulsion over a wide range of composition. Selecting surfactant and co-surfactant in right proportion is necessary for the efficient design of SMEDDS and for the solubilization of drug in the SMEDDS. Generally co-surfactant of HLB value 10-14 is used. Organic solvents like ethanol, propylene glycol, polyethylene glycol are able to dissolve large amount of either drug or hydrophilic surfactant in lipid base and are suitable for oral delivery, so they can be used as co-surfactant for SMEDDS [29].

5. Other excipients: Various pH adjusters, flavouring agents and antioxidants agents to increase the stability and compliance of SMEDDS formulation. Few free radicals (ROO-, RO-, -OH) generated during formulation approach may damage drug and induce toxicity. Lipids undergo auto-oxidation forming peroxides ions and pH of the solution also may accelerate hydrolysis of lipid. 30 Thus to maintain the stability, lipophilic antioxidants like α-tocopherol, propyl gallate or BHT are used.

Formulation Design: Formulation of SMEDDS involves the following steps.

(1) Physicochemical Studies
(2) Construction of pseudoternary phase diagram.
(3) Preparation of SMEDDS.
(4) Characterization of SMEDDS.

(1) Physicochemical Studies:

1. Solubility Study of the Drug: Solubility study of the drug is carried in various edible oils. An excess amount of drug is mixed with required amount of selected oil and sealed in a vial. The mixture is then shaken for 48 h in a temperature regulated environment at about 30 ± 0.5 ºC. The mixture is then transferred to centrifuge and mixed at 3000 rpm for 5 min which is followed by filtration using 0.45 mm membrane filter. The filtrate is diluted using suitable solvent and spectrophotometrically quantified using the suitable solvent as a blank. Each experiment is being carried out in triplicate [31].

2. Screening of Surfactant: Emulsification ability of various surfactants will be screened. Surfactant will be added to of the selected oily phase (300 mg). The mixture will be gently heated at 40–45 °C for 30 seconds to attain homogenization of components. The mixture, will be weighed and diluted with distilled water to 50 mL to obtain a fine emulsion. The ease of emulsion formation will be scrutinized by counting the number of volumetric flask inversions to give a uniform emulsion and were observed visually for relative turbidity. The resulting emulsions were allowed to stand for 2 h and transmittance will be observed. The surfactant forming a clear emulsion with fewer inversions and higher transmittance will be selected [32].

3. Screening of Co-surfactant: Various co-surfactants will be screened for SMEDDS formulation. The screening of co-surfactants will be conducted on the basis of percent transparency and ease of emulsification. Mixtures of co-surfactant, selected surfactant and selected oil phase will be prepared and evaluated in the same manner as described in the above section on surfactant screening [32].

(2) Construction of Pseudo Ternary Phase Diagram: The pseudo ternary phase diagrams will be constructed using the water titration method. A series of Emulsions will be prepared by varying mass ratio of oil to S_{mix} from 9:1 to 1:9. The ratio of Tween 80 to PEG 400 will be optimized by varying their mass ratio from 1:0, 1:1, 2:1, 3:1, to 4:1.

Each pre-concentrate mixture will be titrated drop-wise with distilled water at room temperature and agitated after each drop. The end point of the titration will be taken as the point when the solution become cloudy and turbid, and the quantity of water required will be recorded.

The pseudo ternary phase diagram will be established to delineate the area of microemulsion and boundary of phases. The pseudo ternary phase diagrams will be plotted using Prosim software [33].

How to Read a Typical Ternary Diagram: The following points may be useful to read and understand ternary diagram in an easy way. The three corners of the typical ternary diagram represent three components, that is, A, B and C. The arrow towards BA indicates increase in proportion of A from 0% concentration (at point B) to 100% concentration (at point A), the arrow towards AC indicates the increase in proportion of C from 0% concentration (at point A) to 100% concentration (at point C), and similarly the arrow towards CB indicates the increase in proportion of B from 0% concentration (at point C) to 100% concentration (at point B). Composition at point "O" can be known by the following:

(i) Drawa line that is parallel to CB from point O towards AB. The point where this line intersects with AB indicates the percent composition of A at point O(X).

(ii) Then, percent composition of B at point O can be known by drawing a line that is parallel to AC towards BC. The point where this line intersects with BC indicates the percent composition of B at point O (Y).

(iii) Similarly, the percent composition of C at point O can be known by drawing a line that is parallel to AB towards AC (Z).

