IJMPR 2023, 7(4), 81-89

International Journal of Modern Pharmaceutical Research

www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Review Article

SJIF Impact Factor: 5.273

A REVIEW ON SELF NANO EMULSIFYING DRUG DELIVERY SYSTEM

Chandana L.*, Snehalatha[1], Subhan Sab[1], Nagaraja T. S.[1] and Chethan Patel D. N.

Department of Pharmaceutics, SJM College of Pharmacy, Chitradurga-577502 Karnataka, India.

Received on: 22/02/2023

Revised on: 12/03/2023

Accepted on: 02/04/2023

***Corresponding Author**

Chandana L.

Department of Pharmaceutics, SJM College of Pharmacy, Chitradurga-577502 Karnataka, India.

ABSTRACT

A large proportion of novel pharmacologically active molecules developed in recent drug discovery programmes are lipophilic and poorly soluble, posing a significant challenge for pharmaceutical researchers to improve the oral bioavailability of such drug molecules. Among the different approaches, SNEDDS has received more attention due to improved oral bioavailability, which allows for dose reduction. SNEDDS is an isotropic mixture of oil, surfactant, co-surfactant and drug that forms an oil-in-water emulsion in aqueous environment under gentle agitation. Low energy emulsification tmethods and high energy emulsification methods can both be used to create nano emulsions. The self nano-emulsifying drug delivery system (SNEDDS) can improve the water solubility of poorly water soluble drugs in BCS classes II and IV. This review describes composition, preparation of components, mechanism of self emulsification, biopharmaceutical aspects and evaluation of self nano-emulsifying drug delivery system(SNEDDS) for enhancement of oral bioavailability of poorly water soluble drugs.

KEYWORDS: Self nano emulsifying drug delivery system, bioavailability, surfactant, solubility.

INTRODUCTION

The oral route is the most simple and convenient method of noninvasive administration. Oral drug delivery on the other hand, may hamper drug molecules with low aqueous solubility. Approximately 40% of new chemical entities have poor water solubility and pose a significant challenge to the modern drug delivery system resulting in poor oral bioavailability, considerable intra and inter-subject variability and a lack of dosage proportionality. The Biopharmaceutical Classification System (BCS) classifies these drugs as class II pharmaceuticals meaning they have low water solubility but high permeability. To address the poor aqueous solubility, various techniques such as solid dispersion and complexation with cyclodextrins have been already used. These approaches have been beneficial in some circumstances, but they have a number of drawbacks.[1]

In response to this lack in these procedures, the use of nanotechnology in the provision of many drug benefits such as improving drug stability, increasing the permeability or transport of poorly permeable drugs, controlling drug distribution and disposition in the body and targeting drug delivery to the site of action has been recognised. Nanoemulsions for example, are lipid-based drug delivery technologies that have shown promise in enhancing the solubility of drugs that are weakly water soluble.[2]

Self-Nano emulsifying drug delivery system (SNEDDS), self-micro emulsifying drug delivery system(SMEDDS) and self emulsifying drug delivery systems (SEDDS) have all been employed in recent years to increase the oral bioavailability of poorly water-soluble drugs.[3] A self-nano emulsifying drug delivery system (SNEDDS) is an isotropic mixture of oil, surfactant, co-surfactant and drug introduced into aqueous phases under gentle agitation. SNEDDS are easily distributed in the gastrointestinal system and the digestive motility of the stomach and intestine provides the agitation required for self-emulsification.[4] In general, the size range of self-emulsification systems ranges from nanometer to micrometer. Self-Nano emulsification systems have a globule size range of less than 100nm following dispersion in water.[5]

This stable emulsion provides a large interfacial area for drug partitioning between the oil and water phases, which may lead to quicker dissolution rate and enhanced bioavailability. SNEDDS appears to be an attractive choice of formulation because it requires simple and cost-effective manufacturing infrastructure. This is because SNEDDS is a physically stable lipid solution, eliminating the need for a high energy emulsification procedure and thereby lowering manufacturing costs. Furthermore, SNEDDS's faster dissolution rate and more consistent bioavailability imply a lower medication dose, potentially eliminating dose-related side effects.[6]

