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# A Review on self nano emulsifying drug delivery system

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**ABSTRACT** : Self-nanoemulsifying drug delivery systems (SNEDDS) are anhydrous homogenous liquid mixtures consisting of oil, surfactant, drug and co emulsifier or solubilizer, which size upon spontaneously form oil-in-water nano emulsion of approximately 200 nm or less in dilution with water under gentle stirring. Preparation method include. Physical adsorption, Melt granulation, Pour molding method, Spray congealing, spray drying, Extraction- spherization, Lyophilization, positivity charged SEDDS, Drug transport mechanism of SNEDDS. Solid self-emulsifying drug delivery systems combine the advantages of liquid formulation (i.e., enhanced solubility and bioavailability) with those of solid dosage forms (e.g., low production cost, convenience of process control, high stability and reproducibility, and better patient compliance). The oral administration route remains the best choice for drug delivery owing to its safety, patient compliance and capacity or self-administration. In addition to being the most convenient route of administration, oral delivery has been limited owing to the numerous barriers present at the gastro-intestinal (GI) tract. The self-emulsifying formulations can be administered as water-free pre-concentrates those in situ form nano emulsions in the fluids of the gastrointestinal tract. Self nano emulsifying drug delivery systems (SNEDDS) are isotropic mixtures of oil, surfactant, co-surfactant and drug that form fine oil-in-water nano emulsion when introduced into aqueous phases under gentle agitation. n the current research work, losartan potassium (LP) loaded Self Emulsifying Drug Delivery System (SEDDS) was formulated using various ratios of lipids, surfactants and co-surfactants to prevent its first pass metabolism. A pseudo-ternary phase diagram was plotted to establish the emulsification region. Total of eight batches (F1 to F8) were prepared and subjected to different characterizations (thermodynamic study, phase separation, zeta potential and particle size) studies to obtain the optimized formulation. The optimized SEDDS (F8) with 40% oil, 60% surfactant and co-surfactant mixture (Smix) (6:1 ratio) was found to be a thermodynamically stable emulsion, with droplet size at around 204.745.0 nm, surface charge -13.38±1.5 mV and polydispersity index 0.221±0.03. The SEM study

confirmed the spherical shape and even surface of the droplets. The In-vitro drug release profile of optimized formulation exhibited a similar rate and extent of dissolution as compared to the marketed formulation. Further, the optimized formulation had shown equivalent therapeutic efficacy (anti- hypertensive) with respect to the marketed tablet at half of the dose of the drug in SEDDS formulation.

**KEYWORDS:** Self nano emulsifying drug delivery system ( SNEDDS ), Bioavailability, Improved Solubility . Losartan, Self Emulsifying, Drug Delivery System, anti-hypertensive, lipids, surfactants, co- surfactants.

**1.INTRODUCTION :** The self-nanoemulsifying drug delivery systems (SNEDDS) is an emulsion-based system consisting of isotropic anhydrous homogenous liquid mixtures. These mixtures are oil, surfactants, co-surfactants, and also an active drug compound that will produce oil-in-water emulsion into aqueous media by mild agitation. spontaneously form oil-in-water nano emulsion of approximately 200 nm or less in dilution with water under gentle stirring. These are typically meant for oral delivery. SNEDDS have been broadly classified based on the basis of drop- let size obtained after dispersion. If the droplet size of dispersion is in range of 100-250 nm then the SEDDS are termed as SMEDDS (Self Micro Emulsifying Drug Delivery System) while those having droplet size below 100 nm are called SNEDDS . lipid-based formulations to increase the oral bioavailability of poorly water-soluble medicinal molecules. Active lipophilic ingredients are often added to inert lipid vehicles like oils, surfactant dispersions, emulsions, liposomes, self- emulsifying formulations, nano-emulsifying systems, and micro emulsifying systems. Most improve solubilization and permeation by increasing drug surface area. Lipids are used to increase the solubility and oral bioavailability of BCS class II and IV drugs. Most improve solubilization and permeation by increasing drug surface area [1]. Lipids are used to increase the solubility and oral bioavailability of BCS class II and IV drugs. Since self-emulsifying drug delivery systems (SEDDS) are physically stable lipid solutions or dispersions, they are one of the lipid formulations that represent an attractive alternative to orally administered emulsions [4, 26]. This is because SEDDS are one of the lipid formulations that make up self-emulsifying drug delivery systems. Mixtures of natural or synthetic oils, solid or liquid surfactants, and, alternatively, one or more hydrophilic solvents and co-solvents/surfactants are what make up SEDDS .

