International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 21s, 2025
https://theaspd.com/index.php

Self-Emulsifying Drug Delivery System: Emerging Trends And Innovative Approaches In Drug Solubility Enhancement

Divya Palaparthi[1], S.Jeganath[1]
[1]Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology And Advanced Studies (VISTAS), Pallavaram, Chennai - 600117, Tamil Nadu, India.
*Corresponding author jeganaths@gmail.com

Abstract
Self-emulsifying drug delivery systems (SEDDS) are lipid-based formulations designed to enhance the solubility and oral bioavailability of poorly water-soluble drugs. These systems consist of isotropic mixtures of oils, surfactants, and co-surfactants/co-solvents that spontaneously form fine oil-in-water emulsions upon mild agitation in gastrointestinal fluids, increasing surface area for dissolution and facilitating absorption. Recent advancements include the development of self-nanoemulsifying systems (SNEDDS) with nanometer-sized droplets, supersaturable SEDDS (S-SEDDS) to maintain higher drug concentrations, and solid SEDDS (S-SEDDS) for improved stability and handling. Formulation strategies involve careful selection of excipients such as medium- or long-chain triglycerides, non-ionic surfactants like Cremophor® EL or Tween® 80, and co-solvents like Transcutol® P. Applications extend to anticancer, antiviral, anti-inflammatory, and immunosuppressive agents, with potential in transdermal, ocular, and parenteral delivery. However, challenges remain in scaling up production, ensuring long-term stability, preventing drug precipitation, and addressing surfactant-induced gastrointestinal toxicity. Future directions emphasize green manufacturing, safer biocompatible excipients, stimuli-responsive delivery, and integration with nanotechnology for precision medicine. These innovations position SEDDS as a versatile platform capable of overcoming solubility barriers and advancing modern drug delivery.
Keywords: *Self-emulsifying drug delivery systems, Oral bioavailability, Solid SEDDS, Poorly soluble drugs, Lipid-based formulations*

INTRODUCTION

Poor aqueous solubility remains one of the most significant challenges in modern drug development, particularly for the majority of new chemical entities (NCEs) emerging from high-throughput screening. It is estimated that nearly 40–60% of drugs in the development pipeline belong to the Biopharmaceutics Classification System (BCS) Class II and Class IV, where dissolution or solubility is the rate-limiting step in absorption and, consequently, bioavailability [1, 2]. These physicochemical limitations not only compromise therapeutic efficacy but also demand higher doses, increasing the risk of systemic toxicity and variability in pharmacokinetic profiles. Traditional approaches such as salt formation, particle size reduction, and use of co-solvents have been explored extensively, yet their applicability is often limited by physicochemical incompatibilities, instability, or inability to sustain supersaturation in the gastrointestinal (GI) environment [3].

Lipid-based drug delivery systems (LBDDS) have emerged as a powerful alternative for enhancing the oral delivery of poorly water-soluble drugs by leveraging the body's natural lipid digestion and absorption pathways. Among these, self-emulsifying drug delivery systems (SEDDS) have gained particular prominence due to their ability to spontaneously form fine oil-in-water emulsions upon mild agitation in the GI tract, typically provided by gastric motility [4]. Comprising isotropic mixtures of oils, surfactants, and sometimes co-surfactants or co-solvents, SEDDS create microemulsions or nanoemulsions with droplet sizes typically ranging from 20 nm to several hundred nanometers. This significantly increases the surface area for dissolution, maintains the drug in a solubilized state, and facilitates its transport across the intestinal epithelium. Furthermore, SEDDS can promote lymphatic uptake, thereby bypassing the hepatic first-pass effect and improving systemic exposure for lipophilic molecules [5, 6].

The clinical success of several marketed SEDDS-based formulations, such as Neoral® (cyclosporine A), Norvir® (ritonavir), and Fortovase® (saquinavir), has reinforced the practical utility of this technology in overcoming solubility barriers. Moreover, advances in formulation science have enabled the development of self-nanoemulsifying drug delivery systems (SNEDDS) with droplet sizes in the nanometer range, supersaturable SEDDS (S-SEDDS) to delay drug precipitation, and solid SEDDS (S-SEDDS) for improved stability, portability, and patient convenience. These innovations expand the versatility of SEDDS beyond

conventional oral delivery, opening opportunities in parenteral, transdermal, and pulmonary drug delivery routes [7].

