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A Review on SNEDDS

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Abstract:
SNEDDSs are composed of an oil phase, surfactant, and cosurfactant or cosolvent. SNEDDSs characteristics, their ability to dissolve a drug, and in vivo considerations are determinant factors in the choice of SNEDDSs excipients. A SNEDDS formulation can be optimized through a phase diagram approach or statistical design of experiments. The characterization of SNEDDSs includes multiple orthogonal methods required to fully control SNEDDS manufacture, stability, and biological fate. Encapsulating a drug in SNEDDSs can lead to increased drug loading capacity, solubilization, stability in the gastrointestinal tract, and absorption, resulting in enhanced bio-availability. The transformation of liquid SNEDDSs into solid dosage forms has been shown to increase stability and patient compliance.

Keywords: Self-nano emulsifying drug delivery systems (SNEDDS); Solubility improvement; Curcumin and Thymoquinone; Gastrointestinal tract; Combined therapeutic effects.

INTRODUCTION

Nearly 90% of the medication candidates on the market today have limited bioavailability and low water solubility. The formulation design for a particular drug has grown increasingly complicated as a result of these difficult problems. Drug formulators must seek out novel formulation technologies that can guarantee successful therapies for people in need to overcome these obstacles.

Self-nano-emulsifying drug delivery systems (SNEDDS) are relatively more in demand technologically among self-emulsifying formulation systems. These systems have demonstrated the ability to decrease slow,

incomplete drug dissolution and speed up the formation of the drug's solubilized phase, which is highly effective for systemic absorption. SNEDDS are mostly liquid isotropic mixes containing active medicinal ingredients, lipids, surfactants, and water-soluble co-solvents. These mixtures can solidify to form solid SNEDDS. SNEDDS can create ultrafine emulsions (droplet size between 10 and 200 nm) in an aqueous phase, such as the upper portion of intestinal material, with gentle agitation.

Lipid-based self-nano emulsifying drug delivery systems using bioactive oils (SNEDDSs) are appealing nanoparticle dosage forms that offer synergistic therapeutic effects in addition to increased solubility. They also improve the intestinal absorption of poorly water-soluble medications without reducing their effectiveness. It is possible to encapsulate Bio-SNEDDSs in either soft or hard gelatin capsules to preserve their physical and chemical stability and reduce fluctuations in patients' plasma profiles.

The ability of SNEDDS to promote transcellular absorption by increasing membrane fluidity, permitting paracellular transport by opening tight junctions, avoiding the hepatic first-pass effect, lowering cytochrome P-450 metabolism, and safeguarding the drug from enzymatic degradation may be the reason for the enhancement of drug absorption. [27-29]

Both soft and hard gelatin capsules can hold liquid SNEDDS, but doing so has some drawbacks, such as higher production costs, excipients that are incompatible with the capsule's shell and may cause swelling or shrinkage of the shell, formulation leakage, and drug precipitation if kept at lower temperatures.[30] Turning liquid SNEDDS into solid dosage forms will help to solve these problems by increasing the drug's solubility, bioavailability, and stability of solid dosage forms. To convert liquid SNEDDS into S-SNEDDS, several procedures are used, including spray drying, adsorption onto solid carriers, melt extrusion, and melt agglomeration.[31]

The simplest approach is physical adsorption onto solid carriers, which just requires the physical mixing of liquid SNEDDS onto solid carriers to produce free-flowing powders that may then be placed into hard gelatin capsules or compacted into tablets following the inclusion of suitable excipients. [32]

Among all solidification techniques, the adsorbent approach is the simplest, quickest, and most cost-effective to construct. Silica compounds, which have a high ability to adsorb lipids (oils) and produce a free-flowing powder, are the ideal materials for surface adsorption. This free-flowing powder can either be compressed into tablets or encapsulated in hard gelatin capsules using a one-step process.

COMPONENTS OF SNEDDS:

The physical mixture of oil, surfactant, and co-surfactant employed in the formulation of SNEDDS in various literature surveys is used in various ratios. To make the SNEDDS preparation, the majority of the literature uses surfactant and co-surfactant mixtures (Smix) with oil in various ratios.

Oil: The droplet size of the nanoemulsion, drug solubility, and the biological fate of nanoemulsions and pharmaceuticals are all greatly influenced by the physicochemical characteristics of an oil, such as molecular volume, polarity, and viscosity. Therefore, the oil phase is essential in the creation of SNEDDS. Typically, the oily phase for the formulation of SNEDDS is chosen based on its ability to solubilize the selected drug candidate. This helps the SNEDDS achieve the greatest drug loading feasible. The chosen oil must be able to create nano-emulsions with extremely small droplet sizes. As a compromise between the drug's potential for solubilization and the simplicity with which a nanoemulsion with the required qualities may generate, the oily phase is commonly used. Long-chain triglycerides and fixed oils (like soybean oil) with excessively long hydrocarbon chains are known to be challenging to nano-emulsify. Oils with short chains or low molecular volumes, such as medium-chain monoglycerides and fatty acid esters (like ethyl oleate), and oils with moderately long chains (medium-chain triglycerides), on the other hand, are easier to nano emulsify. The nanoemulsion size is directly related to the oil's lipophilicity and the amount of oily phase present in SNEDDS. For example, castor oil, sesame oil, hydrolyzed corn oil, corn oil, olive oil, soybean oil, and soyabean oil isopropyl myristate. We can use one of the therapeutically active ingredients as an oil.

