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SELF-EMULSIFYING DRUG DELIVERY SYSTEM

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ABSTRACT

Self- emulsifying drug delivery system are the unique mixture of oil, solvent surfactant, co-surfactant, co-solvents. These are the effective approach to solving the solubility of poorly soluble drug. From couple of years aqueous solubility is biggest issues to the formulator for formulation and development of novel drug delivery. SEDDSs are Good strategy for enhancement of oral absorption and bioavailability of BCS class 2 and class 4 drugs. For these system oral route is most convenient than other route. Requirement of this system is due to poor solubility and oral absorption of highly lipid soluble drug. Those drug which is formulated by SEDDS will have good pharmaceutical market. These system have ability to form emulsification with the solid as well as liquid dosage form .SEDDS are very quickly dispersed in the gastro-intestinal fluid and making micro or Nano-emulsion containing solubilized drug. These article covers formulation, Evaluation, future aspect and application part of self-emulsifying drug delivery system.

KEYWORDS: Self Emulsifying Drug Delivery System (SEDDS), Solubility, bioavailability

INTRODUCTION

Self- emulsifying oil formulation (SEOF) is a similar name over a self- emulsifying drug delivery system. Oral route is most convenient for chronic drug therapy. SEDDS defined as the unique mixture of oil, solvents, surfactant, co-solvent and co-surfactants[41]. Self-emulsifying drug delivery system is a simplest approach to improve the solubility of poorly soluble drug specially BCS class 2 and 4 by forming fine and stable o/w emulsion. SEDDS can be given orally with hard gelatin and soft gelatin capsule, tablet, pellets, and solid dispersion.

Table: 1 BCS classification of drug[39]

BCS class	Aqueous solubility	Membrane permeability
1	High	High
2	Low	High
3	High	Low
4	Low	Low

In the formulation of self- emulsifying drug delivery system we require surfactants, solvents, co-surfactant, Co-solvents. SEDDS formulation are the simple binary mixture.[24]

Properties of SEDDS[1]

- ✓ They have able to emulsify very rapidly in intestinal fluids
- ✓ They form fine emulsion of o/w
- ✓ Emulsify with solid as well as liquid dosage form
- ✓ Insertion of drug in oil phase done easily.

Advantages of SEDDS

- ✓ Enhancement of oral bioavailability[2]
- ✓ Targeting of drug to be achevied[3]
- ✓ Drug delivery occurs in control rate
- ✓ Ability to form solid and liquid dosage form

Disadvantages of SEDDS

- ✓ Irritation of gastro-intestinal tract due to high amount surfactant present in the formulation[4]
- ✓ Instability of drug due to surfactant[5]
- ✓ Traditional method of dissolution do not work[5]

Dosage forms of SEDDS[6]

Different dosages forms of SEDDS is available for effective delivery of drug

Oral route	Other route
Capsule, sustain/control release tablet, pellets, solid dispersion.	Topical, pulmonary, ocular and parenteral

Structure of self -emulsifying drug delivery system

Factor which play important role in the make –up of self -emulsification system.

-Temperature for stable emulsification.

-Oil-surfactant compatibility.

-Assiduity of surfactants.

Excipients used in the formulation of SEDDS

A) Surfactants

A) Surfactant[6,7]

Most of the surfactants are not suitable to take orally because toxicity, In this case non- ionic surfactants are mostly recommended because less toxic and high hydrophilic-lipophilic balance (HLB). Safety is the most important tool for selection of surfactants. In SEDDS formulation only those surfactants are used where they can suitable with oral administration.

Types of surfactants[8,9]

1) Anionic surfactant

e.g.-Sodium lauryl Sulphate (SLS).

2) Cationic surfactants

e.g.-quaternary ammonium compounds.

3) Ampholytic surfactants (Zwitterionic surfactants)

e.g. –sulfobetaines.

4) Non-ionic surfactant

EX-Sorbitan ester (span), polysorbate (Tween).

B) Oil

The oil shows one of the most important contribution in formulation of SEDDS because of they solubilize the required amount of lipophilic drug and increase the absorption in GI tract.[10,12] Vegetable oil or modified oil are most preferably use for success of the self-emulsifying system[12]. It must be compatible with the drug, surfactant, co- surfactant and solvents. All formulation ingredients are mixed together and form stable formulation.

