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Review Article

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A Review on Formulation Design of Self micro emulsifying Drug Delivery System to Improved Solubility

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ABSTRACT

Poorly Solubility of orally administered drug is major challenge of pharmaceutical industry as nearly 35-40% of newly launched drugs possess poor aqueous solubility which leads to their poor dissolution and low bioavailability, resulting in high intra & inter subject variability & lack of dose proportionality. Self-micro emulsifying drug delivery technique is the one of the process for improving the solvency of the hydrophobic medication. The medications which are insoluble in water can be formulated in this technique by solubilizing it in the lipid vehicle to absorb through the membrane. The lipid and surfactants are utilized to build the solvency of the drug and improve absorption. This improves the dissolution rate of the drug by expanding its solubility. Oral bioavailability of hydrophobic drugs can be improved using SEDDS, and appears most promising. Their dispersion in gastro intestinal (GI) fluid after administration forms micro or nano emulsified drug which gets easily absorbed through lymphatic pathways bypassing the hepatic first pass metabolism. SMEDDS are isotropic mixtures of oil, surfactant, co-surfactant and drug with a unique ability to form fine oil in water microemulsion upon mild agitation following dilution with aqueous phase. This article gives an overview of SMEDDS as a promising approach to effectively tackle the problem of poorly soluble drugs.

Key Words: *Solubility, Dissolution, Absorption. and Bioavailability*

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INTRODUCTION

The oral route is the preferred way of dosing, because this is the easiest and most convenient way of noninvasive administration. Most of drug substance that applied orally today is small molecule that can permeate the intestinal gut membrane by transcellular passive diffusion. This process is determined by physicochemical law and by the properties of the intestinal cells. In addition to its permeability through the gut wall, the availability of drug in the body depends on its ability to dissolve in the gastrointestinal fluid[1].

The solubility or dissolution of the drug substance can be mainly altered on two levels, through material engineering of the drug substance or through formulation approaches. Whatever route is taken to enhance or modify the solubility and/or dissolution of a lead substance. It needs to be scalable to a commercially viable process later on in the development. Besides the aqueous solubility of a drug substance. Its permeability is a second critical aspect for oral bioavailability.The biopharmaceutical classification system (BCS) was introduced in the mid-1990s to classify the drug substances with respect to their aqueous solubility and membrane permeability. Drug substances, for which solubility enhancement can improve the oral bioavailability, are substances that are classified in class 2 (poor soluble/permeable) and class 4 (poor soluble/poor permeable). Especially for class 2 substances, solubility enhancement is part of the strategies to improve the oral bioavailability[2].

Recently, preparation of formulations with lipid base to upsurge the oral bioavailability of drugs with poor aqueous solubility is in trend. Selfdispersing lipid formulations are classified into two categories: (1) Self-emulsifying drug delivery system (SEDDS) and (2) selfmicroemulsifying drug delivery system (SMEDDS).

SMEDDS is homogeneous and isotropic mixture of drug, oil, surfactant, cosurfactant, and cosolvent. Dilution method and water titration methods are used to plot ternary phase diagram for the identification of best emulsifying region. SMEDDS is used to solve the problems of all Biopharmaceutical Classification System (BCS II) drug which possess issues of high molecular weight, low solubility, gastric irritation, enzymatic degradation, pre-systemic first pass-effect, low bioavailability and stability of drug [3,4,5].

Advantages of SMEDDS

SMEDDS formulation has several advantages:

1. Minimizing disturbance with the contact of GIT and gut wall.

2. Deliver peptides that are inclined to enzymatic hydrolysis in GIT.
3. It gives a sustained release of medicaments when a polymer is consolidated.
4. Safe and simple synthesis of SMEDDS.
5. More predictable fleeting profiles of medication assimilation.
6. Particular medication focusing on a particular replace ingestion with absorption window in the GI tract.
7. Drug security from the threatening condition in the gut.
8. The tale approach will upgrade water dissolvability and ultimate improve the availability of the lipophilic medication.
9. It demonstrates large inter and Intra subject variable in absorption prompting variance over plasma profile solid or liquid dosage forms.[6]

COMPONENTS OF SMEDDS

Lipid

Lipids are responsible for the solubilization of hydrophobic drugs, fluidization of the intestinal cell membrane, enhancement of dissolution rate, and solubility in gastrointestinal (GI) fluids, and they further protect the drug from chemical and enzymatic degradation by altering pharmaceutical properties of drug. Most drugs used in SMEDDS are hydrophobic in nature and have greater solubility in triglycerides than surfactants. Hence, they are used in 40–80% concentration[7,8,9].

