Jurnal Sains Farmasi & Klinis
p-ISSN: 2407-7062 | e-ISSN: 2442-5435
homepage: http://jsfk.ffarmasi.unand.ac.id
DOI : 10.25077/jsfk.12.3.217-225.2025

ORIGINAL ARTICLE J Sains Farm Klin 12(3):217–225 2025 | DOI: 10.25077/jsfk.12.3.217-225.2025

# Self-Nanoemulsifying Drug Delivery System (SNEDDS): Challenges and Opportunities in Enhancing Drug Solubility

**Farhad Aulan Sabillah[1], Hannie Fitriani[1]*, Muhammad Sulaiman Zubair[2], & Yandi Syukri[1]**

*[1]Department of Pharmacy, Faculty of Science and Mathematics, Islamic University of Indonesia, Sleman, Yogyakarta*
*[3]Department of Pharmacy, Faculty of Science and Mathematics, Tadulako University, Palu, Central Celebes*

**ABSTRACT:** For oral medications, especially those in BCS Classes II and IV, poor aqueous solubility continues to be a significant formulation challenge. This problem restricts dosage consistency, therapeutic efficacy, and bioavailability. A promising method for improving the solubility and absorption of lipophilic drug compounds is the Self-Nanoemulsifying Drug Delivery System (SNEDDS). With ramifications for the pharmaceutical and medical domains, this narrative review attempts to investigate the synthesis, characterization, difficulties, and possible uses of SNEDDS in improving drug solubility. According to the standards of scientific merit, accessibility, and relevance, a total of 25 articles released within the previous five years were included. When SNEDDS meet gastrointestinal fluids, they spontaneously form nanoemulsions, which improves drug solubility. Oil, surfactant, and co-surfactant make up this system, which is optimized according to zeta potential (±30 mV), polydispersity index (<0.3), and particle size (<200 nm). Numerous studies have shown how well it works to enhance the pharmacokinetics and solubility of medications like thymoquinone, rosuvastatin, and curcumin. However, issues with excipient safety, formulation scalability, and long-term stability still exist. SNEDDS offers a versatile and efficient method for enhancing oral drug delivery, especially for nutraceuticals and health supplements. To fully realize its therapeutic and industrial potential, more research involving clinical validation, regulatory harmonization, and quality-by-design approaches is required.

**Keywords**: **SNEDDS; solubility; bioavailability; nanoemulsion; drug delivery; formulation.**

## Introduction

The optimality of a drug to be absorbed into the body is influenced by several things, including solubility, dissolution, absorption, therapeutic effects, and bioavailability of the drug [1]. Solubility, dissolution rate, absorption rate, therapeutic effect, and bioavailability are some of the factors that affect a drug's optimal absorption in the body. Low water solubility is a significant barrier for medications in Biopharmaceutical Classification System (BCS) classes II and IV, limiting bioavailability, therapeutic efficacy, and dose consistency. The Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) is one of the methods to address this problem [2,3]. SNEDDS is a system consisting of a combination of oil, surfactants, and co-surfactants that can spontaneously form nanoemulsions when in contact with the aqueous phase through mild gastric agitation [4]. SNEDDS, which is a nano-emulsion-based drug delivery system that is formed spontaneously when there is direct contact with gastrointestinal (GI) fluids, is widely used in the formulation of drugs and lipophilic active compounds that have low solubility, with the composition of the oil phase as a solubility enhancer of lipophilic drugs, surfactants as surface tension reducers in forming nanoemulsions and co-surfactants as stabilizers of the emulsion system of SNEDDS preparations [5].

The results of the stable and clear SNEDDS formulation have a particle size below 100 nm [6]. Polydispersity index (PI) is a parameter used to see the level of homogeneity of the resulting particles. While the zeta potential parameter determines the stability of the formulated SNEDDS. The zeta potential value of SNEDDS can estimate the surface properties of nanoemulsion. The ideal value for zeta is greater than ±30 mV [7]. The transmittance percentage of the SNEDDS preparation is one factor to see the level of clarity of the formulated dispersion system. The transmittance percentage value is to find out whether the

**Article history**
Received: 20 Oct 2025
Accepted: 12 Dec 2025
Published: 07 Mar 2026
**Access this article**

***Corresponding Author:** Hannie Fitriani
Department of Pharmacy, Faculty of Science and Mathematics,
Islamic University of Indonesia, Sleman, Yogyakarta, 55584 | Email: hanniefitriani@uii.ac.id

particle size has reached the nanometer range, namely 95% approaching 100% which will produce clear SNEDDS [8].

From the study about SNEDDS sertraline showed that SNEDDS formulation can significantly enhance its solubility and oral bioavailability, showing ~5-fold higher AUC, ~4-fold greater Cmax, and 386% improved relative bioavailability compared to pure sertraline [9]. Beyond physicochemical parameters, several studies documented significant improvements in dissolution rate and in vivo bioavailability. Rosuvastatin-SNEDDS demonstrated a 3.2-fold increase in AUC compared to conventional suspension [10].

