

SELF-EMULSIFYING DRUG DELIVERY SYSTEM – A REVIEW**Anil Kumar Chouhan* Mukesh Mehra and Narendra Gehalot**

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Ujjain, M.P.**ABSTRACT**

The modern study was expected to devise Self-emulsifying drug delivery system. SEDDS absorption and it may get better oral bioavailability of the poorly soluble drug, a combination of modified oils, surfactant, co-surfactant mixtures were screened for their appropriateness in the formulation of Self-emulsifying drug delivery system and work of SEDDS be optimized.. The drug release since these optimized formulations be study and create to be better compared on the way to conventional dosage form. Our study point to that Self-emulsifying drug delivery system can be successfully formulated by adsorption method and dissolution profile. It is hold up by SEM study,

which does not prove verification of precipitation of the drug on the surface of the delivery service. Dissolution studies revealed incredible enhance in dissolution of the drug as compare to market invention.

KEYWORDS: Self –emulsification, oil, surfactant, co-surfactant, dry emulsion.**INTRODUCTION****SEDDS system**

- ✓ SEDDS are defined as a pre-concentrate containing a combination of drug, oil, surfactant, and co-surfactant and, from time to time, co-solvent. Self-emulsifying drug delivery system is a broad term connected with the making of emulsions with a droplet size ranging from a few nanometers to several microns, which can be classify as SMEDDS and SNEDDS. SMEDDS form visible microemulsions with oil droplet ranging between 100 and 200 nm, while SNEDDS are more fresh, with droplet sizes smaller than 100 nm.^[12]
- ✓ The digestive motility of the stomach and intestine provide the campaigning compulsory for self-emulsification in vivo. The advantages of these systems comprise not only

improved drug solubilization. But also improved release and absorption properties due to the already dissolved form of the drug in the formulation and the resulting small droplet size, which provide a large interfacial surface area.^[17]

- ✓ Salt formulation, micronization, inclusion in cyclodextrins, encapsulation in micro/nanoparticles, preparation of solid dispersions, solubility in lipid-based systems, mixed micelles and the use of silica-based mesoporous material have been the main approach studied.
- ✓ Lipid-based formulations include lipid solutions, lipid nano-particles, emulsions, micro emulsions or SEDDS.^[19]

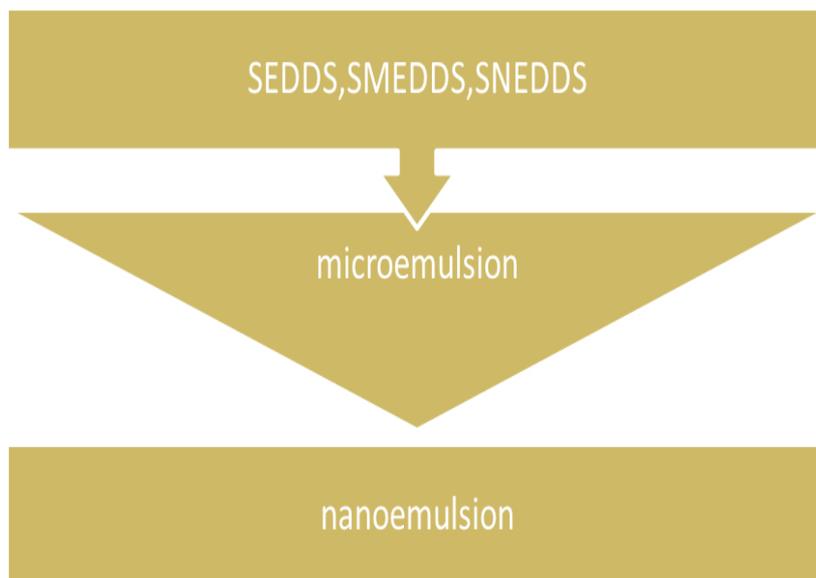
Self-emulsifying drug delivery system development

- ✓ The competence of the oral absorption of a drug composite from the SE formulation depends on many formulation-related parameter, such as surfactant concentration, surfactant, HLB, oil/surfactant ratio and droplet size, all of which establish the self-emulsification facility. Thus, only very exact pharmaceutical excipient combination will lead to capable SE systems.
- ✓ To increase a better concerned of the reasons after successful SEDDS formulation, the selected ten Poorly water soluble drug exhibit dissimilar physicochemical property and resolute their solubility in a range of oils and surfactants.
- ✓ In this case, the Self-MicroEmulsifying Drug Delivery System was collected of Capryol 90, Cremophor EL or Solutol HS15 and Akoline-MCM as the oil phase, surfactant and co-surfactant, respectively. The optimized CFP SNEDDS required a surfactant content of less than 40% to form nanoemulsion, and the droplet size was not synthetic by the pH of the dilution medium.

