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A Comprehensive Review of Solid Self Nano Emulsifying Drug Delivery System (S-SNEDDS) Technology to Enhance Nanoemulsion Stability

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ABSTRACT: Patients and practitioners prefer oral medication administration for systemic or local treatment due to its convenience and pleasurable experience. Nevertheless, numerous oral pharmaceutical formulations encounter various delivery challenges as a result of the hostile conditions of the gastrointestinal tract and a multitude of physiological barriers, including gastrointestinal architectural traits, biochemical variables, and physiological factors. Nanoparticle technology is often employed to surmount these challenges. Nanoemulsions, a form of nanotechnology, have been shown to improve the bioavailability and solubility of active pharmaceutical ingredients. However, despite these advantages, they often encounter adjustment challenges related to physical and chemical stability, necessitating the development of advanced delivery systems to ensure their therapeutic efficacy. Furthermore, liquid dosage forms may present several limitations for oral administration, such as inadequate masking of unpleasant tastes in the absence of flavoring agents or sweeteners, as well as difficulties in achieving accurate doses. Another potential method to enhance the stability of the drugs is the Solid Self Nano Emulsifying Drug Delivery System (S-SNEDDS). This lipid-based drug delivery device utilizes a particular porosity carrier and a Liquid SNEDDS compaction process. The S-SNEDDS formulation is a potential method of delivering medications for active substances not soluble in water, sensitive to light, or unstable in liquid form. It also exhibits benefits such as excellent stability, straightforward scalability, consistent content distribution, precise dosage accuracy, and improved patient adherence. Encapsulation of hydrophobic pharmaceuticals protects against the aqueous environment, impeding hydrolysis and enhancing the drug's stability when exposed to moisture. Another mechanism of S-SNEDDS is the controlled release mechanism, which can also enhance the drug's stability in terms of its chemical composition and therapeutic effectiveness. Therefore, S-SNEDDS have the potential to provide a viable approach to improving the stability of nanoemulsions.

Keywords: **nanotechnology; nanoemulsions; S-SNEDDS; stability.**

Introduction

Oral medications are the most common, convenient, and widely used route of administration, as they offer advantages such as painless, unassisted administration and increased patient compliance compared to other routes such as intramuscular, intravenous, and pulmonary. However, some compounds failed in research and development due to their low solubility and bioavailability upon oral administration [1]. The gastric mucin-bicarbonate barrier, enteral enzymes, and small oral surface area are a few physical characteristics that may also make it more difficult for the body to absorb medications when taken orally. Additionally, insufficient time for gastrointestinal tract absorption is a common cause of low bioavailability. Time may need to be increased at the absorption site if the drug does not dissolve easily or cannot cross the epithelial layer (for example, if the drug is highly polar and ionizable). In such cases, bioavailability can be low and highly variable. Previous gastrointestinal surgery (such as bariatric surgery), physical activity, age, genetic phenotype, gender, disorders (malabsorption syndrome and achlorhydria), and stress may also affect drug bioavailability [2].

All these limitations can be overcome by applying nanotechnology approaches to drug delivery mechanisms. In previous research, nanotechnology has been effectively used in various pharmaceutical formulations to increase oral bioavailability [3]. Nanoscale drug design has been studied a lot. It is the most advanced technology used for nanoparticles because it has many potential benefits, such as the ability to change properties like solubility, drug release profile, diffusivity, bioavailability, and immunogenicity. As a result, this may lead to the improvement and development of convenient administration routes, lower toxicity, fewer side effects, better biodistribution, and longer drug

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life cycles [4].

Various nanosystems have been produced, including carbon nanotubes, paramagnetic nanoparticles, dendrimers, nanoemulsions, etc. Nanoemulsions systems have much potential as drug delivery systems because they can make drugs that are hard to dissolve in water more soluble, dissolve faster, and be more bioavailable when taken by mouth. It can be defined as "an oil-in-water (o/w) or water-in-oil (w/o) emulsion with an average droplet diameter ranging between 50 and 1000 nm" [5]. Characterized by their submicron-sized droplets, nanoemulsions offer several advantages including improved drug dissolution rates, increased surface area for absorption, and enhanced stability of active pharmaceutical ingredients (APIs). However, despite these benefits, the physical and chemical stability of nanoemulsions can be challenging, often necessitating the development of advanced delivery systems to maintain their efficacy. Liquid dosage forms may have many oral disadvantages, such as not covering the unpleasant taste of formulations without flavoring agents or sweeteners, inappropriate dosage adjustment, etc. Consequently, solid dosage forms may be preferred in general. Solid nanoemulsions (SNE) is a highly recommended dosage form due to its strength, scalability, and ability to obtain all the benefits of a liquid system. Therefore, this nanoparticle system is expected to increase the bioavailability and therapeutic profile of drugs that are difficult to dissolve in water [5].

Solid Self Nano-emulsifying Drug Delivery System (S-SNEDDS) is one of the lipid-based drug delivery systems with a compaction system called Liquid Sel Nano-emulsifying Drug Delivery System (SNEDDS) using a specific porous carrier. The S-SNEDDS formulation was developed by converting SNEDDS into powder form via spray drying, freeze-drying, spray cooling, melt granulation, melt extrusion/extrusion spheronization, or solid carrier adsorption [6]. The S-SNEDDS dosage form provides many benefits, such as high stability, ease of scale-up, content uniformity, dosage accuracy, and increased patient compliance. The S-SNEDDS formulation provides a promising drug delivery system for active substances poorly soluble in water, photosensitive, and unstable in liquid dosage forms which combining the advantages of SNEDDS (increased solubility and bioavailability) by protecting drug degradation, facilitating drug lymphatic transport, inhibiting P-gp-mediated multidrug efflux, increasing the area under the curve (AUC) and maximum concentration (Cmax) and reducing the time to reach Cmax. (Tmax) [7,8]. And solid dosage forms (high stability) during handling and storage in a wide selection of dosage forms [9].

A previous study shows S-SNEDDS preparations can increase the stability and bioavailability of a medicinal compound, characterized by the absence of physical or chemical changes during the specified time. Therefore, this literature review aims to explore the current advancements in solid SNEDDS technology and its efficacy in enhancing the stability of nanoemulsions. By analyzing recent research and developments, we seek to provide a comprehensive understanding of the formulation strategies, characterization techniques, and potential applications of solid SNEDDS in modern drug delivery systems.

Methods

This article was created by reviewing journal information relevant to all aspects of S-SNEDDS nanotechnology. Literature studies were conducted by searching PubMed, ScienceDirect, and Google Scholar references using Perish and Publish 8. The inclusion criteria for this narrative review include journals published in the last ten years (2014–2024); peer-reviewed journal articles including original research, review articles, and meta-analyses; research papers discussing the formulation, characterization, and evaluation of S-SNEDDS; and the exclusion criteria including studies published more than ten years ago; articles not explicitly related to S-SNEDDS or nanoemulsion stability; articles from non-peer-reviewed journals, magazines, or opinion pieces; duplicate studies without adding new insights. There were 852 articles obtained from searches using keywords in the form of "Solid Self Nano-emulsifying Drug Delivery System (S-SNEDDS) AND Stability," "Formulation S-SNEDDS enhance stability," "S-SNEDDS AND nanoemulsions" and "Nanoemulsions AND stability." The article selection stages were completed by adjusting the inclusion criteria and research objectives to full text until 56 articles that could be used as a template for writing articles were obtained.