In majority studies have shown SNEDDS can improve solubility and pharmacokinetics, most focus on optimizing a single drug formulation with in vitro evaluation. Comprehensive analyses across various drug classes, particularly comparing BCS II and IV applications, remain limited. Moreover, issues such as industrial scalability, long-term physicochemical stability, and regulatory pathways are rarely addressed [11,12]. Recent SNEDDS formulation techniques for synthetic and natural compounds are compiled in this review, which also highlights opportunities, challenges, and physicochemical performance, to identify obstacles and suggest solutions for the development of sustainable, efficient SNEDDS, the goal is to examine formulation elements, particle properties, stability data, and reported bioavailability improvements.

## Methods

To integrate findings from multiple studies pertaining to the creation and use of the SNEDDS in improving drug solubility and bioavailability, this article was written using a narrative review approach. This method was chosen because it was adaptable in providing a thorough account, especially when it came to outlining the opportunities and difficulties of SNEDDS from a technical and clinical standpoint.

Three important scientific databases Google Scholar, PubMed, and ScienceDirect were used to perform a thorough literature search. "SNEDDS," "self-nanoemulsifying drug delivery system," "solubility enhancement," "bioavailability improvement," and "formulation challenge" were among the keywords that were used. Boolean operators, such as ("SNEDDS" OR "Self-Nanoemulsifying") AND ("Solubility" OR "Bioavailability") AND ("Formulation" OR "Stability"), were used to refine pertinent results.

The active ingredient's name and BCS classification, the composition of SNEDDS (oil, surfactant, and co-surfactant), important formulation parameters, and documented bioavailability enhancements were among the data taken from studies that qualified. A consolidated table provided a summary of these findings.

## Result and Discussion

Twenty-five articles in all satisfied the requirements for inclusion in this review. Both synthetic and natural active pharmaceutical ingredients that were primarily categorized as BCS II or IV drugs with low aqueous solubility were included in these studies. In majority, the oil phase consisted of medium-chain triglyceride (MCT)-based oils such as Capmul MCM, Maisine, or Capryol 90, along with co-surfactants such as PEG 400, propylene glycol, or Transcutol and non-ionic surfactants such as Tween 20, Tween 80, or Cremophor EL. This combination typically produced nanoemulsions with zeta potential values ranging from -50 mV to +29 mV, particle sizes ranging from 5.2 to 300 nm, and PDI values below 0.3. In comparison to traditional formulations, several studies documented a notable improvement in drug solubility and dissolution rate. For instance, when compared to suspension forms, rosuvastatin-containing SNEDDS had a 3.2-fold higher bioavailability due to particle sizes as low as 14.69 nm with PDI <0.5 [10]. Compared to traditional suspensions, curcumin-loaded SNEDDS increased bioavailability by up to five times and decreased particle size to 28.53 nm [13]. While thymoquinone-based SNEDDS produced droplet sizes of 67.7 nm and displayed improved absorption profiles, some characterization parameters were not disclosed [4]. In a similar vein, cinnarizine formulations showed improved dissolution rates and particle sizes of 200–300 nm with PDI 0.75 [12].

Variability in solubility results according to formulation composition was also disclosed by the collected data. Better dissolution performance was correlated with formulations that used medium-chain oils in conjunction with high-HLB surfactants, which tended to produce smaller droplet sizes and higher clarity (percent transmittance >80%) [14] On the other hand, formulations with low zeta potential values or suboptimal surfactant-to-oil ratios frequently showed instability over storage, higher PDI, or larger particle sizes [15,16].

A qualitative evaluation of the reviewed literature reveals recurrent issues like industrial scalability, preserving long-term physicochemical stability, and meeting regulatory requirements, even though the summary table only includes the formulation composition and important

physical parameters. The discussion section delves deeply into these elements as well as prospects for targeted drug delivery and integration with other nanotechnology-based systems.

Numerous studies addressing the formulation and characterization of SNEDDS for a range of bioactive compounds, both natural and synthetic, were successfully identified by this review. Table 1 which includes the formula composition, physical parameters, and performance evaluation of each formulation, provides a summary of the data collected. The SNEDDS formulations used medium-chain triglyceride oils such as Capmul MCM, Maisine, or Capryol 90 combined with high-HLB surfactants, such as Tween 20 or Tween 80 and co-surfactants, such as PEG 400 or Transcutol P [11]. This combination was consistently effective in generating uniform particle size distribution, with droplet sizes typically below 200 nm and PDI values <0.3 [15]. For example, rosuvastatin-SNEDDS achieved a particle size of 14.69 nm with PI <0.5 [10], mahogany seed extract-SNEDDS showed 12.21 nm with good transmittance clarity (15), and curcumin-SNEDDS resulted in 28.53 nm with PI 0.129 [13].