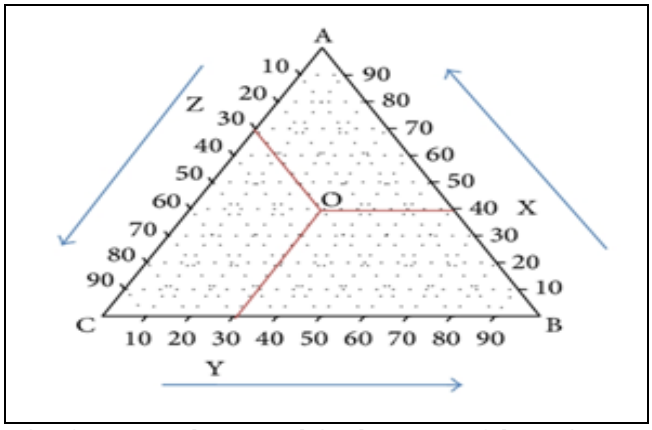

FIG. 3: TERNARY DIAGRAM INDICATING THE COMPOSITION OF A, B, AND C AT POINT O

Preparation of SMEDDS: The preparation involves the addition of drug to the mixture of oil, surfactant, and co-surfactant and then it should be subjected to vortexing [34]. In some cases, drug is dissolved in any one of the excipients and the remaining excipients are added to the drug solution [35].

Then, the solution should be properly mixed and tested for the signs of turbidity. After equilibration at ambient temperature for 48 hours, the solution should be heated for the formation of clear solution, if required. Depending on the final volume, the formulation should be stored in capsules of suitable size [36].

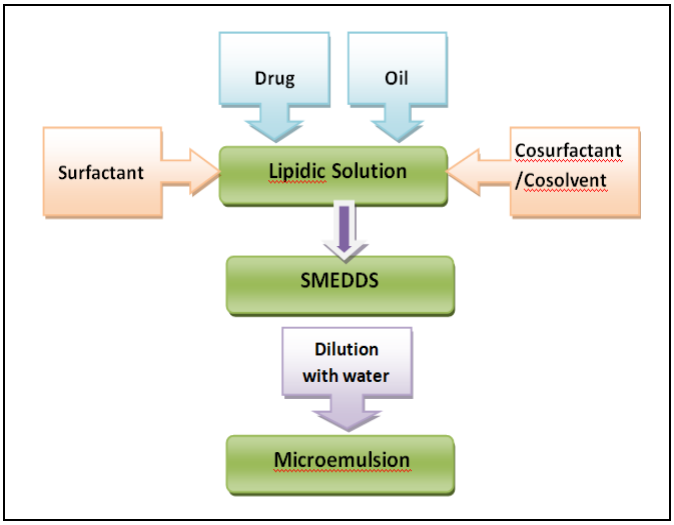

FIG. 4: GENERAL STRATEGY OF FORMULATING SMEDDS TO MICROEMULSION

Characterization of SMEDDS:

1. Macroscopic Evaluation: Macroscopic analysis will be carried out in order to observe the homogeneity of Micro emulsion formulations. Any change in colour and transparency or phase separation occurred during normal storage condition (37 ± 2 ºC) will be observed in optimized Micro emulsions formulation [37].

2. Visual Assessment: To assess the self-emulsification properties, formulation will be introduced into 100 ml of water in a glass flask at 25 ºC and the contents will be gently stirred manually. The tendency to spontaneously form a transparent emulsion will be judged as good and it will be judged bad when there will be poor or no emulsion formation. Phase diagram will be constructed identifying the good self emulsifying region [38].

3. pH and Viscosity Measurement: The pH of SMEDDS will be measured by pH meter and the viscosities will be measured to determine rheological properties of formulations. The viscosity of the prepared SMEDDS Batches will be determined by using Brookfield viscometer using a spindle in triplicate [39].

4. Thermodynamic Stability Studies:

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 will be conducted, and the formulations will be examined for stability at these temperatures.

II. Centrifugation Test: Formulations will be centrifuged at 3,500 rpm for 30 min, and then looked for phase separation [40].

5. Dilution Studies: Optimized formulations will be subjected to 50, 100, and 1000 fold dilution with distilled water, 0.1N hydrochloric acid, pH 4.4 phthalate buffer, and pH 7.4 phosphate buffer. The resultant diluted emulsions will be checked manually for any physical changes such as coalescence of droplets, precipitation, or phase separation after 24 h storage [41].

6. Droplet Size and Polydispersity Index (PDI) Determination: Photon correlation Spectroscopy (PCS) or dynamic light scattering (DLS) or Laser Diffraction Techniques are used to determine droplet size of emulsion. Zetasizer equipments are used for measurement of particle size which are able to measure sizes between 10 and 5000 nm [42].

7. Zeta Potential Measurement: Zeta potential for Micro emulsion will be determined using Zetasizer HSA 3000 (Malvern Instrument Ltd., UK). Samples will be placed in clear disposable zeta cells and results will be recorded. Before putting the fresh sample, cuvettes must be will behed with the methanol and rinsed using the sample to be measured before each experiment [43].

8. Transmittance Test: Stability of optimized Micro emulsions formulation with respect to dilution will be checked by measuring Transmittance through U.V. Spectrophotometer (UV-1700 SHIMADZU). Transmittance of samples will be measured at particular wavelength and for each sample three replicate assays were performed [44].

9. Determination of Self Emulsification Time: The emulsification time of SMEDDS will be determined according to USP 22, dissolution apparatus 2. Required amount of formulation will be added drop wise to 500 ml purified water at 37 ºC. Gentle agitation will be provided by a standard stainless steel dissolution paddle rotating at 50 rpm. Emulsification time will be assessed visually [44].

