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REVIEW

Solidification of SNEDDS Using Mesoporous Carriers (2020–2025): A Review of Design, Biopharmaceutical Enhancement, and Therapeutic Impact

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Abstract: Self-nanoemulsifying drug delivery systems (SNEDDS) have been widely developed as a practical approach to enhance the bioavailability of poorly water-soluble drugs through nanoscale emulsification. To improve the stability and practicality of liquid systems, solidification is commonly performed to obtain solid SNEDDS (S-SNEDDS) by incorporating appropriate solid carriers. Among various options, mesoporous materials have attracted significant attention due to their high surface area, tunable pore sizes, and excellent adsorption capacity. This review aims to summarize and critically analyze recent advances in mesoporous-based S-SNEDDS, focusing on formulation design, solidification strategies, and associated biopharmaceutical outcomes. The review is based on research articles published between 2020 and 2025 retrieved from reputable scientific databases (PubMed, ScienceDirect, Taylor & Francis, Springer, Scopus, and Web of Science) and selected for their relevance to mesoporous carriers and S-SNEDDS development. Findings reveal that carriers such as mesoporous magnesium alumino-metasilicate (eg, Neusilin®) and mesoporous silica (eg, Syloid®) have primarily been reported in studies employing physical adsorption. These systems generally exhibit favorable micromeritic properties and solid-state characteristics, suggesting successful drug incorporation within the carrier matrix and improved physical stability. These systems consistently demonstrate enhanced dissolution and permeation, and subsequently translate into superior pharmacokinetic and pharmacodynamic performances. Overall, the solidification of SNEDDS using mesoporous carriers successfully yields systems with desirable physical properties and improved in vitro and in vivo performances. Future research should address regulatory considerations for mesoporous excipients, deepen mechanistic insights into drug–carrier interactions, and include comparative evaluations among different carriers to support clinical and industrial advancement.

Keywords: S-SNEDDS, mesoporous carriers, solubility enhancement, adsorption method, bioavailability

Introduction

Poor aqueous solubility remains a significant barrier to the oral delivery of Biopharmaceutics Classification System (BCS) Class II and IV drugs, often resulting in suboptimal dissolution, limited absorption, and inadequate therapeutic performance.[1] Lipid-based formulations offer an attractive means to address these limitations, with self-nanoemulsifying drug delivery systems (SNEDDS) emerging as one of the most effective approaches to improve the solubility and bioavailability of poorly water-soluble drugs.[2,3] SNEDDS are composed of oil, surfactant, and cosurfactant, and are therefore referred to as nanoemulsion preconcentrates.[4] In the Lipid Formulation Classification System (LFCS), most SNEDDS are categorized as Type III formulations, which contain oils and relatively high levels of surfactants that

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promote rapid self-emulsification.[5] By spontaneously forming oil-in-water nanoemulsions upon mild agitation in the gastrointestinal (GI) fluids, SNEDDS significantly increase the drug's surface area for dissolution and facilitate lymphatic transport, thereby circumventing extensive first-pass metabolism.[6] Compared with other lipid-based carriers, SNEDDS offer distinct advantages in terms of thermodynamic stability, ease of scale-up, and the ability to be readily converted into solid dosage forms without compromising their self-emulsification properties.[7–9]

Although liquid SNEDDS (L-SNEDDS) effectively enhance drug solubility and absorption and show acceptable physical stability, their practical application is often limited by handling difficulties, incompatibility with certain capsule shells, and the risk of drug precipitation during long-term storage. To overcome these limitations and improve formulation robustness, solidification strategies have been developed to convert liquid systems into solid SNEDDS (S-SNEDDS), which can be further processed into dosage forms such as tablets, capsules, or pellets.[10,11] Various techniques have been investigated for the solidification of SNEDDS, including spray drying, freeze-drying, hot-melt extrusion, and physical adsorption onto adsorbents.[12–16] Among these approaches, physical adsorption has gained particular attention because it enables efficient loading of L-SNEDDS and offers a relatively simple process compared to spray drying or hot-melt extrusion.[17]

Conventional adsorbents, such as non-mesoporous silicas (eg colloidal silicon dioxide), have been used to solidify SNEDDS. Still, their limited pore volume and lower liquid uptake often limit loading capacity and may compromise overall formulation performance.[18] To address these limitations, mesoporous materials have emerged as a promising alternative.[19] These structural attributes enable more efficient entrapment of L-SNEDDS, enhance powder flow, and support the stabilization of drugs in a molecularly dispersed or amorphous state.[20,21] Advances in material science have further expanded the potential of mesoporous carriers through the development of ordered mesoporous silicas such as MCM-41 and SBA-15, as well as engineered silica-based excipients, including mesoporous silica and magnesium alumino-metasilicate, which offer improved compressibility and higher loading capacity.[22–25] Despite these advantages, important considerations remain regarding potential drug–excipient interactions, altered release behavior due to excessive adsorption, and the need to address emerging regulatory and safety requirements for silica-based carriers in oral pharmaceutical products.[26]

The rapid expansion of SNEDDS-based technologies has extended their application beyond conventional oral delivery toward broader pharmaceutical and biopharmaceutical uses. In particular, the integration of mesoporous materials into SNEDDS has opened new opportunities for achieving higher drug loading and enhanced physical stability. Despite these advances, variations in carrier properties, adsorption mechanisms, and formulation design strategies continue to influence system performance and require systematic evaluation. Therefore, this review focuses on recent developments in mesoporous-based S-SNEDDS, highlighting key formulation strategies and their implications for physical stability, biopharmaceutical performance, and future pharmaceutical applications. The limitations and future directions in this field are also discussed to provide a comprehensive understanding and guide future research on the rational design of S-SNEDDS developed with mesoporous carriers.

Basic Principles for SNEDDS Solidification

SNEDDS are isotropic mixtures consisting of oils, surfactants, and co-surfactants that spontaneously form fine oil-in-water nanoemulsions upon mild agitation in aqueous environments such as gastrointestinal fluids.[4,8,27] The droplets, with diameters under 200 nm, provide a large interfacial surface area that enhances the dissolution rate and absorption of poorly water-soluble drugs, especially those classified as BCS Class II and IV.[28–30] The self-emulsification process occurs due to a reduction in the interfacial tension between oil and water, allowing the formation of thermodynamically stable emulsions with minimal external energy input. Consequently, SNEDDS can maintain drugs in a solubilized form within the gastrointestinal milieu and improve the consistency of oral absorption.[31,32]

L-SNEDDS offer significant advantages in terms of biopharmaceutical performance. They can markedly enhance the apparent solubility and oral bioavailability of poorly water-soluble drugs. The nano-sized droplets formed upon dispersion provide a large surface area for drug diffusion. At the same time, the surfactants present in the system can modulate intestinal membrane permeability, further promoting drug absorption. In some cases, L-SNEDDS also facilitate lymphatic transport, thereby bypassing hepatic first-pass metabolism and improving systemic exposure.[29,31,33,34] Despite these

benefits, the practical application of L-SNEDDS remains limited by factors such as potential changes in formulation performance during long-term storage, risk of leakage, and limited compatibility with conventional solid dosage form manufacturing. To overcome these drawbacks, transforming liquid SNEDDS into solid forms, known as S-SNEDDS, has emerged as a promising approach.[13,35]

Solidification of SNEDDS aims to overcome the handling, stability, and manufacturing challenges associated with liquid SNEDDS. Converting liquid systems into solid forms enhances stability, improves dosage accuracy, and facilitates development into conventional solid dosage forms such as tablets, capsules, or pellets. Additionally, S-SNEDDS can minimize capsule leakage, facilitate large-scale production, and improve patient compliance. However, the solidification process may alter self-emulsification efficiency or drug-release behavior due to adsorption or interactions with the solid carriers, requiring careful optimization of carrier type and processing conditions. Solid carriers play a pivotal role in converting liquid SNEDDS into solid dosage forms while retaining the SNEDDS's self-emulsifying properties.[11,36]

Overview of Mesoporous Particles

According to the IUPAC classification, porous materials are categorized by pore diameter as microporous (<2 nm), mesoporous (2–50 nm), and macroporous (>50 nm). Among these, mesoporous materials have attracted particular attention for pharmaceutical applications because their pore size range enables both efficient molecular accommodation and controlled confinement of drug molecules. Mesoporous materials possess a well-organized porous network with high specific surface area, tunable pore size, and large pore volume. These features enable effective adsorption and entrapment of liquid formulations such as SNEDDS within their pore channels. The capillary-driven absorption of the liquid phase converts it into a solid form while preserving its self-emulsifying properties upon reconstitution. The confined mesoporous environment can also restrict molecular mobility, thereby helping maintain the amorphous or molecularly dispersed state of poorly water-soluble drugs and enhancing their physical stability.[37–39]

Among different classes of porous solids, mesoporous silica materials are the most extensively investigated due to their favorable combination of physicochemical and biological properties. They exhibit large and accessible surface areas, substantial pore volumes, mechanical robustness, and chemical inertness, along with good biocompatibility, low toxicity, and cost-effectiveness. These attributes make mesoporous silica a versatile and promising carrier platform for various drug delivery applications, including the solidification of lipid-based systems.[37–40] Previously, non-porous silica such as colloidal silicon dioxide (fumed silica) was widely used as a solid carrier for lipid-based formulations owing to its very high surface area and strong adsorptive capacity. However, colloidal silicon dioxide lacks internal mesopores that can provide spatial confinement for drug molecules or liquid formulations.[38] Recent comparative studies have demonstrated that mesoporous carriers offer superior performance in terms of drug loading, dissolution enhancement, and release control compared with non-porous colloidal silicon dioxide.[38,41]

Mesoporous silica materials are broadly classified into ordered and non-ordered types, depending on the regularity of their pore structures and synthesis methods. Ordered mesoporous silica, such as MCM-41, SBA-15, and KIT-6, is typically synthesized via surfactant-templated sol–gel methods that yield uniform, predictable pore architectures. These ordered systems enable precise control over pore geometry and surface functionality, thereby supporting efficient drug adsorption and tunable release behavior.[38,42,43]

In contrast, non-ordered mesoporous silica is a commercially available pharmaceutical excipient produced via precipitation or modified fumed-silica processes. Although its pore structure is irregular, this material provides a high specific surface area (200–700 m^2/g) and large pore volume (0.6–1.8 cm^3/g), making it a highly effective adsorbent for lipid-based formulations. Beyond pure silica, silicate-based materials such as mesoporous magnesium aluminometasilicate have also been widely employed as pharmaceutically safe adsorbents for the solidification of lipid-based delivery systems.[38,39]

S-SNEDDS Development Using Mesoporous Carriers

The solidification of SNEDDS using mesoporous materials has been widely investigated, resulting in formulations that will hereafter be referred to as mesoporous-based S-SNEDDS. These systems have been primarily developed for drugs

with poor aqueous solubility, particularly those classified as BCS Class II and Class IV, owing to SNEDDS's inherent ability to enhance drug solubilization, dissolution rate, and intestinal permeability.[44]

Typically, these systems originate from conventional L-SNEDDS formulations comprising an oil phase, a surfactant, and a co-surfactant. The formulation strategy aims to create isotropic mixtures that form fine oil-in-water (O/W) nanoemulsions spontaneously upon dilution in GI fluids. The selection of the oil phase is a crucial step, commonly guided by solubility screening of the drug in various lipids to ensure maximum solubilization and thermodynamic stability of the preconcentrate. In most cases, medium-chain triglycerides or semisynthetic lipids are used because they dissolve lipophilic drugs and promote rapid emulsification.[45,46] However, recent studies have increasingly explored the incorporation of bioactive oils as the lipid phase.[47] One widely used bioactive oil is black seed oil. This oil not only serves as an effective solubilizing vehicle owing to its high linoleic and oleic acid content, but also offers a range of pharmacological benefits.[48] These dual-functional properties have been leveraged to develop SNEDDS formulations for drugs such as glibenclamide, atorvastatin calcium, and curcumin. The bioactive oil enhances drug solubility and potentially contributes to therapeutic synergy, thereby improving overall pharmacodynamic outcomes.[49–51]

The choice of surfactant is crucial for determining the emulsification efficiency of SNEDDS in the gastrointestinal environment. Nonionic surfactants with high hydrophilic–lipophilic balance (HLB) values, typically above 12, such as Cremophor RH 40, Cremophor EL, Tween 20, and Tween 80, are particularly suitable for forming oil-in-water nanoemulsions. In the gastrointestinal tract, these hydrophilic surfactants promote the dispersion of the lipid phase into intestinal fluids, producing stable oil droplets that are further solubilized by bile salts and phospholipids. Beyond emulsification, certain nonionic surfactants also enhance membrane fluidity and inhibit efflux transporters such as P-glycoprotein, thereby improving drug absorption and overall bioavailability.[52–54] Co-surfactants such as Transcutol® P, propylene glycol, and PEG 400 are frequently included to complement the surfactant system. Their amphiphilic and low-viscosity characteristics further reduce interfacial tension and increase the flexibility of the interfacial film, thereby enhancing emulsification spontaneity and expanding the nanoemulsion region in the pseudo-ternary phase diagram.[8,55]

The performance of L-SNEDDS is generally characterized by droplet size, polydispersity index (PDI), percentage transmittance, and emulsification time. These critical quality attributes determine the in vivo fate of the formulation: smaller, more uniform droplets provide a larger surface area for drug release, and high transmittance reflects optical clarity and efficient dispersion. At the same time, shorter emulsification time indicates rapid self-emulsification within the GIT.[4,56] Once an L-SNEDDS exhibits desirable nano-emulsification behavior, it can be transformed into an S-SNEDDS by incorporating the formulation onto a suitable solid carrier. Among the various carriers employed for this purpose, mesoporous materials have gained considerable attention. Based on the studies reviewed, S-SNEDDS can be further developed into multiple solid dosage forms depending on the characteristics of the incorporated drug, including tablets, HPMC capsules, gelatin capsules, and enteric-coated capsules.