Self-emulsifying drug delivery system bioavailability

- ✓ Self-emulsifying drug delivery system find better the oral bioavailability of Poorly water soluble drug by attractive the solubility and keep the drug in a dissolved state, in small droplets of oil, during its transit through the GIT.
- ✓ The improvement of the oral bioavailability has been qualified to dissolution increase of drug, larger surface area provided by the fine emulsion droplets, improved diffusion across the unstirred aqueous layer, and enlarged mucosal permeability due to high content of surfactants and also by the long chain oil that promotes lipoprotein mixture by subsequent lymphatic absorption.

- ✓ The tool by which these factors act are closely connected to the formulation components and properties of the formed emulsions such as fast emulsification, mean size of the droplets and zeta potential. Factor acting on the bioavailability of hydrophobic drugs make as self-emulsifying drug delivery system.



Sedds, Smedds, Snedds

Dosage form of SEDDS

- ✓ **Dry emulsion-** It is mostly oil in water emulsion, changed keen on solid by using various techniques such as spray drying, using solid carrier adsorption or freeze drying technique (Patel A et al 2008; Charman SA, 1992; Constantinides PP, 1995). Dry emulsion may be re separate in water previous to use. These are actually powders in which Emulsification spontaneously occurs in vivo or behind experience to an aqueous solution.(Sapra et al., 2012; Jang DJ et al., 2006).
- ✓ **Self-emulsifying capsule-** After management of capsules has conservative liquid formulations, microemulsion droplets structure and subsequently disperse in the GIT to reach sites of absorption. Though, if irreversible phase division of the microemulsion occurs, an improvement of drug absorption cannot be estimated. Used for handling this difficulty, sodium dodecyl sulfate was extra into the SE formulation (Itoh K, 2008).
- ✓ **Self-emulsifying sustained release tablet-** To reduce considerably the quantity of solidifying excipients necessary for conversion of Self-emulsifying drug delivery system into solid dosage forms, a gelled Self-emulsifying drug delivery system have been developed by Patil et al. keen on their study, colloidal silicon dioxide was select as a

gelling agent for the oil-based systems, which served the dual reason of dropping the amount of compulsory solidifying excipients and aid in slow down of the drug free (Sapra K et al., 2012; Vasanthavada M & Serajuddin A T, 2007).

- ✓ **Self-emulsifying sustained /controlled release pellets** - Pellets having several encouragement over conventional solid dosage forms like minimizing the inter subject and intra subject variability of plasma profiles and also reduce the GI irritation without lower the bioavailability of drug. These are the various unit dosage forms. (Tang Bo et al, 2008).
- ✓ **Self-emulsifying beads** - These are ready as a solid dosage form using less quantity of excipient. Paradkar with Patil formulate an isotropic formulation of loratidine consisting Cremophore EL, Capmul MCM and Captex 200. By use solvent evaporation technique the SE mixture overloaded into poly propylene beads. The consequences indicate that self-emulsifying bead can be formulate as a solid dosage form with less quantity of solidifying agents (Wadhwa J et al., 2011).
- ✓ **Self-emulsifying nanoparticle**- ready by by nanoparticles technology. Single of the solvent be injection, in this process the prepared melt lipid mass contained lipid, surfactant and drug. This is drinkable and dried to get nanoparticles. By this method 100 nm size unit with 70-75% drug loading effectiveness was obtained.
- ✓ **Self-emulsifying solid dispersion** - To surmount the difficulties related to manufacturing and solidity SE solid dispersion be formulate. It also enlarge the dissolution time and bioavailability of water soluble drugs. Use. (Tang Bo et al, 2008).
- ✓ **Self-emulsifying suppositories**- Some investigators prove that solid SEDDS can not only enlarge GI adsorption but can also are used to advance rectal and vaginal absorption. By with self-emulsifying technique suppositories of Indomethacin have been ready. (Kim JY & Ku YS, 2000).
- ✓ **Self-emulsifying implants**- Research in the field of SE implants has very much enhance the efficacy and function of solid self-emulsifying formulation for example Carmustin is a therapeutic agent use in the treatment of malignant brain tumors but it has small biological half-life.^[15]

Need Of Self-Emulsifying Drug Delivery System

- ✓ Oral delivery of poorly water-soluble complex is to pre-dissolve the compound in a appropriate solvent and fill up the formulation into capsules.

- ✓ The main benefit of this approach is that predissolving the compound overcomes the preliminary rate limiting step of particulate dissolution in the aqueous atmosphere inside the GI tract.
- ✓ Though, a potential problem is that the drug may precipitate absent of solution as the formulation disperses in the GI tract, particularly if a hydrophilic solvent is used.
- ✓ But the drug can be dissolved in a lipid vehicle there is less prospective for precipitation on top of dilution in the GI tract, as partitioning kinetics willpower support the drug remaining in the lipid droplets. (Amidon, G., et.al. 1995).

