Review Article

A Literature Review on Self Nanoemulsifying Drug Delivery System (SNEDDS)

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ABSTRACT

The Lipid-based drug delivery system is extensively reported within the literature for the enhancing drug solubility, permeability, and bioavailability. A considerable majority of novel pharmacologically active constituents produced in recent drug discovery programs are lipophilic and poorly soluble, posing a significant problem for pharmaceutical researchers enhancing the oral bioavailability of such drug molecules. Self-nano emulsifying drug delivery systems (SNEDDS), are the viable oil-based approaches for drugs that exhibit low dissolution rate and inadequate absorption. Ever since the progress of SNEDDS, researchers have been focusing on the challenges of BCS Class II and Class IV Drugs for enhancing water Solubility of poorly water-soluble drugs. SNEDDS is a Validate method for enhancing the solubility and bioavailability of lipophilic compounds. It's the isotropic mixture of oil, surfactant, co-surfactant molecules and it also containing co-solvent molecule. which spontaneously form oil-in-water nano emulsion of approximately 200 nm or less in size upon dilution with water under gentle stirring. It's Drug delivery system Which possess thermodynamically and kinetically stability. The physicochemical properties, drug solubilization capacity considerably regulates the selection of the SNEDDS components. The compositions of the SNEDDS are often optimized with the assistance of phase diagrams. Further to optimize SNEDDS can be done with the help of statistical experimental design. It's a Novel drug delivery system which is applicable for the parenteral, Ophthalmic, intranasal and cosmetic drug delivery system. And therefore, the present review describes Preparation, components, mechanism of self-Nano emulsification, biopharmaceutical aspects, characterization methods and applications of Self-nanoemulsifying drug delivery system (SNEDDS).

Keywords: Nano-emulsion, Oral delivery, Poor bioavailability, Self-emulsifying drug delivery system, surfactant, co-surfactant, Pseudo ternary phase diagram, In-vitro dissolution etc.

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INTRODUCTION

Self-nanoemulsifying drug delivery systems (SNEDDS) are regarded as nanoemulsion preconcentrates or as anhydrous forms of the nanoemulsion. Self-nanoemulsifying Drug Delivery system (SNEDDS) is an isotropic mixture of the natural or synthetic oil, surfactants and co-surfactants and, alternatively, Aqueous media were followed by one or more hydrophilic solvents and co-solvents/surfactant's ability to generate fine oil-in-water (O/W) nano-emulsions under mild agitation conditions[1]. The size range of globules in the self-nano emulsifying Drug Delivery System is less than 100nm when dispersed in water[2]. Recent years Self-Nano emulsifying Drug Delivery System (SNEDDS), self-micro emulsifying Drug Delivery System (SMEDDS) and self-emulsifying drug delivery systems (SEDDS) is employed to enhance the aqueous solubility of BCS Class II and Class IV Drugs which are having poorly water-soluble in nature. By using the medium chain tri glycerides oils and non-ionic surfactant the self-nano-emulsifying Drug Delivery system was formulated, it was crucial for oral ingestion[3]. The drug was submitted to a dissolution rate that limited absorption; the drug was also subjected to SNEDDS, which is critical for improving rate as well as drug absorption and reproducibility of plasma drug concentration profiles[4]. The SNEDDS is important to yield an outsized interfacial area for partitioning of drug between oil and aqueous phase. Having preferable rate of drug dissolution and increases bioavailability of drug formulation[5]. The Self-Nanoemulsifying drug delivery system, which is thermodynamically Stable and Translucent Non-ionized Dispersion of oil-in-water and water-in-oil Nano emulsion was stabilized by the addition of Surfactant and Co-surfactant Molecule[6]. The Self-Nanoemulsifying Drug Delivery System is additionally referred to as Nanoemulsion, Miniemulsion, ultrafine emulsion, Submicron emulsion[6]. Under the mild agitation the oil-in-water nano emulsion of Self-Nanoemulsifying drug delivery system (SNEDDS) followed by aqueous media to form stable oil-in-water nano emulsion.

Selection of Appropriate Drug Candidates for SNEDDS

The SNEDDS System is a Novel Approach to Enhance Oral Bioavailability of Drugs that are Poorly Water-Soluble drugs. In the Biopharmaceutical classification system (BCS) can Categorize into Four Classes, comparison to Class I and

Class III drugs, Class II and Class IV drugs have lower aqueous solubility.