These mixtures are isotropic in nature. Candidates for this formulation concept include pharmaceutical substances that have adequate solubility in mixtures of lipids, surfactants, and co-solvents (or co-surfactants). SEDDS are able to disperse easily throughout the gastrointestinal tract, and the agitation that is required for the self-emulsification-dispersion process is provided by the digestive motility of the stomach and intestine. SEDDS are usually liquid or soft gelatin capsules) . Solid dosage forms are preferred over liquid preparations due to manufacturing ease, patient convenience, accuracy, and stability. Combining lipid-based drug delivery systems with solid dosage forms overcomes the drawbacks of liquia formulations. Some attempts were made to solidify liquid SEDDS

Metaprolol is a naturally long-acting beta-blocker. and according to the Biopharmaceutical Classification System, it is a drug that has low solubility [10], However, in the essential drug list maintained by the World Health Organization, it is presented in an immediate-release dosage form. Patients suffering from heart failure, hypertension, and ischemic heart diseases have been the subjects of research on metaprolol, which is now commercially available in 3.125-, 6.25-, 12.5-, and 25-mg tablet strengths.

SNEDDS are useful for pre-dissolving poorly water-soluble compounds and filling capsules. Pre- dissolving the compound overcomes the rate-limiting step of particulate dissolution in the Gl tract. The drug may precipitate in the Gl tract if a hydrophilic solvent is used (eg polyethylene glycol). If the drug is dissolved in a lipid vehicle, there is less chance of precipitation in the Gl tract, as partitioning kinetics favour the drug remaining in the liquid droplets. 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. [2] Self emulsifying drug delivery systems have been shown to be successful in improving the oral.

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. [2] Self emulsifying drug delivery systems have been shown to be successful in improving the oral. bioavailability of and lipophilic drugs. poorly water soluble

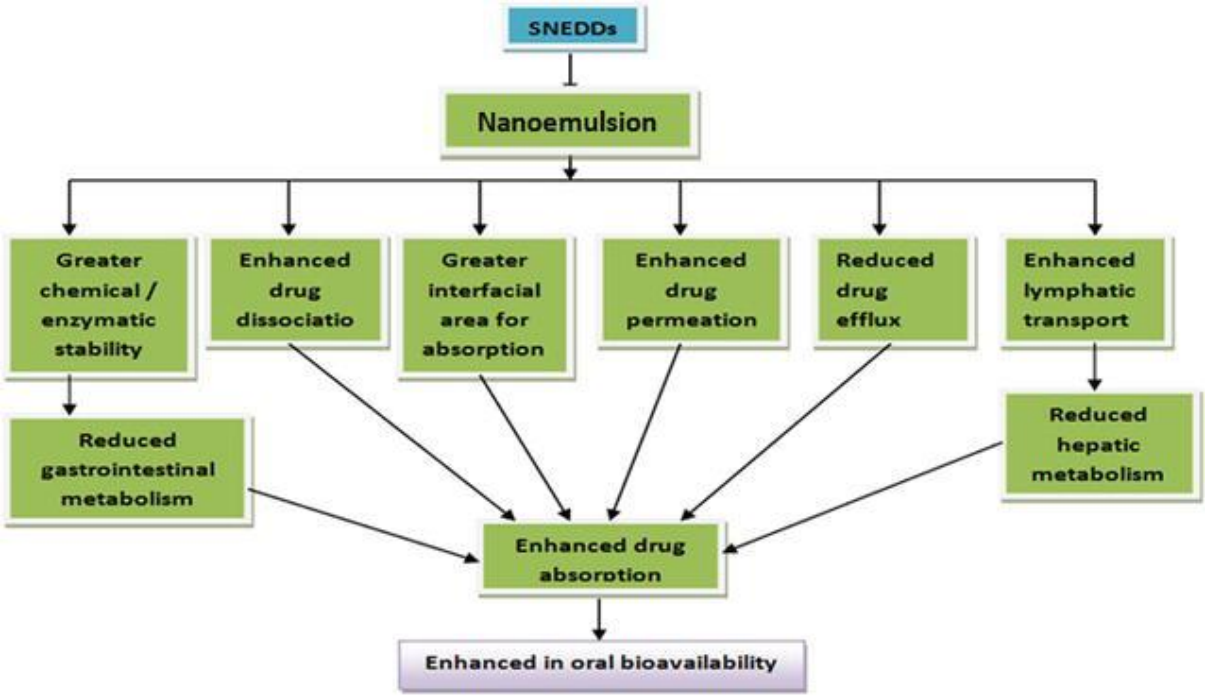
Self emulsifying drug delivery systems (SEDDS) also called as self emulsifying oil formulation which are mixtures of oils and surfactants, ideally isotropic, and sometimes containing co-solvants, which emulsify spontaneously to produce fine oil in water emulsion when introduced into aqueous phase under gentle agitation. [4],[5] nanoemulsifying (SNEDDS), microemulsifying (SMEDDS) and Self- self- self- emulsifying drug delivery systems **(**SEDDS) to improve the oral bioavailability of poorly water- soluble drugs.