Result and Discussion

Nanoemulsions Properties

Nanoemulsions are heterogeneous colloidal dispersions with relatively small droplet sizes (20–200 nm) known as submicron emulsions or mini-emulsions. The formulation of nanoemulsions is divided into two types: oil-in-water (O/W) type and water-in-oil (W/O) type, prepared by nanoemulsification technology [10,11]. W/O

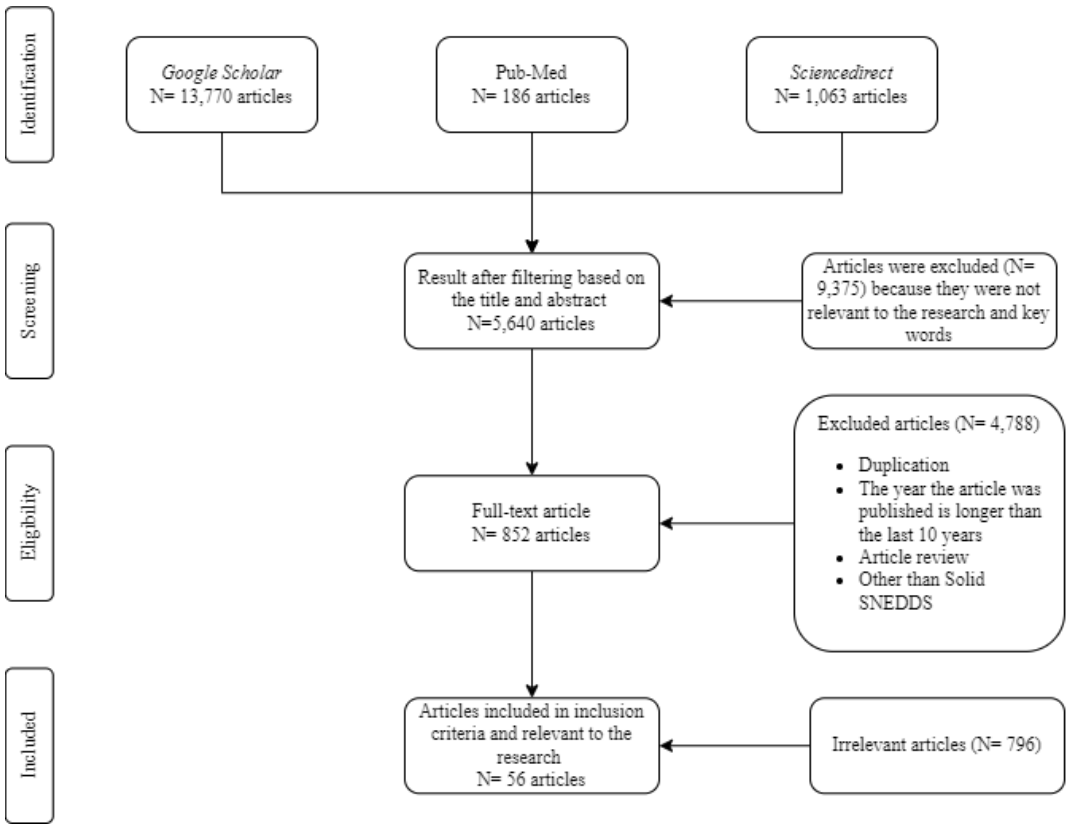

Figure 1. Flow chart of the article selection process in the review.

nanoemulsions consist of small drops dispersed in an oil phase, while O/W nanoemulsions contain a few oil drops dispersed in an aqueous phase [12]. The emulsifiers in nanoemulsions act as stabilizers and facilitate the formation of nanodroplets; in W/O nanoemulsions, the emulsifier used is lipophilic or hydrophobic, while in O/W nanoemulsions, a hydrophilic emulsifier is used [13].

The potential advantages of nanoemulsions have been used as a carrier or vehicle system in pharmaceutical, food, beverage, cosmetics, and other fields. In several studies, nanoemulsions act as encapsulation systems for lipid compounds to protect them through the gastrointestinal system and increase their bioaccessibility, which is also influenced by carrier oil type, emulsifier type, and oil drop size.

Besides the small particle size, the high surface area of the nanoemulsion droplets makes them suitable for encapsulating and delivering bioactive compounds. Compared to conventional emulsions, nanoemulsions can enhance kinetic stability due to their small droplet sizes, which prevent phase separation and creaming and extend the shelf life of products. The bioavailability and solubility of nanoemulsions may be increased due to the particle size of nanoemulsions being better at facilitating the absorption of bioactive compounds in the gastrointestinal tract [11].

S-SNEDDS Properties and Formulation Methods

The drug preparation in the S-SNEDDS formula offers several advantages compared to L-SNEDDS and nanoemulsions. First, the S-SNEDDS formulation provided increased stability and longer shelf life due to reduced susceptibility to phase separation and degradation. Another main benefit lies in improving the drug loading capacity, which allows higher solubility and bioavailability of drugs. Ease of handling and transportation is also one of the advantages of S-SNEDDS preparations because there is no need to worry about spills, leaks, and damage, which are generally associated with preparations in liquid form. In addition, the solid form facilitates better control over dose uniformity, a critical factor for accurate administration. S-SNEDDS also contributes to increased bioavailability by promoting rapid drug dispersion and absorption in the gastrointestinal tract. Lower resistance to environmental factors such as temperature and humidity increases overall toughness during storage and transportation. In addition, flexibility in dosage forms is a significant asset, as S-SNEDDS can be easily integrated

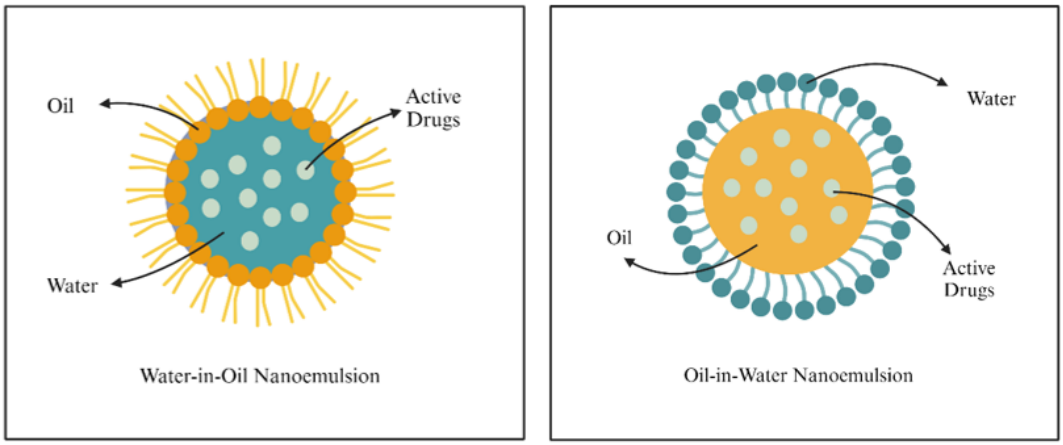

Figure 2. Types of nanoemulsions [13].

into various forms, such as tablets or capsules, offering diversity in administrative forms and meeting various patient preferences. It is essential to recognize that the choice between solid and liquid SNEDDS depends on the characteristics of the particular drug, therapeutic goals, and patient needs. All these advantages make S-SNEDDS a promising approach in drug formulation development and potentially increase treatment effectiveness [14,15].

Generally, the techniques used to formulate S-SNEDDS from L-SNEDDS include conventional adsorption on an inert carrier (surface adsorption technique), extrusion-spheronization, spray drying, and wet granulation. The most widely and economically used approach is the adsorption of liquid SNEDDS on the surface of a porous carrier. The adsorption method offers the advantages of high oil loading capacity, lower processing losses, more straightforward formulation, easy conversion of the solidified formulation into tablets, and low cost [16].