Under the Self-Nanoemulsifying Drug Delivery System, Class II and Class IV drugs can increase their aqueous solubility and oral bioavailability. The SNEDDS is Important to Prevent Problem of Enzymatic Degradation Associated to Class I drugs and Class III drugs and Improved Solubility and Bioavailability[7].

Based on the solubility and permeability analysis a schematic Representation about Biopharmaceutical Classification System (BCS) having four classes of system which is shown in Figure No.1[8].

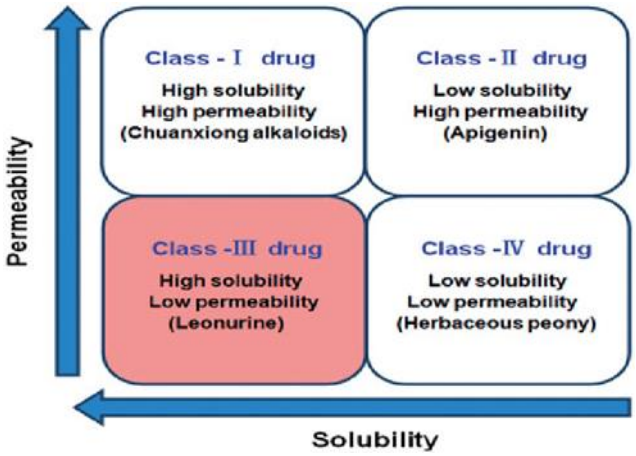

Figure 1: Biopharmaceutics classification system

Lipidized forms of Class II and Class IV drugs enhance their absorption by bypassing the barrier of reduced water insoluble solubility, and illustrate their dissolution in GI through membrane transfer to the bile-salt mixed micellar phase. through which absorption happens readily[9]. this regard, the properties of the drug, including water solubility, log P, do not provide sufficient insight into the suitability of a lipid-based formulation as they cannot predict the vivo effects[10].

Advantage of SNEDDS

- SNEDDS improve the pharmacokinetics of the administered drug, which reduces dosage frequency[11].
- They possess higher drug payload.
- SNEDDS are highly stable formulation and uncomplicated manufacture techniques.
- Drug diffusion with SNEDDS allowed for a wider distribution in the stomach and GI tract, thus reducing the irritation caused by excessive contact between the gut walls and the drugs[12].
- The drug is protected from the aggressive environment in the GI tract by SNEDDS.
- SNEDDS manage controlled drug delivery profile.
- In terms of surface interfacial area, SNEDDS facilitate for better drug partitioning between water and oil[13].
- SNEDDS improve the rate and extent of drug absorption.
- SNEDDS enables the selective drug targeting towards precise absorption window in GI tract[14].

Disadvantages of SNEDDS

- Traditional dissolve procedures are ineffective for SNEDDS because they rely on digestion prior to disintegration[15].
- For strength evaluation, SNEDDS in vitro models require more research and validation.
- More research into the in vitro-in vivo correlations of SNEDDS is needed[15].
- Drugs' chemical instabilities.
- Surfactant concentrations in the formulation are higher (30–60%)[16].
- Higher production cost.
- Lower drug incompatibility and stability.
- Possibility of drug leakage and precipitation[16].

Factors Affecting SNEDDS

- SNEDDS aren't suitable for the Drugs, which are administered at very high dose.
- The drug's solubility in water is limited, and lipids are the most difficult to administer by SNEDDS[17].
- The capability of SNEDDS to maintain the drug in a solubilized state is significantly determined by the drug's solubility in the oily phase.
- Sometimes there might be a risk of precipitation if the surfactant or co-surfactant is contributing to a greater extent for drug solubilization[17].

COMPOSITION Of SNEDDS

The SEDDs is mainly composed of the following[18]:

Drugs,

Oil,

Surfactant,

Co-surfactant,

Co-solvents.

