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Self-Nanoemulsifying Drug Delivery Systems (SNEDDS): An innovative Approach

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Abstract:

Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) represent an innovative and efficient 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 Satranidazole and Ofloxacin—two potent antimicrobial agents used in the treatment of mixed bacterial and protozoal infections, particularly in the gastrointestinal and genitourinary tracts. Both drugs exhibit solubility and permeability limitations that restrict their oral bioavailability and therapeutic efficacy. The SNEDDS approach utilizes an isotropic mixture of oils, surfactants, and co-surfactants that spontaneously form fine oil-in-water nanoemulsions upon mild agitation in gastrointestinal fluids, facilitating enhanced absorption. The review highlights key formulation aspects including selection of oil phase, surfactant, and co-surfactant based on solubility studies, emulsification efficiency, and construction of pseudo-ternary phase diagrams. Evaluation parameters such as globule size, zeta potential, emulsification time, thermodynamic stability, drug loading efficiency, and in vitro drug release are critically discussed. The SNEDDS formulation of Satranidazole and Ofloxacin offers a promising strategy for improving oral bioavailability, providing rapid onset of action, and achieving synergistic antimicrobial activity with reduced dosing frequency and gastrointestinal side effects.

Keywords: SNEDDS; Satranidazole; Ofloxacin; Nanoemulsion; Bioavailability enhancement; Solubility improvement; Antimicrobial therapy.

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. Such medications benefit greatly from SNEDDS.

There are several academic articles stating that SNEDDS performance is independent of meals and that SNEDDS give repeatability of plasma profile.

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.

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

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. [5]

Need for Study

Satranidazole, an antiprotozoal drug, and Ofloxacin, a broad-spectrum fluoroquinolone antibiotic, are frequently co-administered for the management of mixed anaerobic and aerobic infections, particularly in gastrointestinal and gynecological conditions. However, both drugs suffer from significant limitations in conventional oral dosage forms. Satranidazole exhibits poor aqueous

solubility and variable absorption, leading to inconsistent plasma concentrations and reduced therapeutic efficacy. Similarly, Ofloxacin, although moderately soluble, demonstrates limited bioavailability due to pH-dependent solubility and first-pass metabolism. These shortcomings often necessitate higher doses, which increase the risk of dose-related side effects such as gastrointestinal irritation and microbial resistance.

To overcome these issues, there is a pressing need for a drug delivery approach that can enhance solubility, improve dissolution rate, and ensure consistent bioavailability of both drugs.

The Self-Nanoemulsifying Drug Delivery System (SNEDDS) provides an attractive solution by delivering the drugs in a pre-dissolved, nano-sized form that readily disperses in gastrointestinal fluids, enhancing absorption and therapeutic effectiveness.

Thus, developing and evaluating a SNEDDS formulation of Satranidazole and Ofloxacin could not only improve patient compliance through reduced dosing frequency but also achieve better therapeutic outcomes by minimizing variability and maximizing bioavailability.

Methods for Preparation of Self-Nanoemulsifying Drug Delivery Systems (SNEDDS)[6-9]

Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) are isotropic mixtures of oils, surfactants, and co-surfactants that form nanoemulsions (20–200 nm) upon dilution in gastrointestinal fluids.

Their preparation involves simple mixing, solubility screening, and optimization via pseudo-ternary phase diagrams.

Simple Mixing Method

Principle:

Drug is dissolved in a blend of oil, surfactant, and co-surfactant to form a clear isotropic preconcentrate.

Procedure:

1. Perform solubility studies in oils (e.g., Capryol, Labrafac), surfactants (e.g., Tween 80), and co-surfactants (e.g., Transcutol).
2. Mix oil + surfactant + co-surfactant in various Smix ratios (1:1 to 1:4).
3. Add drug and stir until a clear mixture forms.
4. Store in airtight vials.

Aqueous Titration Method (Pseudo-Ternary Phase Diagram Method)

Principle:

Determines the optimal ratio of oil, surfactant, and co-surfactant for nanoemulsion formation.

Procedure:

1. Prepare different Smix ratios (1:1, 2:1, 3:1).
2. Add oil in varying proportions.
3. Titrate with water and observe clarity/transparency.
4. Construct pseudo-ternary diagrams using the water titration method.
5. Select compositions falling within the nanoemulsion region.

Heating and Mixing Method

Principle: Useful for drugs with high melting points or poor solubility.

Procedure:

1. Heat oil, surfactant, and co-surf actant (40–60°C).
2. Dissolve the drug completely.
3. Cool to room temperature to obtain an isotropic system.

Solid SNEDDS (S-SNEDDS) Preparation Methods

A. Adsorption onto Solid Carriers

Principle:

Liquid SNEDDS is adsorbed onto porous excipients to form free-flowing powder.

B. Spray Drying Method

Principle:

SNEDDS is spray-dried with solid carriers to obtain a dry particulate system.

Method:

1. Prepare SNEDDS emulsion.
2. Mix with carriers (e.g., lactose, maltodextrin).
3. Spray dry at controlled temperature.

C. Freeze Drying (Lyophilization)

Principle: Diluted SNEDDS is frozen and sublimed using cryoprotectants (mannitol/ trehalose).

D. Melt Granulation Method

Principle: Lipid excipients melt and bind powders during granulation, forming S-SNEDDS.

Microemulsion-Based SNEDDS Optimization

Principle: Sometimes a microemulsion is prepared first to identify stable nanoemulsion regions, followed by SNEDDS formulation.

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