Review Article

Self-Emulsifying Drug Delivery System (SEDDS)

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ABSTRACT

Self-emulsifying drug delivery systems (SEDDS) are lipid-based formulations that have received a lot of attention recently in an effort to increase the oral bioavailability of drug that aren't highly water soluble. They are made up of isotropic mixture of natural or synthetic oils with surfactants and cosurfactants that self-emulsify to generate O/W nano or micro-emulsions when exposed to GI fluids while being mildly stirred up by the peristaltic motions of the GI tract (GIT). The typical droplet size should be between 20 and 200 nm. The oral absorption of drugs from SEEDS is greatly influenced by a number of variables, including surfactant concentration, oil/surfactant ratio, polarity of the emulsion, droplet size and charge. Due to the drug's increased solubility and decreased stomach irritability, this formulation enhances the bioavailability. Because over 40% of novel therapeutic molecules are being hydrophobic in nature suggests that SEDDS experiments will go on and that new therapeutic molecules created as SEDDS will eventually be available on the pharmaceutical market.

Keywords: Self-emulsifying drug delivery systems, isotropic, emulsions, bioavailability.

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INTRODUCTION

Self-emulsifying drug delivery systems (SEDDS), which are lipid-based formulations, have received a lot of attention recently in an effort to increase the oral bioavailability of medications that aren't highly water soluble[1]. SEDD are isotropic mixture of drug, oil, surfactant and co-surfactant. When put into an aqueous phase while being gently stirred, SEDDS spontaneously emulsify to generate fine oil-in-water emulsions. Medium-chain triglyceride oils and non-ionic surfactants, which are less hazardous, have recently been used to manufacture SEDDS. Following oral administration, these systems cause mild gastric movement and the formation of fine emulsions (or microemulsions) in the GIT. SEDDS can be used to dissolve hydrophobic medications so that they could be administered as concentrated solutions in a unit dosage form for oral administration, skipping the dissolution step that typically restricts the absorption of such medications. As a result, the process of hydrophobic medication absorption could take place independently of other circumstances that might have a favourable or unfavourable impact[2].

By significantly increasing their solubility and enhancing their dissolving characteristics, SEDDs are utilized as efficient method to increase the GIT absorption and oral bioavailability of poorly water-soluble medicines. SEDD formulations are also available in liquid (L-SEDDs) and solid (S-SEDDs) forms. In addition to easier process control, it is suggested that S-SEDDs will offer higher stability, reproducibility, and patient compliance[3].

Advantages [4]

- Quick Onset of Action.
- Scale-up and Manufacturing Simplicity.
- Ability to distribute peptides in the GIT that are susceptible to enzyme hydrolysis.
- Reduction in the Drug Dose.
- increased capability for loading drugs.

FORMULATION OF SEDDS

When creating a SEDDS, the following factors need to be taken into account:

Based on the drug's solubility, oils, surfactants, and co-solvents are chosen. SEDDS formulation is made by combining the medicine with an oil, surfactant, and cosolvent mixture. Design of the best SEDDS necessitates pre-formulation solubility and phase diagram studies because the medicine interacts with the self-emulsifying process to some amount when added to SEDDS, changing the optimal oil-surfactant ratio[4,5].

Preparation of SEDDS

By using a pseudo-ternary diagram, find out the stable nano emulsion region for that particular SEDD formulation. Consequently, the formulation was made using a particular

range of surfactants. Four sites were chosen from each phase diagram in the area where the water percentage is zero. The drug was introduced right away to the oil phase in a vial and blended with the aid of a vortex mixer. The oil-drug mixture was vortexed after a sufficient amount of S-mix was added, and then it was homogenized for 10 minutes. The amount of oil in each formulation was kept constant while the concentration of the surfactant mixture varied[5].

Excipients

a) Oil

In the SEDDS formulation, the oil is one of the most crucial excipients since it can solubilize the required dose of lipophilic dug.

Depending on the molecular make-up of the triglyceride, the lipophilic medication can either assist self-emulsification or increase the proportion of lipophilic drug delivered by the intestinal lymphatic system, enhancing absorption from the GI tract. For the creation of self-emulsifying formulations, long and medium chain triglyceride (LCT and MCT) oils with various saturation levels have been employed[6].

b) Surfactant

For the design of self-emulsifying systems, a variety of compounds with surfactant capabilities may be used, but the options are constrained because so few surfactants are suitable for oral use. The non-ionic surfactants with a comparatively high hydrophilic-lipophilic balance (HLB) are the ones that are most frequently advised. An important consideration when selecting a surfactant is safety[6].

The four main groups of surfactants are:

- Anionic surfactants
- Cationic surfactant
- Ampholytic surfactants
- Nonionic surfactants

c) Co solvent

The formation of an ideal SEDDS requires rather large concentrations of surfactants (often more than 30% w/w), hence the quantity of surfactant can be decreased via cosurfactant inclusion. Cosurfactant and surfactant work together to reduce interfacial tension to a very small, momentary negative value.