Mesoporous Carriers in the Solidification of SNEDDS

The incorporation of mesoporous materials as solid carriers has emerged as a transformative strategy in the development of S-SNEDDS. These materials, characterized by high surface area and tunable pore size, enable efficient conversion of liquid SNEDDS into free-flowing powders while preserving or even enhancing nanoemulsification performance.[38] Recent studies have highlighted various mesoporous carriers, such as mesoporous silica, mesoporous magnesium alumino-metasilicate, mesoporous silica nanoparticles, and mesoporous mannitol as promising excipients that facilitate drug loading, improve physical stability, and maintain rapid self-emulsification upon reconstitution.

Mesoporous Magnesium Alumino-Metasilicate (MAS)

Mesoporous magnesium alumino-metasilicate (MAS) is a synthetic amorphous inorganic material and is among the most widely used mesoporous carriers in the development of S-SNEDDS. A commercially available example of this material is Neusilin®. Its high surface area (±300 m^2/g) and large pore volume (1.82 ± 0.55 cm^3/gram), high oil adsorbing capacity (2.7–3.4 mL/g), and its high water adsorbing capacity (2.4–3.1 mL/g) enable efficient adsorption of lipid formulations while maintaining rapid re-emulsification in aqueous media.[37,57–59] MAS is available in several pharmaceutical grades, including UFL2, US2, and S1/S2, which mainly differ in particle size, flowability, and oil adsorption

capacity. Among these, the US2 grade is the most commonly employed in S-SNEDDS due to its moderate particle size (~100 μm), high oil adsorption capacity, and excellent compressibility, making it suitable for direct compression and capsule filling. In contrast, the UFL2 grade, which possesses a much smaller particle size (~2–3 μm) and higher surface area, offers superior dispersibility but reduced flowability, which may complicate downstream processing.

MAS (US2) has been widely applied as a solid carrier in the development of S-SNEDDS for various poorly water-soluble drugs, including Aprepitant, Benidipine, Bosentan, Camptothecin, Capsaicin, Curcumin/Lansoprazole, Curcumin/Piperine, Fenofibric Acid, Fosfestrol, Glimepiride, Morin Hydrate, Omeprazole Hydrochloride, Palbociclib–Letrozole, Plumbagin, Posaconazole, Rhubarb Free Anthraquinones, Tamoxifen/Resveratrol, and Valsartan (Table 1).[17,20,28,51,59–77] MAS (US2) belongs to the mesoporous carrier category, with a pore size of approximately 18.76 ± 1.89 nm.[58] In terms of performance, MAS (US2) has demonstrated superior functionality as a solid carrier, as shown in the aprepitant S-SNEDDS study, where it exhibited a higher liquid adsorption capacity than mesoporous silica, retaining up to 2 g of L-SNEDDS per gram. Although magnesium calcium silicate (Florite® R) demonstrated the highest oil adsorption capacity (5 g/g), the resulting powders were sticky and poorly flowing. In contrast, MAS (US2) provided an optimal balance between adsorption efficiency and powder flow properties, making it the most suitable carrier for solidifying SNEDDS formulations.[60]

Table 1 Summary of Mesoporous Magnesium Aluminometasilicate (MAS)–Based S-SNEDDS

Active Ingredients/BCS	L-SNEDDS System and Solidification System	L-SNEDDS and S-SNEDDS Characteristics	Final Product/Reference
Aprepitant/Class II	Liquid: • Oil: Imwitor® 988 • Surf: Cremophor® RH40 • Co-S: Transcutol®P Solid: • Carrier: MAS (US2) • Optimum ratio: 1.5:1 • Physical absorption method (Dropwise, manual mixing)	Liquid: • DS: 14.48 ± 1.80 nm • PDI: 0.061 Solid: • HR: 1.22 • CI: 18.07%	Powder[60]
Benidipine/Class II	Liquid: • Oil: Labrafil M 2125 cs • Surf: Cremophor EL • Co-S: Transcutol P Solid: • Carrier: MAS (US2) • Optimum ratio: 1:1.15 • Physical absorption method (manual mixing)	Liquid: • DS: 156.20 ± 2.40 nm • PDI: 0.25 • ZP: −17.36 ± 0.18 mV • ET: 65.21 ± 1.95 s • %T: 99.80 ± 0.70%	Hard HPMC capsules[17]
Bosentan Monohydrate/Class II	Liquid: • Oil: Maisine® • Surf: Cremophor® RH 40 • Co-S: Labrasol® Solid: • Carrier: MAS (US2) • Optimum ratio: 1.25:1 • Physical absorption method (manual mixing)	Liquid: • DS: 17 nm • PDI: 0.180 Solid: • AOR: 22.6° • HR: 1.22 • CI: 18% • Pore diameter: 14.4 Å • SBET, m^2/g: 165 • SBHJ, m^2/g: 245 • Micropore volume (cc/g): 0.082 • DS: <50 nm • PDI: <0.5	Tablet[61]
Camptothecin/Class IV	Liquid: • Oil: omega oil • Surf: Cremophor-RH40 • Co-S: Labrafil-M2125 Solid: • Carrier: MAS (US2) • Physical absorption method (dropwise, manual mixing)	Liquid: • DS: 47 nm • PDI: 0.176 • ZP: −35.2 mV • ET: 21 ± 0.38 s • %T: 98.42 ± 1.82% Solid: • AOR: 15.34 ± 0.06° • HR: 1.16 ± 0.04 • CI: 9.45 ± 0.05%	Hard gelatin capsule[62]

(*Continued*)

Table 1 (Continued).

Active Ingredients/BCS	L-SNEDDS System and Solidification System	L-SNEDDS and S-SNEDDS Characteristics	Final Product/Reference
Capsaicin/Class II	Liquid: ● Oil: Isopropyl myristate ● Surf: Labrafil ● Co-S: Ethanol Solid: ● Carrier: MAS (US2) ● Physical absorption method (dropwise, manual mixing)	Liquid: ● DS: 62.04 ± 2.37 nm ● PDI: 0.43 ± 0.29 ● ET: 18.19 ± 0.46 s ● %T: 98.90 ± 1.24% Solid: ● AOR: 15.22 ± 0.04° ● HR: 1.10 ± 0.03 ● CI: 9.33 ± 0.03% ● DS: 52.86 nm ● ZP: −22.80 mV	Hard gelatin capsule[63]
Curcumin and Lansoprazole/Class IV & II	Liquid: ● Oil: Black seed oil ● Surf: Cremophor EL ● Co-S: Imwitor 988 Solid: ● Carrier: MAS (US2) ● Optimum ratio: 1:1 ● Physical absorption (Manual mixing)	Liquid: ● DS: 13.8 ± 0.2 nm ● PDI: 0.12 ± 0.02 ● ZP: −21.3 ± 0.6 mV	Capsule[66]
Curcumin and Piperine/Class IV & II	Liquid: ● Oil: Black Seed Oil ● Surf: Cremophor RH40 ● Co-S: Labrasol Solid: ● Carrier: MAS (US2) cured ● Optimum ratio: 1:1 ● Physical absorption (Dropwise,manual mixing)	Liquid: ● DS: 22.01 nm ● PDI: 0.211 ● ZP: + 0.906	Hard gelatin capsules[77]
Curcumin and Piperine/Class IV & II	Liquid: ● Oil: Black seed Oil and Imwitor 988 ● Surf: Cremophor RH40 ● Co-S: Transcutol P Solid: ● Carrier: MAS (US2) ● Optimum ratio: 1:1 ● Physical absorption (Dropwise,manual mixing)	Liquid: ● DS: 51 nm	Powder[51]
Fenofibric Acid/Class II	Liquid: ● Oil: Kollisolv® MCT 70 ● Surf: Cremophor RH 40 ● Co-S: Transcutol HP Solid: ● Carrier: MAS (US2) ● Physical absorption method (manual mixing)	Liquid: ● DS: 28.77 ± 3.07 nm ● PDI: 0.18 ± 0.33 ● ZP: −12.90 ± 1.31mV ● ET: 54.81 ± 2.94 s ● %T: 99.63 ± 0.64 Solid: ● DS: 29.77± 4.97 nm ● PDI: 0.54± 0.06	Powder[67]
Fosfestrol	Liquid: ● Oil: Soybean oil ● Surf: Labrasol ● Co-S: Labrafil M2125 Solid: ● Carrier: MAS (US2) ● Physical absorption method (Dropwise, manual mixing)	Liquid: ● DS: 52 nm ● PDI: 0.158 ● ZP: −36.4 mV Solid: ● AOR: 15.34 ± 0.06° ● HR: 1.16 ± 0.04 ● CI: 9.45 ± 0.05%	Powder[68]
Glimepiride/Class II	Liquid: ● Oil: Black seed oil ● Surf: Tween 80 ● Co-S:PEG 400 Solid: ● Carrier: MAS (US2) ● Physical absorption method (manual mixing)	Liquid: ● DS: 34.64 ± 2.01 nm Solid: ● AOR: 32.38°	Tablet[59]

(*Continued*)

Table 1 (Continued).

Active Ingredients/BCS	L-SNEDDS System and Solidification System	L-SNEDDS and S-SNEDDS Characteristics	Final Product/Reference
Morin Hydrate/Class IV	Liquid: • Oil: Labrafil M 1994 CS • Surf: Cremophor RH 40 • Co-S: Transcutol HP Solid: • Carrier: MAS (US2) • Optimum ratio: 1: 2 • Physical absorption method (manual mixing)	Liquid: • DS: 31 ± 1.5 nm • PDI: 0.124 ± 0.02 • ZP: −9.4 ± 1.4 mV • ET: 58 ± 2.8 s • %T: 98.12 ± 0.8% Solid: • AOR: 24.06 ± 0.44° • HR: 0.67 ± 0.21 • CI: 7.96 ± 0.14% • DS: 52 ± 4.25 nm • PDI: 0.133 ± 0.06 • ZP: −12.4 ± 2.52 mV	Powder[69]
Omeprazole Hydrochloride/Class II	Liquid: • Oil: Capryol 90 • Surf: Cremophor RH 40 • Co-S: Ethanol Solid: • Carrier: MAS (US2) • Optimum ratio: 2:1 • Physical absorption method (manual mixing)	Liquid: • DS: 19.11±3.11 nm • PDI: 0.18±0.05 • ZP: - 3.9±1.56 mV Solid: • AOR:25.36±0.29° • HR: 1.10±0.00 • CI: 9.04±0.14%	Enteric Coated Hard Gelatin Capsules[70]
Palbociclib-letrozole/Class II and class I	Liquid: • Oil: Maisine • Surf: Cremophor RH-40 • Co-S: Labrasol Solid: • Carrier: MAS (US2) • Physical absorption method (manual mixing)	Liquid: • DS: 71 ± 3 nm • ZP: - −31 ± 2 mV • %T: 99.26 ± 1.71% Solid: • AOR: 6.23 ± 0.08° • HR: 1.23 ± 0.03 • CI: 10.02 ± 0.04%	Powder[71]
Plumbagin/Class II	Liquid: • Oil: Capmul MCM • Surf: Tween 20 • Co-S: Propylene glycol Solid: • Carrier: MAS (US2) • Physical absorption method (manual mixing)	Liquid: • DS: 58.500 ± 1.170 nm • PDI: 0.228 ± 0.012 • ET: 17.660 ± 1.520 s • ZP: − 28.200 ± 1.200 mV • %T: 99.200% ± 0.600 Solid: • AOR: 29.67 ± 0.98° • HR: 1.14 ± 0.03 • CI: 13.32 ± 2.84% • DS: 105.600 ± 1.110 nm • ZP: − 30.460 ± 1.960 mV	Powder[72]
Posaconazole/Class II	Liquid: • Oil: Capmul MCM • Surf: Tween 20 • Co-S: Acrysol K140 Solid: • Carrier: MAS (US2) • Optimum ratio: 3:1 • Physical absorption method (manual mixing)	Solid: • DS: 11.9 nm • PDI: 0.495 • ZP: −39.9 mV	Powder[73]
Rhubarb Free Anthraquinones	Liquid: • Oil: Capryol 90/ethyl oleate • Surf: Cremophor RH 40 • Co-S: Transcutol HP Solid: • Carrier: MAS (US2) • Optimum ratio: 1:1 • Physical absorption method (dropwise, manual mixing)	Solid: • DS: 33.48 ± 13.88 nm • PDI: 0.182 ± 0.01 • ZP: −14.2 ± 5.24 mV • AOR: 26.00 ± 1.00° • HR: 1.20 ± 0.01 • CI: 16.67 ± 0.58%	Tablet[74]

(*Continued*)

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Table 1 (Continued).