Oil used in SEDDS formulation[11]

- Corn oil
- Olive oil
- Oleic acid
- Sesame oil
- Hydrogenated soyabean oil

- Hydrogenated vegetable oil
- Soyabean oil
- Peanut oil
- Beeswax

C) Co-solvent

The co-solvents helps to dissolve solute in to solvents. lipid soluble and water soluble drug dissolve in the base by adding co-solvents. By determining the molecular weight we can examine the physical state of the excipients at the room temperature. Co-solvents form miscible liquid of hydrophilic and hydrophobic drug[5,12]

Example of co-solvents

- Polyethylene glycol
- Polypropylene glycol
- Glycerin
- Ethanol

Formulation of self-emulsifying drug

1) Single component lipid solution

It is a lipid based formulation in which the drug molecules are solubilized in single excipients like PEG, vegetable oil. Basically the PEG acts as water miscible solvents. Gastrointestinal tract increases or raises the emulsification which plays important role in the drug release and absorption[13]

2) Self- emulsifying formulation

This system is a mixture of surfactants, co-surfactants, oil, co-solvents and the solubilized drug which is orally compatible. Concentration of all these mixture is showing effect in the emulsification. For self- emulsifying drug delivery system droplet size range is 100 nm and for SMEDDS it is 50 nm[14]

3) Self- emulsifying solid dispersion formulations

In these formulation solvents get totally solubilizes the drug. It will directly improve the absorption of drug which is to be formulated. These formulations contain dispersion of the drug in the matrix of the excipients then afterwards they get converted in to their solubilized

form. It will civilize in the dissolution of the drug.[15] Solid dispersion of these formulations directly amends the solubility of poorly soluble drug substance.

4) Turbidity measurement

For checking the dispersion of system whether done at equivalence point rapidly with respective to time[16]

5) Droplet size

Optical microscopy is mainly used for the determination of emulsion droplet size. This factor perform important role in the self –emulsification because this will decide the bioavailability and stability of drug[40]

6) Zeta potential measurement

For the identification of charge on the droplet. Due the free fatty acid the charge on the oil droplet is negative in self- emulsifying drug delivery systems[38]

7) Determination of emulsification time[17]

In this self –emulsification time, dispensability, appearance and flow ability is to be determined.

Evaluation of self –emulsifying drug delivery system[23]

1) Thermodynamics stability test[18]

Chosen details were subjected to various thermodynamic stability tests (Centrifugation, Heating cooling cycle and Freeze thaw cycle), to avoid selecting metastable formulation.

2) Centrifugation

Chosen formulations from phase diagram were centrifuged at 3500 rpm for 30 minute and watched for phase separation, creaming and splitting. Formulation that are steady were taken for warming cooling cycle.

3) Heating cooling cycle

Stability of Nano-emulsions on variety of temperature was considered by H/C cycle. Six cycles between refrigerator temperature 40^0C and 45^0C with storage at every temperature for not less than 48 hours, formulation, that are steady at these temperatures, were subjected to Freeze thaw cycle.

4) Freeze thaw cycle

Three stop thaw cycles between - 21C and +25oC with capacity at every temperature for not less than 48 h was completed for the formulation. Details, which passed by these thermodynamic stretch tests, were further taken for the dispersibility tests for surveying the efficiency of self-emulsification.

5) Dispersibility test

The effectiveness of dispersibility was surveyed utilizing a USP XXII dissolution apparatus type 2. Every formulation (0.5 ml) was added to 500 ml refined water kept up at 37±0.5◦C, with paddle rotating at 50 rpm for gentle agitation. The in vitro performance of the formulation was visually surveyed utilizing the evaluating system as indicated below[19]

System	Term
system A	Rapidly framing (inside 1min.) EX-Nano-emulsion
system B	Rapidly framing, slight less clear EX-emulsion
system C	Fine smooth emulsion that shaped inside 2 min.
System D	Dull, grayish white emulsion, ease back to emulsify (longer than 2 min.)
System E	Formation showing either poor or negligible emulsification

6) Effect of PH and robustness

Formulation were subjected to 50, 100, 1000 and 3000 fold dilution with refined water, 0.1M HCl and recreated intestinal liquid (pH 6.8). The resultant weakened emulsions were checked physically for any physical changes, for example, (coalescence of droplet, precipitation or phase separation) after 24 h keeping[2]

7) Viscosity[21]

Brookfield DV III ultra V6.0 RV cone and plate rheometer (Brookfield Engineering Laboratories, Inc, Middleboro, MA, axle # CPE40) was utilized to decide the thickness of various plans at 25±1.0°C.