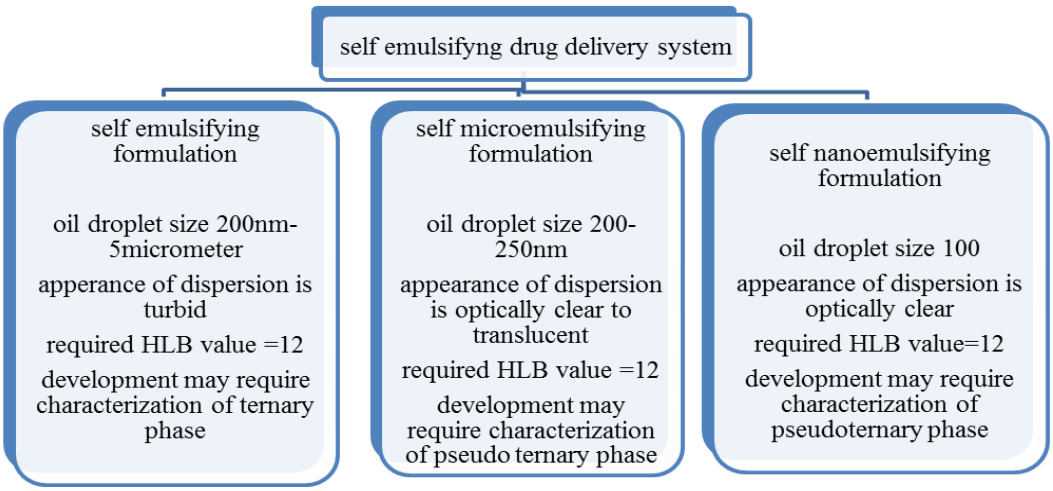

Figure 1: Difference between SEDDS, SMEDDS and SNEDDS.

Advantages[7]

- Rapid onset of action.
- Oral bioavailability enhancement.
- Safe delivery of peptides which are degraded due to enzymatic hydrolysis in GIT.
- Enhanced drug loading capacity with SNEDDS.
- Reduction in dosage of drug.
- Easy in scale up (pilot plant) process.
- No impact on digestion process of lipid.

Disadvantages

- Production costs are high.
- Challenges regarding the validation of different components.
- Problems with drug compatibility.
- Less drug loading due to leakage.
- Traditional dissolution methods do not work.
- High concentration of surface active agent in formulation may cause irritation to GIT.
- Volatile co solvents of SNEDDS migrate into capsule shells, cause precipitation of hydrophobic drugs.

Types of nanoemulsion (SNEDDS)[8]

1) Water-in-oil nanoemulsion (w/o) water droplet was distributed in continuous phase oil.
2) Nanoemulsion of oil in water (o/w). Oil droplets were distributed in continuous phase water.
3) Nanoemulsion with bi-continous morphology.

In which the surfactant was soluble in both the oil and water phases and the droplet was dispersed in both the oil and water phases

Selection of Appropriate Drug Candidates for SNEDDS

The snedds system is a novel approach for improving the oral bioavailability of poorly water-soluble drugs. In comparison to class I and class III drugs, class II and class IV drugs have lower aqueous solubility, according to the biopharmaceutical classification system (BCS).Class II and class IV drugs can improve their aqueous solubility and oral bioavailability by using the self-nanoemulsifying drug delivery system. The snedds is important for preventing enzymatic degradation problems associated with class I and class III drugs, as well as improving solubility and bioavailability.[9] Based on the solubility and permeability analysis, a schematic representation about biopharmaceutical classification system (BCS) having four classes of system which is shown in figure no.2.[10]

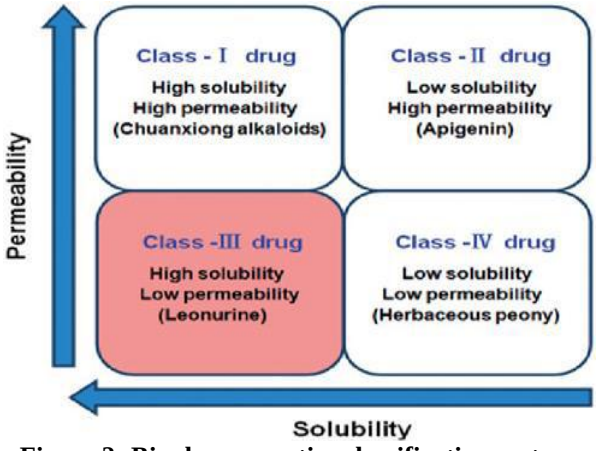

Figure 2: Biopharmaceutics classification system.

Factors affecting SNEDDS performance

Identifiable and variable factors that may affect the performance of SNEDDS may include but not limited to the following:

Nature and Dose of the Drug

Drug molecules with higher effective therapeutic concentration requirements typically do not present as possible candidates for SNEDDS development unless they have exceptionally high solubility in at least one of the components of SNEDDS, particularly the lipophilic phase. The most challenging drugs to administer by SNEDDS are those with poor solubility in water and lipids, often with log p values of around 2. The drug's solubility in oil phase has a significant impact on SNEDDS ability to keep the drug dissolved.

Concentration of Surfactant or Co- surfactant
As dilution of SNEDDS will cause the surfactant or co-surfactant's solvent capacity to decrease, there may be a risk of precipitation if these substances are more heavily involved in the solubilization of the drug.

Polarity status of lipid phase
One of the most important elements controlling the performance of drug-loaded lipid-based formulations is the nature and degree of the polarity of the oil/lipid phase. Essentially, the type of forces present in the system as well as the affinity of drug molecules for the oil or water phase, are strongly dependent on the polarity factor. The polarity of the lipid phase directly governs drug release from Nano emulsions and it is determined by the HLB, the chain length and degree of unsaturation of the fatty acid and the molecular weight of the micronized drug. The formulation with the highest polarity was found to have the highest drug release rate.[11]

Mechanism of self emulsification
According to Reiss, self-emulsification occurs when the entropy shift that favouring dispersion is greater than the energy required to increase the surface area of the dispersion. The free energy of the conventional emulsion is a direct function of the energy required to form a new surface between the oil and water phases and can be expressed by equation 1.