Drugs

SNEDDs are often prepared for drugs that have a poor water solubility. For most circumstances, BCS class II and class IV medicines are often used in manufacture of SNEDDs. Physicochemical parameters of the drug, such as log P, pKa, molecular structure and weight, presence of ionizable groups, and quantity, all have a significant impact on SNEDDS performance[19]. High melting point drugs with log P values of about 2 are poorly suitable for SNEDDS. While, lipophilic drugs having log P values greater than 5,

are good candidate for SNEDDS[20]. Examples include Itraconazole, nifedipine, vitamin E, simvastatin, danazol, ketoconazole, mefanimicacid, carbamazepine, glibenclamide, cyclosporine-A, amphotericin B, furosemide, acetazolamide, ritonavir, paclitaxel etc[21].

Table 1: Types of drugs used in SNEDDs

Class II Drugs	Class IV Drugs
Artemeter	Albendazole
Carbamazepine	Acetazolamide
Dapsone	Azathioprine
Efavirenz	Bifonazole
Ezetimibe	Didancosine
Folic Acid	Furosemide
Griseofulvin	Indinavir
Haloperidol	Mesylate
Ibuprofen	Nelfinavir

Oil

The oil phase has great importance in the formulation of SNEDDS as physicochemical properties of oil such as molecular volume, polarity and viscosity significantly govern the spontaneity of the nano emulsification process, droplet size of the Nano emulsion, drug solubility and biological fate of Nano emulsions., it's mainly related to O/W nano emulsion. The oil is crucial for maximum solubilizing ability for selected drug candidate is important for selection of oily phase for Nanoemulsion Formulation. This is often most important approach having the high drug loading ability. The naturally also as synthetically occurring the mixture of oils and fats are triglycerides contain in long chain fatty acids in order to decrease the degree of unsaturation and is important to prevent oxidative degradation[22]. The nano emulsion size is directly proportional to the lipophilicity of the oil and concentration of oily phase in SNEDDS. Investigations by Anton and Vandamme and Sadurni[23], support the aforementioned statement. Interestingly, Long-chain triglycerides, in contrast to medium-chain tri-, di-, and mono-glycerides, have demonstrated a greater ability to enhance lymphatic transport of drugs (responsible for preventing first-pass metabolism of drugs)[24], whereas medium-chain mono- and di-glycerides have greater solubilization potential for hydrophobic drugs and permeation-enhancing properties[25]. Hence, it's going to be difficult for single oily component to possess optimum properties with reference to nano emulsification and drug delivery. In certain cases, employing a mixture of oils also can be used to meet optimum properties of the oily phase. For nanoemulsions and microemulsions an analogous concept has been utilized. For instance, a mixture of fixed oil and medium-chain triglyceride is used in certain cases to have good balance between drug loading and emulsification[26]. Due to their inability to solubilize higher drug concentrations, edible oils are not included in the SNEDDS formulation. Due to the creation of improved emulsification systems with more surfactants acceptable for oral administration, hydrolyzed vegetable oils are used. They propose formulation and physiological remuneration. Medium-chain semi-synthetic chemicals, referred to as amphiphilic compounds that possess surfactant characteristics, are substituting the oils in SNEDDS[27].

Table 2: Type of oil used with drug in SNEDDS

Oil	Drug
Palm kernel oil	Ibuprofen
Castor oil	Cyclosporin-A
Captex 500	Furosemide
Capmul MCM C8	Glibenclamide
Lemon oil	Diclofenac Sodium

Surfactants

Surfactant are defined as molecules and ions are adsorbed at interface. It's having ability to prevent the interfacial tension and provide interfacial area. The selection of surfactant is additionally critical for the formulation of SNEDDS. Surfactant properties such as hydrophilic-lipophilic balance (in oil), cloud point, viscosity, and affinity for the oily phase have a significant impact on the nanoemulsification process, self-nanoemulsification region, and hence nanoemulsion droplet size[28]. The concentration of the surfactant with in the SNEDDS has considerable influence on the droplet size of nanoemulsions[29]. The acceptability of the elected surfactant for the desired route of administration and its regulatory status must also be considered during surfactant selection.

CLASSIFICATION SURFACTANT MOLECULE

The four main groups of surfactants are[30]: -

Cationic surfactants.

Anionic surfactants.

Ampholytic surfactants.

Non-ionic surfactants.

Cationic surfactants

The hydrophilic group or head of an ionic surfactant carry a net charge. The surfactant is called Cationic surfactant if the charge is positive. Cationic surfactants are mainly primary, secondary, tertiary amines and quaternary ammonium salts of higher alkyl groups such as octadecyl trimethyl ammonium chloride, C12-14 alkyldimethylbenzyl ammonium chloride.

