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A review: self emulsifying drug delivery system

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ABSTRACT

Most favorite route of drug administration is the oral route for administration for many formulations and has dominated over all other routes of administrations. The main disadvantage of oral drug formulations is low and unpredictable bioavailability that results from unfortunate aqueous solubility. Nearly about 42% of upcoming chemical molecules show bad water solubility that is the main problem for modern drug delivery system, just because of their low bioavailability. The current study is basically on the purpose of to formulate a Self Emulsifying Drug Delivery System which enclose lipophilic drug. Many drugs like loratadine wich exploring the potential of transporter for such system. The self micro emulsifying drug delivery systems is the one isotropic mixture of oil with surfactant as well as with co- surfactant and drug with a distinctive capability for forming fine oil in water micro-emulsion in the lead to mild shakeup following dilution along aqueous phase. When compared to other techniques self emulsifying drug delivery system came up with strong attention just because of enhanced oral bioavailability enabling decrease in dose amount, High steady sequential profiles of drug absorption and the size of particle of formulations may influenced by type of oil, as that liquid paraffin made small size of particle which may ranges below 2 microns.

Keywords: Self emulsifying drug delivery system, lipid based formulations, oral bioavailability, poorly water soluble drugs

INTRODUCTION

Self emulsifying drug delivery system is one of the most accepted and commercially feasible formulation technologies for overcome many problems. There are different self emulsifying drug delivery systems are as self emulsifying oil formulation (SEOF) and second one is self micro emulsifying drug delivery system SMEDDS. The effectiveness of lipophilic drug is often slowed down because of their poor aqueous solubility that leads to very low absorption after in vivo administration.

SEDDS is typically bring into being opaque emulsions through a droplet sizing in 100 to 300 nm though SMEDDS form clear micro emulsions by way of a droplet size of below 50 nm in addition the concentration of oil in SMEDDS is below 20 % when it is compared to 40-80% in SEDDS. We can conclude that a mixture of oil and surfactants is required to form self-emulsifying drug delivery systems (SEDDS) which is ideally isotropic and also sometimes it contains some co-solvents then it emulsify spontaneously for producing a fine oil-in-water emulsions after bring into aqueous phase under a very mild agitation.

The chain triglycoside oils and nonionic surfactants are nowadays in trend to prepare the self emulsifying drug delivery system mainly because of its less toxic nature. The drugs like HIV protease are very poor water soluble, glycoprotein inhibitors and drugs like anticancer those are having problems to produce and uphold a good solubility in gastrointestinal tract. The self-emulsification process is preceded during creation of liquid crystals and gel phases.

The isotropic mixtures of oil and a surfactant that forms SMEDDS formulations and a co surfactant may be a solubilizer with a active ingredient.

The ability to form fine oil-in-water microemulsions is the basic principle of self emulsifying drug delivery system that formed below a mild shacking which is further pursued dilution by aqueous phases as SEDDS are isotropic mixtures of drug, oil and surfactant and cosurfactant, that form fine emulsion or lipid droplets, sizing between 100 nm to below 50 nm for self- micro emulsifying drug delivery systems on dilution with physiological fluids. 5,9.15,17

Benefits of smedds 1,16

There are the following benefits of self micro emulsifying drug delivery systems as listed below,

- Improvement in oral bioavailability
- Dosage form development of SEDDS dry emulsions

Improvement in oral bioavailability 19

Bioavailability can be altered by the dissolution rate that also main limitation dependant for drug absorption for many drugs those is poorly water soluble. The drug those are solubilised and micro emulsified form ranging between 1- 100 nm and then succeeding increase in the specific surface area that allow further efficient drug convey through the intestinal aqueous boundary layer and during the absorptive brush border membrane leading to enhanced bioavailability. [1]

Dosage form development of SEDDS Dry emulsions 2,3,4,5,6,7

The powders from of emulsion with SEDDS in which emulsion are spontaneously occurs in vivo when they exposed into an aqueous solution. These dry emulsions may be used for preparation of tablets and capsules as well. All typically dry emulsion formulations are prepared as oil/ water emulsions that containing a solid carrier may be lactose, maltodextrin, in the aqueous phase by,

- Revolving evaporation
- Freeze-drying
- Spray drying

The solid state glass emulsions in the form of dry known as 'foam' was obtained by rotary evaporation using with heavy mineral oil and sucrose. These emulsifiable glasses contain the benefit of using no surfactant.