10. Electro Conductivity Study: The SMEDDS system contains ionic or nonionic surfactant, oil, and water. This test will be performed for measurement of the electro conductive nature of system. The electro conductivity of resultant system will be measured by electro conductometer [45].

11. Drug Content: The optimised preweighed SMEDDS formulation will be dissolved in suitable solvent. The extract will be analysed spectro-photometrically against the standard solvent solution of drug [45].

12. *In-vitro* Diffusion Studies: The quantitative *in-vitro* release test will be performed in 900 ml purified distilled water, which is based on USP 24 method. SMEDDS will be placed in dialysis bag during the release period to compare the release profile with conventional tablet. 10 ml of sample solution will be withdrawn at predetermined time intervals, filtered through a 0.45 µ membrane filter, dilute suitably and analyzed spectro-photometrically [46].

Solidification Techniques for Transforming Liquid Smedds to Solid SMEDDS: SMEDDS mainly exist in two forms either liquid or solid form. Most of the SMEDDS are limited to liquid dosage forms, because many excipients used in SMEDDS are not solids at room temperature.

SMEDDS are kinetically stable, spontaneous and require low energy input in emulsion formation process in comparison with traditional emulsion formulation that are thermodynamically unstable.

However, liquid SMEDDS formulations can also be solidified to improve stability, reproducibility, and patient compliance as few issues may take place when filled in capsules such as the incompatibility of components with the capsule shell when kept for long term.

Different techniques are used for conversion of liquid SMEDDS into solid SMEDDS such as encapsulation of liquid and semisolid SMEDDS, spray drying, adsorption to a solid carrier, melt extrusion *etc.* [47]

1. Encapsulation of Liquid and Semisolid Self-emulsifying Formulation: Capsule filling of a liquid and semisolid formulation is one of the most common and simplest technique with suitability for both low dose potent drug and high dose drug loading (up to 50%) for conversion to solid SMEDDS. For liquid formulation, direct filling and sealing of capsule are possible whereas for a semisolid formulation, they are heated to a minimum of 20 °C above the melting temperature which will be followed by active component incorporation with continuous agitation into the capsule and sealing it [48].

2. Spray Drying: Liquid or semisolid formulation of SMEDDS is prepared by mixing the essential components *i.e.,* oil phase, aqueous phase, surfactants, co-surfactants and drug and is prepared for spray drying. This formulation is then introduced into a spray of droplets in a drying chamber under controlled temperature and airflow condition, where the volatile phase (*e.g.* water present in the system) gets vaporized forming dry particles which can be either prepared into tablet or capsule formulation. The atomizer, the temperature, the most suitable airflow pattern and the drying chamber design are selected according to the drying characteristics of the product and powder specification [49].

3. Adsorption to a Solid Carrier: Various adsorbent like magnesium trisilicates, silica, magnesium hydroxide, talcum, aerosil 200 is used to absorb liquid or semisolid SMEDDS forming free-flowing powders or granules depending upon the drug characteristics. The process is simple and involves the addition of liquid SMEDDS into carriers by mixing in blenders. Thus obtained powder can be directly filled into a capsule or can be proceeded to tablet formulation by mixing of suitable excipients. Good content uniformity is obtained with high-level absorption (up to 70% w/w) by use of suitable adsorbent. At recent times, various nanoparticle absorbents like carbon nanotubes, charcoal, bamboo charcoal, silicon dioxide are also used [50].

4. Melt Granulation: Melt granulation encompasses the technique of addition of binders to the formulation which relatively melts at a low temperature resulting in the formation of granules. This process is more relevant to that of spray drying as it omits drying phase and one step granulation is achieve. The mixture is subjected to impeller with specified impeller speed, binder particle size and viscosity and total mixing time. Gelucire 1 is commonly used as a binder which is derived from mixtures of mono-/di-/tri-glycerides and polyethylene glycols (PEG) esters of fatty acids [50].

CONCLUSION: Self-microemulsifying drug delivery systems are recent and effective approach for the augmentation of oral bioavailability of many poor water soluble drugs provided that the drug should be potent with high lipid solubility. Some bioactive molecules have poor aqueous solubility, limited dissolution rate and low bioavailability creating different problems during formulation. The presence of only a few drugs products formulated as SMEDDS made available into the commercial market signifies the difficulties in formulating poorly water-soluble drug compounds into such formulation. Self-emulsifying drug delivery system is the most promising approach for formulation in case of such a drugs. The low solubility nature of drug makes them less soluble and bioavailable. Formulating drugs in a microemulsion form is a facile method for enhancing their solubility and bioavailability. Self-micro emulsifying drug delivery system (SMEDDS) has in recent times emerged as one of the most fascinating approaches to improve the solubility, dissolution and oral absorption for poorly water-soluble drugs. The fact of SMEDDS being one of the novel and versatile approaches to improve the bioavailability of approximately 40% of poorly water-soluble drugs implies that the study on SMEDDS must continue so that more drugs compounds formulated as SMEDDS will reach the pharmaceutical market in near future.

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CONFLICTS OF INTEREST: Nil

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