Active Ingredients/BCS	L-SNEDDS System and Solidification System	L-SNEDDS and S-SNEDDS Characteristics	Final Product/Reference
Tamoxifen and Resveratrol/Class II	Liquid • Oil: Capmul MCM • Surf: Tween 80 • Co-S: Trancutol HP Solid: • Carrier: MAS (US2) • Physical absorption method (manual mixing)	Liquid: • DS: 104.5 nm • PDI: 0.211%T: 94% Solid: • DS: 92.54 ± 3.98 nm • PDI: 0.208 ± 0.012 • ZP: −13.5 ± 0.87 mV • %T: 96.00 ± 0.90	Powder[28]
Valsartan/Class II	Liquid: • Oil: Ethyl oleate • Surf: Cremophore RH-40 • Co-S: Transcutol HP Solid: • Carrier: MAS (UFL2) • Optimum ratio: 1:2 • Physical absorption method (manual mixing)	Liquid: • DS: 19.90 nm • ZP: −20.57 ± 1.16 mV • PDI: 0.074 ± 0.01 Solid: • AOR: 22.39 ± 0.76° • HR: 1.14 ± 2.03 • CI: 12.29 ± 1.84% • DS: 39.40 ± 1.05 nm • ZP: −9.10 ± 0.95 mV • PDI: 0.21 ± 0.02	Hard gelatin capsule[75]
Valsartan/Class II	Liquid: • Oil: Sesame oil • Surf: Tween 80 • Co-S: PEG 400 Solid: • Carrier: MAS (US2) • Physical absorption method (manual mixing)	Liquid: • DS: 173.9 nm • PDI: 0.184 • ZP: −31.2 mV Solid: • AOR: 34.03° • HR: 1.14 • CI: 12.40%	Tablet[76]

Abbreviations: AOR, Angle of repose; BCS, Biopharmaceutics Classification System; CI, Carr's index; Co-S, Co-surfactant; DS, Droplet size; ET, Emulsification time; HR, Hausner ratio; L-SNEDDS, Liquid self-nanoemulsifying drug delivery system; MAS, magnesium alumino-metasilicate; PDI, Polydispersity index; S-SNEDDS, Solid self-nanoemulsifying drug delivery system; %T, Percentage transmittance; ZP, Zeta potential.

Similarly, in the development of benidipine-loaded S-SNEDDS, MAS (US2) again demonstrated superior performance compared with colloidal silicon dioxide and granular mesoporous silica. It exhibited the highest oil adsorption capacity and produced powders with excellent flowability and a smooth, dry appearance at an L-SNEDDS-to-carrier ratio of 1:1.5. This optimized ratio ensured efficient drug loading and rapid dissolution, thereby selecting MAS (US2) as the preferred mesoporous carrier for further formulation studies.[17] Comparable findings were observed in the development of morin hydrate-loaded S-SNEDDS, where MAS (US2) outperformed colloidal silicon dioxide in terms of micromeritic behavior and powder handling. The formulation prepared with MAS (US2) at a 1:2 (L-SNEDDS: carrier) ratio exhibited excellent flow properties and a uniform, free-flowing powder. At the same time, the colloidal silicon dioxide-based S-SNEDDS showed poor flow and slight agglomeration in the powder bed.[69]

In the development of rhubarb anthraquinone (RhA)-loaded S-SNEDDS, various water-soluble adsorbents (dextrin, lactose, mannitol, NaCl, $NaHCO_3$) and water-insoluble adsorbents (SiO_2, MAS (US2), microcrystalline cellulose, $CaCO_3$, PVPP) were evaluated for their oil adsorption capacities. Among these, MAS (US2) and SiO_2 demonstrated the highest adsorption efficiency, producing non-sticky, free-flowing powders suitable for solidification. The SNEDDS powder prepared with MAS (US2) also showed a significantly higher zeta potential ($p < 0.05$) than the liquid formulation, indicating enhanced physical stability.[74] Similarly, in valsartan-loaded S-SNEDDS, both MAS (US2) and MAS (UFL2) exhibited higher adsorption efficiency than granular mesoporous silica, irregular mesoporous silica, and calcium phosphate. MAS (UFL2) achieved the highest adsorption capacity (2.28 ± 0.15 g L-SNEDDS/g carrier) with excellent flow characteristics (angle of repose 22.39 ± 0.76°, Hausner ratio 1.14 ± 2.03, and Carr's index 12.29 ± 1.84%). The fine, porous microstructure of MAS (UFL2) favors internal adsorption over surface coating, thereby enhancing the uniformity and physical stability of the final solid system.[76]

Further insight into the mesostructural characteristics of MAS (US2) was obtained from Brunauer–Emmett–Teller (BET) analysis conducted on bosentan-loaded S-SNEDDS. MAS (US2) exhibited a surface area of 342 m^2/g, a pore diameter of 12.3 nm, and a pore volume of 0.171 cm^3/g, confirming its mesoporous structure. After SNEDDS loading, these parameters decreased substantially, with the surface area reduced to 145–156 m^2/g and the pore volume to 0.072–0.077 cm^3/g, indicating efficient pore filling by lipid components while maintaining sufficient structural integrity for rapid re-emulsification upon aqueous dispersion.[20,61]

To further enhance its performance, MAS (US2) was modified via a solvent-evaporation "curing" process using 10% polyvinylpyrrolidone (PVP K-30), as demonstrated in curcumin- and lansoprazole-loaded S-SNEDDS formulations. This modification was intended to overcome the limitations imposed by small mesopores (1–50 nm), which may hinder emulsification and drug release. The curing process partially blocked the smallest pores, reducing the BET surface area from 399.2 to 286.4 m^2/g and the pore volume from 1.82 to 1.50 cm^3/g, while slightly increasing the average pore diameter from 18.3 to 21.2 nm. This adjustment improved pore accessibility and surface wettability, prevented oil entrapment, and facilitated rapid emulsification. Consequently, the dissolution efficiency of curcumin and lansoprazole increased by 1.8- to 2.7-fold compared with the unmodified MAS, demonstrating that the cured MAS enhances S-SNEDDS performance through optimized pore architecture and surface characteristics.[66]

Collectively, these findings confirm that MAS, particularly the US2 and UFL2 grades, offers a favorable balance of porosity, adsorption capacity, and flowability, making it one of the most versatile and practical mesoporous carriers for S-SNEDDS. Its tunable physicochemical characteristics and modifiable surface properties further enhance its potential to improve the stability, dispersibility, and dissolution performance of lipid-based formulations.

Mesoporous Silica (MS)

Besides mesoporous magnesium alumino-metasilicate, mesoporous silica (MS) is another widely used inorganic carrier in the development of S-SNEDDS. A commonly used, commercially available non-ordered mesoporous silica is Syloid®. It is mainly available in FP- and XDP-type grades, which differ in particle size, surface area, and powder-flow properties. Among these, the FP 244, XDP 3050, and XDP 3150 grades have been widely utilized in the development of S-SNEDDS.[58] As summarized in Table 2, mesoporous silica has been extensively applied in S-SNEDDS formulations containing atorvastatin calcium, curcumin, duloxetine, docosahexaenoic acid, ginkgolides, glibenclamide, nifurtimox, benznidazole, and ropinirole, primarily targeting BCS class II and IV drugs.[26,49,50,78–83]Structurally, mesoporous silica consists of amorphous silica particles with aggregated, irregular morphology and interconnected mesopores, providing a large specific surface area and substantial pore volume for efficient entrapment of lipid formulations, as well as rapid desorption and re-emulsification upon contact with aqueous media.[39]

Table 2 Summary of Mesoporous Silica–Based S-SNEDDS

Active Ingredients/BCS	L-SNEDDS System	L-SNEDDS and S-SNEDDS Characteristics	Final Product/References
Atorvastatin Calcium/Class II	Liquid: • Oil: Black seed oil • Surf: Tween 80 • Co-S: Propylene glycol Solid: • Carrier: MS (244 FP) • Optimum ratio: 1:1 • Physical absorption method (manual mixing)	Liquid: • DS: 46.62 nm • ZP: −35.2 mV	Powder[78]
Atorvastatin/Class II	Liquid: • Oil: Imwitor 308 • Surf: Tween 80 • Co-S: Propylene glycol Solid: • Carrier: MS (244 FP) • Physical absorption method (manual mixing)	Liquid: • DS: 10.5 nm	Capsule[50]

(*Continued*)

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Table 2 (Continued).

Active Ingredients/BCS	L-SNEDDS System	L-SNEDDS and S-SNEDDS Characteristics	Final Product/References
Curcumin and Duloxetine/Class IV and II	Liquid: • Oil: Castor oil • Surf: Tween 80 • Co-S: Transcutol P Solid: Carrier: MS (244 FP)	NA	Powder[79]
Docosahexaenoic Acid/Class II	Liquid: • Oil: Labrafil® M1944 CS • Surf: Tween 80 • Co-S: Transcutol P Solid: • Carrier: MS (XDP 3150) • Physical absorption method	Liquid: • DS: 43.51 ± 1.36 nm • PDI: 0.186 ± 0.053 • ZP: −19.20 ± 1.21mV Solid: • AOR: 24.22±0.32° • HR: 1.09±0.001 • CI: 23.63±2.12% • FR: 4.74±0.21 g/s • DS: 57.32 ± 1.87 nm • PDI: 0.261 ± 0.043 • ZP: - 16.6 ± 2.18 mV	Tablet[80]
Ginkgolides/Class IV	Liquid • Oil: Caprylic/ capric triglyceride • Surf: HS-15 • Co-S: Transcutol HP Solid: • Carrier: MS (XDP3050) • Optimum ratio: 1:1.5 • Physical absorption method	Liquid: • DS: 35.38 ± 1.80 nm • ZP: −3.36 mV Solid: • DS: 32.67 nm • ZP: −3.42 mV	Gastric Floating Tablets[81]
Glibenclamide/Class II	Liquid: • Oil: Black seed oil • Surf: Cremophor El • Co-S: Capryol 90 Solid: • Carrier: MS (XDP3050) • Optimum ratio: 1:1.25 • Physical absorption method	Liquid: • DS: 24.9 ± 0.2 nm • PDI: 0.35 ± 0.036 • ZP: −24.3 ± 8.1mV	Powder[49]
Nifurtimox and Benznidazole/Class IV and II	Oil: • Oil: Capryol 90 • Surf: Labrasol • Co-S: Labrafil M1944 CS Solid: • Carrier: MS (XDP3050) • Optimum ratio: 2:1 • Physical absorption method (manual mixing)	Liquid: • DS: 132 ± 7 nm • PDI: 0.610 ± 0.056 • ZP: −33.1 ± 2.4 Solid: • AOR: 25.97 ± 2.28° • HR: 1.21 ± 0.009 • CI: 15.82 ± 3.33%	HPMC Caspules and tablet[82]
Ropinirole/Class I	Liquid: • Oil: Capmul MCM EP • Surf: Tween 20 • Co-S: Acrysol EL 135 Solid: • Carrier: MS (244 FP) • Optimum ratio: 1: 4 • Physical absorption method (manual mixing)	Liquid: • DS: 96.71 nm • PDI: 0.370 • ET: 22s • %T: 98.90% Solid: • AOR: 33.8° • HR: 1.154 • CI: 12.7%	Tablet[83]
Triple Combination Therapy/Class II	Liquid: • Oil: Capmul MCM • Surf: Tween 20 • Co-S: PEG 400 Solid • Carrier: MS (244 FP) • Physical absorption method	Liquid: • DS: 99.5 ± 10.2 nm • PDI: 0.593 ± 0.011 • ZP: - 30.4 ± 2.4 mV Solid: • DS: 99.3 ± 0.8 nm • PDI: 0.583 ± 0.14 • ZP: −29.7 ± 2.2 mV	Powder[26]

Abbreviations: AOR, Angle of repose; BCS, Biopharmaceutics Classification System; CI, Carr's index; Co-S, Co-surfactant; DS, Droplet size; ET, Emulsification time; FR, Flow rate; HR, Hausner ratio; HPMC, Hydroxypropyl methylcellulose; L-SNEDDS, Liquid self-nanoemulsifying drug delivery system; MS, mesoporous silica; PDI, Polydispersity index; PEG, Polyethylene glycol; S-SNEDDS, Solid self-nanoemulsifying drug delivery system; %T, Percentage transmittance; ZP, Zeta potential.

