JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue

JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)

An International Scholarly Open Access, Peer-reviewed, Refereed Journal

SNEDDS: Self-Nanoemulsifying Drug Delivery System

Nazmeen Kausar,

Department of Pharmaceutics, RBVRR Women's College of Pharmacy, Affiliated to Osmania University, Hyderabad.

ABSTRACT:

The lipid- based drug delivery is extensively reported within the literature for the enhancing drug solubility, permeability, and bioavailability. Self-Nano emulsifying drug delivery systems (SNEDDS) are one of the emerging strategies developed to tackle the issues associated with the oral delivery. Self-Nano emulsifying drug delivery systems (SNEDDS), which are Isotropic mixtures of oils, surfactants, solvents, and co-solvents/surfactants, can be used for the formulations to improve the over absorption of drug it depends on many formulations related parameters, such as surfactant concentration, Oil /surfactant ratio, polarity of the emulsion, droplet size and charge, all of which in essence determine the self-emulsification ability. With the growing interest in this field, it is an increasing need for selection of excipients guidelines to obtain effective and safe delivery system with improved bioavailability. The aim of this study is to present the composition, role of various excipients, factors, Biopharmaceutical aspects affecting the formulation.

Keywords: Bioavailability, Self-Nano Emulsifying Drug Delivery Systems (SNEDDS), lipid formulation classification system (LFCS).

INTRODUCTION:

SNEDDS are defined as isotropic mixtures of natural or synthetic oils, solid or liquid surfactants, one or more hydrophilic solvents and co-solvents/surfactants. Their potential is to enhance the bioavailability is due to their ability to spontaneously form a stable oil-in-water (o/w) emulsion once agitated with the aqueous phase at a low energy requirement. Upon oral administration the stomach's digestive motility provides the necessary emulsion (20-200nm) with a large interfacial area for the drug absorption.

This spontaneous formation is a result of the interaction between the drug, lipid carriers, and surfactants within the formulation. The result is a uniform and stable nano emulsion that maximizes the drug's solubility and bioavailability. However, being liquid in nature has several problems, such as rancidity, leakage or incompatibility with the capsule shell, drug precipitation during manufacturing or in storage. Applications of SNEDDS are vast, spanning from oral to topical and parenteral drug delivery in particular their role in improving the delivery of poorly water-soluble drug has opened new avenues for treating various medical conditions more effectively. As research and development in this field continue to advance, SNEDDS promised to play a pivotal role in the future of pharmaceutical science.

Selection of Appropriate Drug Candidates for SNEDDS

The SNEDDS system is a novel approach to enhance oral bioavailable of drugs that are poorly water-soluble drugs in biopharmaceutical classification system can categorize into four classes, comparison to Class I and Class III drugs, Class II and Class IV drugs have lower
aqueous solubility.

In the Biopharmaceutical Classification System (BCS), Class II and Class IV drugs have lower aqueous solubility compared to Class I and Class III. However, SNEDDS can effectively increase the solubility and oral bioavailability of Class II and Class IV drugs. This system addresses issues of enzymatic degradation associated with Class I and Class III drugs while improving overall drug solubility and bioavailability.

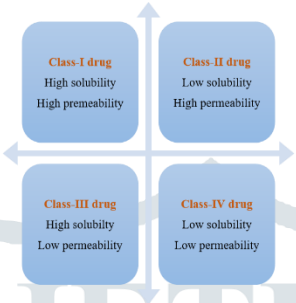

Figure 1: Biopharmaceutics Classification System

ADVANTAGE OF SNEDDS

- SNEDDS improves the pharmacokinetics of the administered drug which reduces dosage frequency.
- SNEDDS managed controlled drug delivery profile.
- In terms of interfacial area SNEDDS facilitate for better drug partitioning between water and oil.
- SNEDDS are most stable formulation and uncomplicated manufacture techniques.
- They possess high drug payload.
- Drug diffusion with SNEDDS allowed for a wider distribution in the stomach and GI tract, thus reducing the irritation caused by excessive contact between the gut walls and the drugs.
- The drug is protected from the aggressive environment in the GI tract by SNEDDS.
- SNEDDS manage controlled drug delivery profile.
- In terms of surface interfacial area, SNEDDS facilitate for drug partitioning between water and oil.
- SNEDDS improve the rate and extent of the drug absorption.
- SNEDDS enables the selective drug targeting towards precise absorption window in GI tract.

Disadvantages of SNEDDS

- Traditional dissolve procedures are not effective for SNEDDS because they rely on digestion prior to disintegration.
- For good evaluation, SNEDDS in vitro study require more research and validation.
- More research into the in vitro-in vivo correlations of SNEDDS is needed.
- Drugs' chemical instabilities.
- Surfactant concentrations in the formulation are higher (30-60%).
- Higher production cost.
- Lower drug incompatibility and stability.
- Possibility of drug leakage and precipitation.