$\Delta G = \Sigma N \pi r2 \sigma$

Where,

G = the free energy associated with the process,

N = the number of droplets of radius r,

σ = represents the interfacial energy.

The two phases of an emulsion tend to separate over time, reducing the interfacial area. The emulsion is then stabilised by emulsifying agents, which form a monolayer of emulsion droplets, lowering interfacial energy and forming a barrier to prevent coalescence.[12] When the free energy necessary to produce the emulsion in a self-emulsifying system is either very low, positive, or negative, the emulsion process occurs spontaneously. Emulsification includes destabilisation through contraction of local interfacial regions and requires relatively little energy input. For emulsification to occur, the interfacial structure must be free of surface shearing resistance. Emulsification can be associated with the ease by which water penetrates into the various liquid crystals or phases get formed on the droplet's surface. When a binary mixture (oil/non-ionic surfactant) is added to water, an interface forms between the oil and aqueous continuous phases followed by water solubilization within the oil phase due to aqueous penetration through the interface, which continues until the solubilization limit is reached close to the interface.

Further, aqueous penetration will result in the formation of the dispersed liquid crystalline phase. As the aqueous penetration proceeds, eventually all materials close to the interface will be liquid crystal, the actual amount depending on the surfactant concentration in the binary mixture once formed, rapid penetration of water into the aqueous cores, aided by the gentle agitation of the self-emulsification process causes interface disruption and droplet formation. The high solubility of these self-emulsified systems to coalescence is considered to be due to liquid crystal interface surrounding the oil droplets.[13] and the process of absorption of self emulsifying drug delivery system has shown in figure no.3.

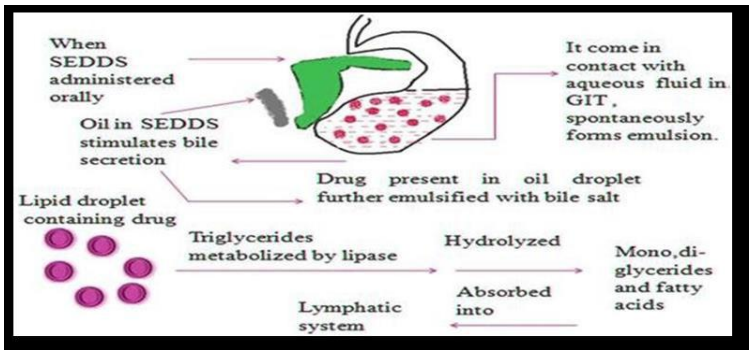

Figure 3: Process of absorption of self emulsifying drug delivery system.

Composition of SNEDDS[14]
The SNEDDs is mainly composed of the following

1. Drugs
SNEDDs are often developed for drugs that are poorly soluble in water. SNEDDs are often prepared using BCS class II drugs. Examples include itraconazole, nifedipine, vitamin E, simvastatin, danazol, ketoconazole, mefanimicacid, carbamazepine, glibenclamide, cyclosporine-A, and ritonavir.

2. Surfactant
There are numerous compounds with surfactant properties that may be used in the design of self-emulsifying systems, but the choice is limited because very few surfactants are orally suitable because safety is a major determining factor in choosing a surfactant. Natural emulsifiers are favoured since they are thought to be safer than synthetic surfactants. The non-ionic surfactants with a reasonably high hydrophilic lipophilic balance(HLB) have been the most widely recommended

(HLB). Surfactant concentrations ranging from 30-60% are employed to create stable SNEDDs.

The four main groups of surfactants are:

1. **Anionic surfactants:** Potassium laurate, sodium lauryl sulphate.
2. **Cationic surfactant:** Quaternary ammonium halide.
3. **Ampholytic surfactants:** Sulfobetaines**.**
4. **Nonionic surfactants:** Sorbitan esters (Spans), poly –sorbates (Tweens).

3. Oils

SNEDDs were designed using long chain triglyceride and medium chain triglyceride oils with varying degrees of saturation. Although unmodified edible oils are the most natural base for lipid carriers, their poor capacity to dissolve large amounts of hydrophobic drugs and relative difficulties in efficient self emulsification limit their usage in SNEDDs. GELUCIRE, an unique semi synthetic medium chain triglyceride-containing molecule has recently replaced medium chain triglycerides. Other appropriate oil phases and fats include commonly used oils and fats such as olive oil, corn oil, soya bean oil, and animal fats. Disadvantage of evaporating into the shell of soft or firm gelatin capsules resulting in drug precipitation.

4. Polymers

Inert polymer matrix constituting 5 to 40% of the composition relative to weight, which is not ionizable at physiological pH and capable of producing matrix is employed. Examples include hydroxyl propyl methyl cellulose, ethyl cellulose and others.

PREPARATION OF SNEDDS

The Self-Nanoemulsifying drug delivery system (SNEDDS) is Prepared by two ways.