Thymoquinone-SNEDDS exhibited droplet sizes of 67.7 nm with improved absorption [2], whereas cinnarizine-SNEDDS, despite larger particle sizes of 200–300 nm and PDI of 0.75, still showed better solubility and dissolution than traditional formulations [12]. Furthermore, bedaquiline-SNEDDS with particle size around 98.88 nm demonstrated good stability and enhanced biopharmaceutical performance [17]. However, not all articles comprehensively reported their characterization data, which complicates direct comparisons across studies.

The potential of SNEDDS in enhancing physicochemical and biological performance of bioactive has shown from buckwheat flavonoid-loaded SNEDDS exhibited a particle size of 121.4 ± 3.2 nm, PDI 0.21 ± 0.02, and zeta potential −31.5 mV, indicating good stability and uniform droplet distribution. The formulation significantly increased the aqueous solubility and antioxidant activity compared to the crude extract, with a 4.8-fold enhancement in oral bioavailability confirmed through in vivo evaluation. These findings further strengthen the evidence that SNEDDS not only improves dissolution and absorption of lipophilic compounds but also maintains bioactivity during the delivery process, underscoring its versatility in pharmaceutical and nutraceutical applications [5].

## SNEDDS Mechanism of Action

Based on the theory proposed by [18], the emulsification mechanism requires a condition where there is a change in entropy in supporting a dispersion that is greater than the energy required so that it will increase the dispersion surface. The free energy (ΔG) resulting from conventional emulsions is the negative energy of the energy required to form a surface in two phases, namely the oil phase and the water phase which produce a stable emulsion. Free energy (ΔG) is represented by the equation:

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

Information:
ΔG = Free energy
N = Total droplets
r = Droplet radius
σ = Interfacial energy

The mechanism of emulsion formation/ emulsification of SNEDDS occurs through mixing between the water phase and the oil phase at a constant temperature and light stirring. *Self-emulsification* begins when the entropy energy in the dispersed phase or the entropy change that supports the dispersion process exceeds the maximum limit of the energy required to increase the surface area of the dispersion [19].

## Composition of SNEDDS Formulation

A key factor in SNEDDS performance is formulation composition. As shown in combining medium-chain triglyceride oils (Capmul MCM, Maisine, and Capryol 90) with high-HLB surfactants (Tween 20, Tween 80) and co-surfactants (PEG 400, Transcutol P) typically results in better dissolution, smaller droplets, and increased clarity [1,8]. On the other hand, as seen in cinnarizine and niclosamide [2,7] SNEDDS, suboptimal surfactant-to-oil ratios or mismatched HLB values can result in larger droplet sizes, higher PDI, and decreased stability. Stability also depends on zeta potential; values above ±30 mV, like in heparin SNEDDS −36.8 mV [5], aid in preventing droplet aggregation and preserving long-term physical stability.

## Characterization of SNEDDS

The characterization process of SNEDDS is divided into several processes, namely particle size testing, polydispersity index (PI), measurement of percent transmittance, and zeta potential. Particle size testing is carried out to determine the effect of minimum dispersion and volume required for particle size. According to the characteristics, the particle size of SNEDDS ranges from