MS (244 FP) possesses comparable mesoporous characteristics, with a surface area of approximately 330 m^2/g, a pore volume of about 1.8 cm^3/g, and an average pore diameter of around 16–17 nm. The main distinction lies in its much smaller particle size (approximately 3–5 μm) compared with MS (XDP 3050) (around 50 μm). This finer particle size results in a higher specific surface area and oil adsorption capacity but leads to relatively poorer flowability. Consequently, MS (244 FP) is more suitable for powder- or granule-based S-SNEDDS, whereas MS (XDP 3050), with its larger particle size and superior flow behavior, is preferred for direct compression and large-scale manufacturing applications.[57]

In the development of DHA-loaded S-SNEDDS, various adsorbents, including hydrophobic carriers MS (XDP 3150), MS (244 FP), colloidal silicon dioxide (200 grade), microcrystalline cellulose PH102, magnesium stearate, and lactose) and hydrophilic carriers (sodium carboxymethylcellulose), were compared in terms of oil adsorption capacity. Among these materials, MS (XDP 3150) exhibited the highest adsorption efficiency, requiring only 300 mg to solidify one unit dose of liquid SNEDDS, followed by colloidal silicon dioxide (410 mg) and MS (244 FP) (460 mg). In comparison, magnesium stearate showed the lowest adsorption efficiency (1600 mg). The S-SNEDDS prepared using MS (XDP 3150) exhibited good flow and compressibility, with an angle of repose of 24.22 ± 0.32°, a Hausner's ratio of 1.09 ± 0.001, and a Carr's index of 23.63 ± 2.12%.[80]

Similarly, MS (244 FP) demonstrated favorable performance in the solidification of ropinirole-loaded SNEDDS compared with granulated fumed silica and MAS (UFL2), producing optimal pre-compression properties at a 1:4 (mL:g) liquid-to-adsorbent ratio, with a Carr's index of 12.7, a Hausner's ratio of 1.154, and an angle of repose of 33.8°.[83] Furthermore, MS (XDP 3050), which was employed in the development of S-SNEDDS containing nifurtimox and benznidazole, exhibited good flowability with an angle of repose of 25.97 ± 2.28°, a Hausner's ratio of 1.21 ± 0.009, and a Carr's index of 15.82 ± 3.33%. This grade also enabled high drug loading of nifurtimox- and benznidazole-loaded SNEDDS (2:1, w/w), achieving nearly complete dissolution compared with commercial tablets.[82]

Collectively, MS–based carriers provide a favorable combination of liquid adsorption capacity, powder flowability, and chemical inertness for S-SNEDDS solidification. While MAS generally exhibits higher lipid uptake and greater compactness, MS offers superior powder uniformity and physical stability. These complementary characteristics make MS a reliable inorganic carrier, particularly suited for formulations in which both chemical compatibility and processing performance are critical to achieving consistent, physically stable S-SNEDDS systems.

Mesoporous Silica Nanoparticles

Mesoporous silica nanoparticles (MSNs) are nanostructured materials composed of an amorphous silica matrix containing a highly ordered network of mesopores with diameters typically ranging from 2 to 50 nm. MSNs have emerged as a versatile platform in modern drug delivery systems due to their unique physicochemical characteristics and structural tunability. Their large specific surface area, adjustable pore size, and well-defined porous architecture enable high drug loading capacity, controlled release behavior, and enhanced stability of incorporated therapeutics. Additionally, their chemical inertness, biocompatibility, and favorable degradation profile make them suitable for various administration routes.[19,24,43,84]

In a recent study, SMB-7-type MSNs were used to stabilize carvedilol-loaded L-SNEDDS containing Peceol, Tween 80, and Labrasol. The solidification was achieved via spray drying under optimized conditions to ensure a homogeneous coating and minimal lipid loss. The optimized S-SNEDDS formulation, prepared at a 2:1 L-SNEDDS: MSN ratio (1000 mg L-SNEDDS to 500 mg MSN), exhibited excellent reconstitution properties, forming a stable nanoemulsion and maintaining a high degree of supersaturation. Compared to pure carvedilol, this system significantly enhanced drug solubility (approximately 400-fold), dissolution rate (5.7-fold at 60 min), and oral bioavailability, as evidenced by 21.7-fold and 15.7-fold increases in AUC and Cmax, respectively.[85]

These findings confirm the role of mesoporous silica nanoparticles as a versatile platform that combines the advantages of solid adsorption and lipid-based delivery. By stabilizing the supersaturated state and preventing drug recrystallization, MSNs effectively enhance dissolution kinetics and systemic exposure, offering a promising strategy to improve the biopharmaceutical performance of poorly water-soluble drugs.[85]

Mesoporous Mannitol

Another mesoporous carrier explored for S-SNEDDS is mesoporous mannitol (MPM). This material combines the inherent advantages of mannitol (high water solubility, good biocompatibility, and low hygroscopicity) with a mesoporous architecture that enhances surface area and adsorption capacity. Although its application in drug delivery remains relatively limited compared with mesoporous silica-based materials, MPM provides a hydrophilic, low-cost, and pharmaceutically acceptable alternative for the solidification of lipid-based formulations.[86,87]

A recent study employed mesoporous mannitol as a solid carrier for piperine-loaded L-SNEDDS, formulated with Peceol, Tween 80, and Labrasol as lipid components. The mesoporous mannitol was synthesized by spray drying a mixture of D-mannitol and ammonium bicarbonate (1:1 w/w), with ammonium bicarbonate serving as a subliming pore-forming agent. This process generated a highly porous mannitol structure with a specific surface area of 4.192 m^2/g, approximately twice that of unmodified mannitol. The resulting mesoporous framework enabled efficient adsorption of the liquid SNEDDS within its pores while maintaining the self-emulsifying property upon reconstitution.[88]

In a separate study, mesoporous mannitol was developed as a soluble carrier for a pitavastatin supersaturated self-nanoemulsion (SSNE), using a Design of Experiments (DoE) approach to optimize the pore structure systematically. The effects of templating agent type, concentration, and solid loading were investigated. The findings indicated that ammonium carbonate was the most suitable templating agent, producing mesoporous mannitol with a favorable surface area, pore size, and flowability. Increasing the templating agent concentration significantly enhanced the pore size and volume, whereas higher solid loading reduced both parameters. Notably, the incorporation of pitavastatin SSNE into the optimized mesoporous mannitol produced a solid SSNE with nanodroplet formation behavior identical to that of the liquid SSNE, confirming that the solidification process preserved the self-emulsifying characteristics.[89]

Collectively, these findings underscore mesoporous mannitol as a promising hydrophilic mesoporous carrier for the solidification of both conventional and supersaturated SNEDDS, offering structural tunability, enhanced drug dissolution, and the ability to maintain nanoemulsion integrity without relying on silica-based excipients.

Preparation Methods of Mesoporous-Based S-SNEDDS

The transformation of liquid SNEDDS into solid intermediates is a critical step that enhances formulation stability, enables the development of solid dosage forms, and improves patient acceptability. The choice of preparation method significantly influences the physical properties, emulsification behavior, and overall biopharmaceutical performance of the resulting S-SNEDDS.

The preparation of L-SNEDDS generally follows straightforward, well-established procedures. The process usually begins by dissolving a hydrophobic drug in a selected lipid phase to enhance solubilization and loading efficiency, followed by the addition of a surfactant and a co-surfactant until a homogeneous, isotropic mixture is obtained. Mixing is typically assisted by mechanical energy using a magnetic stirrer or vortex mixer to ensure uniformity. However, in several studies, the drug was directly incorporated into the premixed oil-surfactant-co-surfactant system to improve solubilization and prevent drug precipitation during storage.[8]

Based on the reviewed studies, the primary method for solidifying SNEDDS with mesoporous carriers is physical adsorption, also known as surface adsorption. The principle of this method is that L-SNEDDS naturally adheres to the carrier's porous surface via capillary action and surface wetting, forming a uniform powder without solvents or heat. Typically, liquid SNEDDS are manually blended with the mesoporous carrier either by gradually adding the liquid formulation onto the carrier or by introducing the carrier into the liquid formulation until a uniform, free-flowing powder is obtained. Only a few studies have reported the use of mechanical stirring to enhance mixing.[17,60] This technique is simple, solvent-free, and suitable for thermolabile drugs, making it the most widely applied approach in S-SNEDDS preparation. It is predominantly used with non-ordered mesoporous carriers, including MAS and MS. These properties allow efficient entrapment of lipid-based formulations while preserving their self-emulsifying behavior upon reconstitution (Figure 1).

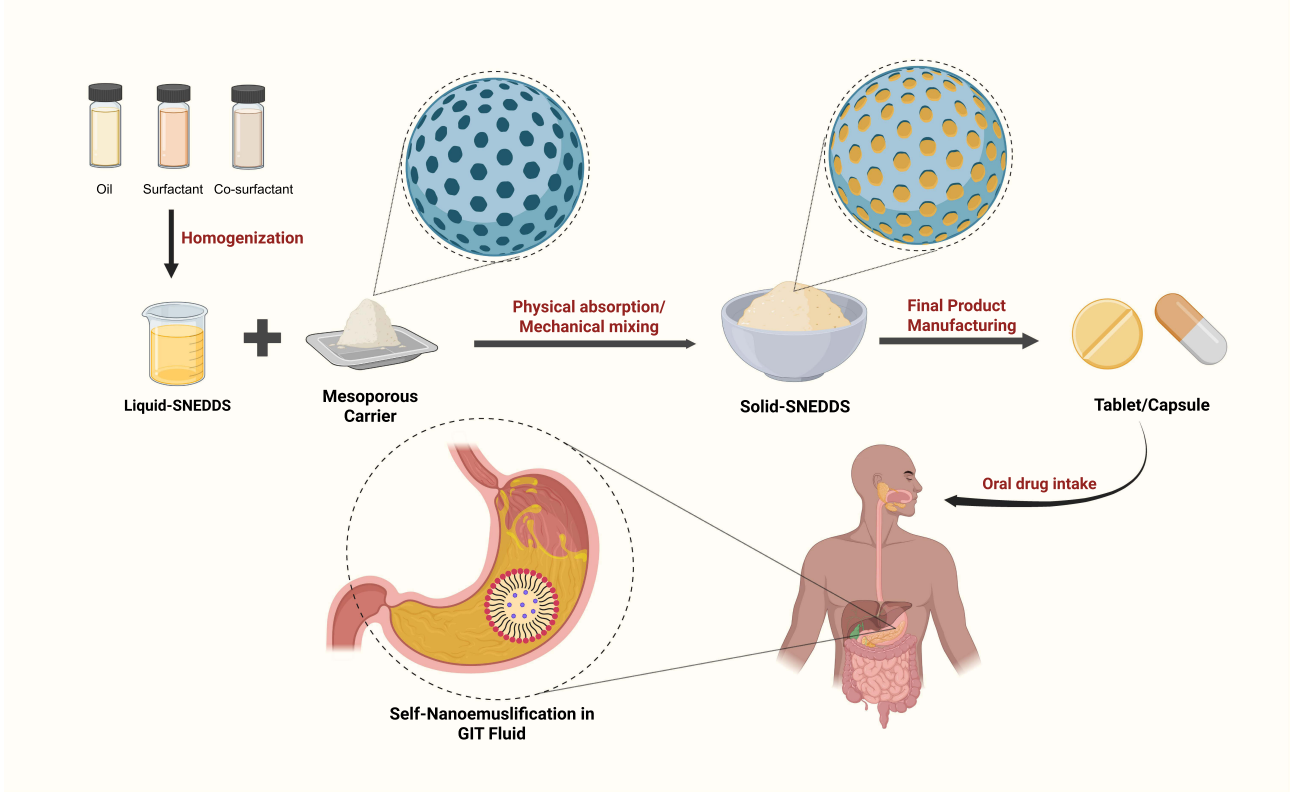

Figure 1 Illustration of Mesoporous-based S-SNEDDS.

In addition to adsorption, a few studies have employed spray drying to obtain S-SNEDDS, particularly when using MSNs or mesoporous mannitol as carriers. In these cases, the preformed liquid SNEDDS is dispersed in an aqueous medium with the mesoporous carrier, and the mixture is subsequently spray-dried under controlled conditions to achieve rapid solidification and uniform particle formation. Although less common, this approach provides better control over particle morphology and scalability for specific carrier systems.[85,88]

Physicochemical Characteristic of Mesoporous-Based S-SNEDDS

Comprehensive characterization is critically important for understanding how mesoporous carriers influence the physical properties, structural integrity, and performance of S-SNEDDS. The transformation from liquid to solid form must preserve the system's self-emulsifying efficiency while ensuring acceptable flowability and stability for downstream processing. Therefore, various solid-state and physicochemical analyses have been employed to evaluate morphology, crystallinity, thermal behavior, and intercomponent interactions within mesoporous carrier-based S-SNEDDS.

Crystallinity and molecular dispersion are typically assessed using differential scanning calorimetry (DSC) and powder X-ray diffraction (PXRD). The disappearance or reduction of characteristic melting endotherms and diffraction peaks of the API after adsorption indicates its conversion to an amorphous or molecularly dispersed state within the carrier matrix. This transformation is generally beneficial for enhancing dissolution rate and bioavailability, as demonstrated in several S-SNEDDS formulations containing poorly soluble drugs.[17,62]

Fourier transform infrared spectroscopy (FTIR) or Raman spectroscopy is also commonly employed to evaluate potential chemical interactions between SNEDDS components and the mesoporous carrier. In most cases, minimal peak shifts or the absence of new peaks suggest that physical adsorption predominates rather than chemical bonding, confirming the compatibility of lipid excipients with silica-based or other mesoporous carriers.[17,62]

Morphological examination, typically conducted using scanning electron microscopy (SEM) or transmission electron microscopy (TEM), provides insight into the surface topology and distribution of lipid components within the carrier

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matrix. When liquid SNEDDS is adsorbed onto mesoporous materials, the formulation tends to fill the internal pores and uniformly coat the surface. This morphological transformation confirms efficient entrapment of lipid droplets within the porous network while maintaining a dry, free-flowing powder.[17,80]

Micromeritic properties, including bulk density, tapped density, Hausner ratio, and angle of repose, are commonly evaluated to determine powder flowability. These evaluations are an essential parameter for processes such as capsule filling or tablet compression. The high specific surface area and porous architecture of mesoporous carriers contribute to favorable compressibility and uniform distribution of the lipid-based formulation.[70,72]

Collectively, these analyses confirm that incorporating mesoporous materials into S-SNEDDS promotes desirable physical and structural features, consistent with theoretical expectations of enhanced surface area and molecular confinement. Nevertheless, despite the general agreement between empirical findings and theoretical predictions, not all studies have comprehensively evaluated every physicochemical aspect. Some investigations remain limited to basic characterization, leaving gaps in understanding the full spectrum of solid-state interactions and microstructural organization. Expanding these analyses across future studies would therefore strengthen the mechanistic understanding and design optimization of mesoporous-based S-SNEDDS systems.

