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Review Article

A Review on Self Nanoemulsifying Drug Delivery System (SNEDDS)

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ABSTRACT

Self-nanoemulsifying drug delivery systems (SNEDDS) have emerged as a promising approach for improving the oral bioavailability of poorly water-soluble drugs, particularly those classified under Biopharmaceutics Classification System (BCS) Class II and IV. SNEDDS are isotropic mixtures of oils, surfactants, and co-surfactants that spontaneously form fine oil-in-water nanoemulsions upon mild agitation in gastrointestinal fluids. This unique property enhances drug solubilization, promotes faster dissolution, and facilitates lymphatic transport, thereby bypassing first-pass metabolism. Over the past decades, significant advancements have been made in the selection of excipients, optimization techniques, and characterization methods to ensure stability, efficacy, and patient compliance. SNEDDS offer advantages such as ease of manufacturing, scalability, and protection of labile drug molecules, yet challenges remain in drug precipitation control, in-vivo predictability, and regulatory standardization. This review highlights the formulation strategies, mechanistic insights, recent technological advancements, and potential clinical applications of SNEDDS, aiming to guide future research and industrial translation.

INTRODUCTION

Almost 50% of the new drugs discovered recently have poor solubility problem and most of them encounter poor bioavailability problem when formulated as oral dosage form. [1,2] The poor water solubility of the drug leads to poor bioavailability with wide inter- and intra-subject variations, presenting the formulation scientists challenge to formulate them as oral dosage form. These poorly soluble molecules can be classified according to the Biopharmaceutics Classification System (BCS) either as class II or class IV (figure 1). According to BCS classification (Fig 1), class I drugs are highly soluble and highly permeable. BCS class II and class IV drugs are poorly soluble compounds while class III drugs have permeability issues associated with them. To overcome the poor aqueous solubility problem, many approaches have been exploited such as, particle size reduction, complexation with cyclodextrins, salt

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formation, solid dispersions, use of surfactant, nanoparticles, etc. [3-9]

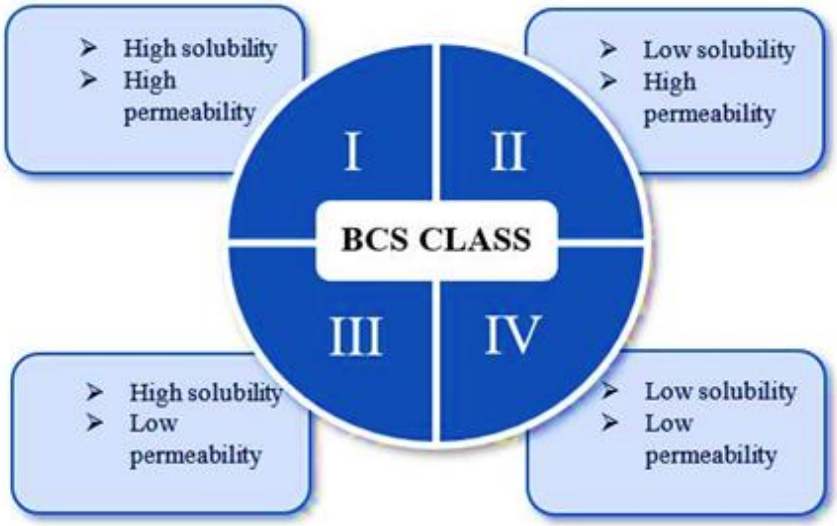

Figure 1. Biopharmaceutics Classification System (BCS)

