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SELF EMULSIFYING DRUG DELIVERY SYSTERM: A REVIEW

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Abstrat: Formulators have always favored the oral route, which has dominated over alternative administration routes. Low and inconsistent bioavailability, primarily due to inadequate water solubility, is the main issue with oral medication formulations. Because of their limited bioavailability, over 40% of novel chemical entities have poor water solubility and pose a serious threat to the current drug delivery method. Drugs can become more soluble in water through a bunch of processes, including complex formation, solid dispersion, and salt production, but the Self Emulsifying Drug Delivery System (SEDDS) is receiving more attention as a means of enhancing the pharmaceuticals that are lipophilic and soluble. Ideally, SEDDS are isotropic blends of medication, oil, surfactant, and/or co surfactant. After being administered, these systems spread quickly in the gastrointestinal system. fluid, producing solubilized dug micro- and nano-emulsions.This results in in situ medication solubilization that allows it to be absorbed through lymphatic channels, avoiding the first-pass hepatic impact. This review provides a thorough overview of SEDDS, which shows promise as a solution to the issue of poorly soluble compounds.

Keywords: self emulsifying drug delivery system, solubility, bioavalability, poorly-soluble, surfactants, cosurfactants.

Introduction: Recently, formulation scientists who specialize in the medical field sector have faced intriguing issues related to the synthesis of inadequately soluble in water molecules. The issue of low bioavailability is linked to the poor water solubility of around 35–40% of novel medication candidates when administered orally. A bunch of initiatives have been undertaken in the oral formulation of such drugs to adjust the dissolution profile and thereby enhance the absorption rate, such as lowering particle size, using wetting agents, co-precipitation, and preparing solid dispersions. Recently, there has been an increased focus on lipid-based formulations as a means of increasing the bioavailability of drugs with limited water solubility. Among numerous such delivery methods, such as drug inclusion in oils, surfactant dispersion, emulsions, and liposomes, one of the most prominent is self-emulsifying drug delivery systems (SEDDSs). The underlying principle of this system is its capacity to dilute by aqueous phases and then, with mild agitation, produce fine oil-in-water (o/w) microemulsions[1]. Drug, lipid, and surfactant mixes that are isotropic in nature and often incorporate a single or several hydrophilic cosolvents or coemulsifiers with

droplet sizes differing from several microns to a few nanometers are termed as self-emulsifying drug delivery networks. [2].

Advantages Of SEDDS:

1. Dose reduction of drug.
2. Control of drug profile.[2]
3. Palatibility issue are less. [4]
4. Protection from GIT enviroment of drug.[3]
5. medication that is specifically targeted to a certain GIT absorption window.[3]

Mechanism Of Action:

Mechanism of action of self-emulsification happens when the energy needed to enhance the dispersion's surface area is less than the entropy shift that favors dispersion. The unbound energy needed to form a fresh surface between the phases of water and oil determines the typical emulsion and is expressed by the following equation:[5]

$$\Delta G == \Sigma N \pi r_2 \sigma \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots$$

where N is the quantity of droplets of radius r, σ represents the energy interfacial with time, and the process-related free energy is represented by Δ G. (ignoring the free energy of mixing).[6]

The preceding equation makes it clear that the greater energy level makes it unfavorable for an oil and water phase to spontaneously establish an interface. As of yet, there is no proof that the system often known as SEDDS may spontaneously emulsify in the correct thermodynamic sense[7]. The two phases of the emulsion will naturally want to separate from one another in order to reduce the interfacial area and, consequently, the free energy of the system. As a result, Typical emulsifying agents create a monolayer over the emulsion droplets, lowering the interfacial energy and preventing coalescence, which stabilizes the emulsions created by aqueous dilution[8]. When an emulsion forms spontaneously in a self-emulsifying system, the free energy needed to do so is either very low, positive, or negative[9].

Composition Of Self-emulsifying Drug Delivery System

To create sedds, four essential components must be present. Which are described below:

- API(DRUG)
- Oils
- Surfactants
- Co-surfactants / Co-solvents

DRUG(API):

It is preferable in order to raise the solublility of drugs with high permeability as well as poor solubility, like Danazol and Diclofenac.[10]

Oils:

Oils are regarded as one of the key ingredients in sedds formulations. It expedites the procedure of self-emulsification and aids in the solubilization of the drug's lipophilic component[11] via means of the intestinal lymphatic system, enhancing the GIT's absorption capacity[12]. SEDDS is formulated using triglyceride oils, both medium and long chain, with varying saturation levels[13]. Amphiphilic in nature, medium chain

triglycerides exhibit greater solubility and movement at the lipid/water interface. Using Cremophor RH40, which promotes the development of micro emulsion, along with long chain triglycerides high level of focus. Oils included in the preparation include sesame oil, peanut oil, and maize oil of SEDDS[14].