Stability Performances of Mesoporous-Based S-SNEDDS

Maintaining storage stability is essential to ensure consistent performance of SNEDDS formulations that are designed to enhance drug solubilization and bioavailability. Although liquid SNEDDS are generally more stable than conventional nanoemulsions because they are stored as pre-concentrates that form nanoemulsions only upon dilution, they may still experience long-term instability, such as drug precipitation, leakage, and chemical degradation, particularly with thermolabile or moisture-sensitive drugs. To overcome these issues, the transformation of liquid SNEDDS into solid forms using mesoporous carriers has been widely explored as a practical approach to improve physical and chemical stability while maintaining self-emulsifying capability.[90]

Mesoporous carriers improve stability by adsorbing the liquid formulation into their porous matrices, thereby immobilizing the lipid phase, limiting molecular mobility, and reducing exposure to environmental factors such as moisture, oxygen, and light. Various studies have shown that solidified systems remain stable under accelerated storage conditions. For example, benidipine-loaded S-SNEDDS stored for 6 months at 40 ± 2 °C and 75 ± 5% relative humidity showed no change in emulsification efficiency, droplet size, transmittance, or drug release, indicating excellent physical and chemical stability.[17] Similarly, bosentan-loaded S-SNEDDS tablets remained stable for up to twelve months under different storage conditions (4 °C, 25 °C/60% RH, and 40 °C/75% RH).[20,61] The formulation retained uniform drug content and physical appearance, with only slight discoloration observed at the highest temperature and humidity, while no statistically significant differences ($p > 0.05$) were detected in tablet properties or drug release performance. Comparable outcomes have been reported for other drugs such as camptothecin, capsaicin, fosfestrol, morin hydrate, palbociclib–letrozole, and posaconazole, which consistently maintained their droplet size, emulsification efficiency, drug content, and dissolution profiles after 3–6 months of accelerated storage. Collectively, these findings demonstrate that mesoporous-based S-SNEDDS possess excellent physical and chemical stability, even under stringent conditions, supporting their potential for long-term pharmaceutical use.[62,63,68]

In contrast, liquid SNEDDS are commonly more susceptible to physical and chemical degradation under similar conditions. For example, curcumin-loaded liquid SNEDDS retained only about 38% of the initial drug content after 6 months of accelerated storage, whereas the corresponding solidified system maintained more than 85%. Similarly, rhubarb anthraquinone liquid nanoemulsions showed up to 16% degradation after 10 days of light and temperature exposure, whereas the S-SNEDDS tablets exhibited less than 5% loss.[74] Other comparative studies have shown that S-SNEDDS exhibit slower degradation kinetics, higher decomposition activation energy, and longer shelf life than their liquid counterparts, confirming that solidification markedly enhances formulation stability.

These consistent observations demonstrate that solidification significantly enhances the stability of SNEDDS through multiple mechanisms, including the immobilization of the liquid phase within mesopores, reduced drug mobility, and the moisture-adsorbing and protective properties of silica-based carriers, which suppress hydrolytic and oxidative degradation. In addition, the solid matrix prevents leakage and phase separation while ensuring reproducible emulsification upon

reconstitution. Overall, mesoporous-based S-SNEDDS provide superior physical and chemical stability compared with liquid systems, offering a more reliable platform for the long-term delivery of poorly soluble and unstable drugs. However, stability evaluation has not been consistently performed across studies, even though it is a critical parameter in determining the robustness and shelf life of these systems. Among the available reports, there remains considerable variability in testing duration, storage conditions, and the quality attributes assessed, which makes direct comparison difficult. Therefore, standardized stability protocols, preferably aligned with ICH guidelines, are essential to enable meaningful comparisons and to strengthen the evidence supporting the long-term stability of mesoporous-based S-SNEDDS.

Biopharmaceutical Performance of Mesoporous-Based S-SNEDDS

The development of mesoporous-based S-SNEDDS primarily aims to address the biopharmaceutical limitations of poorly water-soluble drugs, particularly those in BCS Class II and Class IV. By combining the self-emulsifying capability of SNEDDS with the high surface area and adsorption capacity of mesoporous carriers, these systems are expected to influence several key parameters governing oral drug performance. Potential impacts may include changes in dissolution and drug release behavior, membrane permeation, and pharmacokinetic profiles, which collectively determine drug absorption and bioavailability. These aspects will be further discussed in the following sections, supported by experimental evidence and comparative findings across various mesoporous carriers and drug models.

Impact on Drug Release Behavior

SNEDDS are intrinsically designed to enhance the dissolution of poorly water-soluble drugs by forming fine oil-in-water nanoemulsions upon aqueous dilution. This spontaneous emulsification process generates droplets in the nanometer range, thereby markedly increasing the interfacial surface area for drug partitioning into the surrounding medium. Moreover, the drug's solubilization in the lipid-surfactant mixture helps maintain it in a supersaturated state, delaying precipitation and thereby improving overall dissolution and absorption. The presence of surfactants and co-surfactants further facilitates wetting and dispersion, thereby overcoming the dissolution-rate limitation typically observed with BCS Class II and IV compounds.[9,91,92]

Across multiple studies, S-SNEDDS consistently demonstrated markedly enhanced dissolution behavior compared to pure drugs or suspensions, while maintaining dissolution efficiency comparable to L-SNEDDS and often superior to marketed formulations (Table 3). This overall trend indicates that transforming L-SNEDDS into a solid form can effectively preserve the system's nanoemulsification capacity, providing both enhanced biopharmaceutical performance and improved physical stability. In the majority of cases—such as aprepitant, curcumin, piperine, benidipine, palbociclib, and bosentan—the extent of release increased from less than 30% for the pure drug to over 80–95% within one hour from the S-SNEDDS formulation.[60,71] These improvements are attributed to the molecular dispersion of the drug within the isotropic SNEDDS matrix, which facilitates the spontaneous formation of nanosized droplets upon hydration and substantially increases the surface area available for dissolution. The mesoporous carriers further contribute by enabling rapid capillary wetting and re-emulsification through their large pore volumes and surface areas, thereby maintaining a transient supersaturated state that supports *pH-independent* solubilization.

However, exceptions were noted in several studies, such as the omeprazole hydrochloride S-SNEDDS formulated with MAS (US2) and filled into enteric-coated capsules, in which the pure drug exhibited higher apparent dissolution (~80%) than the S-SNEDDS (~60%), comparable to the marketed capsules (~60–70%). This discrepancy can be attributed to the dissolution conditions, in which 20 mg of drug dispersed in 900 mL of medium was far below its solubility limit (82.3 mg/L), allowing the pure drug to dissolve rapidly without requiring emulsification. In contrast, the S-SNEDDS underwent an initial liberation and re-emulsification step before drug release, resulting in a slower apparent dissolution under these sink conditions. Nevertheless, S-SNEDDS still showed advantages over marketed products due to faster, more uniform dissolution at intestinal pH, attributed to the pre-solubilized drug and rapid nanoemulsion formation, which provides a larger surface area for release.

Compared with L-SNEDDS, most solid systems showed comparable or only slightly lower dissolution rates, indicating that adsorption onto mesoporous carriers generally does not compromise emulsification efficiency. For

Table 3 Drug Release Profile of Mesoporous-Based S-SNEDDS

Active Ingredients/Carriers	Methods	Time	% Drug Release	
			Other Samples	S-SNEDDS
Aprepitant/MAS (US2)[60]	In vitro dissolution study (type II) in SLS 2,2% and buffer pH 1,2; 4,5; 6,8	1 h	Emend® Capsule: 2.2% SLS: ~ 22 µg/mL pH 1.2: ~9 µg/mL pH 4.5: ~4 µg/mL pH 6.8: ~1 µg/mL Micronised aprepitant: 2.2% SLS: ~13 µg/mL pH 1.2: ~4 µg/mL	S-SNEDDS: 2.2% SLS: ~23 µg/mL pH 1.2: ~16 µg/mL pH 4.5: ~18 µg/mL pH 6.8: ~17 µg/mL
Atorvastatin calcium/MS (244 FP[50]	In vitro dissolution study (type II) in phosphate buffer (pH 6.8	30 min	Pure drug: ~ 70% L-SNEDDS: ~95%	S-SNEDDS: ~95%
Atorvastatin/MS (244 FP)[78]	In vitro dissolution study (type II) in phosphate buffer (pH 6.8)	5 min	Pure drug: 7.3%	S-SNEDDS: 88.2%
Benidipine/MAS (US2)[17]	In vitro dissolution study (type II) in 0.1 N HCl (pH 1.2)	15 min	Pure drug: 58.8% Commercial drug: 60.15%	S-SNEDDS: >85%
Bosentan/MAS (US2)[61]	In vitro dissolution study (type II) in 1% SLS and biorelevant media (FaSSIF, FeSSIF, FaSSIF-V2, FeSSIF-V2)	90 min	Reference tablet: • 1% SLS: 100% • FaSSIF: 32.4% • FeSSIF: 11% • FaSSIF-V2: 22.3% • FeSSIF-V2: 22.1%	S-SNEDDS tablet: • 1% SLS: 88% • FaSSIF: 80% • FeSSIF: 82% • FaSSIF-V2: 82% • FeSSIF-V2: 88%
Camptothecin/MAS (US2)[62]	In vitro dissolution study (type I) in 0.1N HCl	20 min	Pure drug: 22.72%	S-SNEDDS in hard gelatin capsule: 99.33 ± 0.26%
Capsaicin/MAS (US2)[63]	In vitro dissolution study (type I) in buffer solution pH 1.2	15 min	Pure drug: 16.61% L-SNEDDS: 87.36%	S-SNEDDS in hard gelatin capsule: 85.19%
Carvedilol/MSN[85]	In vitro dissolution study (type II) in distilled water solution pH 1.2	1 h	Pure drug: ~3%	S-SNEDDS: ~14%
Curcumin and Lansoprazole/MAS (US2)[66]	In vitro dissolution study (type II) in 0.1N HCl pH 1.2 and buffer phosphate pH 6.8	HCl: 1 h Buffer: 1 h	Pure drugs: In HCl: Curcumin: NA Lansoprazole: ~3% (pH 6.8)	S-SNEDDS: Curcumin: ~35% (pH 1.2) and ~40% (pH 6.8 in 120 min) Lansoprazole: ~24%
Curcumin and Piperine/MAS (US2)[77]	In vitro dissolution study (type II) in 0.1N HCl pH 1.2 and buffer phosphate pH 6.8	HCl: 2 h Buffer: 2 h	Suspension: Curcumin: 12.41% Piperine: 17.49%	S-SNEDDS: Curcumin: 65.13% Piperine: 81.56%
Curcumin and Piperine/MAS (US2)[51]	In vitro dissolution study (type II) in SGF pH 1.2 and SIF pH 6.8	HCl: 2 h Buffer: 2 h	Pure drug: Curcumin: ~0% Piperine: ~23%	S-SNEDDS: Curcumin: 60% Piperine: 77%
Docosahexaenoic Acid/MS (XDP 3150)[80]	In vitro dissolution study (type II) in 0.1 N HCl and 0.2 M phosphate buffer pH 6.8	90 min	pH 1.2: L-SNEDDS: 102.92 ± 5.78% Marketed drug: 42.14 ± 3.15% Pure drug: 14.21 ± 2.47% pH 6.8: L-SNEDDS: 98.11 ± 3.78% Marketed drug: 38.73 ± 2.19% Pure drug: 10.15 ± 1.12%	pH 1.2: S-SNEDDS powder: 95.84 ± 4.45% S-SNEDDS tablet: 93.69 ± 4.34% pH 6.8: S-SNEDDS powder: 91.25 ± 4.09% S-SNEDDS tablet: 88.35 ± 3.87%
Fenofibric Acid/MAS (US2)[67]	In vitro dissolution study (type I) in phosphate buffer pH 6.8	1 h	Pure drug: 54%	S-SNEDDS in hard gelatin capsule: 98.07±0.86%

(*Continued*)

Table 3 (Continued).

