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Review Article

A Comprehensive Review on SNEEDS: A Simple Tool to Enhance Drug Solubility

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A B S T R A C T

Many new and current therapeutic compounds still face significant obstacles in their oral delivery due to poor solubility in water, due to this there is poor dissolution, ineffective absorption, and low bioavailability. One of the most promising lipid-based technologies among the different formulation techniques investigated to overcome these constraints is Self-Nanoemulsifying Drug Delivery Systems (SNEDDS). SNEDDS is mixtures of oils, surfactants, and co-surfactants. when this exposed to gastrointestinal fluids it rapidly and spontaneously undergo nanoemulsification, producing ultra-fine droplets that maintain the solubility of lipophilic medications. This review offers a thorough overview of SNEDDS, covering their underlying mechanisms, formulation components, physicochemical factors controlling self-emulsification, and selection criteria for appropriate drug candidates.

The importance of pseudoternary phase diagrams in optimizing compositions, the wide range of approaches to characterization that determine their structural and functional performance and both traditional and sophisticated methods for SNEDDS preparation are all summarized in the article. The review also discusses the current issues with scale-up, stability, and clinical translation, as well as the benefits, drawbacks, and broad pharmaceutical applications of both liquid and solid SNEDDS. So these is versatile platform to enhance the therapeutic effectiveness of poorly water-soluble medications can be seen by emerging trends in computational modeling, quality-by-design techniques, and alternative administration routes.

KEYWORDS: Self-nanoemulsifying systems, bioavailability, nanoemulsion,Pseudo-ternary phase diagram,lipid-based formulations, solubility enhancement, pseudo tertary phase diagram,surfactants,solid- SNEDDS, L-SNEDDS**.**

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INTRODUCTION

Many different drug substances and possible therapeutic candidates are investigated for effective disease treatment in drug development. However, the effectiveness of a medicinal product's delivery to the intended– site is just as important to its success as the drug's pharmacological activity. To get the desired therapeutic result, delivery systems for drug are essential for transporting the active medicinal ingredient in a controlled, effective, and safe manner. By removing physiological barriers and reducing adverse effects, these systems improve the drug's stability, bioavailability, and patientcompliance[1].

Oral, parenteral, transdermal, pulmonary, and targeted delivery systems are just a few of the complicated delivery methods that have been developed over time to maximize therapeutic efficacy. A key component to current pharmaceutical research is the development of such modern delivery technologies, which allow for the efficient use of both new and existing drug molecules.[2]Among various administration routes, the oral approach remains the most commonly used and convenient due to its non-invasiveness, simple to administration,improved patient compliance, safety, and potential for self-administration.The poor solubility and low bioavailability of many recently developed therapeutic agents pose a major obstacle to oral administration, even though it is still the most popular method of drug delivery.[3]

The physical and chemical characteristics of the drug (such as dissociation constant, hydrophobicity, solubility), dosage form design, gastric emptying rate, circadian rhythm fluctuations, food intake, interaction with excipients,

intestinal metabolism, and efflux transporter activity are all factors that affect oral bioavailability. Furthermore, hepatic first-pass metabolism dramatically lowers the systemic availability of numerous medications taken orally.[4]

Lipid-based formulations have become a very effective method because they improve solubilization, promote lymphatic uptake, and reduce drug loss. Self-emulsifying systems, such as SEDDS, SMEDDS, and SNEDDS, have drawn a lot of attention among these formulations because of their ease of use, stability, scalability, and compatibility with a variety of lipophilic medications. These systems serve as a promising alternative to traditional methods because they spontaneously form fine emulsions in the digestive tract. This process leads to quick dissolution and better drug absorption.[5,6]Self-emulsifying systems are usually mixtures of surfactants, co-surfactants, and oils; co-solvents may also be present. When these mixtures come in contact with GI fluids and experience gentle agitation from gastric movement, they quickly form oil-in-water emulsions.As a result, the drug gets incorporated into tiny droplets, which provides a larger surface area for dissolution, better permeability, and improved bioavailability[7,8]