Preparation of Liquid SNEDDS

The Pseudoternary phase diagram was used to identify an important approach for preparing self-nanoemulsifying drug delivery system using the surfactant/co-surfactant ratio and oil/surfactant/co-surfactant ratio. Several series of the formulation were carried out using different concentrations of oil, surfactant and Cosurfactant. The oil and surfactant were weighed in appropriate proportions and the drug was dissolved in this mixture which was then stored at room temperature.

Preparation of Solid SNEDDS

It is the second most important method for preparation of Self nanoemulsifying drug delivery systems (SNEDDS). If necessary, the drug was added to an accurately weighed amount of oil in screw-capped vials and melted in a water bath. The surfactant and cosurfactant were then added to the oily mixture by using positive displacement pipette and agitated with a vortex to achieve a homogenous solution. Solid Self nanoemulsifying drug delivery system (SSNEDDS) was prepared by adding selected liquid SNEDDS dropwise onto suitable novel adsorbents such as Neusillin and thoroughly mixed with glass rod. The resulting damp product was sieved through seive no. 120 and dried at room temperature.[15]

METHODS FOR PREPARATION OF SNEDDS

Active pharmaceutical ingredient, excipient, polymers and emulsifier are all used in the preparation of SNEDDS. There are several methods for creating a self nano-emulsifying drug delivery system, but they are primarily divided into two categories:

A. High-energy-emulsification.

B. Low-energy-emulsification.

The high-energy-emulsification method includes higher pressurized-homogenization (HPH), Ultra sonication and Micro-fluidization. The low-energy method includes Phase-inversion, Spontaneous emulsification.[16]

A. High energy approach.

For the formation of nanoemulsion high energy is applied and is mainly based on the selected composition of mixture and also on the mixture containing surfactant, cosurfactant, cosolvents and other functional compound. The emulsification undergoes mechanical processing to from nanoemulsion.[17]

1. High Pressure Homogenizer

It is one of the most essential devices for detecting and preparing nano emulsions, primarily for the production of nanoemulsions. This procedure is important in which the oil/water surfactant mixture was pumped under very high pressure using a resistive valve. The creation of very fine emulsion droplets is caused by the extremely high shear stress. The droplet size reduction during homogenization process is explained by the combination of two theories, turbulence and cavitation. The high velocity of the resultant mixture imparts significant energy to the liquid in the homogenizer valve resulting in intense turbulent eddies of the same size as mean diameter droplet (MDD). Droplets were apart from Eddie currents, causing droplet size to decrease. Simultaneously, the pressure decrease across the valve causes cavitation, which forms further eddies and disruption of droplets. Reducing the gap size ultimately increases the pressure of the droplet resulting in a higher degree of cavitation. This approach can produce emulsion droplets with diameters of <100 nm if there is sufficient amount of surfactant present to thoroughly cover the oil-water interface formed and the adsorption kinetics are high enough to avoid droplet coalescence.[18]

2. Microfluidization

It is an important technique for preparing nanoemulsion. Micro fluidization is accomplished by the use of a device known as a Micro Fluidizer. This device is used in a high pressure positive displacement pump (500-300 PSI) that forces the product through an interaction chamber made up of small channel droplets known as micro channels. The product flows via the micro channels onto the

impingement area, producing very small particles in the submicron range resulting in Nanoemulsion. In the inline homogenizer, two solutions having a mixture of aqueous phase and oil phase systems are combined to generate a coarse emulsion. The coarse emulsion is processed with a micro fluidizer before being transformed into a homogenous, clear and stable nanoemulsion.

3. Sonication Method

It is useful for determining size of droplet and for reducing droplet size of conventional emulsion using sonication process. It is only suitable for small batches of nanoemulsion.[19]

B. Low energy approach

It is also known as the condensation method, it requires little energy to create nanoemulsions and is based on phase transitions that occur during the emulsification process. To produce nanosized emulsion droplets, this approach dependent on modulation of interfacial phenomena or phase transitions as well as intrinsic physicochemical properties of surfactants, co-surfactants, and oil. The low energy approach is interesting since it uses the system's stored energy to generate smaller droplets. This emulsification can be caused by changes in parameters that affect the system's hydrophilic lipophilic balance (HLB) such as temperature, composition and so on. The following are the most often utilised low-energy emulsification methods.

1. Solvent displacement method

The solvent displacement approach utilised in polymeric nanoparticles has been adapted for spontaneous nanoemulsion production. Oily phase is dissolved in water-miscible organic solvents such as acetone, ethanol and ethyl methyl ketone in this process. The organic phase is poured into an aqueous phase containing surfactant to produce a spontaneous or rapidly developing nanoemulsion due to organic solvent rapid diffusion. Vacuum evaporation is used to remove the organic solvent from the nanoemulsion.

