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Self emulsifying drug delivery system-a promising tool to enhance dissolution of poorly soluble drugs

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ABSTRACT

Oral route offers a convenient way of dosing medications, but the hurdle is low erratic bioavailability. The various challenges faced by the pharmaceutical scientists leads to the improve bioavailability enhance the approach of self emulsifying drug delivery system (SEDDS) .It has gained exposure of their ability to increase solubility and improve the bioavailability of poorly soluble drugs. SEDDS being a lipid based formulations consists of oils, surfactants, dispersions, solid lipid nanoparticles, liposomes and emulsions. SEDDS encompasses many different concepts but it more generally encountered for hydrophobic drugs being encapsulated as unit dosage forms for per oral administration. Hence, Self Emulsifying drug delivery system is a promising approach for enhancement of dissolution of lipophilic drugs, address the ethical and value concern of society large by reducing the ever growing pressure of erratic drug bioavailability. This review focuses the importance and techniques of SEDDS as an efficient technique for enhancing the dissolution rate.

Key words: Self Emulsifying Drug System, Lipophilic drugs, Dissolution, Bioavailability.

1. INTRODUCTION

In drug discovery and development, solubility plays a vital role in every step to import high bioavailability and to achieve required pharmacological action [1]. Due to poor aqueous solubility, the efficacy of lipophilic drug is being lowered to great extent resulting in poor bioavailability [2]. During last two decades colloidal vehicles exploration marked the glory of enhancement of solubilisation and stability of lipophilic drugs [3]. The concept of self emulsifying drug delivery system offers great potential benefits in solving absorption problems enabling reduction in dose by protecting drug against hostile environment in gut [4].

Conventional SEDDS are mostly prepared in liquid form which has several disadvantages like low stability and low loading of drugs [5]. SEDDS are the isotropic mixture of oils and surfactants which are emulsified in aqueous media with mild agitation. The size ranges from 100nm (SEDDS) to less than 50nm for self-micro emulsifying drug delivery system(SMEDDS) on dilution with physiological fluid [6]. In SEDDS, the drug is in dissolved form, the size of droplet being small renders a large interfacial area facilitates drug absorption [7].

1.1. Advantages

a. Drug delivery profile can be controlled.
b. Low dosing of drugs.
c. The drug can be efficiently protected from given environment
d. Efficient drug absorption [8].

2. EXCIPIENT CLASS

2.1. Oil

It can facilitate self emulsification and increase the drug fraction of lipophilic drug which may enhance the drug absorption from gastrointestinal tract [9]. A number of natural product oils is widely used which is suitable to encapsulate oral formulation products[10]. A number of long chain triglyceride oils with different degrees of saturation widely used in SEDDS formulation [11]. Unmodified edible oils are not used owing to the poor solubility in hydrophobic drugs [12].

2.2. Surfactant

Non-ionic surfactants are mostly used in SEDDS due to toxicity and it cause mild reversible changes in the intestinal wall permeability [13]. The concentration of surfactant used ranges from 30 to 60% w/w of the formulation [14]. Surfactants exhibit their mechanism of action by being amphiphilic in nature has the ability to solubilise highly in hydrophobic drug compounds, hence it can prevent the drug precipitation within

gastrointestinal lumen and a prolonged action can be achieved [15].

2.3. Co-Solvents

The major purpose of adding Co-solvents in SEDDS is to dissolve larger hydrophilic surfactant or hydrophobic drug in lipid base . Eg:- Diethylene glycol monoethyle ether, polyethylene glycol. The increase in amount of co-solvent enhancing the drug dissolution from the formulation [16].

2.4. Formulation mechanism of self emulsification

Reiss theory states that the occurrence of self emulsification is due to entropy change causing dispersion to be greater than the energy required to increase the dispersion surface area [17]. It can be described by the equation

$DG=SN_1Pr_12S$

Where,

"DG"=free energy associated with the process (ignoring the free energy of mixing).

"N"=number of droplets;"**r"**=radius of droplets and **"S"**= interfacial energy [18].

2.5. General formulation approach

The basic general formulations to be considered for developing lipid base formulations are

- The solubility of drug in the formulation as such and upon dispersion (for SEDDS)
- The rate of digestion (for formulations susceptile to digestion).
- The solubilization capacity of the digested formulation.

2.6. Formulation

The method of preparing SEDDS involves various steps

2.6.1. Preparation of phase diagram

Solubilising the drug and pharmaceutical ingredient, in a mixture of surfactant, co-surfactant and solvent.

The oil phase and others are mixed by heating if necessary to solublised drug and mixed thoroughles. The emulsion can be added to suitable dosage form such as soft or hard filled gelatin capsule and allowed to cool.

2.6.2. Types of SEDDS

(i) Oral Delivery

(ii) Topical delivery

(iii) Parenteral drug delivery

(iv) Occular& Pulmonary delivery

2.6.2.1. Oral delivery:

(i) Self emulsifying capsule

(ii) Self emulsifying controlled release pellets

(iii) Self emulsifying sustained/controlled release tablets

(iv) Self emulsifying solid dispersions.

2.6.2.1.1. Self emulsifying capsule

A capsule containing conventional liquids, self emulsifying formulations eventually after administration is dispersed in GIT fluid in to micron size droplet so as to reach the absorption site.HPMC plays a predominant role by preventing precipitation in SEDDS [19]. Even by the addition of suitable solid carriers such as adsorbents, polymers in the liquid self emulsifying ingredients can be filled into capsule as solid (or) semi-solid state effectively. Even the drug loading capacity is low like lipophilic compounds; this system provides a good chemical stability [20].