Anionic Surfactants

The hydrophilic group or head of an ionic surfactant carry a net charge. If the charge is negative, the surfactant is called anionic surfactant. Anionic Surfactant commonly

fatty acid soaps, sodium lauryl sulfate, sodium laureth polyoxyethylene ether sulfate, sodium cetyl polyoxyethylene ether phosphate, soybean phospholipids(lecithin), carboxyl (RCOO-), sulphonate (RSO3 -) or sulphate (ROSO3-). Potassium laurate, sodium lauryl sulphate.

Ampholytic surfactants / Zwitterionic surfactants

The surfactant unit consist of both charges Positive also as negative Charge.

Sulfobetaines are good example.

Non-ionic surfactants

The hydrophilic group has no charge, but it can contain strong polar functional groups like hydroxyl or polyoxyethylene, which gives it water solubility (OCH2CH2O).

Sorbian esters (Spans) and polysorbates are good instances (Tween 20).

Non-ionic surfactant molecules are more stable than ionic surfactant molecules, and they are nontoxic and thermodynamically stable molecules with a reasonably high hydrophilic lipophilic balance (HLB) to generate stable SNEDDs. 30-60% surfactant concentration is employed to form stable SNEDDs[31]. The SNEDDS formation causes with the higher surfactant and co-surfactant and oil ratios to the lipid mixtures of molecules and it is responsible for enhancement of oral bioavailability of poorly water-soluble Drugs.

Table 3: Type of surfactants utilized in marketed SNEDDS:

Surfactant	Marketed drug product	Drug
Cremophor RH 40	Neural soft gelatin capsule	Cyclosporine A
Span 20	Kaletra tablet, soft gelatin capsule	Lopinavir
Polysorbate 80	Lipofen hard gelatin capsule	Fenofibrate
Gelucire 44	Targretin soft gelatin capsule	Bexarotene

The surfactant concentration is mostly determined by the size of the droplet molecule used in the preparation of emulsification and Nano emulsification. This is often important for stabilization of oil Droplet under a part of surfactant system. The surfactant concentration is mainly depending on size of droplet the surfactant concentration was increases ultimately size of droplet was increases. It's important Component of preparation of Nanoemulsion system for improving the solubility of poorly water soluble drugs[32].

Co-surfactant

It is similar function to surfactant unit. Co-surfactant was added alongside surfactant unit or combination of surfactant unit in order to capable to increases the ability of the Surfactant to improving water solubility of poorly water-soluble drug. The most important role of co-surfactant in SNEDDS is reduction of oil-water interface and provide the larger surface area and allow the spontaneous formation of nanoemulsion. The SNEDDS formulations require for higher surfactant concentrations (> 30% w/w), which can be condensed with the addition of a co-surfactant. These, in combination with surfactants, reduce the interfacial tension to a -ve value, at which point it expands to form fine droplets, which are then adsorbed with higher amounts of surfactant and surfactant/co-surfactant until the interfacial tension returns to a +ve value. This process is named "spontaneous emulsification." The addition of co-surfactants into SNEDDS isn't obligatory for many non-ionic surfactants[33]. In SNEDDS Co-surfactants with HLB values ranging from 10 to 14 are employed in SNEDDS. Alcohols with medium-chain lengths, such as hexanol, pentanol, and octanol, are hydrophilic co-surfactants that minimize the interface between oil and water, facilitating for impulsive microemulsion formation[34].

Table 4: Co-Surfactants Used for SNEED

Co-surfactant	Chemical name	HLB
Akoline MCM	Caprylic/capric glycerides	5-6
Capmul MCM-C8	Glyceryl caprylate	5-6
Caproyl 90	Propylene glycol mono caprylate	6
HCO-60	PEG-60 hydrogenated castor oil	14
Labrafil 1944 CS	PEG-6 apricot kernel oil	4
Lauroglycol 90	Propylene glycol monolaurate	5
Lauroglycol FCC	Lauroglycol FCC	4
PEG 400	Polyethylene glycol 400	11.6

Co-solvents

Usually an effective self-emulsifying formulation requires a high concentration of surfactant. Accordingly, co-solvents like ethanol, propylene glycol and polyethylene glycol are required to facilitate the dissolution of large quantities of hydrophilic surfactant. These co-solvents sometimes play the role of the co-surfactant with in the microemulsion system. On the opposite end, alcohol and other volatile co-solvents have the drawback of evaporating into the shell of soft or hard gelatin capsules, resulting in the precipitation of the drug[35].