**Table 1.** Results of the SNEDDS opportunities and challenges analysis.

| Active Ingredients | Formula | Research result | Reference |
|---|---|---|---|
| Rosuvastatin | Oil: Capmul Mcm Ep<br>Surfactant: Tween 20<br>Co-Surfactant: Transcutol P | Particle Size: 14.69 nm<br>PI : < 0.5<br>Zeta Potential:- 4.09 mV | [10] |
| Genkwanin | Oil: Maisine Cc<br>Surfactant: Labrasol Alf<br>Co-Surfactant: Transcutol | Particle Size: 94.58 nm<br>PI : 0.14<br>Zeta Potential:- 14.56 mV | [11] |
| Cinnarizine | Oil: Oleic Acid<br>Surfactant: Cremophor El<br>Co-Surfactant: Imwitor 308 | Particle Size: 200- 300 nm<br>PI Index : 0.75<br>Zeta Potential:- 20- 10 mV | [12] |
| Thymoquinone | Oil: Almond Oil<br>Surfactant: Tween 80<br>Co-Surfactant: PEG 200 | Particle Size: 67.7 nm<br>PI: Not listed in the article<br>Zeta Potential: Not listed in the article | [4] |
| Isotretinoin | Oil: Tea Tree Oil<br>Surfactant: Labrasol<br>Co-Surfactant: Transcutol | Particle Size: 217.67 nm<br>PI : Not listed in the article<br>Zeta Potential: Not listed in the article | [31] |
| Cefpodoxime Proxetil | Oil: Clove Oil<br>Surfactant: Tween 20<br>Co-Surfactant: P EG 400 | Particle Size: 300 nm<br>PI : Not listed in the article<br>Zeta Potential: Not listed in the article | [24] |
| Mahogany Seed Extract | Oil: Mahogany Oil<br>Surfactant: Tween 80<br>Co-Surfactant: Peg 400 | Particle Size: 12.21 nm<br>Transmittance Percentage: 84.7%<br>PI: Not listed in the article<br>Zeta Potential: Not listed in the article | [32] |
| Isotretinoin | Oil: Castor Oil<br>Surfactant: Cremophor El<br>Co-Surfactant: Transcutol Hp | Particle Size: 64.36 nm<br>PI : 0.22 | [33] |
| Ravucunazole | Oil: Soy Lecithin<br>Surfactant: Labrasol<br>Co-Surfactant: Miglyol | Particle Size: 200 nm<br>Zeta Potential:- 50 mV | [34] |
| Docetaxel | Oil: Ethyl Oleate<br>Surfactant: PEG 600<br>Co-Surfactant: Tween 80 | Particle Size: 20-110 nm<br>PI: Not listed in the article<br>Zeta Potential: Not listed in the article | [14] |
| Improved oral delivery of non-oncology drugs | Oil: Soybean Oil<br>Surfactant: Tween 80<br>Co-Surfactant: Span 80 | Particle Size: 41 nm<br>PI : 0.189<br>Zeta Potential:- 27.1 mV | [35] |

| Active Ingredients | Formula | Research result | Reference |
|---|---|---|---|
| Pitavastatin | Oil: Cinnamon Oil<br>Surfactant: Tween 80<br>Co-Surfactant: P EG 400 | Particle Size: 104 nm<br>PI : 0.198<br>Zeta Potential:- 29 mV | [36] |
| Zaleplon | Oil: Lavender Oil<br>Surfactant: Sorbeth-20<br>Co-Surfactant: HCO-60 | Particle Size: 87 nm<br>PI : 0.33<br>Zeta Potential: Not listed in the article | [3] |
| Clopidogrel | Oil: Acrysol K 150<br>Surfactant: Captex 500<br>Co-Surfactant: Transcutol P | Particle Size: 5.2 nm<br>Zeta Potential:- 29 mV | [37] |
| Rosuvastatin | Oil: Cinnamon Oil<br>Surfactant: Cremophor Rh 40<br>Co-Surfactant: Transcutol P | Particle Size: 81.8 nm<br>PI : 0.209<br>Zeta Potential: 1.53 mV | [15] |
| Anticancer Drug Candidate | Oil: Capryol 90<br>Surfactant: Kolliphor Rh40<br>Co-Surfactant: Transcutol Hp | Particle Size: 17.8 nm<br>PI : 0.14<br>Zeta Potential:- 4.36 mV | [17] |
| Bedaquiline | Oil: Caprylic Acid<br>Surfactant: Propylene Glycol<br>Co-Surfactant: Transcutol-P | Particle Size: 98.88 nm<br>PI : 0.32<br>Zeta Potential: 21.16 mV | [23] |
| Niclosamide | Oil: Cremophor-Rh40<br>Surfactant: Propylene Glycol<br>Co-Surfactant: PEG 400 | Particle Size: 19.86 nm<br>PI : 0.103<br>Zeta Potential:- 21 mV | [38] |
| Albendazole | Oil: Oleic Acid<br>Surfactant: Tween 20<br>Co-Surfactant: PEG 600 | Particle Size: 89.2 nm<br>PI : 0.278<br>Zeta Potential: Not listed in the article | [26] |
| Remdesivir | Oil: Black Seed Oil<br>Surfactant: Tween 80<br>Co-Surfactant: Imwitor 988 | Particle Size: 247 nm<br>PI : 0.441<br>Zeta Potential: + 29 mV | [16] |
| Furosemide | Oil: Oleic Acid<br>Surfactants:<br>Co-Surfactant: PEG-400 | Particle Size: 116 nm<br>PI :<br>Zeta Potential:- 6.22 mV | [13] |
| Curcumin-Loaded Bioactive | Oil: Black Seed Oil<br>Surfactant: Imwitor 988<br>Co-Surfactant: Kolliphor El | Particle Size: 28.53 nm<br>PI : 0.129<br>Zeta Potential:- 22.17 mV | [39] |
| Multi-Drug-Containing Bioactive | Oil: Black Seed Oil<br>Surfactant: Capmul Mcm<br>Co-Surfactant: Transcutol P | Particle Size: 70.90 nm<br>PI : 0.534<br>Zeta Potential:- 19.1 mV | [21] |