2. Phase Inversion Composition Method (Self nanoemulsification Method)

It creates nanoemulsions at room temperature without the use of organic solvents or heat. In their study, Forgirani et al. discovered that kinetically stable nanoemulsions with reduced droplet size (50nm) can be produced by adding water step by step into a surfactant in oil solution while gently stirring and maintaining a steady temperature. Although the components utilised in the above study were not of pharmaceutical quality, it has opened the door to designing pharmaceutically acceptable nanoemulsions using a similar approach.[20]

3. Phase Inversion Temperature (PIT) method

It is an important method for preparing nanoemulsion and microemulsion. The approach is mostly dependent on the response to temperature. Many physical changes occur in this procedure including physicochemical changes, particle size and *in vivo - in vitro* drug release rate. These approaches also make use of the change in spontaneous emulsion formation. The non-ionic surfactant can be obtained by changing the temperature of the system. The forces in transition forms, O/W nanoemulsion at low temperature and W/O nanoemulsion at high temperature.[21]

FORMULATION OF SNEDDS

A detailed understanding of the spontaneous nanoemulsification process as well as the physicochemical and biological properties of the components employed in the production or development of SNEDDS, is required for successful formulation. The following elements influence the phenomena of self nanoemulsification:

- The physicochemical nature and concentration of the oily phase, surfactant, and cosurfactant or solubilizer (if present).
- The component ratio, particularly the oil to Smix ratio (surfactant:cosurfactant).
- The temperature and pH of the aqueous phase where nanoemulsification would occur.
- The drug's physicochemical qualities, such as hydrophilicity and lipophilicity, pKa, and polarity.

When developing SNEDDS, the above mentioned factors should be considered. Furthermore, the acceptability of the SNEDDS components for the chosen route of administration is an important element in the development of SNEDDS.

Steps for formulation of SNEDDS in brief

- Selection of oil, surfactant and co-surfactant on the basis of drug compatibility and solubility study.
- Construction of pseudo-ternary phase diagrams. Selecting ratio of surfactant/co-surfactant and oil on the basis of pseudo ternary phase diagrams.
- Optimization of SNEDDS formula.
- Characterization of Liquid SNEDDS.
- Selection of best formulation from different formulation of SNEDDS based on data obtained after evaluation studies.
- Conversion of the optimized formulation to solid by adsorbing it on an absorbent carrier.
- Characterization of solid SNEDDS.[22]

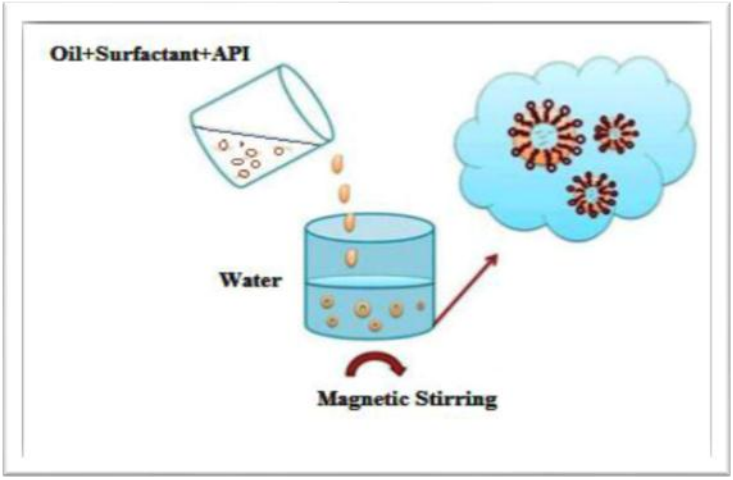

Figure 4: Formulation of SNEDDS.

CONSTRUCTION OF PSEUDO TERNARY PHASE DIAGRAM

This is the initial step before beginning the formulation. It is useful for determining the optimal emulsification region of oil, surfactant, and co-surfactant combinations. Ternary phase diagrams of surfactant, co-surfactant, and oil will be plotted, with each representing an apex of the triangle. The Dilution method and Water Titration method are used to plot ternary phase diagrams.[22] The psedoternary phase diagram is critical for determining the self-Nanoemulsifying drug delivery system (SNEDDS). The Psedoternary phase diagram is a diagrammatic representation of oil, surfactant, and co-surfactant (Smix) and water. Phase titration and Phase inversion methods are used to create a psedoternary phase diagram. The procedure consisted of producing solutions containing oil and various surfactant to co-surfactant weight ratios such as 1:1, 2:1, 3:1 and so on. These solutions were then vortexed for 5 minutes to produce an isotropic mixture that was observed for its appearance (turbid or clear). The turbidity of the samples indicates the creation of a coarse emulsion, whereas a clear isotropic solution indicates the formation of a Nanoemulsion (SNEDDS). Pseudo ternary phase diagrams are created using the values. This diagram corner can indicate a concentration of 100% of each phase component. The diagram is useful for providing information on binary mixtures of two components such as surfactant/cosurfactant, water/drug, or oil/drug.[23]