SEDDS are mixtures of oils and surfactants (similar to the ones mentioned above) that are even and create emulsions (100-300 nm) when exposed to water. This is useful in the dissolution and absorption of drugs. Better versions are SMEDDS which create microemulsions with even smaller droplets (100-250 nm). They are more stable and evenly distributed with the drug. SNEDDS are high-tech implementations, which automatically generate nano-sized oil-in-water emulsions (20-100 nm) in stomach and intestinal fluids[9–11]According to Reiss self-emulsification theory, emulsification begins when the entropy change promotes the oil phase's distribution in water. Upon entering the GI tract, SNEDDS components interact with intestinal fluids to form stable nanoemulsions that facilitate efficient drug transport across biological membranes.[12]

Table 1: How SEDDS, SMEDDS, and SNEDDS Differ from Each Other[13,14]

Parameter	**SEDDS**	**SMEDDS**	**SNEDDS**
Droplet Size	100–300 nm	100–250 nm	<150 nm
Emulsion Type	Emulsion	Microemulsion	Nanoemulsion
Appearance After Dilution	Milky / opaque	Clear to slightly opalescent	Clear / translucent
Emulsification Speed	Moderate to fast	Fast	Very fast / instantaneous
Surfactant Requirement	Moderate	Higher than SEDDS	Optimized; efficient surfactant–co-surfactant use
Drug Loading Capacity	High for lipophilic drugs	Slightly lower than SEDDS	Moderate to high
Stability	Good physical stability	Higher thermodynamic stability	Excellent colloidal stability

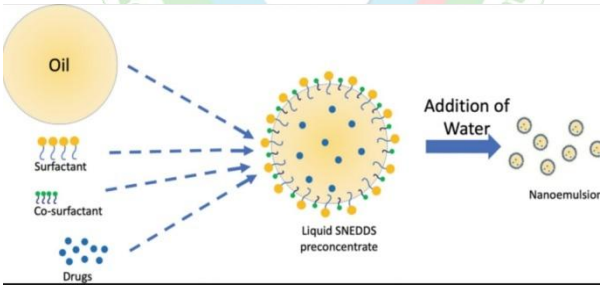

Figure 1: Structure Of SNEDDS[17]

Structurally, SNEDDS are uniform mixtures of surfactants, oil and co-surfactants [As mentioned in Figure 1].SNEDDS enhances the dissolution of water-insoluble drugs by forming small droplets of the drug in a stable. The smaller size disperses the drug, allows it to be absorbed and also allows it to pass through lymph vessels. This increases the amount of drug intake into the body during oral consumption.[15,16]

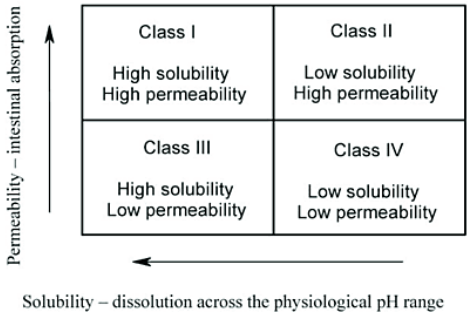

Figure 2: BCS Diagram [20]

BCS Classification

Drugs are divided into four classes by the Biopharmaceutical Classification System (BCS) according to their permeation and soluble properties. Drugs belonging to Classes II, and IV often exhibit poor aqueous solubility and class III low permeation, leading to insufficient intestinal absorption and low systemic bioavailability. Solubilization of weakly water-soluble drugs, therefore, remains challenge indosage forms development. Studies suggest that almost one-third of newly developed chemical entities suffer from low oral bioavailability due to poor dissolution characteristics, necessitating innovative formulation strategies to overcome these limitations.[18,19]

