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A REVIEW ON THE DESIGN OF THE FORMULATION FOR A SELFMICROEMULSIFYING DRUG DELIVERY SYSTEM TO INCREASE SOLUBILITY

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ABSTRACT

A significant issue facing the pharmaceutical industry is the poor aqueous solubility of approximately 35–40% of recently introduced drugs. This results in poor dissolution and low bioavailability, which raises intra- and inter-individual variability and lacks dose proportionality. One method for increasing the hydrophobic drug solvency is the self micro emulsifying drug delivery system. Using this method, pharmaceuticals that are insoluble in water may be made soluble in a lipid carrier so they can pass through the membrane. There are increase the drug's solubility and enhance absorption, lipids and surfactants are added. This increases the drug's solubility and also increases its rate of dissolution. SEDDS has the greatest potential for increasing the oral bioavailability of hydrophobic drug. Their dispersion in GI fluid after delivery results in a micro- or nano-emulsified medication that is readily absorbed through lymphatic routes, avoiding the first pass metabolism in the liver. The special capacity of SMEDDS to generate fine oil in water microemulsion with gentle agitation after dilution with aqueous phase makes them isotropic combinations of oil, surfactant, co-surfactant, and drug. In order to successfully address the issue of poorly soluble drug pharmaceuticals. This article provides an overview of SMEDDS as a promising approach to effectively tackle the problem of poorly soluble drugs.

Keywords: *Solubility, Dissolution, Absorption. And Bioavailability*

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Introduction

Oral administration is the recommended method of dosage since it is the most straightforward and practical non-invasive delivery method. Nowadays, the majority of drugs that are taken orally are tiny molecules that may enter the intestinal gut membrane by transcellular passive diffusion. The physicochemical properties of drug and the characteristics of the intestinal cells govern this process. The drug's capacity to dissolve in the gastrointestinal fluid determines its availability in the body in addition to its permeability through the gut wall [1].

There are two basic ways to modify the solubility or dissolution of drug either by formulating the drug molecule differently or by material engineering. Regardless of the approach used to improve or alter a lead the drug solubility or dissolving. Later on in the development phase, it must be scaled to a commercially viable method in addition to a drug's solubility in water. The pharmacological drug was categorized according to their water solubility and membrane permeability using the Biopharmaceutical Classification System (BCS), which was implemented in the mid-1990s they both class 2 (poor soluble/permeable) and class 4 (poor soluble/poor permeable) drug compounds can have their oral bioavailability improved via solubility method. One of the techniques to increased oral bioavailability and solubility improvement, particularly for class 2 drug [2].

Formulations containing lipid bases have been prepared more frequently recently in an effort to increase the oral bioavailability of drugs with low water solubility. One classifies self-dispersing lipid formulations into two groups:
(1) Self-microemulsifying drug delivery system (SMEDDS) and
(2) Self-emulsifying drug delivery system (SEDDS).

SMEDDS is an oil, surfactant and cosurfactant of homogenous isotropic combination of these ingredients. To find the optimal emulsifying zone, ternary phase diagrams are shown using the dilution method and water titration method. Any drug that has difficulties with large molecular weight, low solubility, stomach irritation, enzymatic degradation, pre-systemic first pass effect, limited bioavailability and stability of the drug can be solved using SMEDDS [3-5].

The benefits of SMEDDS formulation

1-Reducing disruption at the GIT and gut wall interface.
2-Deliver peptides that are predisposed to enzymatic hydrolysis in GIT.
3-Consolidation of a polymer results in a prolonged release of medication.
4-Easy and safe SMEDDS formulation.
5-More dependable ephemeral profiles of drug absorption.
6-A specific drug that targets the GI tract's substitute intake with absorption window.
7-Drug security against the potentially dangerous intestinal illness.
9-It exhibits significant intra- and inter-individual variation in absorption, causing variation in the plasma profile for both solid and liquid dose forms.[6]

Selection Components of SMEDDS

1-Selection of Lipids

Lipids play a crucial role in the solubilization of hydrophobic drugs, the fluidization of intestinal cell membranes, the acceleration of dissolution rates, and the solubility of drugs in gastrointestinal (GI) fluids. Furthermore, by modifying the pharmaceutical properties of the drug, lipids shield it from enzymatic and chemical degradation. In comparison to surfactants, the majority of drug used in SMEDDS are hydrophobic and more soluble in lipids. Therefore, 40–80% concentrations are utilized [7-9].

2-Selection of Surfactants

Surfactant are used at concentrations of 30–60% important in improving the solubility of hydrophobic drugs in oil, dispersing liquid vehicles upon dilution in GI fluids, improving bioavailability by increasing permeability, preventing precipitate formation within the GI lumen, and extending the drug's presence in soluble form, which results in effective absorption. Concentrating at the oil-water interface, they settle in the emulsion's inner stage, or internal phase, creating a microemulsion that is more stable [10,11]

3-Selection of Cosurfactant

SMEDDS requires large doses of surfactants, which may irritate the stomach, in order to reduce interfacial tension. Hence, cosurfactants are used to lower the surfactant's concentration, dissolve a significant quantity of hydrophilic or lipophilic drug in lipid base, and lessen the oil/water interface, which causes a microemulsion to develop instantly. In order to obtain a temporary negative value and provide the interfacial layer enough flexibility, co-surfactants with hydrophile lipophile balance (HLB) values between 10 and 14 are frequently utilized with surfactants [12,13].