Active Ingredients/Carriers	Methods	Time	% Drug Release	
			Other Samples	S-SNEDDS
Fosfestrol/MAS (US2)[68]	In vitro release study (type I) in 0.1 N HCl and phosphate buffer pH 6.8	20 min	Marketed drug: 40.36 ± 2.8% Pure drug: 32.0 ± 3.3%	S-SNEDDS: 98.20 ± 1.3%
Ginkgolides/MS (XDP3050)[81]	In vitro dissolution study (type I) in pH 1.2	1 h	Pure drug: 48.59% (GA) and 46.03% (GB)	S-SNEDDS in capsule: ~98%
Glibenclamide/MS (XDP3050)[49]	In vitro dissolution study (type II) in phosphate buffer pH 6.8	1 h	Pure drug: ~20% L-SNEDDS: 90%	S-SNEDDS: ~85%
Glimepiride/MAS (US2)[59]	In vitro release study (USP type II) in SLS 2,2%	1 h	-	S-SNEDDS: 75.15% – 109.47%
Omeprazole Hydrochloride/ MAS (US2)[70]	In vitro dissolution study (type II) in 0.1N HCl, then 0.01 M phosphate buffer (pH 7.4)	HCl: 2 h Buffer: 1 h	Pure drug: ~ 80% Omisec capsules: ~70% Losec capsules: ~60%	S-SNEDDS in enteric coating capsules: ~ 60%
Morin Hydrate/MAS (US2)[69]	In vitro dissolution study (type II) in phosphate buffer pH 6.8	1 h	Suspension: 18.6 ± 0.4%	S-SNEDDS in hard gelatin capsule: 90 ± 1.8%
Nifurtimox and Benznidazole/ MS (XDP3050)[82]	In vitro dissolution study (USP Apparatus IV, flow-through cell, open-loop) in SGF pH 1.2, then phosphate buffer pH 6.8	2 h	Commercial drug: Nifurtimox: ~19% Benznidazole: ~30%	S-SNEDDS tablet: Nifurtimox: ~90% Benznidazole: ~80%
Piperine/Mesoporous mannitol[86]	In vitro dissolution study (USP type II) in SGF pH 1.2, then phosphate buffer pH 6.8	2 h	Pure drug: ~10% (pH 1.2) ~15% (pH 6.8) L-SNEDDS: ~98% (pH 1.2) ~98% (pH 6.8)	S-SNEDDS: ~98% (pH 1.2) ~98% (pH 6.8)
Palbociclib-letrozole/MAS (US2)[71]	In vitro dissolution study (type I) in 0.1 N HCl and phosphate buffer pH 6.8	20 min	Pure drug: Palbociclib 20.14% Letrozole 31.45%	S-SNEDDS: Palbociclib 99.76% Letrozole 94.86%
Plumbagin/MAS (US2)[72]	In vitro dissolution study (type II) in phosphate buffer pH 7.4	15 min	Pure drug: 30.15% ± 1.01 L-SNEDDS: 93.14% ± 2.02	S-SNEDDS: **90.13% ± 1.99**
Ropinirole/MS (244 FP)[83]	In vitro dissolution study (Dialysis bag method) in phosphate buffer, pH of 7.4	1 h	Pure drug: 30% L-SNEDDS: ~99%	S-SNEDDS: ~99%
Rhubarb Free Anthraquinones/MAS (US2)[74]	In vitro dissolution study (type II) in HCl pH 1.2 and phosphate buffer pH 6.8	4 h	Control tablet: ≤10%	S-SNEDDS tablet: ~80%
Tamoxifen and Resveratrol/ MAS (US2)[28]	In vitro dissolution study (dialysis bag method) in SGF pH 1.2 and SIF pH 6.8	12 h	Suspension: pH 1.2 Tamoxifen ~20% Resveratrol ~35% pH 6.8 Tamoxifen ~20% Resveratrol ~35%	S-SNEDDS: pH 1.2 Tamoxifen ~70% Resveratrol ~79% pH 6.8 Tamoxifen ~80% Resveratrol ~80%
Triple Combination Therapy/MS (244 FP)[26]	In vitro dissolution study (type II) in phosphate buffer pH 6.8	1 h	Pure drug: Candensartan 5,92% ± 1,49 Glibenclamide ~20% Rosuvastatin ~90% L-SNEDDS Candensartan 60.79% ± 3.48 Glibenclamide ~78% Rosuvastatin ~95%	S-SNEDDS: Candensartan ~ 18% Glibenclamide ~65% Rosuvastatin ~75%

(*Continued*)

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Table 3 (Continued).

Active Ingredients/Carriers	Methods	Time	% Drug Release	
			Other Samples	S-SNEDDS
Valsartan/MAS (UFL2)[75]	In vitro dissolution study (type I) in 0.1 N HCl, acetate buffer ph 4.5, phosphate buffer pH 6.8 and distilled water	1 h	Pure drug: pH 1.2 ~9% pH 4.5 ~50% pH 6.8 ~80% Water ~10%	S-SNEDDS in capsule: All media ~90%
Valsartan/MAS (US2)[76]	In vitro dissolution study (type II) in distilled water	10 min	Marketed tablet: ~50%	S-SNEDDS tablet: 97.33%

Abbreviations: FaSSIF, Fasted State Simulated Intestinal Fluid; FeSSIF, Fed State Simulated Intestinal Fluid; HCl, Hydrochloric acid; HPMC, Hydroxypropyl methylcellulose; L-SNEDDS, Liquid self-nanoemulsifying drug delivery system; c, pH, Potential of hydrogen; PDI, Polydispersity index; PEG, Polyethylene glycol; SIF, Simulated intestinal fluid; SGF, Simulated gastric fluid; SLS, Sodium lauryl sulfate; S-SNEDDS, Solid self-nanoemulsifying drug delivery system; USP, United States Pharmacopeia; % drug release, Percentage of drug released; %T, Percentage transmittance.

example, atorvastatin, docosahexaenoic acid, piperine, and ropinirole formulations exhibited nearly identical release in both liquid and solid forms.[80] Minor reductions were observed for capsaicin (85% vs 87%) and plumbagin (90% vs 93%); some curcumin–piperine systems were within an acceptable range and did not alter the overall trend.[63] In more complex formulations, such as the triple-drug S-SNEDDS containing candesartan, glibenclamide, and rosuvastatin, a more noticeable reduction was observed compared to the liquid system. This decrease has been attributed to partial drug retention within the adsorbent's porous structure, possibly due to precipitation of one or more drugs in the mesopores during the solidification process. Such retention is more likely in multi-drug systems where differences in solubility and lipophilicity can lead to competitive adsorption and non-uniform distribution within the carrier, resulting in slower re-emulsification and diffusion into the dissolution medium. In general, however, the solidification process preserved the drug's molecularly dispersed state and maintained dissolution efficiency comparable to that of the liquid system.[26]

Compared with marketed formulations, S-SNEDDS generally provided dissolution rates equal to or higher than those of the marketed formulations. However, the extent of this improvement varied among drugs and dissolution conditions. For example, S-SNEDDS of bosentan, fenofibric acid, nifurtimox–benznidazole, and ginkgolides achieved release of 80–95%. In contrast, marketed products showed moderate to high dissolution, ranging from 40% to 100% depending on the drug and medium.[82] The improved or equivalent performance of S-SNEDDS is attributed to the pre-solubilized nature of the system and the spontaneous formation of nanoemulsion droplets upon hydration, which promote faster release across various pH conditions. Some exceptions were observed, such as omeprazole and lansoprazole systems, which exhibited slightly lower release than both the pure drug and marketed capsules, likely due to the acid-labile nature of these drugs or slower re-emulsification after solidification.[70]

Overall, S-SNEDDS improved the dissolution of poorly soluble drugs compared to pure and marketed formulations, while generally maintaining performance comparable to L-SNEDDS. The observed variations among studies are mainly associated with differences in drug physicochemical properties, formulation complexity, and, importantly, non-standardized testing conditions. Therefore, future studies should ensure the use of harmonized dissolution testing systems for dissolution media, hydrodynamic conditions, and reconstitution procedures, so that the results more accurately reflect the dynamic physiological environment of the gastrointestinal tract and enable more reliable cross-study comparisons. Nevertheless, since in vitro dissolution testing alone cannot fully represent in vivo conditions, the actual performance of S-SNEDDS should ultimately be confirmed through in vivo evaluations, such as pharmacokinetic and pharmacodynamic studies, which more accurately reflect improved absorption and therapeutic efficacy.

Impact on Membrane Permeation

Although only a limited number of studies have evaluated the permeability of S-SNEDDS, the available data consistently show improved membrane transport compared to pure drugs or conventional formulations (Table 4). Overall, S-SNEDDS

Table 4 Permeation Profile of Mesoporous-Based S-SNEDDS

Active Ingredients/Carrier/Reference	Method	Time	% Drug Permeated	
			Other Samples	S-SNEDDS
Bosentan/MAS (US2)[61]	Ex vivo permeability study (Franz diffusion cell) using biorelevant media (FaSSIF, FeSSIF, FaSSIF-V2, FeSSIF-V2)	2h	Reference tablet: FaSSIF: • Flux: 13.9 ± 3.03 μg cm^{-2} min^{-1} • PC: 18.5 ± 0.4×10^{-4} cm min^{-1} FeSSIF: • Flux: 3.99 ± 1.55 μg cm^{-2} min^{-1} • PC: 5.3 ± 2.1×10^{-4} cm min^{-1} FaSSIF-V2: • Flux: 9.58 ± 1.31 μg cm^{-2} min^{-1} • PC: 12.8 ± 1.7×10^{-4} cm min^{-1} FeSSIF-V2: • Flux: 4.42 ± 1.94 μg cm^{-2} min^{-1} • PC: 5.9 ± 2.6×10^{-4} cm min^{-1}	S-SNEDDS tablet: FaSSIF: • Flux: 22.8 ± 14.5 μg cm^{-2} min^{-1} • PC: 30.4 ± 19.4×10^{-4} cm min^{-1} FeSSIF: • Flux: 2.38 ± 1.45 μg cm^{-2} min^{-1} • PC: 3.2 ± 1.9×10^{-4} cm min^{-1} FaSSIF-V2: • Flux: 23.5 ± 22. μg cm^{-2} min^{-1} • PC: 31.3 ± 29.8×10^{-4} cm min^{-1} FeSSIF-V2: • Flux: 23.1 ± 4.39 μg cm min^{-1} • PC: 30.8 ± 5.9×10^{-4} cm min^{-1}
Fosfestrol/MAS US2	In vitro Caco-2 cell permeability assay	-	Pure drug: P_{app}: 13.4 × 10^{-6}cm/s	S-SNEDDS: P_{app}: 62.8 × 10^{-6}cm/s
Palbociclib-letrozole/MAS (US2)[71]	In vitro Caco-2 cell monolayer permeability assay	-	Pure drug: Palbociclib P_{app}: 22.72 × 10^{-6}cm/s Letrozole P_{app}: 44.43 × 10^{-6}cm/s	S-SNEDDS: Palbociclib P_{app}: 87.73 × 10^{-6}cm/s Letrozole P_{app}: 75.85 × 10^{-6}cm/s
Plumbagin/MAS (US2)[72]	Ex vivo permeation study	6 h	Pure drug: • %Cumulative drug permeated: 46,58% • Flux: 1.232 ± 0.080 μg/min • P_{app}: 1.560 × 10^{-4} ± 0.220 cm/min	S-SNEDDS: • %Cumulative drug permeated: 90,36% • Flux: 2.344 ± 0.041μg/min • P_{app}: 2.740 × 10^{-4} ± 0.11 cm/s
Tamoxifen and Resveratrol/MAS (US2)[28]	Non-Everted Gut Sac Permeability Study	2 h	Suspension: • Flux: 0.2298 *mg/cm^2/h* • P_{app}: 11.49 × 10^{-5}cm/s	S-SNEDDS: • Flux: 0.5479 *mg/cm^2/h* • P_{app}: 27.4 × 10^{-5} cm/s

Abbreviations: FaSSIF, Fasted State Simulated Intestinal Fluid; FaSSIF-V2, Fasted State Simulated Intestinal Fluid Version 2; FeSSIF, Fed State Simulated Intestinal Fluid; FeSSIF-V2, Fed State Simulated Intestinal Fluid Version 2; Flux, Drug transport rate per unit area; MAS, magnesium alumino meta-silicate, P_app, Apparent permeability coefficient; PC, Permeability coefficient; S-SNEDDS, Solid self-nanoemulsifying drug delivery system.

exhibited higher apparent permeability coefficients (Papp) and flux values, indicating that the nanoemulsion droplets formed upon hydration effectively enhance drug diffusion across biological membranes.

For example, the permeability of fosfestrol increased nearly fivefold in S-SNEDDS compared with the pure drug, while palbociclib and letrozole also showed marked enhancement in Caco-2 assays. Similarly, plumbagin and the tamoxifen–resveratrol combination demonstrated approximately twofold higher flux and Papp than their respective suspensions. In ex vivo studies, bosentan-loaded S-SNEDDS displayed significantly greater flux and permeability than the reference tablet in most biorelevant media, confirming that nanosized droplets and improved surface wetting promote faster diffusion and partitioning.[20,21,68]

These improvements can be attributed to maintaining the drug in a solubilized, amorphous-like state and to the formation of fine nanoemulsion droplets that increase interfacial surface area and maintain high thermodynamic activity at the membrane surface. Surfactants and co-surfactants may further facilitate permeation by enhancing membrane fluidity. Although current permeability data remain limited, the results strongly suggest that the solidification process preserves and, in some cases, enhances the permeability advantages of liquid SNEDDS, thereby supporting their potential to improve oral absorption.