8) Differential scanning calorimeter

The sample (around 3.00 mg) were put in standard aluminum containers, and dry nitrogen was utilized as effluent gas. All samples were filtered at a temperature slope speed of 5°C/min and the heat flow out of 0 to 250°C.

9) Drug content estimation[22]

SEDDS containing ibuprofen proportional to one was 100 ml volumetric flask containing methanol and blended it well. The extricated arrangement was appropriately diluted and analyzed for drug content using UV spectrophotometer at 221 nm.

10) Drug discharge ponders[22]

The in vitro medicate arrival of plans was controlled by utilizing USP disintegration mechanical assembly II (paddle strategy). The disintegration medium, as per the monograph of ibuprofen in USP, is a pH 7.4 Phosphate cradle. 5 ml of disintegration medium were pulled back each 10 min.

11) Evaluation of anti-inflammatory activity

The evaluation of prepared SEDDS by utilizing rat with the method of carrageenan-induced rat hid paw edema method.[35] The weight of rat is in between 150-200g .place the animal in good condition 12 hours with continuous supply of water. Animal fasted night –over before starting the experiments with feed of water[36]

12) Zeta potential measurements

Use zeta seizer for the suitable measurements 0f micro-emulsion[37]

Future parts of self-emulsifying drug delivery system[24]

Self- emulsifying drug conveyance frameworks are enhance the dissolvability of ineffectively watery solvent medications lipid solvent medications can be conveyed by oral course with SEDDS. it will enhance oral bioavailability. In future, advancement of self- emulsifying drug conveyance frameworks with novel applications in medication conveyance issues connected with the poor dissolvability. SEDDS lessening creation cost. It will enhance soundness and also quiet consistence. In this framework GI disturbance is avoidable and controlled/managed medication is achievable. Changes or option for the routine fluid self-emulsifying drug conveyance framework is strong SEDDS. It is additionally worth calling attention to a few issues to which consideration ought to be paid, for instance physical maturing marvel connected with glyceride, oxidation of vegetable oil, and co-operation amongst medications and excipients. Determination of reasonable excipients is the primary obstacle of creating s-SEDDS. Therefore, these perspectives ought to speak to significant future working heading for S-SEDDS. Subsequently real leaps forward are still required for legitimate improvement of SEDDS.

Utilization of self- emulsifying drug conveyance framework

6) Conveyance framework of self -emulsifying drug utilized in the raises the rate and extent of drug as well as stability of drug and solubility. Following are the some example of drug in which the bioavailability improved by utilization of the self -emulsifying drug conveyance framework. Mostly used for improvements solubility of the poorly soluble drug specially BCS class 2 and 4.

Table; writing covers bioavailability utilizing SEDDS

Sedate	Bioavailability improvement
Exemestane	2.9 folds[25]
Vitamin	2 folds[26]
Vinpocetine	17.3 folds[27]
Ketoprofen	1.13 folds[28]
Gentamycine	5 folds[39]
Halofantrine	6-8 folds[30]
Acyclovire	3.5 folds[31]
Phenytoin	2.3 folds[32]
Carvedilol	3-4 folds[33]
Simvastatin	1.5 folds[34]

CONCLUSION

This work of self- emulsifying drug delivery gives most useful aspect for the poorly soluble drug especially to BCS class2 and 4. In future part it will reduces the cost of mostly pharmaceutical products. SEDDS are the binary mixture of oil, surfactants, Co-surfactants, solvents and co- solvents. Enhancement of bioavailability (rate and extent of drug) is a main application of this system and it is happen by raises the solubility of poorly soluble drug. They form stable formulation of drug over the other systems. SMEDDS is value addition or improved version of SEDDS. Evaluation parameter of self-emulsifying drug delivery frame work help to form safe and effective as well as stable formulation of drug. Improvement of bioavailability and solubility of No. of drugs some of them mention in this article by utilization of self-emulsifying drug delivery system.

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