Despite these advantages, SEDDS are not without challenges. Limitations include low drug loading for hydrophilic compounds, potential precipitation upon aqueous dilution or digestion, chemical instability of excipients, and the possibility of gastrointestinal irritation from high surfactant concentrations. Additionally, translating laboratory-scale SEDDS to industrial production requires careful optimization of excipient ratios, droplet size control, thermodynamic stability, and regulatory compliance. Addressing these limitations has driven research toward novel excipient combinations, green manufacturing techniques, and integration with advanced drug delivery concepts such as targeted, stimuli-responsive, and personalized medicine platforms [8].

This review aims to provide a comprehensive analysis of emerging trends and innovative approaches in SEDDS technology, with a focus on formulation strategies, solidification techniques, novel excipients, and their impact on solubility and bioavailability enhancement. It also explores recent research advancements, practical applications, and potential challenges, offering insights into how SEDDS can evolve into next-generation delivery systems capable of meeting the demands of modern pharmaceutics.

Formulation Considerations

The successful development of a self-emulsifying drug delivery system (SEDDS) relies on the careful selection and optimization of excipients to achieve rapid self-emulsification, stability, and enhanced drug release. The oil phase, such as medium-chain triglycerides (e.g., Capryol® 90, Miglyol® 812) or long-chain triglycerides (e.g., oleic acid, soybean oil), plays a crucial role in drug solubilization and determining droplet size. Surfactants, preferably non-ionic with appropriate hydrophilic–lipophilic balance (HLB) values, such as Cremophor® EL, Tween® 80, or Labrasol®, facilitate emulsification and improve dispersion in the gastrointestinal tract. Co-surfactants or co-solvents like Transcutol® P, propylene glycol, or polyethylene glycol 400 are used to reduce interfacial tension, improve flexibility, and prevent drug precipitation. Drug solubility in each excipient must be assessed to ensure adequate loading without crystallization upon aqueous dilution. Furthermore, thermodynamic stability, compatibility with capsule shell materials, and robustness under gastrointestinal conditions must be optimized to ensure reproducibility, scalability, and patient safety [9].

Applications of Self-Emulsifying Drug Delivery Systems

SEDDS have been successfully utilized for the delivery of various therapeutic agents, including anticancer drugs (e.g., paclitaxel, tamoxifen), antiviral agents (e.g., ritonavir, saquinavir), anti-inflammatory drugs (e.g., celecoxib, ibuprofen), and immunosuppressants (e.g., cyclosporine A, tacrolimus). Beyond oral administration, they have been explored for transdermal, ocular, and parenteral applications due to their ability to enhance drug permeation, protect sensitive molecules, and improve formulation stability. The development of solid SEDDS in the form of pellets, tablets, and capsules further increases storage stability, facilitates large-scale manufacturing, and improves patient compliance, making them a versatile platform for advanced drug delivery [10].

Future Perspectives and Challenges

Green and Low-Energy Technologies

Developing low-energy, eco-friendly self-emulsification methods aligns with the broader push toward sustainability, reducing energy demands and reliance on petrochemical excipients.

Safer, Biocompatible Excipient Design

Given surfactant-associated toxicity risks seen in animal studies, emphasis should shift to milder, gut-compatible surfactants or natural emulsifiers that preserve mucosal integrity and microbiota balance.

Stimuli-Responsive Systems

Incorporating triggers such as pH or enzyme sensitivity could allow targeted and controlled drug release within the digestive tract, enhancing therapeutic precision and reducing off-target effects.

Integration with Precision Medicine

Combining SEDDS with nanotechnology platforms such as polymeric carriers or carrier-free nanoparticles—can enable personalized delivery profiles and programmable release kinetics.

Regulatory and Scale-Up Considerations

To facilitate broader adoption, future efforts must address industrial scalability, reproducibility, and regulatory challenges, particularly in translating formulations into standardized oral dosage forms.

Safety and Long-Term Toxicity Studies

Preclinical insights on GI effects underscore the necessity for systematic in vivo and human studies to gauge chronic safety, microbiome interactions, and inflammatory responses.