Factors affecting SNEDDS

- SNEDDS aren't suitable for the drugs, which are administered at very high dose.
- The drug's solubility in water is limited, lipids are the most difficult to administer by SNEDDS.
- The capability of SNEDDS to maintain the drug in a solubilized state is determined by the drug's solubility in the oil phase.
- Sometimes there might be a risk of precipitation if the surfactant or co-surfactant is to a greater extent for drug solubilization.

Composition of SNEDDS

The SNEDDS is mainly composed of the following.

- ♦ Drugs
- ♦ Oil
- ♦ Surfactant
- ♦ Co-surfactant
- ♦ Co-solvents

Drugs

SNEDDS are prepared for drugs that have a poor water solubility. For most circumstances, BCS class II and class IV drugs are used in manufacture of SNEDDS. Physicochemical parameters of the drug, such as log P, p Ka, molecular structure and weight, presence of ionizable groups, and quantity, all significant impact on SNEDDS performance. High melting point drugs with log P value of 2 are poorly suitable for SNEDDS. While, lipophilic drugs having log P values greater than 5, are suitable for SNEDDS formulation. Examples include Itraconazole, nifedipine, Vitamin E, simvastatin, danazol, ketoconazole, mefenamic acid, carbamazepine, glipalamide, cyclosporine-A, amphotericin B, furosemide, acetazolamide, ritonavir, paclitaxel etc.

Oil

- Oils are soluble in the required dose of the lipophilic drug and facilitate self-emulsification.
- Natural edible oils remain the logical and desired oil ingredients, but they show relatively low drug-loading capacity and poor emulsification efficiency.
- Modified medium-chain triglycerides (MCTs) and long-chain triglycerides (LCTs) are mostly employed to improve the drug solubility in the formulation of SNEDDS.
- MCTs are preferred because of their better solubilizing ability and self-emulsification capacity and it increase the drug transport through the portal vein, but they have a limited capacity to enhance the lymphatic transport of the drugs.
- Conversely, LCTs are by passing the hepatic first pass metabolism and increase the transport of drugs through lymph vessel.
- Thus, a mixture of MCTs and LCTs can be considered to meet the optimum parameters and improve pharmacokinetics.

General Class	Examples	Commercial Name
Fixed oils Medium Chain triglycerides	Castor Oil, Soyabean oil Triglycerides of Capric/ Caprylic acids Triacetin	Miglyol 812, Labrafac CC, Crodamol GTCC Captex 500
Medium chain mono-and diglycerides	Mono and Diglycerides of capric/caprylic acids	Imwitor 742, Capmul MCM
Long chain monoglycerides	Glyceryl momooleate	Peceol,Capmul GMO
Propylene glycol fatty acid esters	Propylene glycol monocaprylate Propylene Glycol dicaprylate/caprate	Capryol 90, Capmul PG-8, Miglyol 840, Captex 200
Fatty acids	Oleic acid Caprylic acid	Crossential O94 -
Fatty acids esters	Ethyl oleate	Crodamol EO
Vitamins	Vitamin E	-

SURFACTANTS:

- Surfactant will improve bioavailability by different mechanism
- Improve drug dissolution
- Increase intestinal epithelial permeability
- Increase tight junction permeability
- Different groups of surfactants can be used for the Nano emulsion stability and formulating of SNEDDS, such as:(i) ionic(ii) cationic(iii) anionic(iv) zwitterionic (v) nonionic.
- The most widely used are the non-ionic surfactants with a relatively high HLB.
- Usually, a stable SNEDDS formulation requires concentration 30% -60% w/w. However; high concentration of surfactant may cause irritation to gastric mucosa. The safety is major considerable parameter for selection of the Surfactant molecule.
- The selection of a particular surfactant for formulation depends upon its HLB value and safety issue.

Co-Surfactant:

- Co-surfactant is similar function to surfactant unit's-surfactant was added along with surfactant until to increases the ability of Surfactant to improving water solubility of poorly water-soluble drug.
- The co-surfactant is able to prevent the Interfacial Fluidity.
- Allow interfacial film sufficient flexibility and reduces its overall effect of surfactant.

Co-Solvent:

Medium chain alcohol C3-C8 are preferred, they increase fluidity of interface and entropy of the system.

Commonly used Co-solvent: Ethanol, Propylene glycol (PG), Polyethylene glycol (PEG), Glycerin, Poloxyethylene.

The newer cosolvents like TranscutolTM and GlycofurolTM have numerous advantages over the traditional ones, including better stability and less volatility.