Design of Formulation SMEDDS

The following steps are involved in formulating SMEDDS.

1) Choosing the active pharmaceutical ingredient (API) for the drug delivery system that self-microemulsifying (SMEDDS).
2) Surfactant screening for emulsifying potential.
3) Selecting the excipients for the SMEDDS.
4) The ability of a drug to dissolve in oils, surfactants, and co-surfactants.
5) The pseudo-ternary phase diagram is built.
6) Setting up the drug delivery system that self- microemulsifying SMEDDS).
7) A factor that affects the drug delivery mechanism that self- microemulsifying
8) SMEDDS characterisation and evaluation.

Drug solubility of oils, surfactants cosurfactants

The ability of drug to dissolve in oils, surfactants, and co-surfactants and the combined properties of these substances were examined for their capacity to dissolve a significant quantity 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 super natantis withdrawn and further analyzed by UV–Visible Spectrophotometer at required nm [14, 15].

Pseudo Ternary Phase Diagram Construction

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 [16-19].

Conclusion

SMEDDS are a potentially effective method for formulation drug molecules with low solubility in water. The oral delivery of hydrophobic drugs is now possible by SMEDDS, which have been shown to improve oral bioavailability substantially. Most of the time, the effectiveness of the SMEDDS formulation depends on the particular situation, thus it is important to carefully consider the formulation's composition. The toxicity of the surfactant being utilized should be considered, as the SMEDDS formulation often uses a rather high concentration of surfactants. Actually, the toxicity and self-emulsification capacity of the surfactant under consideration for application need to be balanced. The size and charge of the oil droplet in the emulsion formed are two other important factors that affect GI absorption efficiency. The versatility of SMEDDS may be demonstrated if problems such as how to forecast the drug's solubilization status in vivo, how lipid systems interact with capsule shell components, and the fundamental process of SMEDDS transport via the GIT are sufficiently addressed. Though these systems have demonstrated their capabilities, not many lipid-based products have reached the market. The reasons for the underutilization of these technologies are unclear, but they most likely stem from our limited understanding of the formulation parameters that yield good in vivo performance and the fact that, in comparison to conventional dosage forms, relatively few in vivo human studies have been published in the literature. More crucially, the development of these self-emulsifying drug delivery devices has been severely hampered by the absence of reliable in vitro assays that accurately predict in vivo performance.

References:

1. Loenberg,R.,&Amiidon,G.L.(2000).Oraldrugabsorption.MarcelDekker,106,137-153.
2. Stegemanna S, Leveiller F, Franchic D, Jongd DH, LindeneH (2007). When poor solubility becomes an issue: From early stage to proof of concept. European journal of pharmaceutical sciences, 249–261.
3. IngleLM,WankhadeVP,UdasiTA,TaparKK (2013).New approachesfordevelopmentandcharacterizationof SMEDDS. Int J Pharm Sci Res; 3:7-14.
4. Agrawal S, Giri TK, Tripathi DK, Alexander A (2012). A review on novel therapeutic strategies for enhancement of solubility for hydrophobic drugs through lipid and surfactant based SMEDDS: A novel approach. Am J Drug Disc Dev; 2:1-41.
5. Chaus HA, Chopade VV, Chaudhri PD (2013). Self-emulsifying drug delivery system: A review. Int J Pharm ChemSci; 2:34-44.
6. Kalamkar, P., Pawar, K., Baddi, H., Thawkar, B., Yevale, R., Kale, M. (2016). A Review on "Self-Microemulsifying Drug Delivery System (SMEDDS). Indian Journal of Drug, 4 (3), 361–373.
7. Reddy S, Katyayani T, Navatha T, Ramya G (2011). Review on self-microemulsifying drug delivery systems. Int J Pharm Res Pharm Sci; 2:382-92.
8. Pooja M, Rajni B, Nimrata S (2011). Lipid based SMEDDS for lipophilic drugs: A acquainted review. Int Res J Pharm; 2:75-80.
9. Parmar B,PatelU, Bhimani B,Sanghavi K. SMEDDS: Adominantdosage formwhichimprovebioavailability. Am J PharmTech Res 2012; 2:54-72.
10. Shah I(2011). Development and Characterization of o/w Nanoemulsions form Self-Microemulsifying Mixture-Thesis. p. 1-25.
11. ReddyLH,MurthyRS (2012).Lymphatictransportoforallyadministereddrugs.IndJExp. Biotechnol;40:1097-109
12. KhanA,KhanH,MohamadT,RasulA (2012).BasicsofSMEDDS.JPharmAlternMed; 1:13-20.
13. Parmar B, Patel U, Bhimani B, Sanghavi K (2012). SMEDDS: A dominant dosage form which improve bioavailability. Am J PharmTech Res; 2:54-72.
14. Parakh, D. R., Patil, M. P., Sonawane, S. S., Kshirsagar, S. J. (2016). Application of factorial design approach in development and evaluation of Selfmicroemulsifying drug delivery system (SMEDDS) of mebendazole. Journal of Pharmaceutical Investigation, 47 (6), 507–519
15. Sunazuka, Y., Ueda, K., Higashi, K., Tanaka, Y., Moribe, K. (2018). Combined effects of the drug distribution and mucus diffusion properties of self-microemulsifying drug delivery systems on the oral absorption of fenofibrate. International Journal of Pharmaceutics, 546 (1-2), 263–271.
16. Chou, Y.-C., Li, S., Ho, C.-T., Pan, M.-H. (2020). Preparation and evaluation of self-microemulsifying delivery system containing 5-demethyltangeretin on inhibiting xenograft tumour growth in mice. International Journal of Pharmaceutics, 579, 119-134.

