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A Review of Research Study on - Self Nanoemulsifying Drug Delivery System

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ABSTRACT:

The Self Nanoemulsifying Drug Delivery System (SNEDDS) is a Novel Drug Delivery System for Enhancement of water solubility of poorly water soluble drugs. It is isotropic mixture of oil, surfactant, cosurfactant molecules and it also containing co-solvent molecule. It is Drug delivery system is thermodynamicallyand kinetically stable. The drug delivery system under mild agitation is followed by dilution of aqueous media such as GI fluid and it can from stable O/W Nanoemulsion. Having size of Globules is less than 100nm. It is important type of Drug delivery system to maintain the chemical stability as well as solubility of drug product. The Self Nanoemulsifying Drug Delivery System (SNEDDS) is important application on BCS Class II and Class IV Drugs for improving water Solubility of poorly water soluble drugs. It is important to prevent the interfacial tension and improving the dissolution as well as absorption rate of drug molecule. It is Novel Drug Delivery System is Applicable for parenteral, Ophthalmic, intranasal and cosmetic drug delivery system. And the present review describes Preparation, components, mechanism, of self Nanoemulsification biopharmaceutical aspects, characterization methods and applications of self Nanoemulsifying drug delivery system (SNEDDS) For Enhancement of oral Bioavailability of poorly water soluble drugs.

KEY WORDS: Nanoemulsion, Miniemulsion, Submicron Emulsion, Self-emulsifying, Psedoternary Phase.

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INTRODUCTION:

Self-nanoemulsifying Drug Delivery system (SNEDDS) is isotropic mixture of natural or synthetic oil, surfactants and co-surfactants that have a unique ability of forming fine oil-in-water (O/W) nano-emulsions under mild Agitation followed aqueous media[1]. Self-Nano emulsifying Drug Delivery System having size range of globules is less than 100nm under dispersion of water[2]. Recent years Self-Nano emulsifying Drug Delivery System (SNEDDS), self microemulsifying Drug Delivery System (SMEDDS) and self-emulsifying drug delivery systems (SEDDS) is used to improve the aqueous solubility of poorly water-soluble drugs[2]. The Formulation of self-nano-emulsifying Drug Delivery system was formulated by using medium chain tri glycerides oils and non-ionic surfactant, is important for oral ingestion[3]. The Drug was subjected to the Dissolution rate limiting absorption, the drug was under SNEDDS is important for enhancement of rate as well as Drug absorption and reproducibility of plasma profile of drug concentration[4]. The SNEDDS is one of the Stable Nano emulsion is important to provide a large interfacial area for partitioning of drug between oil and aqueous phase. Having better rate of drug dissolution and increases bioavailability of drug formulation[5]. The Self Nanoemulsifying drug delivery system is thermodynamically Stable and

Transparent or Translucent Non-ionized Dispersion of (o/w) and (w/o) Nano emulsion was stabilized by addition of Surfactant and Co-surfactant Molecule[6]. The Self Nanoemulsifying Drug Delivery System is also known as Nanoemulsion, Miniemulsion, ultrafine emulsion, Submicron emulsion[6].

Table 1 Comparision of Self emulsifying Drug Delivery System (SEDDS) and Self Microemulsifying Drug Delivery System (SMEDDS)

Sr No	SEDDS	SMEDDS	References
1	It is a mix. Drug,oil, surfactant	It is a mix. Drug, oil, surfactant, co-surfactant	7
2	Droplet size was 100-300 nm	Droplet size was less than 50 nm	8
3	Thermodyamically not stable	Transparent appearance	7
4	Turbid appearance	Thermodynamically stable	8
5	Ternary phase diagram is required to optimize the SEDDS	Psedoternary phase diagram is required to optimize SMEDDS	7

Table 2 Comparision of Self Nanoemulsifying Drug Delivery System (SNEDDS) and Self Microemulsifying Drug Delivery System (SMEDDS)

Sr No	SMEDDS	SNEDDS	References
1	It is Self-Micro emulsifying drug delivery system	It is Self-Nano emulsifying drug delivery system	9
2	It is turbid in nature	Less energy required for preparation	10
3	Large amount of energy is required for preparation as compare to nanoemulsion	Less energy required for preparation	11
4	Droplet size is 100-300nm	Droplet size is less than 100nm	12
5	It is thermodynamically stable	It is thermodynamically and kinetically stable	13
6	It is optimized by ternary phase diagram	It is optimized by Psedoternary phase diagram	14