Mechanism of SNEDDS

SNEDDS strengthen the oral delivery of low water-soluble drugs through its unique mechanism of spontaneous emulsification and absorption. When administered orally, the combination of surfactant, oil and co-surfactant are brought with the fluids of the digestive tract. The gentle agitation from gastric motility causes the formulation to spontaneously creates a minute o/w nanoemulsion, with droplet sizes typically below 100 nm.This procedure keeps the medication soluble and stops it from precipitating, making it accessible for absorption during the digestive process.[21]After the formation of the nanoemulsion, the lipid components of SNEDDS were enzymatically broken down by pancreatic and stomach lipases, resulting in the production of free fatty acids and monoglycerides. These digestion products mix with phospholipids, cholesterol, and bile salts to form mixed micelles that retain the solubilized medication. These mixed micelles facilitate the transport of the medication pass through the unstirred water layer of the intestine and promote their absorption through the intestinal epithelium.[22]

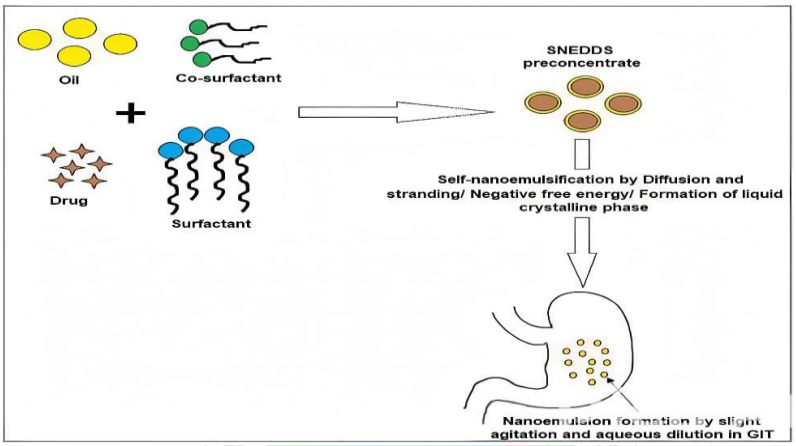

Figure 3: Mechanism of SNEDDS [24]

In addition to improving solubility, the surfactants used in SNEDDS enhance intestinal permeability by reducing interfacial tension and altering membrane fluidity. P-glycoprotein and CYP3A4 enzymes, which are responsiblefor drug efflux and first-pass metabolism, respectively, can be inhibited by certain surfactants. This inhibition results in greater intracellular drug concentrations and reduces the chances of drug being pumped back into the intestinal lumen, thereby increasing systemic availability.[23]

Additionally, highly lipophilic medications included in SNEDDS can avoid hepatic first-pass metabolism by being absorbed through the intestinal lymphatic pathway. The medication enters the lymphatic circulation and effectively reaches the systemic circulation thanks to the formation of chylomicrons within enterocytes.. Overall, the mechanism of SNEDDS involves a combination of enhanced solubilization, enzymatic interaction, micellar transport, and efflux inhibition, resulting in improved bioavailability, stability, and therapeutic efficacy of agents that have less water-soluble.[25]

ADVANTAGES

This delivery systemprovides several advantages over conventional dosage forms and lipid-based formulations[26,27]:

1. By bypassing the dissolution step, they enhance the solubility of fat-soluble drugs, their absorption and availability when ingested orally, and also decrease the difference between those that it causes by eating and those that it causes by not eating.
2. They prevent the degradation of drugs (such as hydrolysis or oxidation) by keeping the drugs in a lipid solution.
3. They assist the patients to take the medicine more comfortably because fewer doses are required, bad tastes are concealed, and numerous types of medicine are possible, including liquids, capsules, small pellets, tablet, or creams.
4. They are able to convert liquid medications into hard tablets or capsules which are more user-friendly, more stable, and convenient.
5. They provide low cost and scalable means to prepare medicines through solidification techniques like spray, freeze drying, fluid bed coating or loading the product on spongy carriers.
6. They slow down the food-related modifications and liver metabolism by consuming surfactants which aid in absorption and lymph transportation.

Disadvantage [28]

1. High surfactant content can lead to gastrointestinal irritation, especially with liquid formulations. Stability

issues can arise, such as drug precipitation or phase separation over time.

2. There is a limited drug loading capacity for highly potent or poorly soluble drugs. Formulation development requires careful optimisation of oils, surfactants, and co-surfactants.