Viscosity Enhancers

The viscosity of emulsions can be altered by using the additional material such as acetyl alcohol's, tragacanth, beeswax and stearic acids etc.

Antioxidant agents

lipophilic antioxidants e.g. alpha tocopherol, Propyl gallate, Ascorbic palmitate stabilize the oil content of SNEDDS formulation.

Polymers

Polymers matrix (inert) present in 5 to 40% w/w, which is not ionizable at physiological pH are able to form matrix.

Examples are hydroxypropyl methyl cellulose, ethyl cellulose, etc.

Preparation of SNEDDS

The Self-Nanoemulsifying drug delivery system (SNEDDS) is Prepared by following two ways.

1. Liquid SNEDDS preparation:

Preparation of self-Nanoemulsifying drug delivery system having the surfactant/co-surfactant ratio and oil/ surfactant/co-surfactant ratio, selected by the Pseudo ternary phase diagram. Different concentrations of oil, surfactant, and Cosurfactant are used to process a number of series of the formulation. The oil and surfactant were weighed in appropriate proportions, and the drug was dissolved in this mixture, which was then stored at room temperature.

2. Solid SNEDDS preparation:

Preparation of Self Nanoemulsifying drug delivery system (SNEDDS). Drug added into accurately weighed amount of oil in a screw capped vials and melted in water bath if necessary. Then with the help of positive displacement pipette the surfactant and cosurfactant are added to the oil mixture and stirred by a vortex to obtain homogeneous solution. Solid Self nanoemulsifying drug delivery system (S-SNEDDS) was prepared by adding selected liquid SNEDDS dropwise on suitable novel adsorbents like Neusillin, Aerosil and are mixed well with glass rod. The damp substance that obtained was sieved no. 120 and dried at room temperature.

METHODS OF PREPARATION OF SNEDDS

- High Pressure Homogenization
- Microfluidizatiion
- Sonication Method
- Phase inversion Method

High Pressure Homogenization

Dissolve the drug, oil, surfactant, and co-surfactant in a suitable solvent to form a clear solution. Transfer the solution to a high-pressure homogenizer. Apply high pressure and force the solution through a narrow gap or small orifice at high velocity. This process subjects the mixture to high shear forces, resulting in the formation of nano-sized emulsions. After homogenization, the solvent is evaporated to obtain the SNEDDS.

Microfludization

Dissolve the drug, oil, surfactant, and co-surfactant in an appropriate solvent to form a clear solution. Load the solution into a microfluidizer. Apply high pressure to force the solution through microchannels or interaction

chambers. As the solution passes through the microchannels, it experiences high shear and cavitation forces, leading to the formation of nanoemulsions. The resulting nanoemulsion is collected and further processed to remove the solvent.

Sonication

Dissolve the drug, oil, surfactant, and co-surfactant in a suitable solvent to form a clear solution. Transfer the solution to a suitable container. Place the container in an ultrasonic bath or sonicate. Apply ultrasonic energy to the solution for a specific duration. The ultrasonic waves create cavitation bubbles in the solution, leading to the formation of nano-sized droplets. Once the desired size is achieved, the solvent is evaporated under reduced pressure or by other suitable means.

Phase Inversion

Prepare two phases: an oil phase containing the drug, oil, and co-surfactant, and an aqueous phase containing the surfactant. Mix the two phases under stirring at a specific temperature. Initially, an oil-in-water (O/W) emulsion is formed. Continue stirring until a phase inversion occurs, resulting in the formation of a water-in-oil (W/O) nanoemulsion. The resulting nanoemulsion is further processed (e.g., solvent removal) to obtain the final SNEDDS.

EVALUATION OF SNEDDS

- Droplet Size (PS) and Polydispersity Index (PDI)
- Visual Inspection
- Self-Emulsification Time
- Robustness
- Percentage of Content
- Drug Content
- Invitro Study
- L-SNEDDS Equilibrium Solubility
- Thermodynamic Stability

Droplet Size (PS) and Polydispersity Index (PDI)

Dilute the SNEDDS formulation with an appropriate dispersant (e.g., water or buffer solution).
Use a suitable particle size analyzer (e.g., dynamic light scattering or laser diffraction) to measure the droplet size distribution.
Record the mean particle size (PS) and the polydispersity index (PDI), which indicates the width of the size distribution (lower PDI suggests better uniformity).

Visual Inspection:

Visually inspect the SNEDDS formulation for any signs of phase separation, creaming, precipitation, or other physical instability.
Record observations and note any changes in appearance over time.

Self-Emulsification Time:

Place a small volume of the SNEDDS formulation in a beaker or vial containing water or simulated gastric fluid.
Observe the time taken for the formulation to spontaneously form a homogeneous emulsion upon gentle agitation.
Record the self-emulsification time as the time elapsed until complete emulsification is achieved.