At this point, the interface would develop into finely dispersed droplets and then absorb more surfactants and surfactant/cosurfactants until their bulk conditions are sufficiently reduced to restore positive interfacial tension. For many non-ionic surfactants, however, the use of co-surfactant in self-emulsifying systems is not required. The choice of surfactant and co-surfactant is essential not only for the creation of SEDDS but also for drug's solubilization[6].

Drug Criteria

Drugs are categorized using the BCS (Bio-pharmaceutical categorization system) according to their permeability and solubility. SEDDS mostly use Class 2 (Low Solubility, High Permeability) drugs eg: Azithromycin, Carbamazepine, Carvedilol, Chlorpromazine, Cisapride Ciprofloxacin[4].

DOSAGE FORMS OF SEDDS

1) Oral delivery:

a) Self-emulsifying capsules:

Microemulsion droplets form after taking capsules containing traditional liquid SEDD formulations, and these then spread out in the GIT to reach the absorption location. An improvement in drug absorption cannot be anticipated if microemulsion phase separation becomes irreversible. Sodium dodecyl sulphate was added to the SEDD formulation to solve this issue[4,11].

b) Self emulsifying sustained / controlled release pellets:

As a multiple unit dosage form, pellets have a number of advantages over conventional solid dosage forms, including the ability to be manufactured with greater manufacturing flexibility, a reduction in intra- and inter-subject variability of plasma profile, and a reduction in GI irritation without compromising drug bioavailability[8].

2) Topical delivery:

The avoidance of the medications hepatic first pass metabolism and associated adverse consequences is simply one of the benefits of topical drug administration over other approaches [4,10].

3) Parenteral delivery:

Due to the extremely small amount of medicine actually delivered at the target site, parenteral administration of drugs with restricted solubility is a significant concern in industry[4].

4) Ocular and pulmonary delivery:

Medicines are often applied topically to the affected area to treat eye diseases. O/w microemulsion have been studied for ocular administration to dissolve poorly soluble drugs, enhance absorption, and achieve prolong release profile[4,10].

EVALUATION

Physical characterization

1) Thermodynamic studies

The kinetic stability of the formulation has traditionally been determined using thermodynamic studies. Any nano emulsion must not exhibit any signs of phase separation, creaming, cracking or coalescence will pass the test.

a) Centrifugation test:

In this experiment, the formulations underwent a 15-minute centrifugation at 6000 rpm. The formulations with

no phase separation passed in this test and were taken for a freeze-thaw stress test.

b) Freeze thaw cycle:

Three cycles of the freeze-thaw cycle were conducted at room temperature, -20°c, and +40°c. Then formulations were kept at each temperature for at least 48 hours[5,9].

2) Identification of self-emulsification time

The self-emulsification time was determined using a USP II dissolution device (Paddle type). In each dissolution vessel, 500 mL of distilled water was placed under continuous stirring (50 rpm) at 37°C. The media was mixed with 100 L of the SEDDS formulation, and the period of time it took for the emulsion to form was measured as the self-emulsification time. Accordingly, a decrease in the emulsification time would result from a rise in surfactant concentration since high surfactant content will increase the water infiltration at the water-oil contact. The creation of liquid crystals causes swelling at the contact, which makes emulsification easier[5].

3) Cloud point measurement

The cloud point was defined as the temperature at which clear emulsion starts to become cloudy. One ml of each formulation was taken, diluted in 200 ml of distilled water, and then placed on the water bath to progressively raise the temperature. By visual inspection, the time for cloud points of stable formulations was recorded in triplicate. A higher cloud point denotes more temperature resistance. Surfactant solubility decreases as temperature rises. The higher cloud point indicates the stability of formulation in GIT[5].

4) Droplet size and zeta potential

The most important factor in the assessment of SEDDS is the size of the droplets following self-emulsification. Smaller droplet size and greater surface area can result in high dissolution and high absorption. The formulations were diluted up to 100 times with distilled water (dilution factor 100), and photon correlation spectroscopy was used to determine the droplet size and polydispersity index of each formulation. Using the Delsa Nano C, the zeta potential was calculated by measuring the light scattering at 25 °C and a 90 ° angle[6,7].

5) Turbidity measurement

By determining whether the dispersion approaches equilibrium quickly and in a consistent manner, this determines effective self-emulsification reproducible time. These measurements are made using turbidity meters, most frequently the Orbeco-Helle and the Hach turbidity meters. Every 15 seconds, the optical clarity of the formulation is measured using an instrument connected to a dissolution device in order to calculate the emulsification time and the clarity of the generated nano- or microemulsion. Additionally, spectroscopic analysis of optical clarity can reveal turbidity[7].

CONCLUSION

Hydrophobic compounds can be delivered by using SEDD formulation, which can be optimized by various methods such as droplet size, zeta potential, polydispersity index etc. For a stable formulation, the surfactant and co-surfactant combination utilized in formulation preparation was essential. Drug formulations with low aqueous stability may be used in self-emulsifying drug delivery systems. The further development of this technology, SEDDS, will open up new opportunities for drug delivery system applications. SEDDS have demonstrated some promise in increasing the oral bioavailability of insufficiently water-soluble and drugs are traditionally dissolved in oils and blended with the appropriate solubilizing agents to create SEDDS.

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