Key Variables Impacting Bioavailability

API molecule's own qualities, dosage form, and interactions with the intricate environment of the absorption site all affect its bioavailability. Key factors include[29,30]:

Physical and chemical properties, such as the solubility of the drug, its oily nature, and its pH dependence. The design in which the medicine is formulated, the excipients, its formation process, and whether or not it is released instantly or gradually. Gut variables including eating, emptiness rate, daily rhythms and general digestive condition. Biological interactions, such as the drug getting in contact with other drugs or food, modulation of enzymes that degrade it, and protein transport (e.g. P-glycoprotein). Patient problems like diseases that may change the extent of drug uptake and its diffusion in the body.

Factors Influencing Self-Emulsification

Several formulation and physiological factors impact self-emulsification efficiency, including [31,32]:

1. HLB Value and Its Role In Surfactant Performance :

It is really important. For the making of oil-in-water nanoemulsions, surfactants possessing an HLB value between 12 and 15 are normally believed to be suitable. This guarantees that the surfactant promotes dispersion in the fluid medium, causing stable nanoscale droplets to spontaneously form when diluted with gastrointestinal fluids.

2. Physiological Conditions:

Things like the temperature and pH of the water can also change how emulsification works. At body temperature (approximately 37°C), the viscosity of oils and surfactants decreases, which promotes rapid emulsification. Alterations in pH between the acidic condition of the stomach and the intestine's nearly neutral environment can also affect ionization and interfacial features of surfactants or co-surfactants, which can make the nanoemulsion less stable.

3. Nature of Co-Surfactant:

Is vital in achieving effective self-emulsification. Co-surfactants reduce interfacial tension further, increase the fluidity of the surfactant film surrounding oil droplets, and prevent coalescence. This facilitates the spontaneous formation of ultra-fine droplets, ensuring better dispersion and long-term stability of the system.

4. Important Physical And Chemical Attributes Of The Drug:

This has a major effect on how nicely self-emulsification works. Highly lipophilic drugs show greater solubility in the oil phase, thereby enhancing drug loading and preventing precipitation during dilution. In contrast, drugs with high melting points or poor solubility in lipidic excipients may limit the performance of SNEDDS. Thus, the compatibility of the drug with excipients is a key determinant of formulation success.

5. Ratio of Oil to Surfactant:

While an excess of surfactant can increase the risk of irritation or toxicity, a higher proportion of oil may result in inadequate emulsification due to insufficient surfactant available to lower the tension between the two surfacesSo, to achieve spontaneous emulsification, the production of small droplet sizes, and enhanced stability of the nanoemulsion, an ideal balance between oil and surfactant is necessary.

Formulation Aspects.

SNEDDS are primarily composed of the following components: a drug that is incorporatedin a blend of oil phase with surfactant, co-surfactant, and may include co-solvents.

1. DRUG

SNEDDS are largely created for medicines with weak water solubility, such as those belonging to BCS Class II and IV. Parameters for suitable candidature for SNEDDS: HLB value requirement is >12, API with a high melting point and a partition coefficient value of about 2 are not suitable. The best candidates for SNEDDS are lipophilic drugs with partition coefficient values greater than 5, Dispersion appearance should be clear, and Globule size: <100 nm.[33]

Table 1: Drug used in SNEDDS with their BCS class and therapeutic uses.[34–43]

Drug (Bcs class)	Drug Class	Therapeutic use	Drug (Bcs class)	Drug Class	Therapeutic use
Embelin II	Anti Inflammatory, Antioxidant	Used for its natural effects in reducing inflammation and fighting cancer.	Ritonavir IV	Antiviral	Used to treat HIV by boosting the effect of other antiviral drugs.
Curcumin II	Anti Cancer , Anti Inflammatory	Helps reduce inflammation and rotects the body from damage.	Lopinavir IV	Antiviral	Used with ritonavir to control HIV infection.
Celecoxib II	NSAID	Used to relieve pain and swelling, especially in arthritis.	Hydrochlorthiazide IV	Diuretic	to treat hypertension, edema, and heart failure
Simvastatin II	Antihyperlipidimic (Statin)	Helps lower cholesterol and protects the heart.	Amphotericin B IV	Antifungal	Treats serious and life-threatening fungal infections .
Docetaxel II	Anticancer	Chemotherapy drug use for many cancer	Furosemide IV	Loop diuretic	Use for acute pulmonary edema,renal failure and hypertension