2.6.2.1.2. Self emulsifying controlled release pellets:

Self emulsifying controlled release pellets is intended to improve the bio-availability by minimizing the gastrointestinal irritation. The pellets were prepared by extrusion spheronisation technology using the reconstituted emulsion as additive. self emulsifying oils, surfactants mixture can be incorporated into pellets which reduces the intrasubject and intersubject variability of plasma profile [21]. Pellets can transform the lipophilic compounds in to aqueous phase, thereby enhancing the bioavailability of drugs being lipophilic in nature [22].

2.6.2.1.3. Self emulsifying sustained/controlled release tablets

Self emulsifying tablets gains more impact due to elimination of adverse effect as well as improvement in penetration efficacy through GI mucosal membrane.inpreparing sustained release tablets surfactants and lipids in combination plays predominant role and amount of solidifying excepients added is reduced., mostly colloidal silicon dioxide selected as gelling agent [23].

2.6.2.1.4. Self emulsifying solid dispersions

Solid dispersions enhance the bioavailability of poorly water soluble drugs by increasing the dissolution rate profile initially.

3. SELF EMULSIFYING SUPPOSITORIES

SEDDS play greater role in rectal/vadsorption achieving therapeutic level for some chronic disease like hepatic etc. Usually

glycyrrhizin with c6 c1s fatty acid excipient for adsorption [24].

3.1. Evaluation

3.1.1. Visual assessment

This test is to identify efficient self emulsification by measuring the turbidity to ascertain dispersion equilibrium within the reproducible time [25]. Fixed quantity of self emulsifying system added to suitable medium (0.1 N HCl) continuous stirring at 50 rpm on magnetic hot plate at appropriate temperature. The turbidity level is monitored by turbidimeter [26].

3.1.2. Thermodynamic stability studies

3.1.2.1. Heating cooling cycle

The formulations are subjected to six cycles between refrigerators temperature with 45^0C storage condition. The whole process is subjected to 48 hr study and the formulation centrifugal test stable done for at these temperatures.

3.1.2.2. Centrifugation

The formulations are centrifuged cycle between 21^0C and 25^oC with storage at each temperature not less than 48 hr .The process is done for 30 minutes with 3500 rpm [27].

3.1.2.3. Dispersibility test:

Usp XXII dissolution apparatus 2 was used to study the efficiency of self emulsification of nano or micro emulsion. To 500 ml of water one milliliter of each formulation was added and the temperature maintained at 37 ± 0.5^oC with 50 rpm. The results of *invitro* performance is tested as following grades.

Grade A: Rapidly forming (within 1 min) nanoemulsion, with clear form or bluish appearance.

Grade B: Rapidly forming having bluish white appearance.

Grade C: Formation of fine milky emulsion rapidly by 2 min.

Grade D: Dull Grayish white emulsion formed, longer than 2 min.

Grade E: Formulation which shows either poor or minimal emulsification with large oil globules present on the surface.

Grade A and Grade B formulation will remain as nanoemulsion when dispersed in GIT while formulation failing in Grade C could be recommended for SEDDS [27]

3.1.2.4. Viscosity determination

As SEEDS system is generally administered in soft or hard gelatin capsule, it is necessary to measure rheological properties of microemulsion by Brookfield Viscometer. This is used to find out the type of system whether it is w/o or w/o. If system shows less viscous nature it is regarded as o/w type and if it is high viscous nature it is regarded as w/o type system [28].

Milling and blending done before filling the solid dispersion in to hard gelatin capsule .the widely used exicipients and geluier 50102, transculol, etc.

3.1.2.5. Turbidimetric ebaluation

The growth of emulsification is monitored bynephloturbidimeter, fixed quantity of self emulsifying system is added to 0.1Nhydrochloric acid under continuous stirring at 50 rpm on magnetic plate at ambient temperature and thus the increase in temperature is measured [29].

3.1.2.6. Droplet size analysis

Photon correlation spectroscopy is used to find the droplet size of emulsions between10 and 5000nm using zetasizer [29].

3.1.2.7. Refractive index and precent transmittance

The refractive index is measured by refractometer. A drop of solution is placed on the slide and it is compared with water (1.333).refractive index and percent transmittance proved the transparency of the formulation , which is measured at particular wavelength using UV spectrophotometer by using distilled water as blank .

3.1.2.8. *Invitro* diffusion study

Invitro diffusion studies are carried out to study the drug release of formulation from liquid crystalline phase around the droplet using dialysis technique.

3.1.2.9. Electroconductivity study

Electroconductometer is used to study the electro conductive nature of system whether the SEDD system contains ionic or non ionic surfactant, oil and water [30].

4. APPLICATIONS

Improvement of solubility and bioavailability as it circeemrents the dissolutions step in care of class II drug (low solubility/high permeability).

- Decrease in gastric irritation.
- Effective delivery of oral hydrophobic drugs.

- Eminent protection of drugs against biodegradation.

Ex : ketoprofen a moderately drug nonsteroidal anti inflammatory drug has low solubility but ketoprofen reported complete drug release if it is formulated as SEDDS in nanocrystalline form [31-33].

5. CONCLUSION

Self emulsifying drug delivery system efficiently improves the dissolution of sparingly soluble drugs by rapid self emulsification. SEDDS system offers a way to improve the rate and extend of oral absorption and to produce more reproducible blood – time profiles. Hence, SEDDS will continue to enable novel applications in drug delivery and solve problems associated with delivery of poorly soluble drugs.

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