- **ADVANTAGES OF SELF NANO EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) :**

- Nanoemulsion (SNEDDS) have a much large surface area and free Energy than micro emulsions(SMEDDS) [15].
- The self Nanoemulsifying drug delivery system is important to improve the Bioavailability[16].
- The ability of nanoemulsion (SNEDDS) to dissolve large quantities of lipophilic Drug, along with their ability to protect the drugs from hydrolysis and enzymatic degradation make them ideal vehicles for the purpose of parenteral transport [17].
- The SNEDDS is important to provide ultra-low interfacial tension and provide a large o/w interfacial areas [18].
- Nanoemulsion (SNEDDS) was formulated in a variety of formulations Such as liquids, sprays,foams, creams, ointments and gels and it is Used as Nanoemulsion in pharmaceutical field as well as used in drug delivery system such as oral, topical and parenteral nutrition[19].
- In Self Nanoemulsifying Drug Delivery System (SNEDDS) is Essential For oils and their maincomponents have the number of applications in medicine, food, beverages, preservation, cosmetics and it is also used for the fragrance and pharmaceutical industries[20].
- It is used as Ayurvedic system and unnani system [21]. The Self Nanoemulsifying drug Delivery System (SNEDDS) having site specific as well as targeted drug delivery system [22].

- **DISADVANTAGES OF SELF NANO EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS)**

- The preparations of Nanoemulsion (SNEDDS) are difficult to prepare because the high pressure homogenizer as well as ultrasonic equipment was available in recent year and the nanoemulsion preparation was expensive [23].

- ❖ The Stability of Self Nanoemulsifying drug delivery system was affected by Temperature and Ph [24].
- ➢ **COMPONENTS:**

In self Nanoemulsifying system is consists,

- ➢ Oil
- ➢ Surfactant
- ➢ Co-surfactant

REVIEW OF RESEARCH STUDY ON SELF NANOEMULSIFYING DRUG DELIVERY SYSTEM:

Meghana S. Kamble had done optimization of self-nanoemulsifying drug delivery system (snedds) of repaglinide using d-optimal mixture experimental design. Repaglinide, which is widely used in treatment of type 2 diabetes, is practically insoluble in water with lowbioavailability (about 50%) and poor absorption characteristics in upper intestinal tract. Self-nanoemulsifying drugdelivery system (SNEDDS) of repaglinide was developed and optimized using D-optimal mixture design to improveits dissolution and solubility. Four formulation variables; the oil phase X1 (Labrafil® M1944CS) and X2(Capmul® MCM-C8), the surfactant X3 (Tween® 80) and the co-surfactant X4 (Transcutol® P) were used in the
design. The prepared eleven formulations were evaluated in vitro for droplet size and % drug release. FormulationF5 was found to be optimum showing 100.05% drug release 53 nm droplet size, 13 s self-emulsification time androbustness to dilution with different media. [25]

Kishor Sagar had done study on design, development and characterization of selfnanoemulsifyingdrug delivery system (snedds) ofnateglinide. In the present investigation an attempt was made to enhance the solubility and dissolution of poorly soluble drug, Nateglinide, by formulating self-nanoemulsifying drug delivery systems (SNEDDS).Phase solubility of Nateglinide was eva luated in various non-aqueous carriers that included oils, surfactants, and co-surfactants. Pseudo ternary phase diagrams were constructed to identify the optimized selfnanoemulsification region. The formulations were characterized for self-emulsification assessment, globule size, polydispersity index, zeta potential, % transmittance, drug content, thermodynamic stability and *in-vitro* dissolution study. [26]

C. Aparna was formulated and evaluated of solid self emulsifying drug delivery sytem of voriconazole. The aim of the present work was to prepare Self emulsifying drug delivery system (SEDDS) of lipophilic anti-fungal drug,Voriconazole for improving its solubility and bioavailability. Various oils, surfactants and co-surfactants were screened for their suitability in the formulation of SEDDS. The prepared formulations were evaluated for parameters like drug content, percentage transmittance and centrifugation test. Pseudoternary phase diagrams were constructed to determine the Nanoemulsion area for each formulation. From the results, F7 (2:1) was found to be the optimized formulation as it exhibited rapid emulsification and required drug content. The drug release from these optimized formulations, Solid Self emulsifying drug delivery systems (SSEDDS) was also studied and found to be better compared to the conventional dosage form. Our studies indicate that SSEDDS can be effectively formulated by adsorption technique. Voriconazole SEDDS with enhanced dissolution rate and bioavailability were successfully formulated and evaluated. [27]