Advantages of self-emulsifying drug delivery system S

- ✓ Improved oral bioavailability enabling reduction in dose (T. Gershanik et al., 1996).
- ✓ Extra consistent temporal profile of drug absorption.
- ✓ Selective targeting of drug(s) towards particular absorption window in GIT.
- ✓ Protection of drug(s) as of the hostile atmosphere in gut.
- ✓ Concentrated variability including food effects.
- ✓ Safety of sensitive drug substances.
- ✓ Liquid before solid dosage forms.

Disadvantages Of Self-Emulsifying Drug Delivery System S

- ✓ Conventional dissolution methods do not work, because these formulations potentially are needy on digestion prior to release of the drug.
- ✓ This in vitro model needs further development and validation previous to its potency can be evaluated.
- ✓ Additional development will be base on in vitro - in vivo correlations and then different prototype lipid based formulations needs to be developed and tested in vivo in an apposite animal model.
- ✓ The drawback of this system include chemical instabilities of drugs and high surfactant concentrations in formulations (approximately 30-60%) which GIT.

Excipients of Self-Emulsifying Drug Delivery Systems

A). Oils: The oil represent one of the most important excipients in the SEDDS formulation not only since it can solubilize the required dose of the lipophilic drug or make easy self emulsification but also and mainly because it can increase the fraction of lipophilic drug transported via the intestinal lymphatic system, thereby greater than ever absorption from the GI tract depending on the molecular character of the triglyceride 28-30. Both long and

medium chain triglyceride (LCT and MCT) oils with similar degrees of saturation have been used for the design of self-emulsifying formulations.^[11]

B). Surfactants: Some compounds exhibiting surfactant properties may be employed for the design of self-emulsifying systems, but the choice is incomplete as very few surfactants are orally acceptable.

- ✓ The four main groups of surfactants are defined as follows-
- ✓ Anionic surfactants
- ✓ Cationic surfactant
- ✓ Ampholytic surfactants
- ✓ Nonionic surfactants^[10]

C). Co-Solvents: The manufacture of an optimum SEDDS requires relatively high concentrations (generally more than 30% w/w) of surfactants, thus the concentration of surfactant can be reduced by incorporation of a co-surfactant. The role of the co-surfactant in concert with the surfactant is to lower the interfacial tension to a very small even transient negative value.^[10]

Commercially available SEDDS

	Drug Formulation	Type of dosage form
1	Astaxanthin	SE Capsules
2	Amlodipine	SE Dry emulsion
3	Diclofenac	SE tablets
4	Nitendipine	Pellets
5	Loratidine	SEF(Beads)
6	Paclitaxel	SE nanoparticles
7	Phenacetin	Solid Dispersion
8	Indomethacin	Suppositories
9	Carmustine	Implants
10	Halofantrine	SEF powder

Evaluation of Self-Emulsifying Drug Delivery System S

- ✓ **Thermodynamic stability study:** The physical stability of a lipid-based formulation is as well crucial to its presentation, which can be harmfully pretentious by precipitation of the drug in the excipient matrix. In addition, poor formulation physical stability can lead to phase partition of the excipient, affecting not only formulation performance, but

visual form as well. In adding up, incompatibilities among the formulation and the gelatin capsules covering can lead to brittleness or deformation, belated disintegration, or incomplete release of drug.^[12]

- **Heat cooling cycle:** Six cycles between refrigerator temperature (40°C) and 45°C by storage space at each temperature of not less than 48 hr is calculated. persons formulations, which are stable at these temperatures, are subjected to centrifugation assessment.
- **Centrifugation:** Passed formulations are centrifuged thaw cycles between 21 °C and +25 °C with storage space at temperature for not less than 48 hr is done at 3500 rpm for 30 min. those formulations that does not show any phase partition are taken intended for the freeze thaw stress test.
- **Freeze thaw cycle:** Three freeze for the formulations. Those formulations passed this test show good quality stability by no phase separation, creaming, or cracking
- ✓ **Dispersibility examination:** The competence of self-emulsification of oral nano or micro emulsion is evaluated using a standard USP XXII dissolution apparatus 2. One milliliter of each formulation be added to 500 mL of water at 37 ± 0.5 0C. A typical stainless steel dissolution paddle rotating at 50 rpm afford gentle agitation. The in vitro presentation of the formulations is visually assess by the following.^[19]

Grade system

- ✓ Grading A: speedily forming (within 1 min) nanoemulsion, have a clear or bluish appearance.
- ✓ Grading B: speedily forming, to some extent less clear emulsion, having a bluish white appearance.
- ✓ Grading C: Fine milky emulsion so as to shaped within 2 min.
- ✓ Grading D: Dull, grayish white emulsion having slightly oily exterior that is unhurried to emulsify (longer than 2 min).
- ✓ Grading E: Formulation, exhibit either poor or minimum emulsification with large oil globules present on the surface. Grade A and Grade B formulation will remain as nanoemulsion when discrete in GIT. While formulation falling in Grade C could be advise for self-emulsifying drug delivery system formulation.