The advantages and disadvantages with these systems are well known and available in number of reviews. However, lipid-based formulations have a great potential to improve oral bioavailability of poor water-soluble drugs by presenting the drug in a solubilized state in colloidal dispersion. Incorporating the lipophilic drug into inert lipid vehicle such as oils (tri-, di- and monoglycerides), surfactant, liposomes, self-nanoemulsifying drug delivery systems (SNEDDS) can improve the poor bioavailability problem associated with lipophilic drugs. The present review describes how SNEDDS can be used as a strategy to improve bioavailability of poorly water-soluble drugs. Various methods of characterization and biopharmaceutical aspects of SNEDDS have been discussed. The authors have tried to explain the effect of the key constituents for the formulation of SNEDDS. The selection criteria of different components and the application of SNEDDS in oral drug delivery are also discussed. SNEDDS are defined as isotropic mixtures of natural or synthetic oils, solid or liquid surfactants or alternatively, one or more hydrophilic solvents and co-solvents/surfactants that have a unique ability of forming fine oil-in-water (o/w) emulsions on mild agitation followed by dilution in aqueous media, such as gastrointestinal (GI) fluids. [10] SEDDS are mixtures of oils and surfactants, ideally isotropic, and sometimes containing co-solvents, which emulsify spontaneously to produce fine o/w emulsions when introduced into aqueous phase under gentle agitation. [11] These lipid-based systems as opposed to the polymeric system are easily taken up by the body. The digestion of these formulations involves dispersion of fat globules into a coarse emulsion of high surface area, enzymatic hydrolysis of fatty acid glyceryl esters (primarily triglyceride lipid) at the oil/ water interface and dispersion of the products of lipid digestion into an absorbable form. The resemblance of their degradation product with end product of intestinal degradation has contributed in their wide acceptance for SNEDDS.

2. Classification Of Lipid Formulation System

Pouton [12] and Pouton and Porter [13] introduced the lipid formulation classification in 2000 in order to identify the factors affecting the in vivo behavior of formulation. One of the main objectives of this classification system is to identify the most suitable formulation system for specific drugs based on their physicochemical properties and the same for the excipients. Table 1

briefly describes the characteristics of different systems.

2.1 Type I

Type I systems consist of formulations which comprise drug in solution in triglycerides and/or mixed glycerides. Typically, lipophilic materials are blends of food glycerides derived from vegetable oils, which are safe for oral ingestion, rapidly digested and absorbed completely from the intestine. Because type I systems do not contain surfactant, these systems exhibit poor initial aqueous dispersion and have very limited ability to self-disperse in water. They depend on digestion by pancreatic lipase/co-lipase in the GI tract to generate more amphiphilic lipid digestion products and promote drug transfer into the colloidal aqueous phase. Theses system are suitable for highly lipophilic drugs (logP > 4), where drug solubility in oil is sufficient to allow incorporation of the required dose. The advantage of type I system lies in the generally regarded as safe status (GRAS) of excipients, simplicity and their compatibility with capsules.

2.2 Type II

Type II lipid formulations (typically referred to as SEDDS) are isotropic mixtures of lipids and lipophilic surfactants (hydro philic-- lipophilic balance (HLB) < 12) that self-emulsify to form fine o/w emulsions when introduced in aqueous media. Self-emulsifying systems are formed when the surfactant con centration exceeds 25%w/w, the optimum concentration range being 30- 40% surfactant. Above 50% surfactant, these systems emulsify slowly due to the formation of viscous liquid crystalline phases at the oil/water interface. Poorly soluble drugs can be dissolved in these systems and encapsulated in hard or soft gelatin capsules to produce convenient single unit dosage forms. Type II lipid-based formulations generate large interfacial areas which in turn allows efficient partitioning of drug between the oil droplets and the aqueous phase from where absorption occurs. An advantage of type II formulations is that they are unlikely to lose solvent capacity on dispersion.

Table 1. Classification of Lipid Formulation system and their characteristics.[12]

No surfactant	Surfactant (moderate HLB)	Surfactant (higher HLB)	Surfactant and co-solvent	High concentration of surfactant and co-solvent
Poor self-dispersion Digestion required	Self-dispersing Will be digested	Self-dispersing May function without digestion	Transparent dispersion May function without digestion	Micelle or mixed micelle Thought to be limited digestion