Surfactant

Surfactants play an important role in the enhancement of solubility of hydrophobic drug in oil, dispersion of liquid vehicle on dilution in GIT fluids, improvement of bioavailability by increasing permeability, prevention of precipitate formation within the GI lumen, and prolonging the presence of drug moiety in soluble form, which results in effective absorption, and 30–60% concentration is used. They concentrate at oil-water interface and settle at inner stage (internal phase) in emulsion and make more stable microemulsion[10,11].

Co surfactant

In SMEDDS, for the purpose of reducing interfacial tension, high concentrations of surfactants is required that may cause gastric irritation. Thus, cosurfactants are employed to lessen the concentration of the surfactant, to dissolve large amount of either lipophilic drug or hydrophilic surfactant in lipid base, and to decrease interface of oil/water which results in immediate formation of microemulsion. Co-surfactants ranging between hydrophile-lipophile balance (HLB) values of 10–14 are widely used with the surfactant to reduce interfacial tension to a great extent to achieve transient negative value and to provide sufficient flexibility to interfacial film[12,13].

Formulation Design:

Formulation of SMEDDS involves the following steps.

1) Selection of active pharmaceutical ingredient (API) for self-micro-emulsifying drug delivery system (SMEDDS).
2) Screening of surfactant for emulsifying ability.
3) Choice of excipients for self-microemulsifying drug delivery system (SMEDDS).
4) The solubility of a drug in oils, surfactant, and co-surfactant.
5) Construction of pseudo ternary phase diagram.
6) Preparation of self-micro-emulsifying drug delivery system (SMEDDS).
7) Factor influencing self-micro-emulsifying drug delivery system.
8) Characterization and evaluation of SMEDDS.

Solubility of a drug in oils, surfactant, and co-surfactant

The dissolvability of medication in oils, surfactant, and co-surfactant: the aggregate of the oils surfactants, and co-surfactants were screened for their attributes to dissolve a tremendous amount of pure drug. An additional quantity of the drug is taken in clear screw cap glass vials that confine oil/surfactant/co-surfactant followed by blending on cyclomixer (vortex mixture). The admixture is shaken and centrifuged. An aliquant part from the supernatant is withdrawn and further analyzed by UV–Visible Spectrophotometer at required nm [14,15].

Construction of Pseudo Ternary Phase Diagram

The different proportions of oil, surfactant, and co-surfactant are agitated to formulate various techniques Fixed quantity of each system is added in a beaker containing 0.1 N HCl at 37°C and the substances are mixed using the magnetic stirrer The clearness of the designed dispersion was visually examined with the help of following grading techniques; A. Denoting the clear micro emulsion formation with bluish ting. B. Denoting a translucent micro emulsion formation had a bluish appearance.

C. Denoting a little less clear emulsion preparation. D. Indicating a clear white emulsion development. E. Signifying the details which had either poor emulsification with huge oil droplets superficially or the emulsion was not developed[16,17,18,19].

CONCLUSION

SMEDDS are a promising approach for the formulation of drug compounds with poor aqueous solubility. The oral delivery of hydrophobic drugs is now possible by SMEDDS, which have been shown to improve oral bioavailability substantially. The efficiency of the SMEDDS formulation is case specific in most instances thus, composition of the SMEDDS formulation should be determined very carefully. Since a relatively high concentration of surfactants is generally employed in the SMEDDS formulation, toxicity of the surfactant being used should be taken into account. In fact, a compromise must be reached between the toxicity and self-emulsification ability of the surfactant that is considered for use. The size and charge of the oil droplet in the emulsion formed are two other important factors that affect GI absorption efficiency. Versatility of SMEDDS could be proved if issues like method to predict solubilisation state of the drug in vivo, interaction of lipid systems with components of capsule shell and basic mechanism of transport of SMEDDS through GIT are adequately addressed. Despite the proven ability of these systems relatively few lipid based product have been commercialized. The reasons underlying the lack of application of these technologies is not clear, but likely reflects the limited knowledge of the formulation parameters that are responsible for good in vivo performance and the fact that relatively few in vivo studies in human have been reported in literature when compared with conventional dosage forms. Perhaps more importantly the lack of effective in vitro tests that are predictive of in vivo performance has significantly hindered successful development of these self emulsifying drug delivery systems.

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