e-ISSN: 2320-4230, p-ISSN: 2961-6085

Journal of Drug Discovery and Therapeutics

Available Online at www.jddt.in

CODEN: - JDDTBP (Source: - American Chemical Society)

Volume 13, Issue 6; 2025, 63-68

A Review on Self-Nanoemulsifying Drug Delivery Systems (SNEDDS)

Dinesh Kumar[1], Rajesh Asija[2], Seema Trimukhe Yadav[3], Anil Goyal[4], Aman Kumar Gupta[5]

[1,5]PG Student, Department of Pharmaceutics, Maharishi Arvind Institute of pharmacy, Jaipur

[2]Principal, Maharishi Arvind Institute of pharmacy Jaipur

[3]Associate Professor, Maharishi Arvind Institute of pharmacy Jaipur

[4]Principal, Agrani College of Pharmacy, Jaipur

Received: 18-09-2025 / Revised: 20-10-2025 / Accepted: 20-11-2025

Corresponding author: Dinesh Kumar

Conflict of interest: No conflict of interest.

Abstract:

The formulation of Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) has emerged as a promising approach to enhance the solubility, dissolution rate, and oral bioavailability of poorly water-soluble drugs. This review focuses on the formulation and evaluation of SNEDDS containing Sitagliptin and Metformin Hydrochloride, two antidiabetic agents that act synergistically to improve glycemic control in type 2 diabetes mellitus. While Metformin exhibits low permeability and Sitagliptin has limited solubility, their combined delivery through SNEDDS offers an innovative platform for improved therapeutic performance. The review discusses the principles of nanoemulsion formation, selection of suitable oils, surfactants, and co-surfactants based on solubility and emulsification efficiency, and optimization using pseudo-ternary phase diagrams. Key formulation and evaluation parameters—such as globule size, zeta potential, and emulsification time, drug loading capacity, thermodynamic stability, and in vitro drug release—are critically analyzed. The potential of SNEDDS to overcome the pharmacokinetic limitations of conventional dosage forms, reduce dose frequency, and improve patient compliance is emphasized. Overall, the combination SNEDDS of Sitagliptin and Metformin Hydrochloride represents a novel strategy to achieve enhanced bioavailability, controlled release, and effective management of type 2 diabetes mellitus.

Keywords: SNEDDS, Sitagliptin; Metformin Hydrochloride; Type 2 diabetes mellitus; Self-nanoemulsifying system.

Introduction

SNEDDS is an isotropic combination made up of surfactant, co-solvent, and occasionally oil. A homogenous, translucent, isotropic, and thermodynamically stable dispersion will form in an aqueous environment. The production of this dispersion is aided by mild agitation, which is in-vivo given by gastrointestinal motility. SNEDDS are physically stable formulations that are simple to make as compared to emulsions, which are delicate and metastable dispersion forms. Because of a reduced susceptibility of formulation performance to pre-

absorptive solubilization and nutritional status, SNEDDS formulations are known to diminish inter- and intra-individual variability in bioavailability. Although SNEDDS formulations have grown in popularity over the past several years, they are not now widely used for a number of reasons. While some attribute the absence of commercial formulation to pharmaceutical development laboratories' customs, others believe it is due to their insufficient understanding of the substance's physico-chemical properties. For the formulation of SMEDDS and lipid formulation, knowledge of the emulsification process, effectiveness of emulsification, and susceptibility of the formulation to digestion is desirable.[1]

Advantages of Self Nano-emulsifying Drug Delivery System

Improvement in oral bioavailability

A significant factor limiting the bioavailability of numerous medications that are poorly water soluble is absorption that is dependent on dissolution rate. The ability of SNEDDS to deliver the drug to the gastrointestinal tract (GIT) in solubilized and nano emulsified form (droplet size between 1-100 nm) and subsequent increase in specific surface area allows for more efficient drug transport through the intestinal aqueous boundary layer and through the absorptive membrane, improving bioavailability.

Decreased in inter- subject and intra-subject variability and food effects

Numerous medications exhibit significant intra- and inter-subject variation in absorption, which reduces the effectiveness of the medication and increases patient non-compliance. Food has a significant impact on how well a medicine works therapeutically in the body. Such medications benefit greatly from SNEDDS.

Ability to deliver peptides that are prone to enzymatic hydrolysis in GIT

The ability of SNEDDS to carry macromolecules such hormones, peptides, enzyme substrates, and inhibitors, as well as their capacity to provide protection from enzymatic hydrolysis, distinguishes them from conventional drug delivery systems. If polysorbate-20 is used as an emulsifier in the formulation of the microemulsion, the intestinal hydrolysis of the prodrug by cholinesterase can be prevented. These systems spontaneously develop without the use of energy or heating, making them suited for thermolabile medications like peptides.