2.3 Type III

Type III lipid-based formulations are defined by the inclusion of hydrophilic surfactants (HLB > 12) and co-solvents such as ethanol, propylene glycol (PG) and polyethylene glycol (PEG). These have the potential to disperse quickly to form fine submicron dispersions, often fine enough to form trans parent dispersions. Type III formulations can be further segregated (somewhat arbitrarily) into type IIIA and type IIIB formulations in order to identify more hydrophilic systems (type IIIB), where the content of hydrophilic surfactants and co-solvents increases and the lipid content reduces. Type IIIB formulations typically achieve greater dispersion rates when compared with type IIIA, although the risk of drug precipitation on dispersion of the formulation is higher given the lower lipid content. The best-known example of a successfully marketed type III is the Neoral cyclosporin formulation. In contrast to the earlier Sandimmune cyclosporin formulation (comprising corn oil, polyoxyethylated glycerides (labrafil M-2125-CS) and ethanol) which formed a coarse

emulsion on dispersion into water, Neoral spontaneously forms a trans parent and thermodynamically stable dispersion with a drop let size below 100 nm when introduced into an aqueous media. These systems mix with water easily and take up so much water that penetration of water into the formulation and subsequent dispersion proceeds rapidly.

2.4 Type IV

Type IV systems are essentially pure surfactants or mixtures of surfactants and co-solvents, do not contain natural lipids and represent the most hydrophilic formulations. These formulations commonly offer increased drug-loading capacity (due to higher drug solubility in the surfactants and co-solvents) when compared with formulations containing simple glyceride lipids and also produce very fine dispersions when introduced in aqueous media. The blending of water-soluble surfactants with co-solvents aids the dispersion of surfactant and reduces the loss of solvent capacity. An example of a type IV formulation is the current capsule formulation of the HIV protease inhibitor amprenavir (Agenerase) which contains TPGS (tocopherol polyethylene glycol succinate) as a surfactant and PEG 400 and PG as co-solvents.

3. Advantages And Disadvantage of SNEDDS Micro/Nanoemulsion

ADVANTAGES:

• Ease oral administration the drug in Self-Nano emulsifying System for Drug Delivery. [14]

• The self- nanoemulsifying drug delivery method enhances bioavailability.[15]

• SNEDDS has low interfacial tension-and a high o/w- interface area.[16]

• Nano-emulsion delivery technologies can enhance therapeutic effectiveness and decrease adverse effects by reducing the overall dosage.[17]

• SNEDDS droplet size are nano (globule less than 100 nm), so area is large thus increase the speed of absorption and reduce variability, thus enhance bioavailability of drug.

DISADVANTAGES:

- Traditional dissolve procedures are ineffective for SNEDDS because they rely on digestion prior to disintegration. [18]
- 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. [18]
- Drugs' chemical instabilities.
- Surfactant concentrations in the formulation are higher (30–60%). [19]
- Higher production cost.
- Lower drug incompatibility and stability. Possibility of drug leakage and precipitation. [19]

SNEDDS are promising approach for the formulation of drug compounds with poor aqueous solubility. The oral delivery of hydrophobic drugs can be made possible by SNEDDS. Hence present work aimed towards formulation of Self Nanoemulsifying drug delivery system of cardiovascular drug for enhanced bioavailability.

4. Composition of SNEDDS

The SNEDDs is mainly composed of the following. [19]

S.N.	Composition
1.	Drugs
2.	Oil
3.	Surfactant
4.	Co-surfactant

4.1 Drug

The most important parameter for SEDDS formulation is the lipophilicity and hydrophobicity of a drug. A drug's log P should preferably be 2. The drug is formulated at a modest dose and should not be subjected to substantial first-pass metabolism. [19].

4.2 Oil

Surfactants lower the interfacial tension by forming an inter facial film, allowing for dispersion. During SNEDDS formulation, the HLB value must be kept in mind. A surfactant with an HLB value greater than 12 is chosen to achieve better emulsification. It helps to disseminate the intended formulation quickly by forming small oil-in-water (o/w) droplets. Nonionic surfactants are commonly used in the formulation of SNEDDS due to their nontoxic nature, despite the fact that they may produce a modest irreversible change in the permeability of the GIT wall. In GIT, a formulation of surface-active com pounds that is 30–60% w/w results in improved self-emulsifi cation. Surfactants in high amounts might irritate the wall of the GI tract. [22-24].

4.3.1 Classification Surfactant Molecule

The four main groups of surfactants are: [25]

Cationic surfactants.
Anionic surfactants
Ampholytic surfactants
Non-ionic surfactants

4.3.1.1 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.