20-200 nm [20]. PI is tested to show the uniformity of particle size distribution of SNEDDS preparations where a low PI <0.3 indicates that the particles are distributed uniformly and stably. Zeta potential is an indicator of the stability of SNEDDS in solution. A zeta potential value of more than 30 mV indicates that the SNEDDS preparation has good stability [21]. A high percent transmittance indicates that the nanoemulsion produced from SNEDDS is clear and the particles are in the nanometer range. A percent transmittance value of more than 80% indicates that SNEDDS has good clarity [22]. Evidence reported by [23] revealed the characterization results were obtained in the form of particle size with an average of 98.88 ± 2.1 nm which indicates the potential for increasing drug bioavailability, PI 0.3 ± 0.09 which indicates that the resulting formulation has a uniform particle size distribution, and a zeta potential of 21.16 mV indicating the stability of the formulation results. The purpose of this literature review is to examine the challenges and opportunities of SNEDDS in enhancing drug solubility.

## Challenges in developing SNEDDS

The studies under review consistently show that SNEDDS is a useful tactic for enhancing the bioavailability and solubility of medications that are poorly soluble in water, especially those in BCS classes II and IV. Dissolution rate is the main obstacle for BCS II medications, and SNEDDS overcomes this by creating nanoparticles that expand the surface area that can dissolve. For instance, when compared to traditional suspensions, SNEDDS loaded with rosuvastatin and curcumin produced droplet sizes below 30 nm, increasing bioavailability by up to five times [6,24]. BCS IV medications, on the other hand, struggle with both low permeability and low solubility. As demonstrated in thymoquinone and bedaquiline formulations, SNEDDS not only increases solubility by decreasing droplet size but also makes it easier for drugs to pass through intestinal membranes through surfactant-mediated permeability enhancement [1,4].

Challenges in the research include production scalability, which calls for more intricate and economical optimization to preserve consistency, long-term formulation stability, which necessitates additional testing, regulation and safety, which involves the use of surfactant and cosurfactant materials that need to be tested for chronic toxicity and potential side effects [4]. The findings of the study highlight issues with production scale optimization, which calls for stringent process control; compatibility and stability, which necessitate additional testing; safety and regulation of the additional materials used; and the requirement for adaptability to other medications where hydrophobic molecules have demonstrated evidence, but in hydrophobic molecules like heparin, which necessitate additional testing [12].

Data on changes after 6 months of storage were collected and showed that the particle size rose from 98.88 nm to 106.04 nm and the PI increased from 0.34 to 0.45 [25]. This indicates that coalescence occurred during long-term storage, lowering the charge efficiency from 98.31% to 76.20%. This demonstrates that long-term storage causes physicochemical instability, which poses a problem for the creation of SNEDDS preparations.

The application of medications containing hydrophobic compounds, like 4-Allylpyrocatechol (APC), which are challenging to formulate in an aquatic base system, highlights the difficulties in developing SNEDDS preparations [26]. To overcome these obstacles, a strategy is required to choose co-surfactants and lipids, such as medium-chain triglycerides (MCTs), which can improve the drug's solubility and distribution. Additionally, this study demonstrated that the zeta potential data of APC-SNEDDS ranged from -16.20 mV to -20.37 mV, in contrast to SNEDDS without active ingredients, which had a value of -9.73 mV. This may result in particle aggregation, which would lessen the emulsion's efficacy.

## Opportunities from SNEDDS

SNEDDS has several opportunities as an alternative in the development of pharmaceutical preparations. The opportunities of SNEDDS are increasing the bioavailability of drugs, increasing the solubility of drugs especially lipophilic, preparations have a large surface area, increasing the interfacial tension on active substances with low interfacial tension. SNEDDS can be customized for Individuals with condition special [25]. SNEDDS increases the bioavailability and effectiveness of drugs. The results of this study indicate the particle size of SNEDDS produced is 14.69 nm; PI <0.5; percent transmittance 99.9%; and zeta potential - 4.09 mV. In this study, a dissolution test was also carried out which showed that SNEDDS showed a faster drug release ability with conventional drugs. Great potential in clinical applications for developing treatment. Technology in the use of SNEDDS provides a potential picture in improving the drug release profile in the GI tract which makes the effects of interacting foods less. The alternative approach provided by SNEDDS provides better bioavailability, increased patient compliance and minimal side effects [27].

Formulation was made with a combination of ingredients, namely CC maisine as oil, Labrasol ALF as

surfactant, and Transcutol HP as co-surfactant. The ratio used was 20:60:20 with small droplet size results and high stability. The particle size results were 94.58 nm ±0.86, PI 0.14 ±0.1, and zeta potential −14.56 ±1.64 mV. In vitro drug release testing the amount of Genkwanin (GKA) released from four formulations (F02, F05, F08, and F11) approximately 50% in 36 hours. Profile release from formulation shows that release fast followed by the phase stable, so that indicates rate release more fast and furious dissolution cumulative higher [11]. According to Noyes–Whitney equation (dC /dt= kDA (Cs-Ct)), the release of GKA is mainly influenced by its solubility Because release fast from SNEDDS does not depend on size drops. With load drug to in size particle micelle or nanoemulsion. There is a significant increase in bioavailability in lipophilic drugs such as GKA which have low solubility, increased clinical efficacy also provides better therapeutic effects in rapid and consistent absorption.