But wherein freeze-drying a process in which a slow cooling rate and the adding up of amorphous cryoprotectants contain the best stabilizing effects. The heat treatment before melting decreases the stabilizing effects.

Approach of spray drying is habitually used in the preparation of dry emulsions here O/W emulsion was preparede and then converted into dry SEDDS by spray-dried for removing the aqueous phase.

Mechanism of self-emulsification 16,,17

The mechanism of self emulsifying drug delivery is depended on apparent from equation that the spontaneous configuration of the interface within the oil and water phases is actively not privileged. Anyway the self-emulsification only occurs when the entropy change that favors dispersion is larger than the energy required boosting the surface area of the dispersion.

The energy needed to create a new surface between the two phases is a direct function of a conventional emulsion.

Equation,

$$\Delta G = \sum_{i} N_i \pi r_i^2 \sigma$$

Where, G is the free energy associated with the process,

N is the number of droplets of radius

Free energy (ΔG) associated is given by the equation radius 'r' and 'σ' is interfacial energy

Consequently the emulsions made from aqueous dilution are stabilized by conventional emulsifying agents that make a monolayer around the emulsion droplets and then reduce the interfacial energy to provide a barrier to coalescence.

Different Dilution phases 13

When the dilution of a SMEDDS formulation done the impulsive bends of the Surfactant layer changes through a number of possible liquid crystalline phases. These drop globule structure can go by from a reversed spherical droplet to a reversed bar shaped droplet, hexagonal phase, lamellar phase, cubic phase and various other structures until, after appropriate dilution, a spherical droplet will be formed again. The illustration of commonly encountered phases, when added the water to an oil and surfactant.

Material of Formulation of Self emulsifying drug delivery system (SEDDS) 2,5,9,15

The different amount of comprising material used to formulate SEDDS as listed below,

- Surfactant
- Co-surfactant
- Oil
- Transcutol P (liquid)
- Solubilizer

Along with the define amount of a drug all above listed excipients are mixed to formulate the SEDDS.

Different excipients used in sedds 1,8,9,8,12

Oils

The long-chain triglyceride and medium-chain triglyceride along with different extent of saturation are used for the design and development of self-emulsifying formulations. The edible oils without any modification provide the most bases for lipid vehicles. They are having difficulties to dissolve big amounts of hydrophobic drugs and their relative difficulty in capable self-emulsification noticeably decrease their use in sedds formulation.

As distinction altered or hydrolyzed vegetable oils have provide broadly to the success of the above systems.

Surfactants

Surfactants category as non-ionic with a comparatively high hydrophilic and lipophilic balance be advocated for the intend of self-dispersing systems and the a variety of liquid or solid ethoxylated polyglycolyzed glycerides and polyoxyethylene 20 oleate (Tween 80) are the most frequently used excipients. Natural Emulsifiers are expected to be more safer than synthetic ones and are recommended for self dispersed lipid formulation.

Co-solvents

A very high concentration is required (above 30% w/w) to produce an effective self-emulsifying system.
There are different organic co-solvents used in sedds as listed below,
Organic solvents mainly suitable for oral administrationas.

- Ethanol
- Propylene glycol (PG)
- Polyethylene glycol (PEG)

These co-solvents may help to dissolve large amounts of either the hydrophilic surfactant or the drug in the lipid base.