C) Turbidimetric estimation: Nepheloturbidimetric assessment is done to check the growth of emulsification. Fixed quantity of Selfemulsifying system is added to fixed amount of

suitable medium (0.1N hydrochloric acid) under nonstop stirring (50 rpm) on magnetic plate at ambient temperature, and the increase in turbidity is measured by a turbidimeter. though, since the time required for whole emulsification is too short, it is not possible to monitor the rate of change of turbidity (rate of emulsification),

D) Viscosity Determine: The SEDDS system is generally administered in easily pourable into capsules and such system should not too thick to create a problem. The rheological properties of the micro emulsion are evaluated by Brookfield viscometer. This viscosities determination conform whether the system is w/o or o/w. If system has low viscosity then it is o/w type of the system and if high viscosities then it are w/o type of the system.

E) Droplet Size Analysis Particle Size Measure: The droplet size of the emulsions is resolute by photon correlation spectroscopy (which analyses the fluctuations in light scattering due to Brownian motion of the particles) using a Zetasizer able to calculate sizes between 10 and 5000 nm.^[5]

DRY EMULSION

Preparation of Dry Emulsion

Preparation of dry emulsion follows the steps given below

- ✓ Liquefy drug in lipophilic solvent.
- ✓ Include aqueous phase containing bulking agents.
- ✓ Outline an emulsion.
- ✓ Eliminate water (Lyophilization, spray drying).
- ✓ Fill up powder into capsules or compress into tablets.

Dry emulsions are prepared by using Spray drying

- ✓ Lyophilization
- ✓ Rotary evaporation

Method

- ✓ Water O/w emulsions is ready with desired % of dry powder mass. The aqueous solution enclose dissolved solid carrier and lipophilic vehicle is homogenized (Faldt P, Bergenstahl B, 1996c) in a elevated speed colloid mill. After that the liquid O/W emulsions were spray dry in a laboratory spray dryer.

- ✓ Reconstitution of liquid emulsions: A whole of 1.0 g of dry emulsion was suspended in 4.0 ml. of distilled water in a 17 ml. container. Later than 1 hour of rotation on approximately 20 rpm, samples are withdrawn for additional characterization.
- ✓ The dry emulsions were store in a well closed containers protected from light at ambient temperature and 400 C in 75% relative humidity chamber created by a saturated NaCl solution.^[12]

Dry Emulsions Necissity

- ✓ Side effects are reduced.
- ✓ Dry emulsions are attractive as they are physically and microbiologically constant formulations.
- ✓ They characterize a possible oral drug delivery system for lipophilic and low soluble drug substances.
- ✓ Used for drug substances require protection next to light or oxidation.
- ✓ Dry emulsions give the majority stable possible effective blood levels over prolonged durations of treatment.^[13]

Dry Emulsions Applications

- ✓ Into the formulation of antifoams.(Chiou WL and Riegelman S, 1971)
- ✓ Into beauty formulations.
- ✓ Into family care wipes, in skin care wipes, in baby care wipes.
- ✓ Into makeup removing wipes.
- ✓ Into bath salt formulations.
- ✓ Into surface coating formulations for e.g: in paints. (Lladser M, 1968).^[15]

Dry Emulsions Properties

- ✓ The variety of rotary atomizer and the rotation rate had no visible effect on the technical property of the dry emulsions have 40% lipid.
- ✓ The reconstitution possessions of the dry emulsions were change by both the type of rotary atomizer and in the rotation rate of the atomizer.
- ✓ The porosimeter density of the dry emulsions is affect by the rotation rate of the atomizer.
- ✓ This is maybe due to a particle size effect caused by the decrease of particle size with improved rotation rate of atomizer.
- ✓ The dry emulsions are cohesive powders have poor flow ability suitable to low density, the size and form of the particles.

- ✓ Dry emulsions have lipid content below 50% reformed the creative emulsion.^[17]

CONCLUSION

Seeds formulation can be optimized used for the delivery of hydrophobic compound with drug load; minimum surfactant application and proper infinite dilution can be achieve devoid of preparation precipitation. Seeds are able to be making use of for the formulations of drugs compound by means of poor water soluble drug. Advance of this technology Seeds resolve continue to allow novel application in drug delivery system.

Seeds have been shown to be rationally successful in civilizing the oral bioavailability of weakly water-soluble and conventional preparation of Self-emulsifying drug delivery system involves dissolution of drugs in oils and their blending with proper solubilizing agents. Dry emulsions are smart since they are physically and microbiologically constant formulations. Dry emulsions give most stable possible successful blood levels over prolonged durations of treatment.

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