17. Zheng, D., Lv, C., Sun, X., Wang, J., Zhao, Z. (2019). Preparation of a supersaturate self-microemulsion as drug delivery system for ellagic acid and evaluation of its antioxidant activities. Journal of Drug Delivery Science and Technology, 53, 101209.
18. Jo, K., Kim, H., Khadka, P., Jang, T., Kim, S. J., Hwang, S.-H., Lee, J. (2020). Enhanced intestinal lymphatic absorption of saquinavir through supersaturated self-microemulsifying drug delivery systems. Asian Journal of Pharmaceutical Sciences, 15 (3), 336–346.
19. Shete, H., Sable, S., Tidke, P., Selkar, N., Pawar, Y., Chakraborty, A. et. al. (2015). Mono-guanidine heterolipid based SMEDDS: A promising tool for cytosolic delivery of antineoplastics. Biomaterials, 57, 116–132.
20. Zhang P, Liu Y. Feng N, Xu J. (2008) Preparation and evaluation of selfmicroemulsifying drug delivery system of oridonin. Int J Pharm.355:269-27.
21. Ghosh PK, Majithiya RJ, Umrethia ML, Murthy RS. Design and development of microemulsion drug delivery system of acyclovir for improvement of oral bioavailability. AAPS Pharm Sci Tech 2006; 7:3-16
22. Wu W, Wang Y, Que L. (2006)Enhanced bioavailability of silymarin by selfmicroemulsifying drug delivery system. Eur J Pharm Biopharm; 63:288-294.
23. Khan BA, Rasul AL. (2012) Basics of Selfmicroemulsifying drug delivery system. Journal of Pharmaceutical Alternative Medicine, 1(1): 13-16.
24. Kohli K, Chopra S, Dhar D. (2010) Selfemulsifying drug delivery systems: An approach to enhance oral bioavailability. Drug Discover Today, 15(21): 958-965.
25. Kyatanwar A., Jadhav K., Kadam V. (2010) Self micro-emulsifying drug delivery system (SMEDDS). Journal of Pharmacy Research, 3(1): 75-83.
26. Kumar A. (2010) Selfemulsifying drug delivery system: Future aspect. International Journal of Pharmacy and Pharmaceutical Sciences, 2(14): 7-13.
27. Kawakami K, Yoshikawa T, Moroto Y, Kanakao E, Takahuani K, Nishihara Y and Masuda K. (2002) Microemulsion formulation for enhanced absorption of poorly soluble Drugs Prescription design. Journal of Controlled Release, 81: 75-82.
28. Maghani N, Suares D. (2013) Selfmicroemulsifying drug delivery system: A promising tool to improve bioavailability. Journal of Pharmacognosy and Phytotherapy, 2(1): 17-21.
29. Patel ND, Patel KV, Panchal LA, Shukla AK, Shelat PK. (2011) An emerging technique for poorly soluble drugs: Self emulsifying drug delivery system. International Journal of Pharma and Biosciences, 2(2): 621-629.
30. Patel AR,Vavia PR. (2005) Preparation and in vivo evaluation of SMEDDS containing Fenofibrate. International Journal of Pharmaceutics, 5(4): 27-34.
31. Reddy S, Katyayani T, Navatha A, Ramya G. (2011) Review on Selfmicroemulsifying drug delivery system (SMEDDS). International Journal of Research in Pharmaceutical Sciences, 2(3): 382-392.
32. Sinde G. (2011) Self microemulsifying drug delivery system: A novel approach for hydrophobic drug. International Journal Pharmaceutical Sciences, 3(1): 988-1005.
33. Shah NH, Carvagal MT, Patel CI, Infild MH, Malick A W. (1994) Self-emulsifying drug delivery system (sdeds) with polyglycolyzed glycerides for improving in vitro dissolution and oral absorption of lipophilic drugs. International Journal of Pharmacology, 106: 15-23.