In addition to solid carrier adsorption techniques, spray-drying methods are the second choice used in the solid formulation of SNEDDS. Better final results indicate this compared to other S-SNEDDS methods. Results were obtained for one of the drugs using the spray drying method. Spray drying is converting a solution, suspension, or emulsion into a dry powder in one step by passing an atomized spray through a high-temperature gas medium [25]. Air is the most preferred choice as a drying gas,

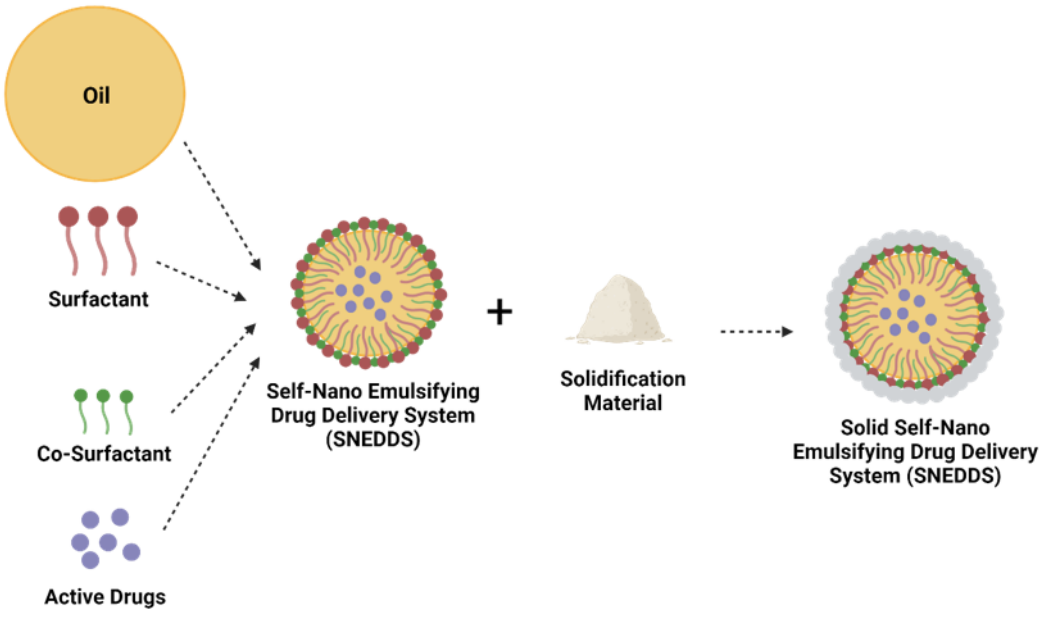

Figure 3. The Preparation of S-SNEDDS [16].

Table 1. Solid Self-Nano Emulsifying Drug Delivery System (S-SNEDDS) Formulation Method.

Active Ingredients	Methods	References
Capsaisin	Surface adsorption technique	[17]
Irbesartan	Spray-drying	[9]
Celexocib	Surface adsorption technique	[18]
Meloxicam	Freeze-drying	[19]
Rifampicin	Surface adsorption technique	[14]
Piperin	Spray-drying	[15]
Darunavir	Surface adsorption technique	[16]
Glimepiride	Surface adsorption technique	[20]
Revaprazan	Spray-drying	[21]
Glipizide	Surface adsorption technique	[22]
Docosahexaenoic acid	Spray-drying	[23]
Sertraline	Spray-drying	[24]

but in some cases, nitrogen gas has also been used. The physicochemical properties of the final product mainly depend on the inlet temperature, air flow rate, feed flow rate, and the type of carrier used [26].

The spray drying technique can be used on laboratory and industrial scales because they are fast, continuous, reproducible, one-step, and, thus, scalable without significant modifications. Successful process change depends on meeting two conditions: scalability and cost-effectiveness. Spray-dried in both. Another advantage is that the powder obtained with spray dried has better flow properties and higher encapsulation/drug loading efficiency. The solid particles obtained have a relatively narrow size distribution on the submicron to micron scale. Therefore, a judicious selection of solid carriers and techniques to strengthen L-SNEDDS is essential [27].

Freeze drying (freeze-drying) or lyophilization is one of the most widely used drying techniques to improve drug stability. This bending process relies on the sublimation of ice from frozen samples followed by desorption in a vacuum [28]. The lyophilization process is based on a sublimation mechanism where the solidified carrier material is converted directly into gas without going through the liquid phase [29]. It consists of three main stages: the freezing stage (solidification), the primary drying stage (ice sublimation), and the last stage, secondary drying, where water desorption occurs [30].

The comparison of S-SNEDDS and Nanoemulsions Formulation based on Drug Stability

Stability is defined as the quality of being stable, and applying this wide concept to pharmaceutical formulations is considered to be the absence of changes in characteristics and properties of the product at the time of its manufacture [31]. Stability study is one of the characterization parameters in every drug preparation. In quality control, characterization plays a central role in ensuring that each batch of drug preparation meets stringent standards regarding stability, uniform distribution and desired drug release. Safety evaluation is another crucial aspect of drug characterization. By understanding the physicochemical properties in detail, potential risks of side effects can be identified and managed appropriately, ensuring the safe use of drug preparation [32].

Chemical stability plays a major role in FPPs where the API is molecularly dispersed, such as in solutions and semisolid and solid formulations. In high-water-content medicines, evaluating microbiological stability is important as it can cause critical healthcare issues. Apart from potency loss and microbiological growth, degradants can appear over time and can lead to toxicity in patients; hence, their quantification is key to determining the overall safety profile of the dosage form. On the contrary, physical instability, including appearance, palatability, uniformity, or dissolution, mostly occurs in solid dosage forms and suspensions. The particle size of suspensions is a crucial factor in determining the biopharmaceutical performance of the formulation. Changes in physical stability are also fundamentally critical in amorphous solid dispersions. Over time, crystallization of the API can take place, and hence, this can cause a profound impact on the dissolution rate of the API and, thus, its oral bioavailability [33,34].

The results from multiple studies on nanoemulsions drug stability offer a collective perspective on their

Table 2. Studies Regarding The Stability of Nanoemulsion Vehicle Systems.

Nanoemulsion Formulation	Stability Parameters	Results	References
Rhodiola rosea	Particle size, polydispersity index, zeta potential, and pH value	In all groups, the particle size increased after 90 days storage and the pH value relative stable. Relatively stable without visible creaming or phase separation after heating applied during production and processing.	[38]
Shrimp oil	Thermal and centrifugal stabilities	The termal stability was lower in the nanoemulsion microfluidized at 6.89 MPa The centrifugal stability of nanoemulsion ranged from 79.6% to 95.6% The particle size average diameter of soy bean increased.	[39]
Diosgenin	Particle size	Has better stability under appropriate pH (<4 or >5), NaCl concentrations (≤0.3M), temperatures (≤60°C), and freeze-thaw cycles (≤2) and storage at 4°C At 80°C the particle size of the nanoemulsion increased	[40]
Black pepper	Particle size, physicochemical properties	The particle size increased gradually as the storage time increased At temperature 25°C ± 5°C with humidity 65% ± 5%, the appearance of the Black pepper nanoemulsion remained unchanged	[11]
Avocado (seed and peel)	Particle size	The particle size of avocado nanoemulsion increased up to 3.05 ± 1.05um after 14 days	[41]

reliability in pharmaceutical applications. Nanoemulsions improve the stability of drugs via a variety of mechanisms. To begin with, the drug solubility and dispersion within the formulation are enhanced due to the prevention of crystallization or precipitation caused by the small particles' high surface area-to-volume ratio. The reduced droplet size also promotes the dissolution of medications with low water solubility, improving drug stability. In addition, nanoemulsions are designed with the purpose of inhibiting phase separation, thereby guaranteeing consistent drug dispersion across the entire formulation. Nanoemulsions droplets provide a protective barrier for pharmaceuticals, shielding them from deterioration caused by external influences such as light, oxygen, and moisture. This helps preserve the drug's chemical composition for an extended period. Finally, nanoemulsions facilitate the formation of smaller droplets, leading to enhanced medication absorption and improved bioavailability, hence contributing to the effectiveness of the treatment. However, it is critical to note that several variables can still affect the stability of nanoemulsions; therefore, formulation design and optimization must be performed carefully to maximize the stability benefits for particular medications [35-37].