4.3.1.2 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 polyoxyethylene ether sulfate, sodium phosphate, cetylsoybean phospholipids(lecithin), carboxyl (RCOO-), sulphonate (RSO3 -) or sulphate (ROSO3-). Potassium laurate, sodium lauryl sulphate.

4.3.1.3 Ampholytic surfactants / Zwitterionic surfactants

The surfactant unit consist of both charges Positive also as negative Charge. Sulfobetaines are good example.

4.3.1.4 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).

Table 2. Classifications of Surfactant

S.N.	General class	Examples	Commercial name
1.	Surbiton easter	Sorbitan monooleate	Span 80
2.	Polysorbates	Polyoxyethylene-20-Sorbitan monooleate	Tween 80

3.	Polyglycolzyed glycerides	Oleoyl macrogol glycerides	Labrafil 1944 CS

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.[26] 30-60% surfactant concentration is employed to form stable SNEDDS. 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.

4.4 Co-surfactant

Co-surfactant lowers the transitory negative value of inter facial tension even further. It gives the interfacial film flexibility so that varied curvatures can be achieved for the creation of different microemulsion concentrations. By adding co-surfactant, the higher amounts of surfactant (approximately 30%) can be simulated. The contact enlargement at this moment results in the creation of finely scattered droplets. It will absorb more surfactant or a higher surfactant/co-surfactant ratio until the film is depleted enough to restore positive interfacial tension. Spontaneous emulsion is formed as a result of this. Co-surfactants are typically made up of medium-chain length alcohols (C_3–C_8). [27]

4.5 Co-solvent

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. (Figure 2) 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 gelatine capsules, resulting in the precipitation of the drug. [28].

5. Mechanism of SNEDDS [29,30]

A quick study of the literature indicates a variety of Nanoemulsion generation methods. The generation of Nanoemulsion droplets is thought to be caused by surfactant-mediated intricate film formation at the oil–water interface. Emulsification happens when the transformation in entropy favouring dispersion is better than the energy required for dispersion surface area amplification and the free energy (G) is negative, according to the thermodynamic theory of Nanoemulsion production. The energy necessary to establish a new surface between the two phases is connected to the free energy in the Nanoemulsion production, as shown in the equation below:

$$\Delta G = \sum Nr2\sigma$$

Where G represents the process's free energy, N is the number of droplets, r is the radius, and σ is the interfacial energy. The two emulsion phases will most likely split, reducing the interfacial area and therefore the system's free energy. Surfactants stabilize the emulsion that arises from aqueous dilution by establishing a single layer around the emulsion droplets, lowering interfacial energy, and preventing coalescence.

6. Methods For Preparation SNEDDS

6.1 High energy approach [31,32]

High mechanical energy is required for the high energy approach which leads the formation of nanoemulsion by mixing surfactants, oil, and co-solvent. Formulation of nanoemulsion extensively uses high energy methods (Figure 3). Strong disruptive forces are provided by the high mechanical energy that are used for breaking up the droplets of large size into droplets of nano size so that nanoemulsions produced would be of high kinetic energy. Basically, SNEDDS require low energy and depend upon the phenomena of self-emulsification.

6.2 High pressure homogenizer [33,34]

High pressure is required for the preparation of nano-formulation. Fine emulsion is formed depending upon the application of high sheer stress. There are two theories that can explain the droplet size including turbulence and cavitation.