Surfactants:

Surfactants possess an amphiphilic nature.They aid in the lipophilic medicinal molecules' solubilization.This keeps the medication from precipitating in the GI lumen. in order that the medication stays for a long period in the lumen. There is widespread usage of some nonionic surfactants with elevated HLB levels. Because surfactants induce changes in biological membrane permeability, they possess the capacity to improve medication absorption. A cationic emulsion is said to have more absorption than an anionic emulsion. A 30 to 60 percent surfactant concentration is needed to produce a stable SEDDS[15-16].

Co-solvents:

For oral administration, co-solvents like ethanol, propylene glycol (PG), and polyethylene glycol (PEG) are ideal as they offer for the dissolving of significant quantities of the medicine or the lipid's hydrophilic surfactant base[17].

Dosage Form Of SEDDS

Dry emulsion:

It is mostly an oil in an emulsion of water that has been solidified via a variety of methods, including spray drying, solid carrier adsorption, and freezing method of drying[6]. Before using, the dry emulsion can be re-dispersed in water. In actuality, these are powders where emulsification happens in vivo on its own or upon exposure to an aqueous solution[10]. Tablets and capsules can be further prepared using dry emulsions. The drug that is barely soluble in water has been utilized with this technique [18].

Self-emulsifying capsule:

When swallowed, capsules containing traditional liquid self-emulsifying formulations spontaneously release microemulsion droplets that travel throughout the digestive system and enhance absorption[19]. Drug precipitation is avoided with this formulation. By employing less surfactant, these formulations reduce gastrointestinal adverse effects[20].

Self-emulsifying solid dispersion:

Solid dispersions are frequently used to accelerate the frequency of dissolution and boost the bioavailability of drugs with limited solubility in water. Manufacturing stability is a significant problem. One popular technique for creating solid dispersions is melt granulation[20].

Self-emulsifying tablets:

Solid self emulsifying drug delivery systems (S SEDDS) have emerged as a solution to address the limitations associated with liquid SEDDS. By transforming semisolid materials into powders using techniques like melt extrusion melt granulation, nanoparticle technology and spray drying S SEDDS offer advantages, over traditional SEDDS. These benefits include improved solubility and bioavailability reduced production costs, enhanced stability and minimized patient complaintsin addition formulations can be combined with solid carriers as colloidal silica, hydroxypropyl methyl cellulose (HPMC), and microcrystalline cellulose (MCC) to produce S SEDDS via adsorption approaches. This innovative approach presents an alternative to overcome the challenges associated with liquid based SEDDS formulations[21-25].

Self-emulsifying nanoparticles:

One way to create it is, by utilizing either the sonication emulsion diffusion evaporation method or the solvent injection approach. In the solvent injection technique, a mixture of melted lipids, drugs, surfactants and lipidss added drop by drop, into a system that isn't solvent. To eliminate particles filtration is. Then the resulting filtrate is dried to yield nanoparticles[20].

Self-emulsifying beds:

During the development of the system just a tiny percentage of substances were used. The SE system was mainly applied to the polystyrene beads, which have internal void structures. This was done through the solvent evaporation technique. The beads are made by combining the monomer styrene, with divinyl benzene. According to reports, these substances are safe for use, in systems chemically stable and can withstand a range of pH levels, humidity levels and temperatures[26].

Self-emulsifying controlled/sustained-release pellets:

Comparing pellets to other traditional solid dose forms reveals significant benefits. These have reduced GI irritations, are simple to make, and exhibit both intra- and inter-subject variability in plasma profiles. For the most part, glyceryl palmitate and glyceryl benzoate are recommended for the creation of pellets with continuous release, such as progesterone and SE nitrendipine pellets[27].

Evaluation Of SEDDS

Various test are conducted for the characterrization and evaluation for sedds.

Visual assesment:

This might offer crucial insights into the mixture's self-emulsifying and micro-emulsifying characteristics, as well as the ensuing dispersion, assessment of the elevated drug solubility, and absorption from the substantial surface area provided by the emulsion. Assessments of turbidity can be applied to ascertain if the dispersion has quickly and reliably reached equilibrium by identifying effective self-emulsifying[4].

Drug content:

The drug is extracted from pre-weighed SEDDS by dissolving it in an appropriate solvent. The solvent extract's drug content is examined using an appropriate analytical technique[28].