Particle size 224.40 ± 15.55, PI 1.00 ± 0.00, and zeta potential -5.57 ± 0.10 in the study shown the efficacy of applying nano formulation to the active ingredient Doxazosin (DOX). Compared to when no nano formulation was used, DOX's surface area, drug solubility, and release rate all increased. Pure DOX exhibits a typical bad release. The corresponding figures are 93 ± 4.47 percent. It should be mentioned that as compared to form pure, DOX formulations, including both nanosuspension and SNEDDS, significantly improve characteristic release (by nearly twice) [1].

### Future Research Directions

Future studies on SNEDDS should focus on several crucial areas to increase their applicability and validate them. Extensive clinical trials are necessary to validate the in vitro and in vivo findings in humans, as most articles still focus on the preclinical stage [28]. A long-term safety assessment of SNEDDS excipients is required, particularly for frequent and high-dose use, because some surfactant or co-surfactant excipients may irritate or have harmful effects on the GI system [29]. Storage stability and production scalability must be considered in the investigation. Particularly for products created with natural materials whose composition changes, successful laboratory formulations may not necessarily translate into consistently high-quality mass production [30]. A novel approach to improving the efficacy and selectivity of therapy is to combine SNEDDS with other drug delivery technologies, such as targeted delivery systems or formulations based on multifunctional nanotechnology [12].

To enable more accurate comparison of results across studies, it is necessary to standardize the methodology for SNEDDS characterization, including physical parameters, dissolution testing, and simulation of GI conditions. Meta-analysis will be made easier by this standardization, which also lowers the possibility of interpretation bias.

## Conclusion

A promising drug delivery method for enhancing the solubility and bioavailability of lipophilic compounds, such as BCS class II and IV medications and natural product-based products, is the use of SNEDDS. According to this review, droplet size, particle distribution, and system stability are all greatly impacted by the choice of oil phase, surfactant, and co-surfactant. Significant increases in dissolution rate and bioavailability have been reported in several studies; however, the findings may not be broadly applicable due to methodological differences and possible publication bias. Long-term stability, long-term excipient safety, regulatory compliance, and production scalability are the primary obstacles in the development of SNEDDS. However, there are also opportunities for development, such as the use of bioactive compounds from natural sources, integration with targeted delivery technologies, and application to different drug classes. Large-scale clinical trials, the standardization of characterization techniques, and the creation of formulations with consistent performance at an industrial scale must be the focus of future SNEDDS research. Overcoming these obstacles could make SNEDDS a viable and efficient drug delivery system for contemporary treatment.

## Conflict of Interest

The authors declare no conflict of interest.

## Acknowledgement

The author would like to thank the grant funds from the Implementation of the Sustainable Development Research Funding Program Inclusivity Scheme 2024 Contract number: 025/E5/PG.02.00/PRPB. INKLUSIVITAS/2024. Number: 2125.a/UN28.

# References


[1]. Al Ashmawy AZG, Alyami MH, Eissa NG, et al. Oral bioavailability enhancement of doxazosin mesylate: Nanosuspension versus self-nanoemulsifying drug delivery systems. ADMET DMPK 2024; 12: 167–176.

[2]. Mardiyanto, Untari B, Anjani R, et al. SOLID SELF NANO EMULSIFYING DRUG DELIVERY SYSTEM (SOLID SNEDDS) OF MEFENAMIC ACID: FORMULA OPTIMIZATION USING AEROSIL®-200 AND AVICEL® PH-101 WITH FACTORIAL DESIGN. International Research Journal of Pharmacy 2020; 11: 25–31.

[3]. Ali SA, Alhakamy NA, Hosny KM, et al. Rapid oral transmucosal delivery of zaleplon–lavender oil utilizing self-nanoemulsifying lyophilized tablets technology: development, optimization and .... Drug Deliv. Epub ahead of print 2022. DOI: 10.1080/10717544.2022.2115165.

[4]. Radwan MF, El-Moselhy MA, Alarif WM, et al. Optimization of Thymoquinone-Loaded Self-Nanoemulsion for Management of Indomethacin-Induced Ulcer. Dose-Response; 19. Epub ahead of print 2021. DOI: 10.1177/15593258211013655.

[5]. Zhao Z, Cui X, Ma X, et al. Preparation, characterization, and evaluation of antioxidant activity and bioavailability of a self-nanoemulsifying drug delivery system (SNEDDS) for buckwheat flavonoids. Acta Biochim Biophys Sin (Shanghai) 2021; 52: 1265–1274.