Robustness:

Subject the SNEDDS formulation to various stress conditions such as centrifugation, temperature cycling, and freeze-thaw cycles.

Evaluate any changes in physical appearance, droplet size, and drug content before and after stress testing.

Robust formulations should maintain stability and performance under these stress conditions.

Percentage of Content:

Analyze a sample of the SNEDDS formulation using an appropriate analytical method (e.g., high-performance liquid chromatography, UV-Vis spectroscopy) to quantify the drug content.

Calculate the percentage of drug content relative to the expected concentration based on the formulation recipe.

In Vitro Diffusion Study

Using the dialysis technique, in vitro diffusion tests are carried out to determine the release behavior of formulation from the liquid crystalline phase around the droplet.

Drug Content

The drug is extracted from pre-weighed SNEDDS by dissolving it in a suitable solvent. The drug content in the solvent extract was compared to a standard drug solvent solution using a suitable analytical method.

L-SNEDDS Equilibrium Solubility:

Determine the equilibrium solubility of the drug in the L-SNEDDS formulation.

Mix excess drug with the L-SNEDDS formulation and maintain the mixture under constant agitation for a sufficient period to reach equilibrium.

Analyze the concentration of the dissolved drug in the formulation using an appropriate analytical method.

Calculate the equilibrium solubility of the drug in the L-SNEDDS formulation.

Thermodynamic Stability:

Subject the SNEDDS formulation to accelerated stability testing under specific temperature and humidity conditions (e.g., ICH guidelines).

Monitor changes in physical appearance, droplet size, drug content, and other relevant parameters over time.

Assess the formulation's ability to maintain its physical and chemical stability under stress conditions.

Conclusion

In recent years, developments in SNEDDS research have been extensively investigated for improving the solubility and oral bioavailability of class II drugs. Self-Nanoemulsifying drug delivery system (SNEDDS) is an Isotropic mixture of oils, surfactants, Co-surfactant (Smix) and co-solvent. Under mild agitation, it emulsifies spontaneously in the aqueous phase to yield fine o/w Nanoemulsion. For the formulation of poorly water-soluble drugs, SNEDDS is a good alternative. SNEDDS enhances the dissolution of the drugs due to increased surface area on dispersion and Absorption rate of Drug molecule. The oral delivery of lipophilic drugs is often made possible by SNEDDS, is important to improve oral bioavailability. It is feasible to improve drug release by incorporating polymer into the mixture by using this method. SNEDDS appears to be a unique, industrially viable approach for future development.

References

1. Chandrasekhara Rao B, Vidyadhara S, Sasidhar R L C and Chowdary Y A. Design and Evaluation of Self-Nano emulsified Drug Delivery System (SNEDDS) of Docetaxel by Optimizing the Particle Size using Response Surface Methodology, IAJPS, 1(1), 2014, 35-45.

2. Girish C, Soni, Prajapati S K, Nirvesh Chaudhri. Self Nanoemulsion, Advance Form of Drug Delivery System, World Journal of Pharmacy and Pharmaceutical Sciences, 2014, 3(10), 410-436.

3. Jeevana Jyothi B, Sreelakshmi K. Design and Evaluation of Self-Nanoemulsifying Drug Delivery System of Flutamide, Journal of Young Pharmacists, 3(1), 2011, 4-8.

4. Lundin P, Bojrup M, Ljusberg-Wahren H, Westrom B, Lundin S: Enhancing effects of monohexanoin and two other medium-chain glyceride vehicles on intestinal absorption of desmopressin (dDAVP). Journal of Pharmacology & Experimental Therapeutics, 1997;282(2):585–590.

5. Payal Gupta, Pramod Kumar, Sharma, Nitin Kumar, Yogesh Pawar, Jitendra Gupta. Self_x0002_Nano Emulsifying Drug Delivery System, A Strategy to Improve Oral Bioavailability, World Journal of Pharmacy and Pharmaceutical Sciences, 3(5), 2014, 506-512.

6. Rajinikanth P S, Neo Woei Keat, Sanjay Garg. Self-nanoemulsifying Drug Delivery Systems of Valsartan, Preparation and In-Vitro Characterization, International Journal of Drug Delivery, 4(2), 2012, 153-163.

7. Shafiq S, Shakeel F, Talegaonkar S, Ali J, Roop K. khar, Sanjula B. Formulation development and optimization using nanoemulsion technique- A Review, European Journal of Pharmaceutics & Biopharmaceutics, 2007;8(2): E212-E17.

8. Wang L, Dong J, Chen J, Eastoe J, Li X: Design and optimization of a new self-nanoemulsifying drug delivery system. Journal of Colloid and Interface Science, 2009;330(2):443–448.