Polymers

We use an inert polymer matrix that represents 5 to 40% composition relative to the weight, is non-ionizable at physiological pH, and can form a matrix. hydroxyl propyl methyl cellulose, ethyl cellulose are two examples of surfactants[36].

Mechanism of Self Emulsification

According to Reiss' theory, emulsification occurs when the entropy changes that favours dispersion is greater than the energy required to increase the surface of dispersion, so the free energy(ΔG) of a conventional emulsion is a (negative) direct function of the energy required to create a new surface between the two phases (oil and water phase) and the emulsion was stabilized. The free energy of a traditional emulsion is related to ΔG and can be represented using the equation[34],

$$\Delta G = \sum i \; Ni \; r^2 i \; \sigma$$

Where;

G stands for the process's free energy.

N is the total number of droplets.

r is the radius of the droplets.

σ is the Interfacial energy.

The two phases of an emulsion tend to separate over time, reducing the interfacial area. The emulsion is then stabilized by an emulsifying agent, which forms a monolayer of emulsion droplets, reducing interfacial energy and serves as a barrier to prevent coalescence[37].

PREPARATION OF SNEDDS

The Self-Nanoemulsifying drug delivery system (SNEDDS) is Prepared by two ways.

Preparation of Liquid SNEDDS

It's important method for preparation of self-Nanoemulsifying drug delivery system having the surfactant/co-surfactant ratio and oil/ surfactant/co-surfactant ratio was selected From the Pseudoternary phase diagram. Different concentrations of oil, surfactant, and Cosurfactant were used to process a number of series of the formulation. The oil and surfactant were weighed in appropriate proportions, and the drug was dissolved in this mixture, which was then stored at room temperature[38].

Preparation of Solid SNEDDS

It is the second most vital method for preparation of Self Nanoemulsifying drug delivery system (SNEDDS). Drug was added into accurately weighed amount of oil in a screw capped vials and melted in water bath if necessary. Then by using a positive displacement pipette the surfactant and cosurfactant were added to the oily mixture and stirred with a vortex to obtain homogeneous solution. Solid Self nanoemulsifying drug delivery system (SSNEDDS) was prepared by adding selected liquid SNEDDS dropwise onto suitable novel adsorbents like Neusillin and are mixed well with glass rod. The damp substance that resulted was sieved no. 120 and dried at room temperature[38].

METHODS FOR PREPARATION SNEDDS

High energy approach

The formation of a nano emulsion when using high energy approach is based on the mixture composition, which includes surfactant, co-surfactant, cosolvents, and another functional chemical, and energy is used to prepare the mixture. The emulsion is mechanically processed to become a nanoemulsion[38].

High Pressure Homogenizer

One of the most significant devices for detecting and preparing nano emulsions is the high-pressure homogenizer. Under very high-pressure conditions the oil in water surfactant mixture under very high pressure and therefore the mixture was pumped by resistive valve. The very high shear stress is liable for the formation of very fine emulsion droplets. The droplet size reduction during homogenization is explained by a combination of two theories: turbulence and cavitation. The high velocity of the resultant mixture gives the liquid a lot of energy, which causes severe turbulent eddies the same size as the mean diameter droplet (MDD) within the homogenizer valve. Droplets were aside from Eddie currents resulting in a reduction in droplet size. At the same time, the pressure across the valve drops, cavitation occurs, and more eddies and disruption droplets form. By reducing the gap size, the pressure of the droplet is increased, leading to a higher degree of cavitation. Emulsion droplets with diameters as small as 100 nm are commonly generated using this method whether there is enough surfactant present to completely cover the oil-water interface formed and thus the adsorption kinetics were high enough to prevent droplet coalescence[39].