In one study regarding the drug stability of nanoemulsions vehicle systems (table. 2) using *Rhodiola rosea* as the active compound, stability studies were conducted in different environmental conditions, encompassing temperature, light, and humidity variations. And evaluated by measuring particle size, polydispersity index (PDI), zeta potential, and pH value on day 1, day 30, day 60, and day 90 under different temperatures (25°C, 40°C,

and 4°C). In addition, the organoleptic assessments were carried out after centrifugation, evaluating odor, color, and texture for each formulation. The average particle size of *Rhodiola rosea* nanoemulsions increased over the storage period; however, it remained below 500 nm, indicating acceptable size parameters for nanoemulsion systems. The polydispersity index (PDI) of the *R. rosea* nanoemulsions was 0.34, which, although slightly elevated, is still within the acceptable range for stable nanoemulsions. The zeta potential values of one group showed a gradual weakening of electrostatic repulsion between droplets as the storage period progressed [38]. This decline in zeta potential suggests a reduction in colloidal stability over time, as lower zeta potential values may lead to increased droplet aggregation or coalescence. The stability index for all groups was calculated using the following equation:.

%Stability Index=(Original viscosity score-hange in viscosity score)/(Original viscosity score) x 100. [37,38,42,43]

The stability indices were 67.18% for formula A, 88.62% for formula B, 87.20 for formula C, and 89.27% for formula D, respectively. These results suggest that the optimized R. rosea NEs are highly stable [38].

The formation, stability, and properties of nanoemulsions often depend on the physicochemical properties of the oil phase, e.g., its polarity, water-solubility, interfacial tension, refractive index, viscosity, density, phase behavior, and chemical stability [44]. The selection of appropriate emulsifiers is one of the key elements for successful emulsification and affects the long-term stability of the emulsions obtained. The size of nanoemulsions droplets determines the optical properties, stability, release behavior, and rheology [10,44].

In S-SNEDDS drug stability, the test was conducted at 40 ± 2 °C/75 ± 5% RH for six months. The formulation is packaged in glass bottles and stored in a climate chamber. Samples were taken at predetermined times (0, 1, 2, 3, and 6) to measure globule size, % transmittance, and emulsification time [15].

In previous research of S-SNEDDS formulation of Docosahexaenoic acid (DHA) (table 3.), the stability was conducted by measuring the peroxide content,

Table 3. Studies Regarding The Stability of S-SNEDDS.

S-SNEDDS Formulation	Stability Parameters	Results	References
Capsaicin	Drug content, droplet size, drug dissolution	Initial value of drug content 98.78 ± 0.11; after three months 96.91 ± 0.15. Initial value of droplet size 62.04 2.37; after three months 65.08 2.42. initial value of drug dissolution 94.05% and after three months 92.72%.	[17]
Docosahexaenoic acid (DHA)	Physicochemical properties, particle size, drug content	No change in color; No precipitation of oil; No change in the DHA content, reconstitution time, and particle size.	[23]
Avanafil	Physicochemical properties, drug content, particle size	No change in color, odor, or texture. The drug content decreased to 96.91% after 6 months of storage. The particle size decreased to 14.90 ± 0.12 after 6 months of storage	[45]
Furosemide	Dilution, droplet size, PDI, and in vitro drug release	Droplet size 17.67 nm with PDI 0.502, the drug release 99.51 ± 2.56 and the dilution passed	[46]
Xanthohumol	Droplet size, drug loading, angle of repose	The mean droplet size of aged S-SNEDDS powder 122.65 ± 6.13. The drug loading for fresh S-SNEDDS was 96.84 ± 4.81%, whereas it was 93.11 ± 4.65% for aged S-SNEDDS. The angle of repose for fresh S-SNEDDS was 22.62 ± 1.23, and the angle of repose for aged S-SNEDDS was 24.27 ± 1.21.	[47]

physicochemical parameters including color change, odor, particle size, robustness to dilution, and DHA content under refrigerated and accelerated storage conditions. The peroxide content is an important parameter to determine oxidative stability, and it increases during storage due to oil oxidation. The optimized S-SNEDDS formulation of DHA is physically stable for a period of 3 months under both accelerated and room temperature storage conditions; there is no change in color, no precipitation of oil, no change in the DHA content, reconstitution time, and particle size. It can be concluded that the results of stability studies of S-SNEDDS of DHA are highly stable and can be stored at room temperature for an extended period [48].

It is imperative to acknowledge that the precise stability benefits provided by S-SNEDDS are contingent upon the formulation's design, encompassing the excipient selection, drug characteristics, and intended route of administration. Formulating and optimizing needs and conducting comprehensive stability testing is crucial to ensure the efficacy of the medicine and its stability.

The stability comparison between solid self-emulsifying drug delivery systems (S-SNEDDS) and nanoemulsions highlights a subtle compromise between the properties of the formulations. The solid-state of S-SNEDDS confers intrinsic resistance to oxidation and hydrolysis, thereby augmenting its long-term stability. This characteristic is especially beneficial for pharmaceutical items that need a longer shelf life and are less likely to be affected by external influences. However, their liquid state can present stability issues, such as coalescence and phase separation, even though nanoemulsions provide advantages such as enhanced solubility, rapid absorption, and improved drug bioavailability.

The Effect of S-SNEDDS Formulation on Nanoemulsions Stability

Nanoemulsions might encounter diminished stability due to various factors, including gravitational separation, Ostwald ripening, and coalescence. When smaller droplets dissolve and contribute to the development of larger droplets, Ostwald ripening occurs, resulting in an irregular droplet size distribution and long-term instability. Phase separation can result from coalescence, the merging of adjacent particles caused by inadequate surfactant coverage or unfavorable interfacial conditions [14]. Additionally, because the small droplet size provides insufficient resistance to gravitational forces, the gravitational separation process—also known as creaming—poses a challenge. A combination of these factors influences the potential instability of nanoemulsions. As a result, stability and shelf-life improvements are achievable by implementing meticulously executed formulation and stabilization techniques [36].

S-SNEDDS enhance the stability of nanoemulsions by providing a solid matrix for the emulsion. These solid particles act as stabilizers and contribute to the system's stability. Several mechanisms of S-SNEDDS that help enhance the stability of nanoemulsions involve a variety of complex mechanisms. S-SNEDDS are crucial in enhancing

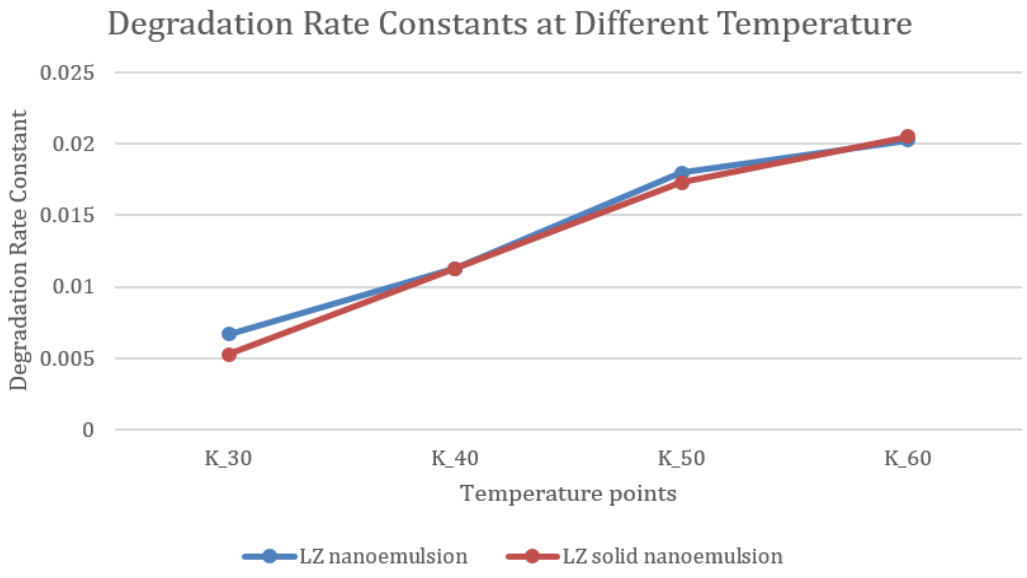

Figure 4. Graph of stability study of Letrozole.

the stability of nanoemulsions. One primary purpose is their capacity to act as a tangible obstacle, creating an organized framework that encloses and protects the emulsified droplets. This matrix effectively stops droplets from merging and joining, which is necessary to prevent the disruptive processes of flocculation and coagulation. The solid parts of these S-SNEDDS give the nanoemulsions mechanical stability by holding the dispersed phase in place and protecting it from gravitational forces that could cause the phases to separate [5].