2. Oil Phase

A key component of SNEDDS, the oil phase controls the emulsification rate, droplet size, and drug solubility. When added to surfactants and co-surfactants, oils create homogenous solutions that, when gently swirled, spontaneously produce fine oil-in-water nanoemulsions.To select an appropriate oil, Drug solubility in different oils is assessed using High-Performance Liquid Chromatography (HPLC) after overnight mixing. A combination of oils may be used to improve drug dissolution.Achieving small droplet size is essential for effective emulsification and enhanced bioavailability.[38]

3. Surfactant

The selection of surfactants in SNEDDS is guided primarily by safety and efficacy. Key considerations include: Preference for edible, naturally derived surfactants over synthetic ones. Optimal surfactant concentrations typically range from 30% to 60% to achieve stable self-emulsifying systems.Non-ionic surfactants are among the most commonly used because they are easy to break up into tiny nano-droplets that have a high HLB value, and are mild on the stomach.They reduce interfacial tension effectively and are considered the safest option for oral delivery. Examples include Tween 80 /20, , Labrasol,Cremophor RH 40 and poloxamers like Pluronic F68. Anionic surfactants can also form good emulsions, but they are less suitable for oral use because they may irritate the gastrointestinal tract, so their use is mostly limited to research studies. Common examples of this type are SLS and SDS. Cationic surfactants create strong emulsification but are rarely chosen for oral SNEDDS due to safety and toxicity concerns; a typical example is cetyltrimethylammonium bromide (CTAB). Amphoteric or zwitterionic surfactants are milder and more biocompatible, and although they are not the first choice for SNEDDS, they are sometimes added to lipid systems for better compatibility—lecithin (phosphatidylcholine) is the main example. In many formulations, combining surfactants offers even better performance, as blends can reduce droplet size and speed up emulsification.[44]

Table 3: Oil, Surfactant and Co-surfactant Systems Used in SNEDDS for Various Poorly Soluble Drugs[45]

Drug	Oil phase	Surfactant	Co-surfactant
Nystatin	Oleic acid	Tween 20/40	Dimethyl sulfoxide or PG
Olmesartan medoxomil	Capryol 90	Cremophor EL or Cremophor RH 40	Transcutol P
Paclitaxel	Sesame oil	Labrasol	Sodium deoxycholate
Fenofibrate	Miglyol 812 + Imwitor 988	Cremophor EL or Cremophor RH 40	(Water-soluble Cremophor RH 40 co-solvent used as needed)
Candensartan cilexetil	Capryol 90	Cremophor RH 40	Transcutol HP

4. Co-Surfactant

Co-surfactants or co-solvents,in addition to SNEDDS, make the emulsification process easier and more efficient. They help by either making the oil–water interface more flexible or by improving how well the drug dissolves in the lipid phase. These components usually have an HLB value between 10–14 or come in the form of common hydrophilic vehicles like ethanol, propylene glycol, glycerol, or PEG. By reduction of the system's dielectric constant or the tension between surfaces, they create a more fluid and hydrophobic environment that encourages the spontaneous formation of fine microemulsion or nanoemulsion droplets. Because they also increase the solubility of lipophilic drugs or surfactants, their presence supports stable nanoemulsions—especially when paired with higher surfactant levels (often above 30% w/w).[46]

Prepration of Snedds [47,48]

Prepration of Liquid SNEDDS

Liquid SNEDDS were prepared by first identifying the most suitable proportions of oil, surfactant, and co-surfactant using a pseudo-ternary phase diagram to locate the self-emulsifying region. After selecting these ratios, the required quantities of each component were accurately measured, and the drug was added to the mixture of oil and surfactant. The blend was gently mixed until the drug completely dissolved and a clear, uniform solution was formed. The final liquid formulation was then kept at room temperature for further analysis.