Micro fluidization

It's a crucial tool for identifying and preparing Nanoemulsion. A device known as a "Micro Fluidizer" is used in Micro fluidization technology. This type of device is used in a high-pressure positive displacement pump (500-300 PSI) that forces the product through the interaction chamber. Micro channels are small channels droplets that are used in high-pressure positive displacement pumps. The product was driven through micro channels and impinged on the impingement area, resulting in very small submicron particles. In the inline homogenizer, two solutions having a mixture of aqueous and oil phase systems are combined and produced, yielding a course emulsion. The coarse emulsion is processed in a micro fluidizer and then further processed to produce a homogeneous, transparent, and stable nano emulsion[40].

Sonication Method

This method is crucial for determining the size of a droplet and for reducing the size of a droplet in a conventional emulsion using a sonication mechanism. It can only be used on tiny batches of Nanoemulsion[40].

Phase inversion Method

This type of method is important for preparation of micro emulsion and Nanoemulsion. The tactic is especially based on the response to temperature. Many physical changes occur during this approach, including physicochemical changes, particle size, and in vivo - in vitro drug release rate. Adjusting the spontaneous emulsion formation is used in these strategies. The non-ionic surfactant is often achieved by changing the temperature of the system. The forcing a transition from o/w nano emulsion was formed at low temperature and w/o Nanoemulsion was formed at higher temperature[41].

Pseudoternary Phase Diagram

Pseudoternary phase diagram is important for determination of SNEDDS. It's diagrammatic representation of oil, surfactant and co-surfactant (Smix), water is known as Pseudoternary phase diagram. It was constructed using the Phase titration and Phase inversion methods. Preparing solutions was step in the process. These solutions, which contained oil and hence had variable surfactant-to-co-surfactant weight ratios, such as 1:1, 2: 1, 3:1, and so on, were vortexed for five minutes, producing in an isotropic mixture. They're being examined to see if they're turbid or clear. The appearance of turbidity in the samples indicates the formation of a coarse emulsion, whereas the appearance of a clear or transparent isotropic solution indicates the formation of a Nanoemulsion (SNEDDS) Percentage of oil, Smix and water. Pseudo ternary phase diagram was created using the values. This diagram corner can illustrate a 100% concentration of each phase's material. The diagram is helpful for presenting information on binary mixtures of two components, such as surfactant/cosurfactant, water/drug, or oil/drug[42]. The Pseudoternary phase diagram is represent mixture of surfactant, co-surfactant, oil, and water phase is shown in Figure No.2[43].

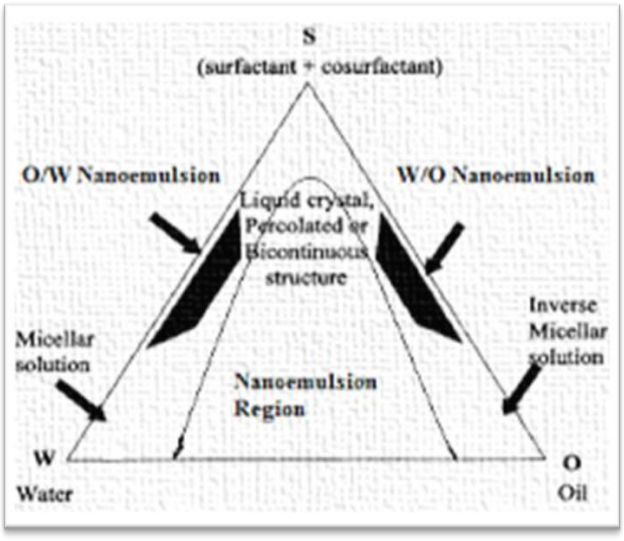

Figure 2: Pseudoternary Phase Diagram

CHARACTERIZATION OF SELF NANO EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS)

Morphological Study

Morphological study is important since it provides information about the formulation's external appearance, such as colour, odour, consistency, density, and look. The transmission electron microscope (TEM) has been used to examine globules in the self-Nano emulsifying drug delivery system (SNEDDS) [44].

Thermodynamic Stability Studies

Physical stability of a lipid-based formulation is also essential for its performance, which might be affected by drug precipitation in the excipient matrix. Furthermore, inadequate formulation physical stability can result in excipient phase separation, affecting not only formulation performance but also visual appearance. Furthermore, incompatibilities between the formulation and, as a result, the gelatin capsule shell might result in brittleness or deformation, delayed disintegration, or inadequate drug release[45-46].