Evaluation of sedds 3,6,8,14,18,19

Evaluation parameter	Description
Particle size	Fresh 1 ml of formulated solution taken and added to 100 ml of 0.1N hydrochloric acid after that the particle sizewas measured using particle size analyzer.
Thermodynamic stability studies	Physical stability of a lipid formulation is quite crucial to its performance that adversely affected by precipitation of the drug particulates in the excipient matrix. Poor formulation physical stability can further create phase separation of the excipient that can affects not only formulation performance, but visual appearance as well. There are certain incompatibilities between the formulation and the gelatin capsules shell can lead to brittleness or deformation, delayed disintegration, or incomplete release of drug.
Centrifugation	Formulations are then centrifuged thaw cycles at 21 0C and +25 0C with storage at each temperature for more than 48 h is done at 3500 rpm for 30 min.
Freeze thaw cycle	Prepared formulations passed this test showed good stability at freezing with no phase separation, creaming, or cracking
Dispersibility test	The efficiency of such self-emulsification of oral nanonised or micronized emulsion is assessed using a standard USP XXII dissolution apparatus 2. One milliliter of each formulation was added to 500 mL of water at 37 ± 0.5 0C. A standard stainless steel dissolution paddle rotating at 50 rpm provided gentleagitation.
In vitro performance	The in vitro performance of the formulations is visually assessed by the following grading system as listed below, **Grade A**: very quickly forming within 1 minutes its forming nanoemulsion, having a clear or bluish appearance. **Grade B**: very quickly forming, it is slightly less clear emulsion, having a bluish white look. **Grade C**: it's a very fine milky emulsion that formed less than 2 min. **Grade D**: it is somehow dull, grayish white emulsion having slightly oily appearance that is slow to emulsify (longer than 2 min). **Grade E**: Some formulation, exhibiting either poor or least emulsification with big oil globules present on the surface.
Turbidimetric Evaluation	The Nepheloturbidimetric evaluation, it is done to monitor the growth of emulsification inside the formulation. Particular amount of Selfemulsifying system is put to fixed quantity of suitable medium of 0.1N hydrochloric acid under continuous stirring at 50 rpm using magnetic plate at 15 to 40 □ temperature.
Viscosity Determination	The formulated SEDDS system is usually administer into soft gelatin or hard gelatin capsules. These rheological properties of the micro emulsion are been evaluated by Brookfield viscometer.
Droplet Size Analysis Particle Size Measurements	The size of the emulsions droplets is determined by using the photon correlation spectroscopy that analyses the fluctuations in light scattering due to Brownian motion of the particles with the help of using a Zetasizer able to measure sizes between 10 and 5000 nm. Light scattering is been monitored at 25°C at a 90° angle then after external standardization with the spherical polystyrene beads.
Refractive Index and Percent Transmittance	The refractive index and the % transmittance ensured the transparency of formulation. The systems refractive index is measured by refractometer by putting drop of solution on a slide and it compare with water (1.333)**.**

Uses of the sedds 7,11,16,18

There are certain applications of the SEDDS as described below,

- Solubility enhancement
- Bioavailability enhancement
- Biodegradation protection

Solubility enhancement

The drug is closed in SEDDS then it increases the solubility as it circumvents the dissolution step in case of Class- Π drug those are Low solubility/high permeability.

Bioavailability enhancement

The different formulation approaches that have been seen to attain the sustained release can increase the bioavailability even it can decrease the gastric irritation include preparation of matrix pellets of nanocrystalline and sustained release microparticles formulations, floating oral systems, as well as transdermal systems of delivery system.

Biodegradation Protection

The self emulsifying drug delivery system is have ability to reduce the degradation as well as it improves absorption that may be particularly useful for drugs those are low solubility and degradation in the GI tract add to a low oral bioavailability. Several drugs are able to get degraded in physiological system just due to its acidic PH in stomach and enzymatic degradation or hydrolytic degradation of the drugs.

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