Ease of manufacture and scale-up

One of the most significant advantages that sets SNEDDS apart from other drug delivery methods, such as solid dispersions, liposomes, nanoparticles, etc., dealing with enhancement of bio-availability, is its ease of fabrication and scale-up. For large-scale manufacture, SNEDDS needs extremely basic and affordable manufacturing facilities such a simple mixer with an agitator and volumetric liquid filling equipment.[2]

Need for formulating SNEDDS

There are a number of solubility improvement technologies that have been published in the literature, as well as several in-depth studies and publications that analyse issues with low water solubility. Basically, a medicine may not dissolve well in aqueous medium or may not dissolve well both in aqueous and organic media. For the first scenario, a variety of formulation strategies are available to increase saturation solubility, including solubilization techniques (solvent mixes, etc.) and specific or non-specific complexation (solid dispersions in polymers or usage of cyclodextrin). However, because they rely on the use of solvents for

formulation formation and pharmaceuticals that are weakly soluble in both aqueous and organic media, most of these procedures are of limited success, if not useless, and other options must be utilised to boost dissolution rate. (salt formation, reduction in particle size, prodrug, etc.).[3]

Dosage Forms from SEDDS [4]

SEDDS are usually limited by liquid dosage forms, because many excipients used in SEDDS are not solid at room temperature. In view of the advantages and limitations of SEDDS, various dosage forms of SEDDS have been extensively exploited in recent years, as they frequently represent more effective alternatives to conventional liquid SEDDS.

Dry emulsions

Dry emulsion formulations are typically prepared from oil in water (O/W) emulsions containing a solid carrier in the aqueous phase by freeze-drying, spray drying or rotary evaporation. The dry emulsions spontaneously disperse in vivo or when exposed to an aqueous solution. Dry emulsions can be used for further preparation of capsules and tablets. A exciting finding in this field is the newly developed enteric-coated dry emulsion formulation, which is potentially applicable for the oral delivery of peptide and protein drugs.

Self-emulsifying sustained/controlled-release tablets

In order to greatly reduce the amount of solidifying excipients required for transformation of SEDDS into solid dosage forms, Patil et al developed a gelled SEDDS. The patent diclosed by Schwarz et al showed that SE tablets are of great utility in obviating adverse effect. Inclusion of indomethacin into selfemulsifying tablets could increase the penetration efficiency through the gastrointestinal mucosal membranes, potentially reducing gastrointestinal bleeding. The newest improvement in the field of self-emulsifying tablet is the self-emulsifying osmotic pump tablet, where the elementary osmotic pump system was the carrier of the self-emulsifying tablet.

Self-emulsifying suppositories: Some investigators proved that Solid-SEDDS could increase not only gastrointestinal adsorption but also rectal/vaginal adsorption. Glycyrrhizin, which barely achieves therapeutic plasma concentrations by the oral route, can obtain fine therapeutic levels for chronic hepatic diseases by either vaginal or rectal self-emulsifying suppositories.

Self-emulsifying implants [5]

Researches on self-emulsifying implants have signifacantly improved the utility and application of solid-SEDDS. Carmustine (BCNU) is a chemotherapeutic agent used to treat malignant brain tumours. However, its short half-life hinders its therapeutic efficacy. In order to enhance its stability and intestinal permeablity, a self-emulsifying system of carmustine was designed and fabricated into wafers with flat and smooth surface by compression molding. The results demonstrated that the self-emulsifying system increased the in vitro half-life of BCNU up to 130 min compared with 45 min of intact BCNU. The in vitro release of BCNU from self-emulsifying PLGA wafers was prolonged to 7 day.

Need for Study

The combination of Sitagliptin and Metformin Hydrochloride is widely used for the management of type 2 diabetes mellitus (T2DM). Despite their effectiveness, to enhance the permeability & thus bioavailability, and gastrointestinal side effects, which can impact therapeutic

efficacy and patient compliance.

Self-nanoemulsifying drug delivery systems (SNEDDS) have emerged as a promising approach to overcome these challenges. SNEDDS enhance the solubility and dissolution of poorly water-soluble drugs, leading to improved absorption and bioavailability.

This formulation can also provide sustained drug release, reduce dosing frequency, and minimize gastrointestinal irritation.

The need for this study arises from the following factors:

Low Solubility and Bioavailability

Sitagliptin has high aqueous solubility, while Metformin Hydrochloride is highly hydrophilic but exhibits poor permeability.

SNEDDS can improve the dissolution rate and enhance intestinal absorption, leading to better therapeutic outcomes**.**

Gastrointestinal Side Effects

Metformin Hydrochloride is associated with gastrointestinal discomfort, including nausea and diarrhea. SNEDDS can facilitate drug absorption in the lymphatic system, reducing gastric irritation.

Improved Patient Compliance

Conventional oral dosage forms require frequent dosing, which may lead to non-adherence. SNEDDS can potentially provide controlled release, reducing the dosing frequency and enhancing patient convenience.