Prepration of Solid SNEDDS

The prepared liquid SNEDDS was then added dropwise onto suitable adsorbents like Neusillin, mixed thoroughly, the material was passed through a 120-mesh sieve and then allowed to dry at room temperature, resulting in the final solid SNEDDS product. For this various technique are used as physical adsorption, spray drying, freeze drying, and melt granulation.

Methods for Preparation of SNEDDS [49,50]

1. Mechanical Energy–Based Method

High-energy techniques employ mechanical forces to generate SNEDDS based on the breakdown of oil droplets into nanoscale. An oil-surfactant-co-surfactant-co-solvent mixture is then subjected to energy, whether through stirring, homogenizing or other high-energy instruments. This spreads the oil to fine drops making the nanoemulsion stable and evenly dispersed. The resulting nanoemulsion tends to be either clear or slightly opaque and its quality is dictated by the selection of oil and surfactant and the energy applied. The methods can be used in the laboratory as well as large scale production.

2. High-Pressure Emulsification Method

Nanoemulsions are mostly prepared by high-pressure homogenization. In this technique the oil water mixture with the surfactants is passed through an extremely small opening with high pressure. During the high shear rate, turbulence, and cavitation the droplet size is reduced to the nanometer level of about 100 nm. The droplets are stabilized and coalescence is inhibited by use of surfactants. Large-scale SNEDDS production, where the droplet size is constant and stable, is especially good with this method as long as the pressure, number of passes, and surfactant concentration are optimized.

3. Microfluidization

Microfluidization is a high-precision method used to prepare uniform and stable nanoemulsions. The technique uses a microfluidizer, which forces the emulsion mixture through micro-channels at very high pressure. Inside the microfluidiser, the streams collide in the interaction chamber, resulting in extremely fine droplets. A coarse emulsion is first formed by blending the oil and water phases with surfactants, and then it is processed through a microfluidiser to reduce the droplet size.The repeated impact and shear forces in the micro-channels produce a transparent, homogeneous nanoemulsion. Microfluidization allows control over droplet size and distribution, improving stability and bioavailability. It is highly reproducible and suitable for scaling up. This method also reduces the risk of droplet aggregation, giving a longer shelf-life to the formulation.

4. Sonication Method

Sonication uses ultrasonic waves to generate intense energy that reduces droplet size in emulsions. When the ultrasonic waves pass through the emulsion, they create alternating high and low-pressure zones that lead to cavitation. Cavitation generates microbubbles that collapse violently, breaking down larger droplets into nanosized particles. This method is generally applied to small-scale batches due to its limited processing capacity. Sonication is especially helpful when accurate control over droplet size is needed. Both the strength and the time of sonication influence how small and consistent the droplets become. The surfactants present in the mixture help stop the droplets from coming back together. Overall, this method creates stable nanoemulsions that can improve the solubility and absorption of drugs with poor water solubility.

5. Phase Inversion Method

In this technique, nanoemulsions form naturally when the temperature or composition of the mixture is altered. It usually uses non-ionic surfactants. At cooler temperatures, the system forms an oil-in-water nanoemulsion, while higher temperatures shift it to a water-in-oil type. This temperature-dependent transition changes the interfacial properties and allows the formation of very small, uniform droplets. The method can also be influenced by altering the ratio of oil, water, and surfactant. Phase inversion can affect particle size, drug release, and in vivo absorption properties. It is considered energy-efficient since it relies on the spontaneous self-assembly of components. This approach works well for drugs that cannot tolerate strong mechanical forces or high temperatures.

Pseudoternary Phase Diagram[51]

The pseudoternary phase diagram is essential for designing and optimising SNEDDS. It provides a diagrammatic representation of the system composed of oil, surfactant, co-surfactant (Smix), and water. Construction of the diagram is typically performed using phase titration or phase inversion methods. Initially, Mixtures of oil and different surfactant–co-surfactant ratios (such as 1:1, 2:1, or 3:1) are prepared and vortexed for about five minutes to obtain uniform, isotropic blends.These mixtures are then visually examined for clarity: turbid samples indicate the formation of a coarse emulsion, whereas clear or transparent solutions indicate successful nanoemulsion (SNEDDS) formation. The percentages