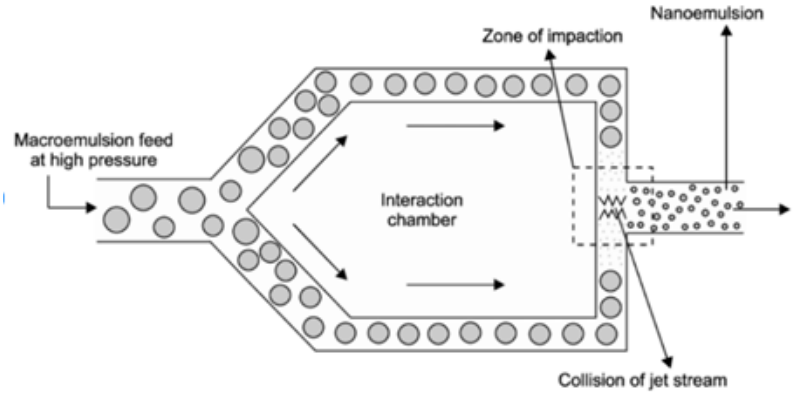

Figure 3. High Pressure Homogenizer

Nano-emulsion of smaller than 100nm droplet size can be produced by this method. Various factors are responsible for the production of droplet size of nanoemulsion using high pressure homogenizers, i.e. type of homogenizer, com position of sample and the operating conditions of homogenizer including time, intensity, and temperature. High pressure homogenization is commonly applied to produce nanoemulsions of food, medicinal, and biotechnological ingredients.

6.3 Micro-fluidization [35,36]

Micro-fluidizer is a device required by the method of micro fluidization. The product is pushed toward the interaction chamber by the positive displacement pump. A microchannel is a small droplet channel found in this system. The product formed is then transferred to the impingement area through the microchannels where nanoemulsion of very fine droplets is produced. Then, course emulsion is produced when the mixture of aqueous phase and oil phase is added into the homogenizer. Further processing leads to the formation of a transparent and homogeneously stable Nanoemulsion.

6.4 Sonication method [36]

One of the useful methods for the formation of SNEDDS is sonication method. With regard to cleaning and operation, the method of

ultrasonication is better as compared to other methods of high energy.

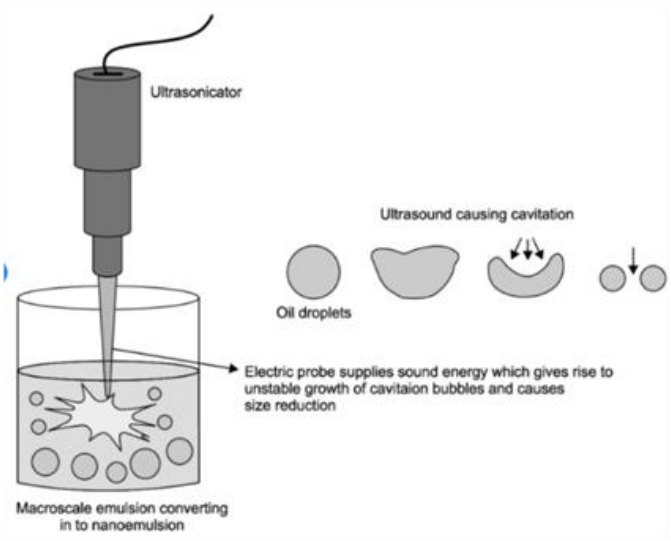

Figure 4. Ultrasonication

In the emulsifications by ultrasonication, the macroemulsions are broken down into nanoemulsion by the cavitation forces provided by the ultrasonic waves (Figure 4). This process reduces the droplet size of the emulsion and leads to an emulsion of nano size. The mechanism of sonication is responsible for the reduction of the droplet size.

6.5 Phase inversion Method [37]

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.

6.6 Pseudoternary Phase Diagram [37-40]

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.

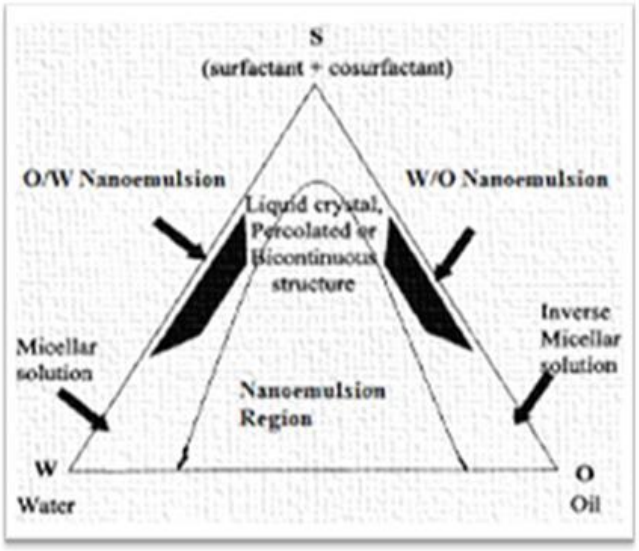

Figure 5. Pseudoternary Phase Diagram

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 (Figure 5). 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. The Pseudoternary phase diagram is represent mixture of surfactant, co-surfactant, oil, and water phase is shown in Figure No.2.