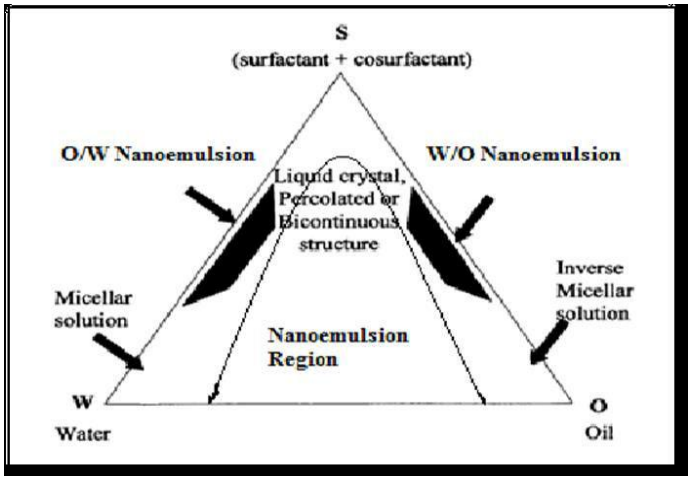

Figure 5: Pseudo ternary phase diagram.

Characterization of Self Nano Emulsifying Drug Delivery System (Snedds)

a) Morphological Study

Morphological analysis is necessary because it offers information about the formulation's exterior appearance. The globules in the self-Nano emulsifying drug delivery system were examined using the transmission electron microscope (TEM).[24]

b) Thermodynamic Stability Studies

Physical stability of a lipid-based formulation is also important for its performance which may be hampered by drug precipitation in the excipient matrix. Furthermore, poor formulation can cause excipient phase separation, affecting not only formulation performance but also visual appearance. as a result the gelatin capsule shell may result in brittleness or deformation, delayed disintegration, or inadequate drug release.

c) Heating cooling cycle

The researchers examined six cycles with temperatures ranging from 40°C to 450°C and storage durations of at least 48 hours at each temperature. The formulations that are stable at these temperatures are subjected to centrifugation testing.

d) Centrifugation

Centrifuged thaw cycles between 21°C and +25°C with storage at each temperature for at least 48 hours are done at 3500rpm for 30 minutes. The freeze thaw stress test is done on formulations that do not have any phase separation.[25-26]

e) Freeze thaw cycle

Freeze thawing was used to test the stability of SNEDDS. The formulations were subjected to three freeze-thaw cycles, with freezing at 4°C for 24 hours and thawing at 40°C for 24 hours. Centrifugation at 3000 RPM was conducted for 5 minutes. The preparations were then tested for phase separation. The formulations that passed this test demonstrated excellent stability with no phase separation, creaming or cracking.

f) Dispersibility Test

To assess the efficacy of self-emulsification of oral nano or microemulsions, a standard USP XXII dissolution apparatus 2 is employed. One millilitre of each formulation was added to 500 mL of water at 37 ± 0.5^{0}C. A standard stainless steel dissolution paddle rotating at 50 rpm offered gentle agitation. To visually analyse the formulation's in vitro performance, the following grading system was utilised. Grade A and Grade B formulations will remain as nano emulsions when dispersed in GIT. A formulation in Grade C may be recommended for the SNEDDS formulation.[27-28]

Table 1: Visual grading system.

Grade	Time for emulsification	Observation	Visual appearance
Grade A	Within 30 seconds	Rapidly forming nanoemulsion which is clear and transparent, high spreadability	Bluish tinge
Grade B	Within 1 min	Rapid nanoemulsion formation which is slightly less transparent, less clear	Bluish white tinge
Grade C	Within 2 min	Rapidnanoemulsion formation which is turbid in nature formed	Milky white tinge
Grade D	Within or longer than 3 min	Nanoemulsion devoid of or slow to minimal emulsification, with non uniform distribution of oil droplets	Dull, grayish white tinge having slightly oily appearance
Grade E	Longer than 3 min	Formulation exhibiting either less, poor or minimal emulsification	Large oil globules

g) Turbidimetric Evaluation

Nepheloturbidimetric analysis is used to track the progress of emulsification. The increase in turbidity was measured using a turbid-meter after a fixed quantity of Self emulsifying system was added to a fixed amount of acceptable medium (0.1N HCL) while continuously stirring (50 rpm) on a magnetic plate at room temperature. When the time required for complete emulsification is too short, it is impossible to monitor the rate of change of turbidity (rate of emulsification).[29]

h) Droplet Size Analysis Particle Size Measurements

To quantify the droplet size of the emulsions, photon correlation spectroscopy (which analyses fluctuations in light scattering owing to Brownian motion of the particles) and a Zeta sizer capable of measuring sizes between 10 and 5000 nm are utilised. After external standardisation with spherical polystyrene beads, light scattering is measured at 25°C at a 90° angle. The nanometric size range of the particle is kept even after 100 times dilution with water, proving the system's compatibility with excess water.[30]

i) Viscosity Determination

The SNEDDS system is often delivered as soft gelatin or hard gelatin capsules. As a result, it is typically easy to pour into capsules and such a system shouldn't be too thick to cause an issue. The rheological parameters of the microemulsion are tested using a Brookfield viscometer. This viscosity determination is consistent with whether the system is water/oil or oil/water. If the system has a low viscosity, it is an o/w system, and if the system has a high viscosity, it is a w/o system.[31]