[6]. Fitriani H, Fitria A, Miladiyah I, et al. Pengembangan Self-Nano Emulsifying System (SNES) Ekstrak Temulawak (Curcuma xanthorrhiza): Formulasi, Karakterisasi, dan Stabilitas. Jurnal Sains Farmasi & Klinis 2021; 8: 332.

[7]. Syukri Y, Kholidah Z, Chabib L. Fabrikasi dan Studi Stabilitas Self-Nano Emulsifying Propolis menggunakan Minyak Kesturi sebagai Pembawa. Jurnal Sains Farmasi & Klinis 2020; 6: 265.

[8]. Kassem AA, Abd El-Alim SH, Salman AM, et al. Improved hepatoprotective activity of Beta vulgaris L. leaf extract loaded self-nanoemulsifying drug delivery system (SNEDDS): in vitro and in vivo evaluation. Drug Dev Ind Pharm 2020; 46: 1589–1603.

[9]. Nair AB, Singh B, Shah J, et al. Formulation and Evaluation of Self-Nanoemulsifying Drug Delivery System Derived Tablet Containing Sertraline. Pharmaceutics 2022; 14: 336.

[10]. Verma R, Kaushik A, Almeer R, et al. Improved pharmacodynamic potential of rosuvastatin by self-nanoemulsifying drug delivery system: An in vitro and in vivo evaluation. Int J Nanomedicine 2021; 16: 905–924.

[11]. Yin HF, Yin CM, Ouyang T, et al. Self-nanoemulsifying drug delivery system of genkwanin: A novel approach for anti-colitis-associated colorectal cancer. Drug Des Devel Ther 2021; 15: 557–576.

[12]. Shahba AA, Tashish AY, Alanazi FK, et al. Combined self-nanoemulsifying and solid dispersion systems showed enhanced cinnarizine release in hypochlorhydria/achlorhydria dissolution model. Pharmaceutics; 13. Epub ahead of print 2021. DOI: 10.3390/pharmaceutics13050627.

[13]. Gul S, Sridhar SB, Jalil A, et al. Solid Self-Nanoemulsifying Drug Delivery Systems of Furosemide: In Vivo Proof of Concept for Enhanced Predictable Therapeutic Response. Pharmaceuticals; 17. Epub ahead of print 1 April 2024. DOI: 10.3390/ph17040500.

[14]. Akhtartavan S, Karimi M, Karimian K, et al. Evaluation of a self-nanoemulsifying docetaxel delivery system. Biomedicine & Pharmacotherapy 2019; 109: 2427–2433.

[15]. Desavathu M. SNEDDS in shell: A novel approach to enhance the solubility of rosuvastatin calcium. Asian Journal of Pharmaceutics (AJP), http://asiapharmaceutics.info/index.php/ajp/article/view/3816 (2020).

[16]. Kazi M, Alanazi Y, Kumar A, et al. Oral Bioactive Self-Nanoemulsifying Drug Delivery Systems of Remdesivir and Baricitinib: A Paradigmatic Case of Drug Repositioning for Cancer Management. Molecules; 28. Epub ahead of print 1 March 2023. DOI: 10.3390/molecules28052237.

[17]. Baral KC, Song JG, Lee SH, et al. Enhanced bioavailability of AC1497, a novel anticancer drug candidate, via a self-nanoemulsifying drug delivery system. Pharmaceutics, https://www.mdpi.com/1999-4923/13/8/1142 (2021).

[18]. H Reiss. Entropy-induced dispersion of bulk liquids. J Colloid Interface Sci 1975; Volume 53, Issue 1: Pages 61-70.

[19]. Buya AB, Ucakar B, Beloqui A, et al. Design and evaluation of self-nanoemulsifying drug delivery systems (SNEDDSs) for senicapoc. Int J Pharm 2020; 580: 119180.

[20]. Inugala S, Eedara BB, Sunkavalli S, et al. Solid self-nanoemulsifying drug delivery system (S-SNEDDS) of darunavir for improved dissolution and oral bioavailability: In vitro and in vivo evaluation. European Journal of Pharmaceutical Sciences 2015; 74: 1–10.

[21]. Kulkarni VR, Kazi M, Shahba AAW, et al. Three-Dimensional Printing of a Container Tablet: A New Paradigm for Multi-Drug-Containing Bioactive Self-Nanoemulsifying Drug-Delivery Systems (Bio-SNEDDSs). Pharmaceutics; 14. Epub ahead of print 1 May 2022. DOI: 10.3390/pharmaceutics14051082.

[22]. Fitria A, Hanifah S, Chabib L, et al. Design and characterization of propolis extract loaded self-nano emulsifying drug delivery system as immunostimulant. Saudi Pharmaceutical Journal 2021; 29: 625–634.