Also, Ostwald ripening can be stopped by adding solid lipid nanoparticles to nanoemulsions as S-SNEDDS. Ostwald ripening is when smaller droplets break apart and spread their contents onto larger droplets. This process significantly contributes to the instability of emulsions. The solid seeds are essential for keeping the nanoemulsions stable over time because they stop Ostwald ripening and ensure that the droplet sizes are spread out more evenly. The composition and surface properties of solid seeds significantly influence the stability of nanoemulsions. By adjusting these parameters, achieving the most effective interactions with both the dispersed and continuous phases is possible, hence improving the overall stability of the emulsion. The gradual release of the dispersed phase from the solid seeds enhances the nanoemulsions's long-lasting stability [49].

One of the studies of nanoemulsion made it into a solid with the active drug Letrozole (LZ), a breast cancer medication. This formulation's stability studies were subjected to accelerated temperature for three months using the degradation rate constant parameter. The result showed (fig 4.) that there was no significant change in Letrozole content at all temperatures through the study interval. Both formulations show increasing degradation rates with increasing temperature. The LZ nanoemulsion generally degrades slightly faster than the LZ solid nanoemulsion at lower temperatures (K_{30} and K_{50}), but the LZ solid nanoemulsion degrades slightly faster at the highest temperature (K_{60}) [50].

In addition, the plot extrapolation determined The degradation rate constant of LZ nanoemulsion at room temperature (K25 = -2.44904), and then shelf-life was calculated, which was 2.6 years. The degradation rate constant LZ solid nanoemulsion at room temperature was (K25 = -2.61978), and the shelf-life was 3.66 years. The optimized SNE-2 has a considerably higher expiration date than NE-3 since the solid demonstrated more stability of solid than liquid preparations [50].

S-SNEDDS improve the stability of nanoemulsions by doing many things, such as creating a physical barrier, stopping merging, stopping Ostwald ripening, and letting control of the interactions. S-SNEDDS exhibit improved stability, making them suitable for many pharmaceuticals, cosmetics, and food applications.

The stability can be increased through various mechanisms:

- Oxidation Protection: The solid state of S-SNEDDS is a barrier to prevent oxidation. This is especially crucial for medications susceptible to oxygen degradation, as the solid form restricts exposure to air and aids in maintaining the chemical stability of the medication [51].
- Encapsulation of Hydrophobic Pharmaceuticals: S-SNEDDS are specifically formulated to enclose hydrophobic pharmaceuticals within a solid matrix. Encapsulation protects against the aqueous environment, impeding hydrolysis and enhancing the drug's stability when exposed to moisture [35].
- Improved Drug Solubility: The primary objective behind the development of S-SNEDDS is to enhance the solubility of the drug, thereby inhibiting any potential crystallization or precipitation. The enhanced solubility enhances the drug's stability in its solid form [52].
- Controlled Release: The solid matrix in self-nanoemulsifying drug delivery systems (S-SNEDDS) facilitates the controlled drug release, ensuring a consistent and sustained drug concentration over time. Implementing this controlled release mechanism can enhance the drug's stability in terms of its chemical composition and therapeutic effectiveness [53].
- Convenience of Handling and Storage: Solid formulations offer greater ease of handling and storage than liquid formulations. They exhibit reduced susceptibility to problems such as leakage, coalescence, and phase separation, enhancing the medicinal product's overall stability [54].

S-SNEDDS Effectiveness Based on Drug Bioavailability

Drug stability directly impacts drug bioavailability, determining the pharmaceutical formulation's solubility, chemical integrity, and release kinetics. Stable drugs retain their initial characteristics, guaranteeing appropriate absorption and dissolution within the gastrointestinal tract. Stability fluctuations may result in degradation, modified solubility, or unsuitable release rates, all of which have

Table 4. Effectiveness of S-SNEDDS Formulation on Drug Bioavailability.

Drugs/Active Compounds	Bioavailability	References
Piperine	T_{max} (hour): 2 t1/2 (hour): 7,23 ± 0,39 Ke (hour): 0,096^{-1} ± 0,006	[15]
Clopidogrel	C_{max} (µg/mL): 24,81± 3,07 T_{max} (jam): 0,5 $AUC_{0-\infty}$ (µg hour/mL): 48,79 ± 14,84	[56]
Revaprazan	C_{max} (µg/mL): 132,9 ± 27,2 T_{max} (hour): 3,7± 1,4 t1/2 (hour): 7,4± 6,5	[21]
Sertraline	C_{max} (µg/mL): 1,43 ± 2,65 T_{max} (hour): 6 AUC_{0-36} (µg hour/mL): 1233,83 ± 42,65	[24]
CoQ10	C_{max} (µg/mL): 1± 0,300 T_{max} (hour): 4 t1/2 (hour): 40,430± 6.37 AUC_{0-t} (µg hour/mL): 38,55± 3,42	[57]

adverse effects on the absorption and bioavailability of the drug [54].

S-SNEDDS has a significant influence on the pharmacokinetics of drugs given to patients. This effect is primarily reflected in increased bioavailability, as seen by higher plasma concentrations and faster absorption kinetics. Pharmacokinetic studies consistently show a decrease in the time to peak concentration (Tmax) and an increase in peak concentration (Cmax), indicating the efficiency of S-SNEDDS in increasing drug absorption. Additionally, the expansion of the area under the concentration-time curve (AUC) emphasizes sustained and improved drug exposure over time [55].

Based on the obtained pharmacokinetic parameters, the drugs formulated in S-SNEDDS in Table 3 have good pharmacokinetic values. Compared with drugs or active substances made by conventional methods, the maximum concentration of SNEDDS solid drugs is higher, and the maximum time required is also shorter. The in-vitro dissolution results of solid clopidogrel SNEDDS showed high clopidogrel drug release. This could be because of how quickly the nano-delivery system forms a preconcentrate after liquid SNEDDS is released from the carrier compound's surface. The surface area of this carrier compound contributes to drug release. Also, tests done on living things show that clopidogrel SNEDDS is 9.07 times more bioavailable than other clopidogrel drugs (Plavix), as shown by the Cmax and Tmax values. This shorter time is obtained as a result of the lymphatic absorption of the drug into the systemic circulation of the nanometric formulation. The bioavailability of clopidogrel is also increased by blocking CYP3A4-mediated first-pass

metabolism in the liver. This lets more of the drug enter the systemic circulation and is linked to a faster rate of clopidogrel absorption [56].

The increased absorption of S-SNEDDS may be due to increased solubility. It is possible for drug compounds that are dissolved in either L-SNEDDS or S-SNEDDS to go straight into the GIT as nanoemulsions droplets, skipping Nanoemulsions of Nanoemulsions of oil and water that are smaller than 50 nm can get into the absorption site through the pathway used in the formulation, which can protect the drug from enzymatic degradation. Nonionic surfactants make drugs more soluble and dissolvable, lower the interfacial surface tension, and help drugs pass through epithelial cells [58].