Amit Kumar Nayak had done Study on A Solid Self-Emulsifying System for Dissolution Enhancement of Etoricoxib. Self-emulsifying drug delivery system offers a solution to improve the oral bioavailability of poorly aqueous soluble drugs. Etoricoxib, a nonsteroidalanti-inflammatory drug (NSAID) is a selective cycooxygenase-2 (COX-2) inhibitor. The poor aqueous solubility of etoricoxib resultsvariable dissolution rate, which is the major cause of poor bioavailability. In the current study, formulation of solid self-emulsifying systems forthe dissolution enhancement of etoricoxib was attempted. The self-emulsifying tablet of etoricoxib containing goat fat and Tween 60 admixturewas formulated by pour moulding technique using a plastic mould. The weight uniformity, drug content, liquefaction time, and in vitro dissolutionin simulated gastric fluid of the formulated tablets were evaluated. There was increase in in vitro drug release with increase in Tween 60 contentand decrease in goat fat content. The etoricoxib release in simulated gastric fluid followed the non-Fickian diffusion model (anomalousbehaviour). [28]

Dr.M. Sunitha Reddy had done Study on Formulation and *in-vitro* Characterization of Solid Self Nanoemulsifying Drug Delivery System (s-SNEDDS) Of Simvastatin. The Present Work Is To Prepare Solid Self Nanoemulsifying Drug Delivery System (S-Snedds) Of A Poorly Water

Soluble Drug Simvastatin With Crospovidone As Carrier To Enhance Dissolution Rate Of Simvastatin. Based On Solubility Studies And Pseudo Ternary Phase Diagrams Five Liquid Snedds Were Prepared With Selected Systems In Various Proportions And Evaluated For Self Emulsification Time, Phase Separation And Precipitation Of The Drug, Robustness To Dilution, Percentage Transmittance, Thermodynamic Stability Studies, Droplet Size, Pdi And Zeta Potential. Prepared S-Snedds Showed "Good" Flow Properties And 94.192±1.39% Drug Content. Reconstitution Properties Showed Spontaneous Nano Emulsification With Droplet Size 16.27 Nm And Pdi 0.276. Results Of In-Vitro Dissolution Revealed That % Drug Released Form S-Snedds Is Higher Than That Of Pure Drug And Marketed Tablet. Results Of Accelerated Stability Study For 6 Months Showed That Formulation Was Stable And Does Not Alter The Dissolution Rate Of Simvastatin. The Results Of Present Study Have Proved The Potential Use Of Snedds To Improve Solubility And Dissolution Rate Of Poorly Water Soluble Drug Simvastatin. [29]

Komal Parmar had done study on Design, characterization and in-vitrostudiesSelf nano-emulsifying drug delivery system for Embelin. The objective of the study was to prepare solid self-nanoemulsifying drug delivery system (S-SNEDDS) containing Capryol-90 as oil phase for the delivery of Embelin, a poorly water soluble herbal active ingredient. Box-Behnken experimental design was employed to optimise the formulation Optimised liquid formulations were formulated into free flowing granules (S-SNEDDS) by adsorption on the porous materials like Aerosil 200 and Neusilin and thereby compressed into tablet. *In vitro*dissolution studies of SNEDDS revealed increased in the dissolution rate of the drug. TEM analysis exhibited sphericalglobules. Further, the accelerated stability studies for 6 months revealed that S-SNEDDS ofEmbelin are found to be stable without any significant change in physicochemical properties.Thus, the present studies demonstrated dissolution enhancement potential of porouscarrier based S-SNEDDS for poorly water soluble herbal active ingredient, Embelin. [30]