- **Black seed oil (therapeutically active excipient):**

Black seed oil is used to produce chemically rich SNEDDS for the first time. Thymoquinone (THQ), thymohydroquinone, dithymoquinone, thymol, carvacrol, nigellicine, nigellidine, and -hedrin are the active components in fixed oil made from pure seeds. With 4.59 mg/g of Black seed oil, THQ (2-isopropyl-5-methylbenzo-1, 4-quinone) has been used to identify the majority of the primary effects. THQ is the component with the highest bioactivity, but because it is a hydrophobic molecule, it is difficult to saturate (549-740 mg/ml in aqueous solutions), which limits its use in pharmaceutical formulations.

- **Surfactant: :** For the creation of SNEDDS, selecting the proper surfactant is important. The process of nano emulsification, the self-nano emulsification region, and the size of the nanoemulsion droplets are all greatly affected by the HLB value (in oil), cloud point, viscosity, and affinity of the surfactant for the oily phase. The amount of surfactant in SNEDDS has an important influence on the droplet size of nanoemulsions. It is important to consider a surfactant's regulatory status and suitability for the desired route of administration when selecting one. Non-ionic surfactants are the most common ones employed in the creation of SNEDDS. Although the non-ionic surfactant is polar and does not carry a charge, it gets its water solubility from very hydrophilic groups like polyoxyethylene or hydroxyl, like tween, span, kolliphore, etc. The non-ionic surfactant SMEDDS formulation is used to construct a stable self-nano emulsifying drug delivery system with high HLB values and surfactant capacity ranges of 30–60% w/w of the preparation. (SMEDDS). The preparation rapidly disperses in fluid media and produces oil/water droplets quickly due to polar groups and high HLB surfactants. Non-ionic surfactants are amphiphilic by nature and have a respectably high hydrophobic drug solubilization capability.

- **Co-surfactants: :** For the creation of SNEDDS, selecting the proper surfactant is important. The process of nano emulsification, the self-nano emulsification region, and the size of the nanoemulsion droplets are all greatly affected by the HLB value (in oil), cloud point, viscosity, and affinity of the surfactant for the oily phase. The amount of surfactant in SNEDDS has an important influence on the droplet size of nanoemulsions. It is important to consider a surfactant's regulatory status and suitability for the desired route of administration when selecting one. Non-ionic surfactants are the most common ones employed in the creation of SNEDDS. Although the non-ionic surfactant is polar and does not carry a charge, it gets its water solubility from very hydrophilic groups like polyoxyethylene or hydroxyl, like tween, span, kolliphore, etc. The non-ionic surfactant SMEDDS formulation is used to construct a stable self-nano emulsifying drug delivery system with high HLB values and surfactant capacity ranges of 30–60% w/w of the preparation. (SMEDDS). The preparation rapidly disperses in fluid media and produces oil/water droplets quickly due to polar groups and high HLB surfactants. Non-ionic surfactants are amphiphilic by nature and have a respectably high hydrophobic drug solubilization capability.
- **Co-solvent:** Co-solvents enhance the solubility and facilitate the large-scale hydrophilic surfactant or drugs dissolving in the lipid base. They lower the overall negative impact of the surfactant. Examples include propylene glycol, polyethylene glycol, and ethanol (suitable for oral administration). Solvents can serve as co-surfactants even in nanoemulsion systems. Alcohols and other volatile co-solvents, on the other hand, have the disadvantage of evaporating into the soft gelatin or hard-sealed gelatin capsule shells in conventional SNEDDS, leading to drug precipitation. These excipients are rarely utilized in conjunction with hard gelatin capsule formulations because of their hygroscope and subsequent effects on gelatin moisture content, which may compromise capsule physical integrity. Poorly water-soluble drugs for soft gelatin capsules are prepared using propylene glycol, a humectant and plasticizing monomer solvent that is approved for use in pharmaceutical formulations.
- **Other components:** various constituents may be flavors, antioxidant agents, and pH adjusters.

CONCLUSION

Despite the above-mentioned enhancements and modifications, SNEDDSs still need to have a few issues fixed before they can be considered commercially viable. Understanding the mechanisms of action of different SNEDDS formulations, pharmacokinetic research, particularly on human subjects, and cost-effectiveness should be prioritized in future studies. They should also focus on its commercial use.

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