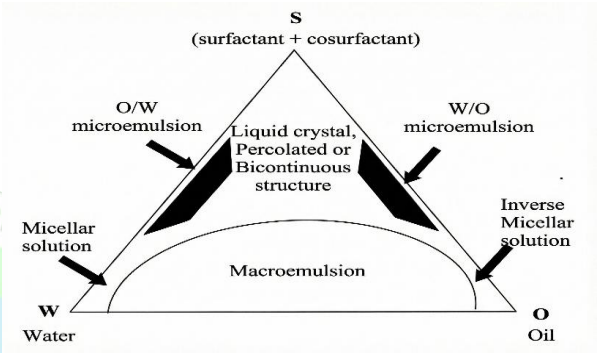

Figure 4: Pseudoternary Phase Diagram[52]

Of oil, Smix, and water are used to create the pseudoternary phase diagram, with each corner representing 100% of one component. This diagram can also show binary mixtures, such as surfactant/co-surfactant, water/drug, or oil/drug. Overall, it serves as an important tool for identifying the self-emulsifying region and optimizing the formulation of SNEDDS.

Characterization of SNEDDS[53–55]

Morphological Study

The morphology will offer an insight into the morphological features of SNEDDS. TEM and SEM are the techniques applied to investigate droplet or particle size, shape, and surface characteristics. TEM validates the nanoscale uniformity and lack of aggregation of globules and SEM surface morphology and porosity in solid SNEDDS, which guarantee the integrity of formulations.

Solubility Studies

To determine the most appropriate formulation constituents, the solubility of the drug was determined in different oils, surfactants, and co-surfactants. Each vehicle was added an excess of drug and the mixtures were shaken under controlled temperature until equilibrium was attained. Upon centrifugation and filtration of the undissolved drug, the content of the drug in the clear layer was determined by either USA spectroscopy or HPLC. Measurements were performed in triplicate and components that appeared to be the soluble ones were chosen to be subject of further formulation studies.

Measurement of Droplet Size

A photon correlation spectrophotometer with a Zetasizer was used to measure droplet size as a key parameter that affects the release and bioavailability of SNEDDS after proper dilution. The uniformly-sized droplets are smaller in size, which means that they self-emulsify effectively, and stability of the formulation is superior, and the large or non-uniform droplets mean that the formulation will not perform well.

Viscosity

Viscosity assessment evaluates the flow properties and rheological behavior of SNEDDS, which are critical for capsule filling and oral administration. Brookfield cone and plate viscometers are commonly used to determine the shear-dependent viscosity in centipoises (cP). Low-viscosity formulations, typically associated with oil-in-water systems, ensure easy handling and rapid self-emulsification, whereas high-viscosity formulations may indicate water-in-oil systems or excessive surfactant content, potentially affecting dosing consistency.

Refractive index (RI) and percent transmittance are optical parameters used to find the transparency and physical stability of SNEDDS. RI is measured with a refractometer, and minor changes over time indicate thermodynamic stability and structural integrity. Percentage transmittance, measured with a UV-visible spectrophotometer, reflects the clarity of the formulation; values approaching 100% indicate a homogenous, transparent nanoemulsion. These parameters together confirm that the formulation maintains its optical properties during storage.

Polydispersity Index (PDI)

The polydispersity index gives the value for uniformity in the droplet size across SNEDDS, providing insight into formulation homogeneity. Measured using photon correlation spectroscopy on a Zetasizer, a low PDI value (<0.3) indicates a uniform nanoemulsion with consistent particle size, whereas higher PDI suggests a heterogeneous system with potential aggregation. Maintaining a low PDI is crucial for reproducible drug release and bioavailability.

Zeta Potential

Zeta potential gives the surface charge present on SNEDDS droplets and serves as a predictor of colloidal stability. Using a Zetasizer and applying the Smoluchowski theory, formulations with high absolute zeta potential values (≥ ±30 mV) are considered electrostatically stable, minimizing the risk of aggregation or coalescence. This parameter is particularly important for long-term storage and for ensuring consistent drug delivery performance.