Dispersibility Test:

SEDDS is put through a dispersibility test to determine how well it disperses into an emulsion and to classify the size of the resultant globules. A typical USP dissolving device 2 (Paddle Type) is used to carry it out. 500 ml of water are mixed with 1 ml of each formulation at 37 + 0.5 °C while the paddle is spinning at 50 rpm. The SEDDS formulation produces a variety of mixtures or gels following titration with water, from which the grading system may be used to evaluate the formulation's in vitro performance[29].

Rheological Properties Determination:

The SEDDS technology may be used to soft gelatin capsules; however, in these cases, it must have significant flow characteristics for processing. When a formulation is diluted to 5% v/v water, its rheological parameters (viscosity, flow, thixotropy, static yield, and creep value) are measured using rotating viscometers, digital instruments connected to a coaxial measuring device or a cup and bob[10].

Thermodynamic Stability Studies:

The effectiveness of a formulation based on lipids is contingent upon its stability, since it may result in unfavorable consequences such as drug precipitation inside the matrix excipient solution[30]. Since drug precipitation within the matrix excipient can negatively impact formulation performance, physical stability is crucial. Excipient phase separation can affect a formulation's bioavailability and therapeutic effectiveness because of its lack of physical stability. When the formulation is enclosed within the capsule, an incompatibility placed between the gelatin and the formulation the capsule's shell might also result in brittleness, softness, delayed disintegration, or insufficient drug release. The following points are performed to examine them[19].

a) Heating cooling cycle: There are six cooling and heating cycles, with exposure times of at least 48 hours at each temperature ranging from 4°C (refrigerator cold) to 45°C (high temperature). The centrifugation test is then performed on those formulations, which have proven stable[31].
b) Centrifugation: Formulations that successfully complete the cycle of heating and cooling is centrifuged for 30 minutes at 3500 rpm[32]. For the freeze-thaw stress test, formulations without any phase partition are chosen[14].
c) Freeze thaw strees cycle: Cracking, creaming, or phase separation are absent in formulations that pass this test, indicating strong stability.

Turbidity measurment:

A property used to determine droplet size and self-emulsification time is turbidity. A certain quantity of SEDDS is mixed with a predetermined volume of the suitable medium (phosphate buffer or 0.1 N HCl), and the mixture is magnetically agitated continuously at 50 rpm to maintain the correct temperature. The turbidity is then kept an eye on with a turbidity meter. It is difficult to control the pace of emulsification because the time necessary for full emulsification is too short. Turbidity measurement tracks droplet development following emulsification[29].

Droplet size analysis & Particle size measurements:

Photon correlation spectroscopy was employed, which examines variations in light scattering brought on by Brownian motion, the size of the droplets in the emulsions is ascertained. Using a Zetasizer that can quantify sizes in the range of 10 to 5000 nm. Using spherical polystyrene beads for external standardization, light dispersal is observed at a angle of 90° and 25°C. The technique is compatible overflowing with water considering that even after 100 times diluting with water, the particle's nanometric size range remains preserved [33,34].

Marketed products formulated as self-emulsifying systems:

Brand Name	Compound	Dosage Form Capsule	Company	Used as
Neoral	Cyclosporine A/I	Soft gelatin, oral solution	Novartis	Immune Suppressant
Norvir	Ritonavir	Soft gelatin, oral solution	Abbott Lab	HIV antiviral
Lipirex	Fenofibrate	Hard gelatin	Sanofi-Aventis	Antihyperlipoproteinemic
Depakene	Valproic acid	Capsule	Abbott	Anticonvulsant

Conclusion And Future prospet:

SEDDS seems like a good option for lipophilic product development. It is essential to grow the in vitro models used to evaluate oral bioavailability increase since the generation of SEDDS is speculative. Vigilance is required to maintain the quality and uniformity of medications inside lipid structures. It will be required that evaluate any incompatibilities between lipid systems and capsule shell components. The application of lipid formulation has a bright future in light of these obstacles. Future studies ought to focus on studies on human bioavailability, and investigations on the mechanisms of action of these kinds of SEDDS formulations should receive more attention. It is necessary to regulate in vitro methods for assessing the intricate changes brought about by the drug in the gut as well as the drug's solubilization status in vivo. Solid-SEDDSs (S-SEDDSs) being looked upon as a possible substitute for these problems. Such devices need the solidification of liquid self-emulsifying systems into powders (SE capsules, SE tablets, SE pellets, SE beads, and so on) in order to provide various solid dose formulations. When liquid SEDDS are converted to solid dose sizes, the drug release characteristics can be maintained. The contents of GIT that are published cause self-emulsification.

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