Enhanced Stability and Absorption

SNEDDS prevent drug precipitation in the gastrointestinal tract, ensuring stable and uniform drug distribution.

Methods for Preparation of Self-Nanoemulsifying Drug Delivery Systems (SNEDDS)

Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) are isotropic mixtures of oils, surfactants, and co-surfactants that spontaneously form oil-in-water nanoemulsions upon mild agitation in gastrointestinal fluids. Their preparation is simple, solvent-free, and suitable for poorly water-soluble drugs.

SNEDDS are generally prepared by mixing or heating techniques with systematic optimization through solubility studies and pseudo-ternary phase diagrams.

Simple Mixing Method (Conventional SNEDDS Preparation)[6]

Principle: Drug is dissolved in oil, surfactant, and co-surfactant mixture under stirring until a clear isotropic blend is formed.

Procedure:

1. Conduct solubility studies in oils, surfactants, and co-surfactants.
2. Select components showing highest solubility and emulsification ability.
3. Mix oil + surfactant + co-surfactant in appropriate ratios (typically 1:2–1:4).
4. Add the drug and stir until completely dissolved.
5. Optimize ratios using pseudo-ternary phase diagrams.
6. Store the isotropic mixture in airtight containers until use.

Aqueous Phase Titration (Pseudo-Ternary Phase Diagram Method)[7]

Principle: Determines the optimum oil–surfactant–co-surfactant region for nanoemulsion formation.

Procedure:

1. Prepare Smix (surfactant–co-surfactant) in various ratios like 1:1, 2:1, 3:1.
2. Add oil to Smix in varying proportions.

3. Slowly titrate with water while gently stirring.
4. Observe clarity, phase separation, and transparency.
5. Select the nanoemulsion region (transparent, low viscosity).
6. Use this region to choose SNEDDS compositions.

Heating and Stirring Method [8]

Principle: Mild heating helps dissolve drugs with high melting points and improves mixing.

Procedure:

1. Heat the oil phase and surfactants to 40–60°C.
2. Dissolve the drug in the molten mixture.
3. Cool gradually under stirring until a clear mixture forms.
4. Fill into capsules.

Solidification Methods (Solid SNEDDS Preparation) [9]

Solidifying SNEDDS improves stability, handling, and converts liquid SNEDDS to capsules/tablets.

A. Adsorption onto Solid Carriers

- Liquid SNEDDS is adsorbed onto porous materials like Aerosil, Neusilin, Syloid.
- Dry powder is filled into capsules or compressed into tablets.

B. Spray Drying

- Liquid SNEDDS emulsions are atomized into a drying chamber.
- Powder microspheres containing SNEDDS are formed.

C. Freeze Drying (Lyophilization)

Convert SNEDDS into dry powders using cryoprotectants like mannitol or trehalose.

Melt Granulation Method [10]

Principle: The lipid and surfactant melt during granulation, facilitating SNEDDS formation upon hydration.

Reference

1. Akiladevi D, Prakash H, Biju GB, Madumitha N. Nano-novel approach: Self nano emulsifying drug delivery system (SNEDDS)-Review article. Res J Pharm Technol. 2020;13(2):983-90.
2. Kumar RS, Sureshkumar R. A review on solid supersaturable SNEDDS. Res J Pharm Technol. 2020;13(7):3530-5.
3. Senapati PC, Sahoo SK, Sahu AN. Mixed surfactant-based (SNEDDS) self-nanoemulsifying drug delivery system presenting efavirenz for enhancement of oral bioavailability. Biomed Pharmacother. 2016;80:42-51.
4. El-Dakroury WA, Zewail MB, Elsabahy M, Shabana ME, Asaad GF. Famotidine-loaded solid self-nanoemulsifying drug delivery system demonstrates exception al efficiency in amelioration of peptic ulcer. Int J Pharm. 2022;611:121303.
5. Chaudhuri A, Shrivastava N, Kumar S, Singh AK, Ali J, Baboota S. Designing and development of omega-3 fatty acid based self-nanoemulsifying drug delivery system (SNEDDS) of docetaxel with enhanced biopharmaceutical attributes for management of breast cancer. J Drug Deliv Sci Technol. 2022;103117.
6. Pouton CW. Formulation of self-emulsifying drug delivery systems. Adv Drug Deliv Rev. 1997;25:47–58.
7. Shafiq-un-Nabi S, Shakeel F, Talegaonkar S. Formulation of self-nanoemulsifying drug delivery systems using phase diagrams. J Pharm Pharm Sci. 2007;10:434–445.
8. Tang B, Cheng G, Gu JC. Development of solid SNEDDS. Drug Dev Ind Pharm. 2008;34:931–938.

9. Gupta S, Chavhan S, Sawant KK. Self-nanoemulsifying drug delivery systems for enhancing solubility. AAPS PharmSciTech. 2011;12:372–382.
10. Sharma A, Jain CP. SNEDDS based on melt granulation. Asian J Pharm. 2010;4:212-217