Thermodynamic Stability

To check how well the formulations could handle different stress conditions, each one was first centrifuged to see if it separated under force. The stable ones were then taken through gentle heating and cooling cycles, allowing us to observe how they reacted to temperature changes. After that, they went through freeze–thaw cycles, shifting between very cold and normal room temperatures. Formulations that stayed clear and unchanged throughout all these steps were considered truly stable and suitable for further development.

Self-Emulsification Test

The effectiveness of self-emulsification is evaluated by the dilution of a little SNEDDS in aqueous medium in contact with gentle stirring at 37 degC. The time taken in emulsification and the clarity of the created nanoemulsion are noted. The early development of a sharp dispersion suggests that there was good self-emulsification, and it is appropriate to deliver drugs into the gastrointestinal tract.

FTIR Spectroscopy

The FTIR analysis is conducted to determine a potential drug-excipient interaction. The samples are scanned using a specified spectral range and the variation in the characteristic peaks give evidence of chemical compatibility or interactions, which ensures maintenance of drug integrity.

X-Ray Diffraction (XRD)

XRD is applied to evaluate the physical appearance of the drug in SNEDDS to compare diffraction of pure drug, excipient and solid SNEDDS. The decrease or loss of crystalline peaks indicate drug amorphization which would help in increasing solubility.

Differential Scanning Calorimetry (DSC).

DSC is a technique used to determine the thermal behavior of SNEDDS components based on identifying melting transition and interaction-related transitions. Thermograms facilitate the verification that the thermal stability and the lack of unwanted interactions in processing or storing is achieved.

In Vitro Dissolution Investigations.

In-vitro dissolution testing determines drug release in SNEDDS with the help of standardized dissolution equipment and artificial physiological media. The comparison of the release profile with the release profile of the pure drug is done to verify enhanced dissolution that facilitates enhanced solubility as well as bioavailability.

Applications of SNEDDS [56, 57]

Medicinal preparations include ampoules, sterile injections, infusion solutions, oral liquids, eye drops, nose drops, aerosols, gels, ointments, creams, lotions, and pastes.Nasal drug delivery for improved absorption and prolonged mucosal contact.Topical bioavailability of lipophilic drugs: topical drug delivery using the eye.Antimicrobial applications against enveloped viruses, fungi, and spores.Cosmetic applications for controlled delivery of active ingredients and improved skin barrier function.Enhancement of the water solubility and oral bioavailability of poorly water-soluble drugs.Preservation of macromolecules like peptides, hormones and substrates of enzyme activity against enzymatic. degradation.Multipurpose drug delivery preparations such as transdermal, ocular, otic, intranasal, parenteral, pulmonary and others vaccine delivery.

Future Perspective [58, 59]

The main goal of SNEDDS research is to improve how well poorly soluble drugs are absorbed when taken orally. PH-sensitive drugs have problems with liquid SNEDDS, but can be transformed into solid dosage forms to enhance stability.

The future research direction should be on: changing the formulation microenvironment, using porous carriers,and comparison of clinical outcomes, particularly when BCS Class IV drugs are used.The challenges associated with scale-up, including supersaturation and stability can be solved by relying on Quality-by-Design (QbD), Design-of-Experiments (DoE), and more sophisticated computational techniques that comprise physiologically based-pharmacokinetics (PBPK) modeling and artificial intelligence (AI).

CONCLUSION

Self-nanoemulsifying drug delivery systems (SNEDDS) have become a valuable approach for improving the performance of poorly water-soluble drugs. By forming very fine oil droplets when they come into the stomach andcome in contact with digestive fluids, SNEDDS help the drug dissolve faster and get absorbed more efficiently. This leads to better bioavailability, more consistent therapeutic effects, and often lower doses compared to conventional formulations.SNEDDS are also flexible to design because different oils, surfactants, and co-surfactants can be combined to suit the needs of each drug. Their simple manufacturing process, stability, and ability to protect sensitive drugs make them attractive for many therapeutic areas.Overall, SNEDDS offer a practical and effective strategy to overcome solubility and absorption challenges, and they continue to gain importance in modern drug delivery research.

CONFLICT OF INTREST:

The authors do not have any conflicts of interest with this investigation.

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