Furthermore, the overall impact of the S-SNEDDS formulation on various drug compounds showed an improvement pattern regarding pharmacokinetic optimization. A consistent increase in the time required to reach maximum concentration (Tmax) indicates controlled release and sustained absorption of the drug compound. Correspondingly, longer elimination half-times (t1/2) indicate the continued presence of drug compounds in the systemic circulation, potentially providing a more prolonged therapeutic effect. The increased maximum concentration (Cmax) values observed for various drug compounds characterize higher concentration peaks, indicating improved drug absorption kinetics and better availability. This increase in exposure is further emphasized by the rise in the area under the concentration-time curve (AUC), encompassing the cumulative drug concentration over time. These observed trends consistently confirm the potential of S-SNEDDS formulations to increase the bioavailability of various drug compounds. The concurrent pharmacokinetic improvements of various drug compounds emphasize the systematic impact of these formulations on drug absorption, distribution, and overall drug exposure [59].

Increased oral bioavailability of S-SNEDDS is achieved through increased solubility and drug dissolution. Moreover, the main reason for increasing the oral bioavailability of solidified SNEDDS is the selected solid carrier, which provides a high specific area at the absorption site. Higher bioavailability values indicate that the solid carrier increases overall drug and systemic absorption from the gastrointestinal lumen [14].

Conclusion

Solid self-emulsifying drug delivery systems (S-SNEDDS) have the potential to provide a viable approach to improving the stability of nanoemulsions. By integrating the stabilizing characteristics of S-SNEDDS, which include the solid state that offers defense against oxidation and hydrolysis, it is possible to enhance the stability of nanoemulsions. Enclosing nanoemulsions droplets within a solid matrix can help alleviate problems associated with phase separation and droplet coalescence, resulting in a stronger and longer-lasting formulation. The possibility of an innovative drug delivery system being created by combining the desirable properties of nanoemulsions with the stability attributes of S-SNEDDS is an emerging area of research. Nevertheless, it is imperative to thoroughly contemplate formulation design, compatibility, and optimization to exploit the advantages of both technologies efficiently. Further research and advancements in this field may yield novel insights into the potential stabilizing effects of solid self-emulsifying drug delivery systems.

Conflict of Interest

The authors have no conflicts of interest regarding this investigation.

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References

[1]. A. G. Agrawal, A. Kumar, and P. S. Gide, “Formulation development and in vivo hepatoprotective activity of self nanoemulsifying drug delivery system of antioxidant coenzyme Q10.,” Arch. Pharm. Res., 2014, doi: 10.1007/s12272-014-0497-z.

[2]. L. Smith, D. R. Serrano, M. Mauger, F. Bolás-Fernández, M. A. Dea-Ayuela, and A. Lalatsa, “Orally Bioavailable and Effective Buparvaquone Lipid-Based Nanomedicines for Visceral Leishmaniasis.,” Mol. Pharm., vol. 15, no. 7, pp. 2570–2583, 2018, doi: 10.1021/acs.molpharmaceut.8b00097.

[3]. A. Z. Mirza and F. A. Siddiqui, “Nanomedicine and drug delivery: a mini review,” Int. Nano Lett., vol. 4, no. 1, Mar. 2014, doi: 10.1007/s40089-014-0094-7.

[4]. [4] D. Singh, K. Sharma, and N. Bedi, “Tacrolimus loaded liquid and solid self-microemulsion preconcentrates: development and evaluation,” Drug Deliv. Lett., 2017, [Online]. Available: https://www.ingentaconnect.com/content/ben/ddl/2017/00000007/00000001/art00006

[5]. J. Ahmad, S. R. Mir, K. Kohli, K. Chuttani, A. K. Panda, S. Amin, “Solid-Nanoemulsion Preconcentrate for Oral Delivery of Paclitaxel: Formulation Design, Biodistribution, and γ Scintigraphy Imaging,” BioMed Res. Int., 2014, [Online]. Available: https://www.hindawi.com/journals/bmri/2014/984756/

[6]. Ameeduzzafar, I. El-Bagory, N. K. Alruwaili, M. H. Elkomy, J. Ahmad, M. Afzal, N. Ahmad, M. Elmowafy, K. S. Alharbi, M. S. Alam, "Development of novel dapagliflozin loaded solid self-nanoemulsifying oral delivery system: Physiochemical characterization and in vivo antidiabetic activity," J. Drug Deliv. Sci. Technol., vol. 54, p. 101279, 2019, doi: https://doi.org/10.1016/j.jddst.2019.101279.

[7]. R. Nazari-Vanani, N. Azarpira, H. Heli, K. Karimian, and N. Sattarahmady, "A novel self-nanoemulsifying formulation for sunitinib: Evaluation of anticancer efficacy," Colloids Surf. B Biointerfaces, vol. 160, pp. 65–72, Dec. 2017, doi: 10.1016/J.COLSURFB.2017.09.008.

[8]. R. Nazari-Vanani, N. Azarpira, and H. Heli, "Development of self-nanoemulsifying drug delivery systems for oil extracts of Citrus aurantium L. blossoms and Rose damascena and evaluation of anticancer properties," J. Drug Deliv. Sci. Technol., vol. 47, pp. 330–336, Oct. 2018, doi: 10.1016/J.JDDST.2018.08.003.

[9]. A. Nasr, A. Gardouh, and M. Ghorab, "Novel solid self-nanoemulsifying drug delivery system (S-SNEDDS) for oral delivery of olmesartan medoxomil: design, formulation, pharmacokinetic and ...," Pharmaceutics, 2016, [Online]. Available: https://www.mdpi.com/1999-4923/8/3/20

[10]. A. Mushtaq, S. M. Wani, A. R. Malik, A. Gull, S. Ramniwas, G. A. Nayik, S. Ercisli, R. A. Marc, R. Ullah, A. Bari, "Recent insights into Nanoemulsions: Their preparation, properties and applications," Food Chem. X, vol. 18, p. 100684, Jun. 2023, doi: 10.1016/J.FOCHX.2023.100684.

[11]. Y. Nie, Y. Pan, Y. Jiang, D. Xu, R. Yuan, Y. Zhu, Z. Zhang, "Stability and bioactivity evaluation of black pepper essential oil nanoemulsion," Heliyon, vol. 9, no. 4, p. e14730, Apr. 2023, doi: 10.1016/J.HELIYON.2023.E14730.

[12]. S. M. Jafari, "An overview of nanoencapsulation techniques and their classification," Nanoencapsulation Technol. Food ..., 2017, [Online]. Available: https://www.sciencedirect.com/science/article/pii/B978012809436500001X

[13]. M. L. Zambrano-Zaragoza, R. González-Reza, N. Mendoza-Munoz, V. Miranda-Linares, T. F. Bernal-Couoh, S. Mendoza-Elvira, and D. Quintanar-Guerrero, "Nanosystems in edible coatings: A novel strategy for food preservation," Int. J. ..., 2018, [Online]. Available: https://www.mdpi.com/1422-0067/19/3/705

[14]. A. Hussain, F. Shakeel, S. K. Singh, I. A. Alsarra, A. Faruk, F. K. Alanazi, G. V. Peter Christoper, "Solidified SNEDDS for the oral delivery of rifampicin: Evaluation, proof of concept, in vivo kinetics, and in silico GastroPlusTM simulation," Int. J. Pharm., vol. 566, pp. 203–217, 2019, doi: https://doi.org/10.1016/j.ijpharm.2019.05.061.

[15]. A. Zafar, S. S. Imam, N. K. Alruwaili, O. A. Alsaidan, M. H. Elkomy, M. M. Ghoneim, S. M. Alshehri, A. M. A. Ali, K. S. Alharbi, M. Yasir, K. M. Noorulla, S. I. Alzarea, A. S. Alanazi, "Development of Piperine-Loaded Solid Self-Nanoemulsifying Drug Delivery System: Optimization, In-Vitro, Ex-Vivo, and In-Vivo Evaluation.," Nanomater. Basel Switz., vol. 11, no. 11, 2021, doi: 10.3390/nano11112920.

[16]. S. Inugala, B. B. Eedara, S. Sunkavalli, R. Dhurke, P. Kandadi, R. Jukanti, S. Bandari, "Solid self-nanoemulsifying drug delivery system (S-SNEDDS) of darunavir for improved dissolution and oral bioavailability: in vitro and in vivo evaluation," Eur. J. Pharm. Sci., vol. 74, pp. 1–10, Jul. 2015.