j) Stability Study

The stability study is critical for establishing the quality and purity of the Nanoemulsion system. The stability of a formulation determines its tolerance. The mechanical stress conditions (centrifugation at 2000-4000 rpm) and storage temperatures ranging from 4 1 °C to 40 1 °C for varied time intervals were used to examine the stability of several nano emulsion formulations. The impact of mechanical stress conditions on the physiochemical stability of the nano emulsion was determined by calculating the percentage of phase separation, breaking of the nano emulsion or any physical change. There was no visible change in the formulations after 60 minutes of centrifugation at 2000 rpm.[32]

k) Refractive Index and Percent Transmittance

The formulation's transparency was demonstrated by the index of refraction and percent transmittance. By

depositing a drop of solution on a slide, the refractometer measures the system's index of refraction which correlates with the water (1.333). The system's % transmittance at a specific wavelength is determined by using a UV-spectrophotometer and distilled water as a blank. If the formulation is transparent, its index of refraction is similar to the index of refraction of water (1.333) and its percent transmittance is more than 99 percent.[33]

l) *In Vitro* Diffusion Study

In vitro diffusion studies are performed using the dialysis technique to examine the release behaviour of formulation from the liquid crystalline phase around the droplet.

m) Drug Content

The drug is extracted from pre-weighed SNEDDS by dissolving it in a suitable solvent. Using a suitable analytical approach, the drug content in the solvent extract was compared to a standard drug solvent solution.[34]

Application[35]

Improving Water Solubility of Poorly Water-Soluble Drug

The Self-Nanoemulsifying Drug Delivery System (SNEDDS) is vital for improving the water solubility of poorly water-soluble drugs and increasing their oral bioavailability.

Applications of Nanoemulsion in Drug Delivery

Nanoemulsions (SNEDDS) have been applied in a wide range of drug delivery systems, including cosmetics and transdermal drug delivery, cancer therapy, vaccine delivery, cell culture technology. Formulations are important for increasing oral delivery of poorly soluble drugs, ocular and otic drug delivery systems, intranasal drug delivery, parenteral drug delivery, and pulmonary drug delivery, as well as intranasal drug delivery system.

Protection Against Biodegradation

SNEDDS, SMEDDS, and SEDDS are required for the delivery of macromolecules such as peptides, hormones and enzyme substrates all of which are inhibitors that must be protected against enzymatic destruction.

CONCLUSION

Drug development techniques generate a large proportion of lipophilic and poorly soluble new chemical compounds. Self-nanoemulsifying formulations have shown promise in enhancing the bioavailability of such therapeutic agents with low aquoeus solubility. Because of the large surface area, the nanosize of these formulations is responsible for increasing drug dissolution and absorption. The lipidic structure of these systems permits drugs to be delivered to the lymphatic system. The procedures and additives used to produce SNEDDS are inexpensive and simple. SNEDDS has sparked the interest of researchers in a range of fields and has been effective in a variety of commercial applications due to its ease of production and exceptional physical stability. Advances in lipid and surfactant technology, as well as the modification of SNEDDS with other technologies such as polymer sciences and biological targeting, may lead to SNEDDS becoming applicable and delivering significant benefits to pharmaceutical research in the future.

ACKNOWLEDGEMENT

Writer is grateful to thanks managements of SJM College of Pharmacy for their continuous support.

CONFLICTS OF INTEREST

The authorsdeclare that there is no conflict of interest.

REFERENCES

1. Praveen g, nagulu m. Formulation and in-vitro evaluation of self nano emulsifying drug delivery system of nifedipine. Nveo-natural volatiles & essential oils journal, 2021; 8(4): 16751-69.
2. Morakul b. Self-nanoemulsifying drug delivery systems (snedds): an advancement technology for oral drug delivery. Pharmaceutical sciences asia, 2020; 47(3): 205-220.
3. Gupta p, kumar p, sharma nk, pawar y, gupta j. Self nano emulsifying drug delivery system: a strategy to improve oral bioavailability. World j pharm pharm sci., 2014; 3(5): 506-12.
4. Nazzal s, smalyukh ii, lavrentovich od, khan ma. Preparation and in vitro characterization of a eutectic based semisolid self-nanoemulsified drug delivery system (snedds) of ubiquinone: mechanism and progress of emulsion formation. International journal of pharmaceutics, 2002; 235(1-2): 247-65.
5. Chakraborty s. Shukla d, mishra b, and singh, eur j pharm biopharm, 2009; 73: 1-15.
6. P.s.rajinikant, neo woei keat, sanjay garg,self-nano emulsifying drug delivery system(snedds) of valsartan:preparation and in-vitro characterization, international journal of drug delivery, 2012; 4: 153-163.
7. Maruti ts, kisan bobe d, potnis v, dhamane s, suresh pv. A review-self nanoemulsifying drug delivery system (snedds), 2020; 9(7): 2261-2277.
8. Mounika m, desu pk, vanitha k. A review on self nano emulsifying drug delivery system, 2019; 2(1): 12-13.
9. Singh b, bandopadhyay s, kapil r, singh r, katare op. Self-emulsifying drug delivery systems (sedds): formulation development, characterization, and applications. Critical reviews™ in therapeutic drug carrier systems, 2009; 26(5): 427-521.
10. Bangia jk, om h. Nanoemulsions: a versatile drug delivery tool. International journal of pharmaceutical sciences and research, 2015; 6(4): 1363-1375.
11. Buddhadev ss, garala kc. Self-nano emulsifying drug-delivery systems: from the development to the