7. Characterization Of Self Nano Emulsifying Drug Delivery System (SNEDDS)

7.1 Visual evaluation [41]

Visual observation helps in the assessment of self-emulsification. The existence of a clear, isotropic, transparent solution after water dilution of SNEDDS suggests microemulsion pro duction, whereas an opaque, milky white appearance indicates macroemulsion evolution. A lack of precipitation and/ or phase separation suggests that the formulation is stable.

7.2 Analysis of droplet size [42,43]

The size of the droplet is determined by the surfactant's type and concentration. The microemulsion generated during dilution of SNEDDS with water has a very narrow droplet size distribution, which is critical for optimal drug release, in vivo absorption, and stability. Droplet size analysis is done using DLS methods.

7.3 Zeta potential measurement [44]

The zeta potential reflects the emulsion's stability following dilution. If the zeta potential is larger, the formulation remains stable. When compared to particles with either sur face charge, particles with a zwitterion charge exhibit greater biocompatibility and a longer blood residence period.

7.4 Emulsification time [45]

The amount of time it takes to emulsify a formulation is determined by the oil/surfactant and oil phase ratio. This is determined using a basket dissolution equipment, which observes the development of a clear solution under agitation following drop wise formulation addition to a water-filled basket.

7.5 Cloud point determination {46]

The cloud point of a homogeneous solution is the temperature at which it drops its transparency. Above the cloud point, the surfactant normally loses its ability to form micelles. It is determined by progressively raising the temperature of the formulation and spectrophotometrically detecting the turbidity. The cloud point of the surfactant is the temperature at which the percentage transmittance decreases. To maintain self-emulsification, formulations should have a cloud point higher than 37.5 C.

7.6 Viscosity measurements [47,48] 1

A rheometer, Brookfield viscometer having a cone and plate with rotating spindle is used to assess the viscosity of diluted SNEDDS formulations.

7.7 Liquefaction time

That are microemulsions This analysis is performed to determine how long it takes for S-SEDDS to melt in a simulated GI environment without moving. The dosage form, which is threaded to the bulb of a thermometer, is covered in a transparent polyethylene film. The thermometer should then be placed in a round bottom flask with 250mL of simulated stomach juice without pepsin and held at 37 C. After that, the time it takes for the liquefaction to happen is noted.

7.8 Dispersibility test [49-53]

In order to assess the capacity of SNEDDS to distribute evenly inside an emulsion and ascertain the dimensions of the resulting globules, a dispersibility test is performed. 0.1 mL of the prepared SNEDDS was introduced into 250 mL of distilled water and stirred using a magnetic stirrer at 100 rpm, and the duration required for the emulsion development was documented. The SNEDDS formulation creates a variety of mixtures upon dilution with distilled water according to which the in vitro activity may be graded. Grading system.

Table 3. Dispersibility test is performed by Grading system

Emulsion Grade	Description of Emulsion Formed	Formation Time
A	Instantly forms a clear, transparent emulsion	Less than 1 minute
B	Quickly forms a slightly bluish or whitish emulsion	Less than 1 minute
C	Produces a milky or cloudy emulsion	Approximately 2 minutes
D	Creates a slowly emulsifying, dull gray or slightly white mixture that has a subtle oily look	More than 1 minute
E	Outcomes lead to inadequate emulsification, resulting in big oil droplets	More than 1 minute

Scattering techniques [54]