[17]. D. A. Bhagwat, P. A. Swami, S. J. Nadaf, P. B. Choudhari, V. M. Kumbar, H. N. More, S. G. Killedar, P. S. Kawtikwar, "Capsaicin Loaded Solid SNEDDS for Enhanced Bioavailability and Anticancer Activity: In-Vitro, In-Silico, and In-Vivo Characterization," J. Pharm. Sci., vol. 110, no. 1, pp. 280–291, 2021, doi: https://doi.org/10.1016/j.xphs.2020.10.020.

[18]. F.-P. Schmied, A. Bernhardt, V. Baudron, B. Beine, and S. Klein, "Development and Characterization of Celecoxib Solid Self-nanoemulsifying Drug Delivery Systems (S-SNEDDS) Prepared Using Novel Cellulose-Based Microparticles as Adsorptive Carriers," AAPS PharmSciTech, vol. 23, 2022, [Online]. Available: https://api.semanticscholar.org/CorpusID:251281861

[19]. I. Kuncahyo, S. Choiri, and A. Fudholi, "Solidification of meloxicam self-nano emulsifying drug delivery system formulation incorporated into soluble and insoluble carriers using freeze drying method," IOP Conf. Ser. ..., 2019, doi: 10.1088/1757-899X/578/1/012051.

[20]. A. B. Mohd, K. Sanka, S. Bandi, P. V. Diwan, and N. R. Shastri, "Solid self-nanoemulsifying drug delivery system (S-SNEDDS) for oral delivery of glimepiride: development and antidiabetic activity in albino rabbits," Drug Deliv., vol. 22, pp. 499–508, 2015.

[21]. J. H. Park, D. S. Kim, O. Mustapha, A. M. Yousaf, J. S. Kim, D. W. Kim, C. S. Yong, Y. S. Youn, K. T. Oh, Soo-Jeong Lim, J. O. Kim, Han-Gon, C, "Comparison of a revaprazan-loaded solid dispersion, solid SNEDDS and inclusion compound: Physicochemical characterisation and pharmacokinetics," Colloids Surf. B Biointerfaces, vol. 162, pp. 420–426, 2018, doi: https://doi.org/10.1016/j.colsurfb.2017.12.017.

[22]. R. N. Dash, H. Mohammed, T. Humaira, and D. Ramesh, "Design, optimization and evaluation of glipizide solid self-nanoemulsifying drug delivery for enhanced solubility and dissolution.," Saudi Pharm. J. SPJ Off. Publ. Saudi Pharm. Soc., vol. 23, no. 5, pp. 528–540, 2015, doi: 10.1016/j.jsps.2015.01.024.

[23]. N. A. Alhakamy, H. M. Aldawsari, K. M. Hosny, J. Ahmad, S. Akhter, A. K. Kammoun, A. F. Alghaith, H. Z. Asfour, M. W. Al-Rabia, and Shadab Md, "Formulation design and pharmacokinetic evaluation of docosahexaenoic acid containing self-nanoemulsifying drug delivery system for oral administration," Nanomater. ..., 2020, doi: 10.1177/1847980420950988.

[24]. H. O. Ammar, M. M. Ghorab, D. M. Mostafa, and A. M. Ghoneim, "Spray dried self-nanoemulsifying drug delivery systems for sertraline HCl: Pharmacokinetic study in healthy volunteers," Int J Pharm Sci Dev Res, vol. 4, no. 1, pp. 9–19, 2018.

[25]. [P. Sharma, S. K. Singh, N. K. Pandey, S. Y. Rajesh, P. Bawa, and ..., "Impact of solid carriers and spray drying on pre/post-compression properties, dissolution rate and bioavailability of solid self-nanoemulsifying drug delivery system ...," Powder Technol., 2018, [Online]. Available: https://www.sciencedirect.com/science/article/pii/S0032591018305904

[26]. P. Chakravarty and K. Nagapudi, "Importance of Drying in Small Molecule Drug Product Development," Dry. Technol. ..., 2020, doi: 10.1002/9783527802104.ch3.

[27]. S. Kumar, H. M. Khan, M. A. Khan, M. Jalal, S. Ahamad, M. Shahid, F. M. Husain, M. Arshad, M. Adil, "Broad-spectrum antibacterial and antibiofilm activity of biogenic silver nanoparticles synthesized from leaf extract of Phyllanthus niruri," J. King Saud Univ.- Sci., vol. 35, no. 8, p. 102904, 2023, doi: https://doi.org/10.1016/j.jksus.2023.102904.

[28]. E. Trenkenschuh and W. Friess, "Freeze-drying of nanoparticles: How to overcome colloidal instability by formulation and process optimization," Eur. J. Pharm. Biopharm., vol. 165, pp. 345–360, Aug. 2021, doi: 10.1016/J.EJPB.2021.05.024.

[29]. L. C. Capozzi, A. A. Barresi, and R. Pisano, "Supporting data and methods for the multi-scale modelling of freeze-drying of microparticles in packed-beds," Data Brief, vol. 22, pp. 722–755, Feb. 2019, doi: 10.1016/J.DIB.2018.12.061.

[30]. M. Bjelošević, K. B. Seljak, U. Trstenjak, M. Logar, B. Brus, and P. A. Grabnar, "Aggressive conditions during primary drying as a contemporary approach to optimise freeze-drying cycles of biopharmaceuticals," Eur. J. Pharm. Sci., vol. 122, pp. 292–302, Sep. 2018, doi: 10.1016/J.EJPS.2018.07.016.

[31]. A. Z. Mirza and F. A. Siddiqui, "Nanomedicine and drug delivery: a mini review," Int. Nano Lett., vol. 4, no. 1, Mar. 2014, doi: 10.1007/s40089-014-0094-7.

[32]. N. Raval, R. Maheshwari, D. Kalyane, S. R. Youngren-Ortiz, M. B. Chougule, and R. K. Tekade, "Importance of physicochemical characterization of nanoparticles in pharmaceutical product development," in Basic Fundamentals of Drug Delivery, Elsevier, 2018, pp. 369–400. doi: 10.1016/B978-0-12-817909-3.00010-8.

[33]. M. Jamrógiewicz, "Consequences of New Approach to Chemical Stability Tests to Active Pharmaceutical Ingredients," Front. Pharmacol., vol. 7, no. FEB, Feb. 2016, doi: 10.3389/FPHAR.2016.00017.

[34]. S. A. Bernal-Chávez, A. Romero-Montero, H. Hernadez-Parra, S. I. Pena-Corona, Maria L. D. Prado-Audelo, S. Alcala-Alcala, H. Cortes, L. Kiyekbayeva, J. Sharifi-Rad, G. Leyva-Gomez, "Enhancing chemical and physical stability of pharmaceuticals using freeze-thaw method: challenges and opportunities for process optimization through quality by design approach," J. Biol. Eng. 2023 171, vol. 17, no. 1, pp. 1–18, May 2023, doi: 10.1186/S13036-023-00353-9.