Heating cooling cycle

The researchers looked at six cycles ranging from 40°C to 450°C, with storage times of at least 48 hours at each temperature. Centrifugation tests are performed on those formulations that are stable at these temperatures.

Centrifugation

Centrifuged thaw cycles between 21°C and +25°C with storage at each temperature for not less than 48 hours are performed at 3500rpm for 30 minutes. The freeze thaw stress test is performed on formulations that do not exhibit any phase separation[45-46].

Freeze thaw cycle

The stability of SNEDDS was assessed via freeze thawing. Three freeze-thaw cycles were performed on the formulations, with freezing at 4°C for 24 hours and thawing at 40°C for 24 hours. For 5 minutes, centrifugation was performed out at 3000 RPM. After that, the preparations were examined for phase separation. The formulations that passed this test demonstrated excellent stability, with no phase separation, creaming, or cracking[47-48].

Dispersibility Test

A standard USP XXII dissolution apparatus 2 is used to evaluate the efficiency of self-emulsification of oral nano or microemulsions. At 37 0.5 0C, one milliliter of each formulation was added to 500 mL of water. Gentle agitation was provided by a conventional stainless steel dissolution paddle rotating at 50 rpm. The following grading system has been used to visually assess the formulation's in vitro performance[47-48]:

Table 5: Visual Grading System

Grade	Time for Emulsification	Observation	Visual Appearance
Grade A	Within 30 seconds	Rapidly forming nanoemulsion which is clear and transparent, high spreadability	Bluish tinge
Grade B	Within 1 min	Rapid nanoemulsion formation which is slightly less transparent, less clear	Bluish white tinge
Grade C	Within 2 min	Rapid nanoemulsion formation, which is turbid in nature formed.	Milky white tinge
Grade D	Within or longer than 3 min	Nanoemulsion devoid of or slow to minimal emulsification, with non uniform distribution of oil droplets	Dull, grayish white tinge having slightly oily appearance
Grade E	Longer than 3 min	Formulation exhibiting either less, poor or minimal emulsification	Large oil globules

When dispersed in GIT, Grade A and Grade B formulations will remain as nano emulsions. For the SNEDDS formulation, a formulation in Grade C may be recommended.

Turbidimetric Evaluation

The growth of emulsification is monitored by nepheloturbidimetric analysis. Under the continuous stirring (50 rpm) on magnetic plate at ambient temperature, the increase in turbidity was measured by using turbid-meter after a fixed quantity of Self emulsifying system was added to a fixed amount of appropriate medium (0.1N HCL). It is impossible to monitor the rate of change of turbidity when the time required for complete emulsification is too short (rate of emulsification) [49].

Droplet Size Analysis Particle Size Measurements

Photon correlation spectroscopy (which analyses fluctuations in light scattering due to Brownian motion of the particles) and a Zeta sizer capable of measuring sizes between 10 and 5000 nm are used to quantify the droplet size of the emulsions. Light scattering is monitored at the 25°C at an 90° angle, after external standardization with spherical polystyrene beads. Even after the 100 times dilution with water, the nanometric size range of the particle is retained then that proves the system's compatibility with excess water[50].

Viscosity Determination

The SEDDS system is usually administered in soft gelatin or hard gelatin capsules. As a result, it's frequently easy to pour into capsules, and such a system shouldn't be too thick to cause a problem. Brookfield viscometer is used to test the micro emulsion's rheological properties. This viscosities determination conforms whether the system is water/oil or oil/water. If the system has low viscosity, then it's o/w type of the system and if high viscosities then it's w/o type of the system[51].

Stability Study

The stability study is crucial for determining the Nanoemulsion system's quality and purity. The tolerance of a formulation is determined by its stability. The stability of several nano emulsion formulations was evaluated by subjecting them to mechanical stress conditions (centrifugation at 2000-4000 rpm) and storing them at various temperatures ranging from 4 1 °C to 40 1 °C for various time intervals. The influence of mechanical stress conditions on the Physiochemical stability of the nano emulsion was measured by measuring % phase separation, breaking of the nano emulsion, or any physical change. After 60 minutes of centrifugation at 2000 rpm, there was no discernible change in the formulations[52].