Impact on Pharmacokinetic Performance

Not all studies on S-SNEDDS included pharmacokinetic evaluations; however, the available results consistently demonstrate significant improvement in oral bioavailability compared to pure drugs, suspensions, and in several cases, marketed formulations (Table 5). The enhancement observed in S-SNEDDS primarily reflects the intrinsic properties of the SNEDDS system itself, rather than the solidification process. The conversion to a solid form mainly provides

Table 5 Pharmacokinetic Profile of Mesoporous-Based S-SNEDDS

Active Ingredients/ Carrier (Reference)	Method	Pharmakokinetic Parameters		Time	Relative Bioavailability
		Other Samples	S-SNEDDS		
Bosentan/MAS (US2)[20,61]	In vivo pharmacokinetic study using Wistar albino male rats (fasted and fed state, administered orally at a single dose of 50 mg/kg	Reference tablet: Fasted state • $AUC_{0-\infty}$: 9263 ± 4170 ng/mL*h • C_{max}: 2178 ± 1429 ng/mL • T_{max}: 4.67 ± 1.37 h Fed state • $AUC_{0-\infty}$: 8223 ± 2595 ng/mL*h • C_{max}: 1102 ± 355 ng/mL • T_{max}: 4.3 ± 1.367 h	S-SNEDDS : Fasted state • $AUC_{0-\infty}$: 11313 ± 2271 ng/mL*h • C_{max}: 5766 ± 2057 ng/mL • T_{max}: 0.458 ± 0.102 h Fed state • $AUC_{0-\infty}$: 19028 ± 5384 ng/mL*h • C_{max}: 5215 ± 2609 ng/mL • T_{max}: 1.00 ± 0.548 h	24 h	Fasted state: 128% • Fed state: 237%
Camptothecin/ MAS (US2)[62]	In vivo pharmacokinetic study using Wistar albino rats (n=9), administered orally at a single dose of 5 mg/kg	Pure drug: • AUC: 123.00 ± 3.54 ng/mL*h • C_{max}: 131.41 ± 4.12 ng/mL • T_{max}: 0.5 h	S-SNEDDS: • AUC: 2125.36 ± 54.32 ng/mL*h • C_{max}: 172.68 ± 7.68 ng/mL • T_{max}: 10 h	24 h	1727%
Capsaicin/MAS (US2)[63]	In vivo pharmacokinetic study using Wistar albino rats (n=9), administered orally at a single dose of 35 mg/kg	Pure drug: • $AUC_{0-\infty}$: 2782.3 ± 212.8 ng. h. mL^{-1} • C_{max}: 450.36 ± 12.47 ng. h. mL^{-1} • T_{max}: 0.5 h	S-SNEDDS • $AUC_{0-\infty}$: 9973.9 ± 208.4 ng. h. mL^{-1} • C_{max}: 752.85 ± 41.65 ng. h. mL^{-1} • T_{max}: 4 h	24 h	358,48%
Carvedilol/ MSN[85]	In vivo pharmacokinetic study using male Sprague–Dawley rats administered orally at a single dose of 40 mg/kg	Pure drug: • AUC: 4.17 ± 1.02 µ.h/mL • C_{max}: 0.72 ± 0.11 µg /mL • T_{max}: 2.00 ± 0.00 h	S-SNEDDS capsule: • AUC: 90.41 ± 5.91 µ.h/mL • C_{max}: 11.31 ± 1.15 µg /mL • T_{max}: 2 ± 0.00 h	24 h	2168,106%
Curcumin and Duloxetine/MS (244FP)[79]	In vivo pharmacokinetic study using Wistar rats administered orally at single doses of 50 mg/kg for curcumin and 20 mg/kg for duloxetine	Pure drug: Curcumin • $AUC_{0-\infty}$: 367.03 ng/mL*h • C_{max}: 34.18 ng/mL • T_{max}: 2 h Duloxetine • $AUC_{0-\infty}$: 3242.6 ng/mL*h • C_{max}: 294.49 ng/mL • T_{max}: 8 h	S-SNEDDS Curcumin • $AUC_{0-\infty}$: 4061.83 ng/mL*h • C_{max}: 332.18 ng/mL • T_{max}: 2 h Duloxetine • $AUC_{0-\infty}$: 6485.82 ng/mL*h • C_{max}: 588.98 ng/mL • T_{max}: 8 h	24 h	Curcumin: 1106.68% Duloxetine: 200.02%
Fosfestrol/MAS (US2)[68]	In vivo pharmacokinetic study using Wistar rats administered orally at doses of 5 mg/kg	Pure drug: • AUC: 256.20 ± 11.84 ng/mL*h • C_{max}: 40.27 ± 2.57 ng/mL • T_{max}: 1 h	S-SNEDDS: • AUC: 1253.37 ± 27. 6 ng/mL*h • C_{max}: 249.66 ± 9.84 ng/mL • T_{max}: 0.75 h	24 h	489.21%

Glimepiride/MAS (US2)[59]	In vivo pharmacokinetic study using Wistar rats administered orally at single doses of 10 mg/kg	Marketed tablet: • $AUC_{0-\infty}$: 16,729.63 ± 632.37 ng/mL*h • C_{max}: 2158.67 ± 128.81 ng/mL • T_{max}: 2.00 ± 0.00h Non SNEDDS tablet: • $AUC_{0-\infty}$: 8655.33 ± 1556.11 ng/mL*h • C_{max}: 1013.33 ± 97.45 ng/mL • T_{max}: 4.00 ± 0.00 h	S-SNEDDS tablet : • $AUC_{0-\infty}$: 18,562.32 ± 1431.03 ng/mL*h • C_{max}: 2277.00 ± 37.40 ng/mL • T_{max}: 2.00 ± 0.00h	24 h	Marketed tablet: 110.95% Non SNEDDS tablet: 214.46%
Morin Hydrate/MAS (US2)[69]	In vivo pharmacokinetic study using Wistar rats administered orally at single doses of 20 mg/kg	Pure drug: • AUC_{0-t}: 26.37 ± 2.8 µg/mL*h • C_{max}: 3.5 ± 0.6 µg /mL • T_{max}: 4.0 ± 0.2 h	S-SNEDDS: • AUC_{0-t}: 78.32 ± 3.3 µg/mL*h • C_{max}: 7.77 ± 1.6 µg /mL • T_{max}: 3.16 ± 0.3 h	24 h	297%
Palbociclib-letrozole/MAS (US2)[71]	In vivo pharmacokinetic study using Wistar albino rats administered orally at single doses of 5 mg/kg	Pure drug: Palbociclib • AUC: 1910.33 ± 134.21 ng/mL*h • C_{max}: 45.66 ± 4.38 ng/mL • T_{max}: 8 h Letrozole • AUC: 102.87 ± 8.67 ng/mL*h • C_{max}: 39.44 ± 2.43 ng/mL • T_{max}: 1 h	S-SNEDDS: Palbociclib • AUC: 8114.66 ± 537.25 ng/mL*h • C_{max}: 441.66 ± 51.27 ng/mL • T_{max}: 6 h Letrozole • AUC: 786.09 ± 21.56 ng/mL*h • C_{max}: 95.25 ± 6.51 ng/mL • T_{max}: 1 h	24 h	S-SNEDDS palbociclib: 424.77% S-SNEDDS letrozole: 764.19%
Plumbagin/MAS (US2)[72]	In vivo pharmacokinetic study using male Wistar rats administered orally at single doses of 100 mg/kg	Pure drug: • AUC: 2948.500 ± 541.090 ng.h/mL • C_{max}: 262.000 ± 5.831 ng/mL • T_{max}: 3.000 ± 0.343 h	S-SNEDDS • AUC: 13249.160 ± 908.090 ng.h/mL • C_{max}: 743.330 ± 4.080 ng/mL • T_{max}: 2.500 ± 0.548 h	24 h	449.36%
Rhubarb Free Anthraquinones/ MAS (US2)[74]	In vivo pharmacokinetic study using rabbits administered orally at single doses of 1 mg/kg	Control tablet: Aloe-emodin • $AUC_{0-\infty}$: 0.12 ± 0.03 µg/L*h • C_{max}: 0.012 ± 0.0003 µg /L • T_{max}: 3.333 ± 1.155 h	S-SNEDDS tablet: Aloe-emodin • $AUC_{0-\infty}$: 0.193 ± 0.055 µg/L*h • C_{max}: 0.02 ± 0.007 µg /L • T_{max}: 5.333 ± 1.155 h	24 h	160.83%
Tamoxifen and Resveratrol/MAS (US2)[28]	In vivo pharmacokinetic study using albino Wistar rats administered orally at single doses of 1.02 mg/kg tamoxifen and 10.20 mg/kg resveratrol	Suspension: Tamoxifen • AUC: 2290.534 ng/mL.h • C_{max}: 193.206 ng/mL • T_{max}: 3 h Resveratrol • AUC: 18,926.140 ng/mL.h • C_{max}: 3933.471 ng/mL • T_{max}: 1 h	S-SNEDDS Tamoxifen • AUC: 3737.314 ng/mL.h • C_{max}: 321.480 ng/mL • T_{max}: 3 h Resveratrol • AUC: 44,533.762 ng/mL.h • C_{max}: 8022.685 ng/mL • T_{max}: 1 h	24 h	Tamoxifen: 163.16% Resveratrol: 235.30%

(*Continued*)

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Table 5 (Continued).

Active Ingredients/ Carrier (Reference)	Method	Pharmakokinetic Parameters		Time	Relative Bioavailability
		Other Samples	S-SNEDDS		
Valsartan/MAS (UFL2)[75]	In vivo pharmacokinetic study using male Sprague–Dawley rats administered orally at a single dose of 10 mg/kg.	Pure drug: • AUC_{0-24}: 2948.86 ± 351.94 ng/mL.h • C_{max}: 341.68 ± 34.17 ng /mL • T_{max}: 1.50 ± 0.00 L-SNEDDS: • AUC_{0-24}: 5849.22 ± 448.71 ng/mL.h • C_{max}: 1575.55 ± 31.51 ng /mL • T_{max}: 0.50 ± 0.00 h	S-SNEDDS: • AUC_{0-24}: 6711.16 ± 522.51 ng/mL.h • C_{max}: 1660.53 ± 49.82 ng /mL • T_{max}: 1.00 ± 0.00 h	24 h	Pure drug: 227.58% L-SNEDDS: 114.74%
Valsartan/MAS (US2)[76]	In vivo pharmacokinetic study using male Wistar rats administered orally at single doses of 10 mg/kg	Marketed tablet: • $AUC_{0-\infty}$: 35.76 ± 4.04 µg/mL*h • C_{max}: 3.19 ± 0.32 µg /mL • T_{max}: 2.00 ± 0.00 h	S-SNEDDS: • $AUC_{0-\infty}$: 61.94 ± 11.43 µg/mL*h • C_{max}: 7.04 ± 0.90 µg /mL • T_{max}: 1.00 ± 0.00 h	24 h	173.21%

Abbreviations: AUC, Area under the plasma concentration–time curve; C_max, Maximum plasma concentration; h, Hour(s); L-SNEDDS, Liquid self-nanoemulsifying drug delivery system; S-SNEDDS, Solid self-nanoemulsifying drug delivery system; MAS, magnesium alumino meta-silicate; MS, mesoporous silica; T_max, Time to reach maximum plasma concentration; µg, Microgram; µh/mL, Microgram hour per milliliter; ng/mL, Nanogram per milliliter; ng/mL·h, Nanogram hour per milliliter; %, Percentage; Wistar rats, Wistar albino rat model used for pharmacokinetic evaluation.

improved physical stability and easier handling, without diminishing the absorption advantages inherent to liquid SNEDDS.

Across various drugs and carrier systems, S-SNEDDS showed marked increases in AUC and Cmax, while Tmax values were generally shorter or comparable, indicating efficient absorption. For example, bosentan-loaded S-SNEDDS increased AUC by 1.3–2.4-fold under both fasted and fed conditions, and similar enhancements were reported for fosfestrol, glimepiride, plumbagin, and valsartan, with AUC increases of 170–500%. More substantial improvements were observed with carvedilol and camptothecin, which showed bioavailability more than 10-fold higher than their pure forms.[20,21,68]

The improvement in pharmacokinetic behavior is consistent with the well-established mechanisms of SNEDDS. Upon exposure to gastrointestinal fluids, the system forms fine nanoemulsion droplets that provide a large interfacial surface area and maintain the drug in a solubilized, amorphous-like state, promoting rapid dissolution and absorption. The lipid components can facilitate lymphatic transport and reduce hepatic first-pass metabolism, while surfactants and co-surfactants may transiently enhance intestinal permeability.[8,9]

Although the extent of improvement varies with drug properties, lipid composition, and formulation design, the overall trend confirms that solidification does not impair the intrinsic bioavailability-enhancing mechanisms of SNEDDS. Instead, S-SNEDDS preserve these advantages while offering greater stability, ease of processing, and dosage uniformity, supporting their application as a practical oral delivery platform for poorly soluble drugs.