## 1.1 Advantages of self nano emulsifying drug delivery system :

- SNEDDS is a proven method for enhancing the solubility and bioavailability of lipophilic compounds.
- Considering the ease of large-scale production and the robustness of SNEDDS, several formulations techniques are commercially available.
- The stability of SNEDDS can be further enhanced by solidifying liquid SNEDDS

## 1.2.Disadvantages of self nano emulsifying drug delivery system :

- high production cost
- low stability and portability
- low drug loading and different dosage forms.
- Irreversible drug/excipient precipitation may also be problematical Desirable properties of self nano emulsion:




### 1.3Preparation of self nano emulsifying drug delivery system :

A series of SNEDLUS were prepared using oil, surfactant and cosurfactant In all the formulations, the amount of Drug was kept constant. Accurately weighed drug was placed in beaker and oil, surfactart, and co surfactant

were auded. The components were mixed by gentle stirring with magnetic stirrer and the resulting mixture was heated at 40°C, until the drug was completely dissolved The homogenous mixture was stored at room temperature until further use

## 1.4 TECHNIQUES USED FOR SOLIDIFICATION OF SNEDDS :

### 1.4.1 Physical adsorption:

Physical adsorption of 1 SEDDS on the solid carriers is one of the sim pless technique of solidification. In this process, 1-SEDDS are added on solid carrier and mixed either via physical blending with hand or motor pestle on lab scale or via use of blenders. The loading factor is calculat ed as the amount of solid carrier required for adsorption of L-SEDDS so that homogenous powder is obtained. After this, weighed amount of both L SEDDS and carrier are mixed together until a homogenous solid pow der is formed via adsorption of L SEDDS over solid carriers. This powder should be passed through sieves to break any lumps, if present. The result ant powder can be directly filled imo capsules or can be compressed into tablets via addition of some other excipients used for tableting (Zidan AS, et al., 2015). Several carriers like silicon trioxide, syloid have the capacity to absorb large amount of L SEDDS (Tarate B, et al. 2014).

Hydrophilic/hydrophobic nature of carrier on which L. SEDDS have to be adsorbed affect the properties of drug eg L-SNEDDS of ezetimube were prepared with Capryol 90. Lauroglycol FCC. ethyl laurate, Cremophor EL and Transcutol P and adsorbed on hydrophobic colloidal silicon diox ide to form Self Nano Emulsifying Granules (SNEG) X-Ray Diffraction (XRD) indicates that drug is in its amorphous form, but when the same SNEDDS were loaded on magnesium sterate a eutectic mixture is resulted

### 1.4.2.Melt granulation :

Melt granulation is a method in which S-SEDDS are prepared in a single step. In this method, there is no need to prepare L-SEDDS and then adsorb on the solid carrier. In this method, oil eg goat fat, or surfactant which are solid at room temperature are used. All the mixture of oil and surfactant is taken in the desired quantity and heated above the melting point. In this melted mixture drug is added and mixed to form homogenous mixture (Attama AA and Mpamaugo VF, 2006)

### 1.4.3.Pour moulding method :

Self-emulsifying suppositories and tablets can be prepared via pour moulding method. In this method, oil and surfactant are taken and heat ed together until they homogenize completly Drug is added into this homogenous mixture and stir thoroughly. This mixture is now poured into moulds and allowed to settle at a temperature of 4°C. The tablets or suppositories with self-emulsafying ability are taken out from mould and stored at cool place (Attama AA. et al., 2003

**1.4.4.Spray congealing :**

Self-emulsifying microparticles can be produced by spray congealing tech- nology: Radued bed equipment a utilized for this purpose. It uses two flad atomers with a wide orifice opening Le pneumatic nozzle External mming of thund and air of gas occurs outside nozzle orifice, thus atomisa ton can be varied by changing the air pressure without affecting the liquid fhose rate to enable the spraying of high concentration or viscous products The tomperature of food tank containing molten fluid should be kept high er than miting temperature Congealing chamber should be cooled using refrigerator system for solidification of droplets

**1.4.5.Spray drying :**

Spray drying is one of the commonly used technique for the formation of Sin Spray dryer costats of following components viz feed delivery warm agnus heard sit supply, drying chamber, solid gas separator and product collection system. In this technique drug, L-SEDDS and car πως με το or spended in a sabent to form a homogenous system. med to produce liquid droplets with the help of e noudere drys the one the temperature, the most suit dis as the passes and the drying chamber design are uuportant vari aksalating probes horetics (Ainaghi A. et al. 2015.