CONCLUSION

Self-emulsifying drug delivery systems (SEDDS) represent one of the most effective and versatile strategies to address the persistent challenges associated with the poor aqueous solubility and low oral bioavailability of lipophilic drugs. By forming spontaneous fine emulsions or nanoemulsions in the gastrointestinal tract, SEDDS significantly increase the interfacial surface area available for dissolution, maintain drugs in a solubilized state for longer periods, and often facilitate lymphatic transport, thereby reducing the extent of first-pass metabolism. Their adaptability in accommodating both liquid and solid dosage forms enhances formulation flexibility, patient compliance, and commercial viability. Over the past decade, advancements in SEDDS technology have expanded their potential well beyond conventional oral delivery. Innovations such as self-nanoemulsifying systems (SNEDDS), supersaturable SEDDS (S-SEDDS), and solid SEDDS have improved stability, drug loading, and ease of large-scale manufacturing. Furthermore, integration with novel excipients, polymeric carriers, and functional additives has opened avenues for targeted and controlled drug release, enabling SEDDS to address a broader spectrum of therapeutic needs. Despite these advancements, certain limitations must be addressed before the full potential of SEDDS can be realized. Issues such as surfactant-induced gastrointestinal irritation, limited applicability to hydrophilic drugs, precipitation during digestion, and excipient incompatibilities remain significant barriers. On the industrial front, ensuring batch-to-batch reproducibility, maintaining thermodynamic stability, and meeting stringent regulatory standards require continuous research and optimization. Looking forward, the next generation of SEDDS is expected to embrace eco-friendly manufacturing methods, incorporate biocompatible and natural emulsifiers to reduce toxicity, and integrate stimuli-responsive components to enable site-specific or condition-triggered drug release. Coupled with advances in computational modeling, artificial intelligence, and nanotechnology, future SEDDS formulations hold the promise of being more patient-specific, scalable, and sustainable. With these innovations, SEDDS are poised to remain at the forefront of lipid-based drug delivery, offering a robust platform capable of transforming the therapeutic landscape for poorly soluble drugs.

REFERENCES

1.Kalepu S, Nekkanti V. Insoluble drug delivery strategies: review of recent advances and business prospects. Acta Pharm Sin B. 2015 Sep;5(5):442-53.
2.Loftsson T, Brewster ME. Pharmaceutical applications of cyclodextrins: basic science and product development. J Pharm Pharmacol. 2010 Nov;62(11):1607-21.
3.Tambe S, Jain D, Meruva SK, Rongala G, Juluri A, Nihalani G, Mamidi HK, Nukala PK, Bolla PK. Recent Advances in Amorphous Solid Dispersions: Preformulation, Formulation Strategies, Technological Advancements and Characterization. Pharmaceutics. 2022 Oct 16;14(10):2203.
4.Salawi A. Self-emulsifying drug delivery systems: a novel approach to deliver drugs. Drug Deliv. 2022 Dec;29(1):1811-1823.
5.Akula S, Gurram AK, Devireddy SR. (2014). Self-microemulsifying drug delivery systems: an attractive strategy for enhanced therapeutic profile. Int Sch Res Notices 2014:1811.
6.Balakrishnan P, Lee B-J, Oh DH, et al. (2009). Enhanced oral bioavailability of dexibuprofen by a novel solid self-emulsifying drug delivery system (SEDDS). Eur J Pharm Biopharm 72:539–45.
7.Park H, Ha ES, Kim MS. Current Status of Supersaturable Self-Emulsifying Drug Delivery Systems. Pharmaceutics. 2020 Apr 16;12(4):365.
8.Gupta S, Kesarla R, Omri A. Formulation strategies to improve the bioavailability of poorly absorbed drugs with special emphasis on self-emulsifying systems. ISRN Pharm. 2013 Dec 26;2013:848043.
9.Uttreja P, Karnik I, Adel Ali Youssef A, Narala N, Elkanayati RM, Baisa S, Alshammari ND, Banda S, Vemula SK, Repka MA. Self-Emulsifying Drug Delivery Systems (SEDDS): Transition from Liquid to Solid—A Comprehensive Review of Formulation, Characterization, Applications, and Future Trends. Pharmaceutics. 2025; 17(1):63.
10. Rehman FU, Farid A, Shah SU, Dar MJ, Rehman AU, Ahmed N, Rashid SA, Shaukat I, Shah M, Albadrani GM, Kamel M, Altyar AE, Abdel-Daim MM, Shah KU. Self-Emulsifying Drug Delivery Systems (SEDDS): Measuring Energy Dynamics to Determine Thermodynamic and Kinetic Stability. Pharmaceuticals (Basel). 2022 Aug 26;15(9):1064.