Therapeutic Performance of Mesoporous-Based S-SNEDDS

Pharmacodynamic evaluations further support the biopharmaceutical advantages demonstrated by S-SNEDDS in dissolution, permeability, and pharmacokinetic studies. Across therapeutic models, S-SNEDDS consistently produced more substantial or sustained pharmacological effects than those of pure drugs, suspensions, or conventional tablets. This enhancement aligns with improved solubilization, absorption, and systemic exposure observed in prior biopharmaceutical studies, indicating that the pharmacodynamic outcomes largely reflect the intrinsic performance of the SNEDDS system (Table 6).

In cardiovascular models, benidipine-loaded S-SNEDDS significantly reduced blood pressure in hypertensive rats. At the same time, bosentan S-SNEDDS achieved comparable cardiac efficacy and better histological recovery at lower doses than the reference tablet. These results correspond with the increased AUC and Cmax observed in pharmacokinetic studies, suggesting improved absorption and tissue distribution. Similarly, in antidiabetic and anti-inflammatory evaluations, glibenclamide, glimepiride, and plumbagin S-SNEDDS demonstrated significantly greater therapeutic responses and tissue protection, consistent with enhanced bioavailability and stable plasma levels.[20,21,72]

For anticancer and neuroprotective applications, S-SNEDDS formulations of camptothecin, capsaicin, tamoxifen–resveratrol, and fosfestrol showed greater cytotoxic or apoptotic activity in vitro.[28] In contrast, curcumin-based combinations exhibited improved behavioral and neuroprotective effects in vivo.These outcomes can be attributed to the higher cellular uptake and sustained intracellular drug levels achieved through nanoscale solubilization and amorphous dispersion within the SNEDDS matrix.

Collectively, these findings indicate that the superior therapeutic effects of S-SNEDDS primarily result from enhanced biopharmaceutical performance of the SNEDDS system (dissolution, permeability, and bioavailability) rather than from the solidification process itself. The solid form effectively maintains these intrinsic advantages while providing greater stability and improved dosage convenience, resulting in improved pharmacological efficacy across diverse therapeutic classes.

Safety Considerations of Mesoporous-Based S-SNEDDS

Safety is a crucial consideration in the development of mesoporous-based S-SNEDDS, as these systems often require relatively high amounts of surfactants, co-surfactants, and additional carriers such as mesoporous silica. While these components are essential for improving drug solubility and biopharmaceutical performance, their concentrations and potential long-term exposure must be carefully evaluated to ensure safety and tolerability. Moreover, any enhancement in

Table 6 Pharmacodynamic Modulation of Mesoporous-Based S-SNEDDS

Active Ingredients (Reference)	Testing Method	Pharmacodynamic Modulation
Benidipine/Magnesium aluminometasilicate (US2)[17]	In vivo antihypertensive activity test using a fructose-induced hypertensive rat model.	S-SNEDDS of benidipine significantly reduced systolic, mean, and diastolic blood pressure compared to the suspension form ($p < 0.001$)
Bosentan/MAS (US2)[20]	In vivo echocardiography and histopathological assessment in MCT-induced PAH rats	SNEDDS and S-SNEDDS tablets demonstrated improved lymphatic biodistribution, comparable cardiac effects, and superior histological recovery at lower doses compared to the reference tablet.
Camptothecin/MAS (US2)[62]	In vitro anticancer evaluation (MTT assay, mitochondrial membrane potential assay, DAPI staining, flow cytometry apoptosis assay, and Cell cycle arrest)	S-SNEDDS demonstrated significantly greater anticancer efficacy than plain CPT, as evidenced by cytotoxicity, apoptosis induction, and cell cycle arrest ($p<0.05$).
Capsaicin/MAS (US2)[63]	In vitro Cytotoxicity & Apoptosis Study in HT-29 colorectal cancer cell	S- SNEDDS demonstrated markedly enhanced anticancer efficacy compared to pure capsaicin, as evidenced by a 1.9-fold reduction in IC50, 2.55-fold higher apoptosis induction, and significantly greater inhibition of HT-29 colorectal cancer cell viability.
Curcumin and Piperine/MAS (US2)[77]	In vivo behavioral studies in AD-induced rats	S-SNEDDS significantly enhanced learning and memory in AD-induced rats, as evidenced by improved novel object recognition, higher spontaneous alternation, and reduced escape latency in the Morris Water Maze.
Curcumin and Duloxetin/MS (244FP)[79]	In vivo Antineuropathic Activity Study in Chronic Constriction Injury (CCI)-Induced Neuropathic Pain Rat Model	S-SNEDDS significantly alleviated CCI-induced neuropathic pain in rats, restoring pain thresholds, reducing oxidative stress and TNF-α levels, and improving sciatic nerve histology, with superior efficacy compared to their pure drug forms.
Fosfestrol/MAS (US2)[68]	In vitro Cytotoxicity Study	S-SNEDDS showed superior anticancer effects compared with pure FST, with lower IC50 values, higher apoptosis induction, and nearly 2-fold stronger G2/M cell cycle arrest in PC-3 cells.
Glibenclamide/MS (XDP3050)[49]	In vivo Anti-Diabetic Activity in Streptozotocin-Induced Diabetic Rat Model	S-SNEDDS formulation of glibenclamide significantly ($p < 0.05$) reduced blood glucose levels compared to the pure drug and control group.
Glimepiride/MAS (US2)[59]	In vivo Anti-Diabetic Activity in Rats	So-SNEDDS tablets showed significantly superior hypoglycemic effect and pancreatic tissue protection compared to non-SNEDDS and marketed tablets ($P < 0.05$).
Nifurtimox and Benznidazole/MS (XDP3050)[82]	In vitro and In vivo Trypanocidal and In vivo Trypanocidal Studies All	S-SNEDDS demonstrated nanomolar efficacy against *T. cruzi* epimastigotes and amastigotes with acceptable selectivity indexes, significantly reducing parasitemia and enhancing survival in acute murine models of Chagas disease
Palbociclib-letrozole/MAS (US2)[71]	In vitro MTT assay/Flow cytometry (Annexin V-FITC/PI)/ DAPI staining	S-SNEDDS exhibited the most potent cytotoxic and apoptotic effects compared to PCB, LTZ, and the physical combination (PCB + LTZ), showing lower IC_{50} values and a significantly higher proportion of apoptotic cells
Plumbagin/MAS (US2)[72]	In vivo Anti-Inflammatory Activity in Rats	S-SNEDDS exhibited significantly higher ($p < 0.01$) anti-inflammatory activity than pure plumbagin in carrageenan-induced paw edema rats.
Tamoxifen and Resveratrol/MAS (US2)[28]	In vitro Cell Line Studies (Cytotoxicity, Cellular Uptake, and Intracellular Antioxidant Activity Tests)	S-SNEDDS exhibited significantly higher cytotoxicity (lower IC_{50}), enhanced cellular uptake (visualized by confocal microscopy), reduced intracellular ROS generation, and elevated SOD activity compared to the drug suspension.

Abbrreviatons: AD, Alzheimer's disease; CCI, Chronic constriction injury; CPT, Camptothecin; FITC, Fluorescein isothiocyanate; G2/M, Gap 2/Mitosis phase; HT-29, Human colorectal adenocarcinoma cell line; IC_{50}, Half maximal inhibitory concentration; LTZ, Letrozole; MCT, Monocrotaline; MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; MAS, magnesium alumino meta-silicate; MS, mesoporous silica; PAH, Pulmonary arterial hypertension; PCB, Palbociclib; PC-3, Human prostate cancer cell line; ROS, Reactive oxygen species; SOD, Superoxide dismutase; SNEDDS, Self-nanoemulsifying drug delivery system; S-SNEDDS, Solid self-nanoemulsifying drug delivery system; TNF-α, Tumor necrosis factor alpha.

absorption and bioavailability must also be accompanied by confirmation that systemic exposure remains within safe therapeutic limits.[93]

Only a few studies have reported safety assessments of mesoporous-based S-SNEDDS, but the available evidence provides encouraging preliminary indications. In the case of posaconazole-loaded S-SNEDDS, acute, subacute, and chronic toxicity studies in rats showed no signs of toxicity, mortality, or behavioral abnormalities, and liver function parameters remained within normal limits.[73,79] Similarly, the curcumin–duloxetine S-SNEDDS demonstrated high cell viability (>88%) in cell line toxicity assays, confirming the absence of cytotoxic effects even at elevated concentrations.[79]

Although these findings support the biocompatibility and general safety of mesoporous-based S-SNEDDS, further comprehensive investigations are still required. Systematic evaluation of both short- and long-term safety, including potential effects of chronic exposure to mesoporous carriers and high surfactant levels, is essential for broader clinical translation. Therefore, future studies should integrate toxicological profiling with pharmacokinetic and pharmacodynamic assessments to ensure that performance improvements are achieved without compromising safety.

Limitations and Future Perspectives

Mesoporous-based S-SNEDDS have shown significant potential to improve the solubility, permeability, and oral bioavailability of poorly soluble drugs. However, several aspects related to formulation, stability, and safety still require deeper investigation before these systems can be reliably developed for clinical and large-scale pharmaceutical use. From a formulation and manufacturing perspective, most studies, particularly those employing mesoporous alumino-metasilicates as mesoporous carriers, still rely on physical adsorption and manual mixing for solidification. While this approach is convenient and straightforward for early-stage investigations, it offers limited control over critical factors, such as mixing uniformity, adsorption efficiency, and lipid-phase distribution within the pores. These limitations may compromise both reproducibility and scalability. Therefore, future research should prioritize process optimization using more controlled and scalable techniques supported by Quality by Design (QbD) and Design of Experiments (DoE). Applying these systematic approaches would enable a more comprehensive understanding of how formulation and process parameters, including pore size, carrier characteristics, and lipid loading, collectively influence the performance and quality attributes of the final S-SNEDDS product.

In addition to formulation and process aspects, the lack of standardized testing, particularly in dissolution evaluation, remains a significant challenge in assessing mesoporous-based S-SNEDDS. The wide variation in dissolution media, pH, surfactant levels, hydrodynamic conditions, and reconstitution procedures hampers direct cross-study comparison and limits reliable interpretation of data. Therefore, future studies should adopt a minimal standardized dissolution framework with defined biorelevant media, controlled agitation conditions, standardized reconstitution protocols, and appropriate reference systems. Such harmonization is essential to generate more comparable and predictive dissolution data.

In terms of stability, solidification generally improves handling and physical robustness compared with liquid SNEDDS, but it does not eliminate the risk of instability. Possible issues, such as drug recrystallization, phase migration, or degradation within the mesoporous matrix, may occur during storage, especially under high humidity or elevated temperature. These changes can alter droplet formation and drug release upon reconstitution. Although several studies have evaluated the stability of mesoporous-based S-SNEDDS, the available data remain limited and inconsistent in terms of testing duration, conditions, and the quality attributes assessed. This lack of uniformity makes it difficult to draw definitive conclusions regarding long-term performance. Comprehensive stability testing following ICH guidelines, combined with solid-state characterization techniques is therefore essential to confirm the long-term integrity of the system and ensure consistent performance throughout its shelf life.

From a safety perspective, most mesoporous-based S-SNEDDS have not yet undergone detailed toxicological evaluation. Existing studies mainly focus on pharmacokinetic and pharmacodynamic improvements, while long-term safety data remain largely unavailable. The relatively high content of surfactants, co-surfactants, and mesoporous silica carriers used in these systems necessitates careful examination of their chronic toxicity, mucosal compatibility, and potential for organ accumulation. Comprehensive safety assessments are crucial to confirm biocompatibility and ensure that improved bioavailability does not come at the expense of safety.

A clearer understanding of drug–lipid–carrier interactions and the establishment of reliable in vitro–in vivo correlations are also needed to support predictive formulation design and regulatory acceptance. Although most studies report improved dissolution and bioavailability, the quantitative relationship between in vitro and in vivo outcomes remains insufficiently explored.

Overall, mesoporous-based S-SNEDDS represent a promising platform for enhancing the delivery of poorly soluble drugs. Further research should emphasize the development of controlled and scalable formulation processes, the establishment of robust stability and safety data, and a deeper mechanistic understanding to ensure consistent performance, product reliability, and clinical applicability.

Conclusion

Mesoporous-based S-SNEDDS have emerged as a robust and versatile platform to overcome the solubility- and bioavailability-related limitations of poorly water-soluble drugs. The predominance of physical adsorption using mesoporous carriers such as mesoporous alumino meta-silicates and mesoporous silica highlights the practicality of this approach for transforming liquid SNEDDS into solid dosage forms while preserving their functional performance. These systems demonstrate favorable physical performances. Overall, mesoporous-based S-SNEDDS exhibit clear biopharmaceutical advantages over pure drug suspensions and conventional marketed tablets and generally maintain performance comparable to liquid SNEDDS. The observed variations among formulations are mainly attributed to differences in drug physicochemical properties, carrier structure, and adsorption behavior. Importantly, this solidification strategy offers distinct advantages over existing approaches by combining process simplicity, high liquid-loading capacity, preservation of self-emulsification performance, and improved processability into solid dosage forms. Despite these promising attributes, successful translation into clinically and industrially viable products remains contingent on further optimization of scalable manufacturing, long-term stability, and comprehensive safety evaluation. Addressing these aspects, together with deeper mechanistic understanding and standardized performance assessment, will be critical to fully realizing the potential of mesoporous-based S-SNEDDS in advanced oral drug delivery.

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Disclosure

The authors declare that they have no conflicts of interest in this work.

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