**1.4.6.Extruction spheronization :**

SEDDS can also be formulated in the form of pellets via extru sion spheronization. This process includes wet granulation of L SEDDS with solid excipients, followed by extrusion of wet mass, spheronization of extrudates, drying of the spheroids, sizing, and optionally coating of the pellets. The bottom plate is grooved to provide the equipment-particle interactions for rounding the cylindrical pellets

**1.4.6.Lyophilisation :**

Lyophilization can also be used for formulating S SEDDS. In this process. water is evaporated directly via sublimation. It includes several steps 1.e freezing, primary drying, and secondary drying in this process both car rier and L SEDDS are dissolved in a common solvent followed by freezing and sublimation process This method gives a solid product Clarate B, et al. 2014). lain AK, et al. 2014 prepared S SNEDDS using lyophilization technique SNEDDS were diluted in minimum quantity of deionized water and thoroughly mixed with Aerosil 200

**1.4.7.Self emulsifying solid dispersion :**

Self-emulsifying solid dispersions can also be prepared by melting meth od in this method, drug, surfactant and fatty acids are homogenously mixed and slightly heated to get a melted mixture. This melted mixture is

then added to a suitable adsorbent like Aerosil 200 and kept at cool temperature. Solid mass obtained is crushed and passed through sieve of suitable size to obtain fine powder.

### 1.4.8.Positivity charged SEDDS :

Most of the absorptive cells present in the human body carry a negative charge. Due to this reason, positively charged SEDDS have been reported to show better bioavailability as compared to conventional SEDDS. Oppositely charged SEDDS have more time to interact with gastric mucosa via increased adhesion.

## 2. MATERIAL AND METHOD :

(Physicochemical and biopharmaceutical properties) involves the application biopharmaceutical principles to the physicochemical parameters of drug substance and are characterized with the goal of designing optimum drug delivery system. Hence, the goals of preformulation studies are to choose the correct form of a substance, evaluate its physical properties and develop a safe, stable as well as therapeutically effective dosage form. Additionally, physical characters of drug and its interaction with delivery systems ar**e also characterized that make a successful drug delivery system .**

## 3.Characterisation of SNEDDS :

### 3.1.Robustness to diluent :

Robustness to dilution was studied by diluting the formulation with 100 times volumes of various dissolution media viz. O. IN HCl and phosphate buffer (pH 6.8) The diluted nano-emulsions were stored for 12 h and observed for any signs of phase separation or drug precipitation.

### 3.2.Determination of emulsification time

Self-emulsifying formulations can be graded for self-emulsification time, dispersibility and appearance Visual assessment criteria for self-nano-emulsion formed from different formulation.

### 4.Characterization of SNEDDS

### 4.1.Transmission electron microscopy

The nano-emulsion globules were visualized by Transmission Electron Microscope (TEM) (MORGAGNI 2680 FEI, (Holland) Samples were cerd on carbon-coated grid and negatively stained with phosphotungstic acid After drying viewed under the microscope aqueous solution of specimen was viewed under the microscope.

### 4.2.Droplet size analysis

The droplet size and zeta potential of the emulsions was determined at 25°C by dynamic light scattering (DLS)

### 4.3.Zeta potential analysis

Zeta potential analysis with Zeta sizer Nano-ZS (Malvern Instrument Limited, UK) by monitoring at a scattering angle 173°C The nanometric size range of the globule was retained even after 100 times dilution with water which proves the compatibility of the system with excess water.

### 4.4.Drug loading efficiency

50 mg formulation was taken and to it methanol was added to make up the volume to 100 ml The resultant solution was analyzed spectroscopically following suitable dilution. The drug loading efficiency was determined by the following formula.

### 4.6.Drug loading efficiency

Amount of drug known In amount formulation/initial drug load×100 of

### 4.7.Stability study

The physical stability study of the various SNEDDS formulations was performed at 4°C, 25°C and 45°C for 60 days. The SNEDDS was evaluated by visual inspection for physical changes such as color and drug precipitation.

### 4.8.In-vitro dissolution study

Dissolution profiles of the SNEDDS were investigated using the dialysis bag method according to dissolution apparatus 2 in USP 24 in OIN HOT and Phosphate buffer (pH 6.8) (900 mL). The formulation was placed in dialysis bag (MWCO 12000 Medicell International, UK) held to the bottom of the vessel using copper sinkers

The temperature was maintained at 37±0.5°C during the study. At regular time intervals. 3 ml samples were withdrawn and replaced with equal volumes of fresh medium. The withdrawn samples were analysed spectrophotometrically for the drug content.

**5. CONCLUSION :**

In this study, combination of HCO-40, Transcutol HP, and MCT in variable ratios showed rapid emulsification in aqueous media. Meanwhile, systems which form nanoemulsion and are able to retain the drug in a solubilized form after dispersion in aqueous media will be preferred as a carrier for poorly water-soluble drugs. In addition, they were able to introduce the SNEDDS into the dissolution media where it was efficiently transformed into nanoemulsion by the gentle agitation provided in the dissolution experiment Modifying silicon dioxide physical form from amorphous into granulated improved the physical properties of both liquisolid powders and tablets.

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