For the investigation of microemulsion, scattering approaches have been used. Small-angle X-ray scattering (SAXS), DLS, PCS, and small angle neutron scattering (SANS) are some of the techniques used. Structural data provided by SAXS on macromolecules vary in size from 5 to 25nm, as well as repetition distances in partly ordered systems up to 150nm in partially ordered systems. It is used to determine the structure of particle systems at nanoscale or at micro scale, including size of particles, dispersion, morphologies, and the surface-to-volume ratio, among other things. To use SANA is to find droplet shape and size. Micelles, oil-swollen micelles, and mixed micelles, are described by the term 'droplet'. The interference effect of wavelets dispersed from diverse materials in a sample is used in small-angle neutron scattering investigations. The dilution of the sample necessary to reduce interparticle interactions is a fundamental disadvantage of these approaches. The structure and content of the pseudo ternary phases can be altered by this dilution. Despite this, effective determination has been achieved utilizing a dilution procedure that preserves the droplet identity. Incorporating deuterated molecules or protonated, SANS allows for selective increase of the scattering ability of distinct microemulsion pseudo phases. The variation in the frequency of the scattering by the droplets due to Brownian motion is studied using DLS and PCS.

7.10 Test of thermodynamic stability

Physical stability is essential for a formulation's performance, as precipitation of the chemical in the excipient matrix might have a detrimental influence. Excipient step separation can occur as a result of inadequate formulation physical stability, lowering bioavailability, and decreasing therapeutic effective ness. Brittleness, softness, and delayed or partial drug release may arise from incompatibilities among the formulation and the gelatin shell of the capsule. The following cycles are used to carry out these investigations.

7.11 Turbidimetric test [55]

Turbidity is a measurable characteristic that may be used to estimate droplet size and self-emulsification time. After a given amount of SNEDDS is administered to a fixed amount of suitable medium under continual stirring at 50rpm on a magnetic stirrer at optimal temperature, the turbidity is measured using a turbidity meter. As the time required for complete emulsification is too short, the rate of turbidity shift, or rate of emulsification, cannot be measured. Turbidimetric analysis is used to track the growth of droplets following emulsification.

7.12 Determination of self-emulsification time [56]

Using a primitive nephelometer and a rotating paddle to assist emulsification, we investigated the efficiency of emulsification of several formulations of Tween 85/medium chain triglyceride systems. This allowed the emulsification period to be measured. Samples were obtained for particle size using photon similarity spectroscopy after emulsification, and self-emulsified and homogenized systems were compared. The self-emulsification process was studied using light microscopy. The process of emulsification was precisely defined as the erosion of a thin cloud of microscopic particles off the surface of big droplets, rather than a steady decrease in droplet scale.

7.13 In Vitro Diffusion Study [57]

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.

7.14 Drug Content [57]

The drug is extracted from pre-weighed SNEDDS 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.

7.15 Bioavailability Study [57]

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.

Relative Bioavailability (%) = (AUC test/AUC reference) X (Dose reference/Dose test).

8. Limitations [58,59]

The absence of reliable predictive in vitro models for the assessment of SNEDDSs and other lipid-based formulations is one of the barriers to their development. Traditional dissolution procedures are ineffective because these formulations may be dependent on gut digestion prior to drug release. An in vitro model of the duodenum's digestion processes has been constructed to imitate this. Before the strength of this in vitro model can be assessed, it must be refined and validated. In addition, because development will be based on in vitro–in vivo correlations, several prototype lipid-based formulations must be produced and evaluated in vivo in an appropriate animal model. Chemical instability of medications and high surfactant concentrations in formulations (about 30–60%) that irritate the GIT are a few other downsides. Furthermore, it is known that volatile co-solvents in traditional self-micro emulsifying formulations diffuse into the shells of soft or hard gelatin capsules, causing lipophilic drugs to precipitate. Due to the dilution impact of the hydrophilic solvent, the drug's precipitation propensity may be increased when diluted. Simultaneously, validating formulations with several components becomes more difficult.

Applications [60-65]

Lipids, surfactants, and cosolvents make up the SNEDDS formulation. The system may form an o/w emulsion when separated by a water phase with modest stirring. SNEDDS deliver medications in small droplets with a balanced distribution, resulting in improved dissolution and permeability. As medicines can be loaded in the inner phase and supplied via lymphatic bypass sharing, SEDDSs protect drugs from enzymatic hydrolysis by in the GI tract and decrease presystemic clearance in the GI mucosa and hepatic first pass metabolism.

Future perspectives

The primary goal of SNEDDS research has been to enhancement bioavailability in oral drug administration. In SNEDDS, the pH catalysed 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.

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.

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