Refractive Index and Percent Transmittance

Index of refraction and percent transmittance proved the transparency of formulation. The refractometer measures the system's index of refraction by placing a drop of solution on a slide, and it correlates with the water (1.333). With the use of a UV-spectrophotometer and distilled water as a blank, the percent transmittance of the system is determined at a specific wavelength. If the formulation has transparent nature, then index of refraction of system is similar to the index of refraction of water (1.333) and formulation have percent transmittance >99 percent[53].

In Vitro Diffusion Study

Using the dialysis technique, in vitro diffusion tests are carried out to determine the release behavior of formulation from the liquid crystalline phase around the droplet[54].

Drug Content

The drug is extracted from pre-weighed SEDDS by dissolving it in a suitable solvent. The drug content in the solvent extract was compared to a standard drug solvent solution using a suitable analytical method[54].

Bioavailability Study

Based on the self-emulsification properties, particle size data and stability of micro emulsion the formulation is selected for bioavailability studies. The in vivo study is performed to compute the drug after the administration of

the formulation. Pharmacokinetic parameters of the utmost plasma concentration (Cmax) and therefore the drug's corresponding time (tmax) following oral administration is calculated. The following equation to determine the relative bioavailability of the SEDDS formulation compared to the conventional tablet[54].

Relative Bioavailability (%) =

(AUC test/AUC reference) X (Dose reference/Dose test).

APPLICATION

Improving Water Solubility of Poorly Water-Soluble Drug

The Self-Nanoemulsifying Drug Delivery System (SNEDDS) is vital to improved water solubility of poorly water-soluble drug and increases oral bioavailability of poorly water soluble drug[55].

Applications of Nanoemulsion in Drug Delivery

Nanoemulsions (SNEDDS) have been used in a wide range of drug delivery systems, including cosmetics and transdermal drug delivery, cancer therapy, vaccine delivery, cell culture technology, formulations are important for increasing oral delivery of poorly soluble drugs, ocular and otic drug delivery systems, intranasal drug delivery, parenteral drug delivery and pulmonary delivery of drugs as well as intranasal drug delivery system[56].

Protection Against Biodegradation

SNEDDS, SMEDDS, and SEDDS are essential for delivering macromolecules such as peptides, hormones, and enzyme substrates, which are inhibitors that must be protected against enzymatic degradation[57].

CONCLUSION

In recent years, developments in SNEDDS research have been extensively investigated for improving the solubility and oral bioavailability of class II medicines. The transition of liquid SNEDDS to solid SNEDDS reduced the rate of drug degradation but did not totally eradicate it. Self-Nanoemulsifying drug delivery system (SNEDDS) is an Isotropic mixture of oils, surfactants, Co-surfactant (Smix) and co-solvent. Under mild agitation, it emulsifies spontaneously in the aqueous phase to yield fine o/w Nanoemulsion. For the formulation of poorly water-soluble medicines, SNEDDS is a good alternative. SNEDDS enhances the dissolution of the drugs due to increased surface area on dispersion and Absorption rate of Drug molecule. The oral delivery of lipophilic drugs is often made possible by SNEDDS, is important to improve oral bioavailability. It is feasible to improve drug release by incorporating polymer into the mixture using this method. SNEDDS appears to be a unique, industrially viable approach to future development.

FUTURE PERSPECTIVE

The primary goal of SNEDDS research has been to enhancement bioavailability in oral drug administration. In SNEDDS, the pH catalyzed and solution-state degradation of drugs must be assessed. Drug degradation can be reduced by converting SNEDDS to a solid form, but it cannot be prevented in many circumstances. Hence, identifying microenvironment-modulation strategies is essential for enhancing the stability of pH-sensitive drugs. The conversion of liquid SNEDDS to solid dosage forms like tablets and pellets has been the subject of intense research. In addition, inert adsorbents, such as Neusilin, are gaining popularity (Fuji Chemicals, Toyama, Japan) and Zeopharm (J.M. Huber Corp., Edison, NJ, USA) products for converting liquids into powders that help in formulation of solid SNEDDS. However, in order to convert liquid SNEDDS into a solid powder without significantly increasing volume or bulk density, a suitable extremely porous amphiphilic carrier must be identified. The use of SNEDDS in other routes of administration than the oral route is widely investigated. The ability of drug delivery scientists to address these aspects of SNEDDS will influence if the technology can be commercialized.

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