current applications and update of the biopharmaceutical aspect, 2021.
12. Gursoy rn, benita s. Self-emulsifying drug delivery systems (sedds) for improved oral delivery of lipophilic drugs. Biomedicine & pharmacotherapy, 2004; 58(3): 173-82.
13. Divate mp, bawkar su, chakole rd, charde ms. Self nano-emulsifying drug delivery system: a review. Journal of advanced scientific research, 2021; 12(03 suppl 2): 1-2.
14. gautam s, singh ak. Self nanoemulsifying drug delivery system-a novalapproach for improving bioavailability. Journal of drug delivery and therapeutics, 2014; 4(6): 33-8.
15. Gadhave ad. Nanoemulsions: formation, stability and applications. International journal for research in science and advanced technologies, 2014; 3(2): 38-43.
16. Kumar m, bishnoi rs, shukla ak, jain cp. Techniques for formulation of nanoemulsion drug delivery system: a review. Preventive nutrition and food science, 2019; 24(3): 225.
17. Gadhave ad. Nanoemulsions: formation, stability and applications. International journal for research in science and advanced technologies, 2014; 3(2): 38-43.
18. Haritha sp, koteswara rao p. Chakravarthi vedantham. A brief introduction to methods of preparation, applications and characterization of nanoemulsion drug delivery systems. Indian journal of research in pharmacy and biotechnology, 2002; 1(1): 25-28.
19. Patel pk, patel mr, patel kr, patel nm. A review on self-micro emulsifying drug delivery systems. Advance research in pharmaceticals and biological, 2014; 4: 590-8.
20. Kuruvila fs, mathew f, kuppuswamy s. Indo American journal of pharmaceutical science, 2017; 4(3): 651-669.
21. Jain k, kumar rs, sood s, gowthamarajan k. Enhanced oral bioavailability of atorvastatin via oil-in-water nanoemulsion using aqueous titration method. Journal of pharmaceutical sciences and research, 2013; 5(1): 18.
22. Sudheer p, kumar n, puttachari s, shankar um, thakur rs. Approaches to development of solid-self micron emulsifying drug delivery system: formulation techniques and dosage forms–a review. Asian journal of pharmacy and life science, 2012; 2(2): 214-25.
23. Amrutkar c, salunkhe k, chaudhari s. Study on self nano emulsifying drug delivery system of poorly water soluble drug rosuvastatin calcium. World j pharm res, 2014; 3(4): 2137-51.
24. Kapil a, aggarwal g, harikumar sl. Formulation and evaluation of nanosuspension and nanoemulsion of rosuvastatin and their comparative study. Asian journal of biochemical and pharmaceutical research, 2015; 1(5): 101-106.
25. Constantinides pp, pouton cw, meakin bj, morton fs. Self emulsification of veg: oil-non-ionic surfactant mixtures. Acs sympser, 1988; 311(2): 242-55.
26. Sheela a, yadav, dinesh singh, sushil kumar poddar. Influence of components of nanoemulsion system for transdermal drug delivery of nimodipine, asian journal of pharmaceutical and clinical research, 2012; 5(3): 209-214.
27. Dabros t, yeung a, masliyah j, czarnecki j. Emulsification through area contraction. Journal of colloid and interface science, 1999; 210(1): 222-4.
28. Kaur g, chandel p, harikumar sl. Formulation development of self nanoemulsifying drug delivery system (snedds) of celecoxib for improvement of oral bioavailability. Pharmacophore, 2013; 4(4): 120-33.
29. Constantinides pp, pouton cw, meakin bj, morton fs. Self emulsification of veg: oil-non-ionic surfactant mixtures. Acs sympser, 1988; 311(2): 242-55.
30. Vanitasagar s, subhashini nj. Novel self-nanoemulsion drug delivery system of fenofibrate with improved bio-availability. International journal of pharma and bio sciences, 2013; 4(2): 511-21.
31. Sinha mk, ganesh n. Preparation and characterization of nanoemulsion based on papaya seed oil. Vivo scientia, 2015; 4(2): 72-6.
32. Rachmawati h, yee cw, rahma a. Formulation of tablet containing curcumin nanoemulsion. Int j pharm pharm sci., 2014; 6(3): 115-6.
33. Rang mj, miller ca. Spontaneous emulsification of oils containing hydrocarbon, nonionic surfactant and oleyl alcohol. Journal of colloid and interface science, 1999; 209(1): 179-92.
34. Vilas pc, gujarathi na, rane br, pawar sp. A review on self microemulsifying drug delivery system. Pharma science monitor, 2013; 4(1): 3628-3648
35. Gourav dk, jain s. Snedds: a vital role in drug delivery true or myth world journal of pharmaceutical research, 2022; 11(13): 1965-1991.