[23]. Jahan RN, Khan Z, Akhtar MS, et al. Development of Bedaquiline-Loaded SNEDDS Using Quality by Design (QbD) Approach to Improve Biopharmaceutical Attributes for the Management of Multidrug-Resistant Tuberculosis (MDR-TB). Antibiotics; 12. Epub ahead of print 1 October 2023. DOI: 10.3390/antibiotics12101510.

[24]. Jindal, Amulya, Kumar, et al. Physical characterization of clove oil based self Nano-emulsifying formulations of cefpodoxime proxetil: Assessment of dissolution rate, antioxidant & antibacterial activity. OpenNano 2022; 8: 100087.

[25]. Qiu XL, Fan ZR, Liu YY, et al. Preparation and evaluation of a self-nanoemulsifying drug delivery system loaded with heparin phospholipid complex. Int J Mol Sci; 22. Epub ahead of print 2 April 2021. DOI: 10.3390/ijms22084077.

[26]. Alothaid H, Aldughaim MS, Yusuf AO, et al. A comprehensive study of the basic formulation of supersaturated self-nanoemulsifying drug delivery systems (SNEDDS) of albendazolum. Drug Deliv 2021; 28: 2119–2126.

[27]. Verma R, Kaushik A, Almeer R, et al. Improved pharmacodynamic potential of rosuvastatin by self-nanoemulsifying drug delivery system: An in vitro and in vivo evaluation. International journal .... Epub ahead of print 2021. DOI: 10.2147/IJN.S287665.

[28]. Dhaval M, Vaghela P, Patel K, et al. Lipid-based emulsion drug delivery systems—A comprehensive review. Drug delivery and .... Epub ahead of print 2022. DOI: 10.1007/s13346-021-01071-9.

[29]. Shahba AA-W, Mohsin K, Alanazi FK. Novel Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) for Oral Delivery of Cinnarizine: Design, Optimization, and In-Vitro Assessment. AAPS PharmSciTech 2012; 13: 967–977.

[30]. Neslihan Gursoy R, Benita S. Self-emulsifying drug delivery systems (SEDDS) for improved oral delivery of lipophilic drugs. Biomedicine & Pharmacotherapy 2004; 58: 173–182.

[31]. Hosny KM, Alhakamy NA, Al Nahyah KS. The relevance of nanotechnology, hepato-protective agents in reducing the toxicity and augmenting the bioavailability of isotretinoin. Drug Deliv 2021; 28: 123–133.

[32]. Taiyeb M, Hartati H, Arwansyah A, et al. Self-Nanoemulsifying Drug Delivery System (SNEDDS) formulation and molecular docking of mahogany seed extract (Swietenia mahagoni) as anti .... Informatics in Medicine ..., https://www.sciencedirect.com/science/article/pii/S235291482400073X (2024).

[33]. Alfaraj R, Hababah S, Eltayb EK, et al. Isotretinoin self-nano-emulsifying drug delivery system: Preparation, optimization and antibacterial evaluation. Saudi Pharmaceutical Journal 2024; 32: 102063.

[34]. Spósito PÁ, Mazzeti AL, de Castro KCMP, et al. Higher oral efficacy of ravuconazole in self-nanoemulsifying systems in shorter treatment in experimental chagas disease. Exp Parasitol 2021; 228: 108142.

[35]. Patil OB, Manjappa AS, Kumbhar PS, et al. Development of stable self-nanoemulsifying composition and its nanoemulsions for improved oral delivery of non-oncology drugs against hepatic cancer. OpenNano 2022; 7: 100044.

[36]. Ashfaq M, Shah S, Rasul A, et al. Enhancement of the solubility and bioavailability of pitavastatin through a self-nanoemulsifying drug delivery system (SNEDDS). Pharmaceutics, https://www.mdpi.com/1999-4923/14/3/482 (2022).
[37]. Aparna A. Enhancement of Solubility and Dissolution Rate of Clopidogrel by Self-nanoemulsifying Drug Delivery System. Asian Journal of Pharmaceutics (AJP), http://asiapharmaceutics.info/index.php/ajp/article/download/3761/1257 (2020).
[38]. Zhang J, Wang X, Li P, et al. Colistin–niclosamide-loaded nanoemulsions and nanoemulsion gels for effective therapy of colistin-resistant Salmonella infections. Front Vet Sci; 11. Epub ahead of print 2024. DOI: 10.3389/fvets.2024.1492543.
[39]. Kazi M, Nasr FA, Noman O, et al. Development, characterization optimization, and assessment of curcumin-loaded bioactive self-nanoemulsifying formulations and their inhibitory effects on …. Pharmaceutics, https://www.mdpi.com/1999-4923/12/11/1107 (2020).