[35]. I. K. Abbas and S. N. Abddulhameed, "Preparation and Characterization of Bilastine Solid Self-Nanoemulsion using Liquisolid Technique," Al-Rafidain J. Med. Sci. ..., 2023, [Online]. Available: https://www.iasj.net/iasj/download/5e55e7adf49206de
[36]. K. O. Aboalnaja, S. Yaghmoor, T. A. Kumosani, and D. J. McClements, "Utilization of nanoemulsions to enhance bioactivity of pharmaceuticals, supplements, and nutraceuticals: Nanoemulsion delivery systems and nanoemulsion excipient systems" Expert Opin. ..., 2016, doi: 10.1517/17425247.2016.1162154.
[37]. A. F. Alghaith, S. Alshehri, N. A. Alhakamy, and K. M. Hosny, "Development, optimization and characterization of nanoemulsion loaded with clove oil-naftifine antifungal for the management of tinea," Drug Deliv., 2021, doi: 10.1080/10717544.2021.1879314.
[38]. B. Iskandar, H. C. Mei, T. W. Liu, H. M. Lin, and C. K. Lee, "Evaluating the effects of surfactant types on the properties and stability of oil-in-water Rhodiola rosea nanoemulsion," Colloids Surf. B Biointerfaces, vol. 234, p. 113692, Feb. 2024, doi: 10.1016/J.COLSURFB.2023.113692.
[39]. B. Rajasekaran, A. Singh, K. Nilsuwan, L. Ma, R. A. Nazeer, and S. Benjakul, "Shrimp oil nanoemulsions prepared by microfluidization and ultrasonication: characteristics and stability," RSC Adv., vol. 14, no. 9, pp. 6135–6145, Feb. 2024, doi: 10.1039/D3RA07342D.
[40]. L. Guanghui, Liu Qi, G. Anning, R. Luting, Z. Yinghan, G. Weiyun, H. Shenghua, G. Fengyi, P. Xiaoli, "Preparation, stability, and in vitro transport of soybean protein-based diosgenin nanoemulsions," Food Chem. X, vol. 20, p. 100982, Dec. 2023, doi: 10.1016/j.fochx.2023.100982.
[41]. G. R. Velderrain-Rodríguez, L. Salvia-Trujillo, G. A. González-Aguilar, and O. Martín-Belloso, "Interfacial activity of phenolic-rich extracts from avocado fruit waste: Influence on the colloidal and oxidative stability of emulsions and nanoemulsions," Innov. Food Sci. Emerg. Technol., vol. 69, p. 102665, May 2021, doi: 10.1016/J.IFSET.2021.102665.
[42]. A. Inal, H. Yenipazar, and N. Şahin-Yeşilçubuk, "Preparation and characterization of nanoemulsions of curcumin and echium oil," Heliyon, vol. 8, no. 2, p. e08974, Feb. 2022, doi: 10.1016/j.heliyon.2022.e08974.
[43]. Y. Syukri, R. Martien, E. Lukitaningsih, and A. E. Nugroho, "Novel Self-Nano Emulsifying Drug Delivery System (SNEDDS) of andrographolide isolated from Andrographis paniculata Nees: Characterization, in-vitro and in-vivo assessment," J. Drug Deliv. Sci. Technol., vol. 47, no. May, pp. 514–520, 2018, doi: 10.1016/j.jddst.2018.06.014.
[44]. D. Gazolu-Rusanova, I. Lesov, S. Tcholakova, N. Denkov, and B. Ahtchi, "Food grade nanoemulsions preparation by rotor-stator homogenization," Food Hydrocoll., vol. 102, p. 105579, May 2020, doi: 10.1016/J.FOODHYD.2019.105579.
[45]. K. A. B. Soliman, H. K. Ibrahim, and M. M. Ghorab, "Formulation of avanafil in a solid self-nanoemulsifying drug delivery system for enhanced oral delivery," Eur. J. ..., 2016, [Online]. Available: https://www.sciencedirect.com/science/article/pii/S0928098716303396
[46]. S. Sujatha, S. J. Jyothi, R. G. Reddy, and K. Kishore Kumar, "Formulation and Evaluation of Solid Nano Emulsion of Furosemide," World J. ..., 2016, [Online]. Available: https://wjpr.s3.ap-south-1.amazonaws.com/article_issue/1467369952.pdf
[47]. M. Hanmantrao, S. Chaterjee, R. Kumar, S. Vishwas, V. Harish, O. Porwal, M. Alrouji, O. Alomeir, S. Alhajlah, M. Gulati, G. Gupta, K. Dua, S. K. Singh, "Development of Guar Gum-Pectin-Based Colon Targeted Solid Self-Nanoemulsifying Drug Delivery System of Xanthohumol," Pharmaceutics, 2022, [Online]. Available: https://www.mdpi.com/1999-4923/14/11/2384
[48]. H. Singh, S. Nathani, N. Singh, P. Roy, S. Paul, H. Singh Sohal, S. K. Jain, "Development and characterization of solid-SNEDDS formulation of DHA using hydrophilic carrier with improved shelf life, oxidative stability and therapeutic activity," J. Drug Deliv. Sci. Technol., vol. 54, Dec. 2019, [Online]. Available: https://www.sciencedirect.com/science/article/pii/S177322471930303X
[49]. S. Paul, K. F. Asha, I. Z. Alam, M. A. Ali, M. E. Al-Mamun, and M. B. M. Rahman, "Physicochemical reports of gliclazide-carplex solid dispersions and tablets prepared with directly compressible co-processed excipients," Heliyon, vol. 9, no. 12, p. e22899, Dec. 2023, doi: 10.1016/j.heliyon.2023.e22899.
[50]. A. Tarik Alhamdany, A. M. H. Saeed, and M. Alaayedi, "Nanoemulsion and Solid Nanoemulsion for Improving Oral Delivery of a Breast Cancer Drug: Formulation, Evaluation, and a Comparison Study," Saudi Pharm. J., vol. 29, no. 11, pp. 1278–1288, Nov. 2021, doi: 10.1016/J.JSPS.2021.09.016.
[51]. I. K. Abbas, "Self-Nanoemulsifying Drug Delivery System: Liquid, Supersaturable, and Solid Dosage Forms," Al-Rafidain J. Med. Sci. ISSN 2789-3219, 2022, [Online]. Available: https://api.semanticscholar.org/CorpusID:254620166
[52]. S. Ahmad and A. Hafeez, "Formulation and Development of Curcumin-Piperine-Loaded S-SNEDDS for the Treatment of Alzheimer's Disease.," Mol. Neurobiol., vol. 60, no. 2, pp. 1067–1082, 2023, doi: 10.1007/s12035-022-03089-7.
[53]. [53] S. S. Al-Nimry, K. A. Alkhamis, Bashar M. Altaani, "Validation of RP-HPLC Method for Determination of Omeprazole in Dissolution Media and Application to Study in-vitro Release from Solid-SNEDDS," Curr. Pharm. ..., 2022, [Online]. Available: https://www.ingentaconnect.com/content/ben/cpa/2022/00000018/00000002/art00007
[54]. H. Etezadi, A. Maleki, J. D. Friedl, A. Bernkop-Schnurch, "Storage stability of proteins in a liquid-based formulation: Liquid vs. solid self-emulsifying drug delivery," Int. J. ..., 2020, [Online]. Available: https://www.sciencedirect.com/science/article/pii/S0378517320309030
[55]. O. Abdifetah and K. Na-Bangchang, "Pharmacokinetic studies of nanoparticles as a delivery system for conventional drugs and herb-derived compounds for cancer therapy: a systematic review," Int. J. ..., 2019, doi: 10.2147/IJN.S213229.
[56]. E. Abd-Elhakeem, M. H. M. Teaima, G. A. Abdelbary, and G. M. E. Mahrouk, "Bioavailability enhanced clopidogrel-loaded solid SNEDDS: development and in-vitro/in-vivo characterization," J. Drug Deliv. Sci. Technol., vol. 49, pp. 603–614, Feb. 2019.
[57]. M. H. Akhter, A. Ahmad, J. Ali, and G. Mohan, "Formulation and development of CoQ10-loaded s-SNEDDS for enhancement of oral bioavailability," J. Pharm. ..., 2014, doi: 10.1007/s12247-014-9179-0.
[58]. M. A. Rahman and M. Mujahid, "Development of self-nanoemulsifying tablet (SNET) for bioavailability enhancement of sertraline," Braz. J. Pharm. Sci., vol. 54, no. 1, 2018, doi: 10.1590/s2175-97902018000117232.
[59]. Y. R. Han, P. I. Lee, and K. S. Pang, "Finding Tmax and Cmaxin multicompartmental models," Drug Metab. Dispos., vol. 46, no. 11, pp. 1796–1804, Nov. 2018, doi: 10.1124/dmd.118.082636.