Raman Suresh Kumar was formulated and evaluated Self Nanoemulsifying Drug Delivery System of Olanzapine for Enhanced Oral Bioavailability for In vitro, In vivo Characterisation and In vitro -In vivo Correlation. Lipid based self nanoemulsifying drug delivery system (SNEDDS) was explored to improve the oral bioavailability of olanzapine (OLZ), a poorly water-soluble drug candidate, using spontaneous emulsification method. The pharmacokinetic study was conducted on rabbits and the parameters like peak concentration (Cmax), time of peak concentration (Tmax), etc. were evaluated by Wagner nelson method. The *in vivo* studies concluded that there was 1.2 fold and 1.6 fold increase in bioavailability of nanoemulsion when compared with marketed tablet formulation and drug suspension, respectively. From the similarity factor between biorelevent dissolution media and 0.1 N HCl (pH 1.6) it was concluded that the 0.1 N HCl (pH 1.6) can be used for the dissolution of SNEDDS to predict the *in vivo* bioavailability instead of the biorelavent media. The level A correlation with correlation factor 0.97 was achieved, which showed that there is a good correlation between *in vitro* dissolution and *in vivo* bioavailability and the dissolution studies can be used as a surrogate for the *in vivo* studies. [31]

Ali Nasr had done study on Design, Formulation, Pharmacokinetic and Bioavailability EvaluationNovel Solid Self-Nanoemulsifying Drug Delivery System (S-SNEDDS) for Oral Delivery of Olmesartan Medoxomil.the study was to develop a solid self-nanoemulsifying drug delivery system (S-SNEDDS) of Olmesartan (OLM) for enhancement of its solubility and dissolution rate. In this study, liquid SNEDDS containing Olmesartan was formulated and further developed into a solid form by the spray drying technique using Aerosil 200 as a solid carrier.The prepared S-SNEDDS formulae were evaluated for flow properties, differential scanning calorimetry (DSC), scanning electron microscopy (SEM), reconstitution properties, drug content and in vitro dissolution study. It was found that S-SNEDDS formulae showed good flow properties and high drug content. Reconstitution properties of S-SNEDDS showed spontaneous self-nanoemulsification and no sign of phase separation.Results of the in vitro drug release showed that there was great enhancement in the dissolution rate of OLM. To clarify the possible improvement in pharmacokinetic behavior of OLM S-SNEDDS, plasma concentration-time curve profiles of OLM after the oral administration of optimized S-SNEDDS formula (F3) were compared to marketed product and pure drug in suspension.[32]

Rehmana Rashid had done Comparative study on solid self-nanoemulsifying drug delivery and solid dispersion system for enhanced solubility and bioavailability of ezetimibe.

The objective of this study was to compare the physicochemical characteristics, solubility, dissolution, and oral bioavailability of an ezetimibe-loaded solid self-nanoemulsifying drug delivery system (SNEDDS), surface modified solid dispersion (SMSD), and solvent evaporated solid dispersion (SESD) to identify the best drug delivery system with the highest oral bioavailability.The SESD formulation was prepared with the same composition of optimized SMSD. The aqueous solubility, dissolution, physicochemical properties, and pharmacokinetics of all of the formulations were investigated and compared with the drug powder. The drug existed in the crystalline form in SMSD, but was changed into an amorphous form in SNEDDS and SESD, giving particle sizes of approximately 24, 6, and 11 µm, respectively. All of these formulations significantly improved the aqueous solubility and dissolution in the order of solid SNEDDS $ SESD . SMSD, and showed a total higher plasma concentration than did the drug powder. **[33]**

Gamal M El Maghraby had done study on Self emulsifying Liquisolid tablets for enhanced oral bioavailability of repaglinide: In vitro and in vivo evaluation. The aim of this work was to enhance dissolution rate and oral bioavailability of repaglinide. This was achieved by development of liquisolid tablet with the liquid component being self emulsifying drug delivery system (SEDDS). Thus SEDDS was prepared using oleic acid as oil and Tween 20 or its mixture with propylene glycol surfactant/cosurfactant system. Formulations containing different oil concentrations were loaded with various amounts of drug and subjected to in vitro evaluation. Optimum formulations were prepared and evaluated as liquisoild tablets. The in vivo study revealed enhancement of the rate and extent of drug absorption after incorporation into the SEDDS, this was evidenced by the rapid onset of action and higher area above the blood glucose versus time curve compared to the unprocessed drug. Overall, the developed system was able to increase the bioavailability of repaglinide. **[34]**

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