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REVIEW ARTICLE

An Overview on Self Micro emulsifying Drug Delivery System

Patidar Yogita, Gupta Ashish*, Darwhekar Gajanan
Acropolis Institute of Pharmaceutical Education & Research, Indore MP 453771
*Corresponding Email ID: ashish.pharma87@gmail.com

ABSTRACT
Self-micro emulsifying drug delivery systems (SMEDDS) are a promising method for improving the bioavailability of poorly water-soluble drugs. These systems, which form fine oil-in-water microemulsions upon mild agitation in the gastrointestinal tract, eliminate the need for high-energy input and ensure uniform formulations. However, they also present challenges such as the need for precise selection and optimization of components and potential gastrointestinal side effects. SMEDDS are used in the pharmaceutical industry to enhance solubility, particularly for class II and IV drugs. They are preferred for their comfort and painless method, making oral routes the most preferred method for improving oral bioavailability. Emerging technologies and multidisciplinary collaborations are paving the way for next-generation SEDDS, with their adaptability and potential for personalized medicine solidifying their role in modern pharmaceutical development.
Keywords: *Self-Microemulsifying Drug Delivery Systems (SMEDDS), Poorly Water-Soluble Drugs, Oil-in-Water Microemulsions, Surfactants and Co-surfactants.*

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INTRODUCTION

The oral route of administration is the preferred choice for ongoing drug therapy. Researchers were having a difficult time coming up with methods to increase the bioavailability of medications that were not very soluble in water. Given that a medication must dissolve in the gastrointestinal tract (GIT)before being passed Incomplete and irregular absorption might result from inadequate water solubility through the gastrointestinal mucosa [12]. Lipophilic medicines are among the medicinal compounds that suffer from low oral bioavailability. It appears to be difficult to increase their bioavailability while also preventing the oral breakdown of the vulnerable components [10].

A complicated network of physical, chemical, physiological, and anatomical variables that act both independently and in concert to limit drug bioavailability causes about 40% of contemporary drug applications to have low water solubility and obstacles to their successful oral delivery. Many methods, including the use of lipid complexes, nanoparticles, cyclodextrin, surfactants, strong dispersions, and permeation enhancers, are proposed to clarify these issues. For ten years, a lot of research was done on particulate drug delivery systems made up of nanoparticles and microspheres [14]. However, the usage of synthetic polymeric compounds, such as methyl methacrylate, poly (lactic acid), and alkyl cyno-acrylate, has become widespread despite their toxicity. Studies have also been conducted on their toxic metabolite product and their buildup [14, 13].

Research is being done on microemulsions as a potential new colloidal delivery system for lipophilic medications. Microemulsions offer advantages such as superior drug solubilization ability, remarkable thermodynamic stability, increased oral bioavailability, and safety compared to hydrolysis by enzymes. The biggest issue with microemulsions is their awful palatability, which is caused by their high fat content and compromises patient compliance. Furthermore, microemulsions cannot be encapsulated in hard or soft gelatin medicines due to their water content; therefore, anhydrous self-emulsifying drug delivery systems maybe required [9]. Therefore, a lipid-based device called the Self-Micro Emulsifying Drug Delivery device (SMEDDS) was created to improve the oral bioavailability of lipophilic medications. Few

studies have reported improved bioavailability of poorly soluble capsules when they are prepared as SMEDDS. Researchers have experimented with lipid-based administration of lipophilic medications, such as cyclosporine, and have determined that it is feasible. The term "isotropic" refers to self-micro emulsifying drug delivery systems (SMEDDS) [1].

GI fluids and mixtures of natural or synthetic oils, surfactants, and cosurfactants have the entirely unique ability to generate magnificent oil-in-water (o/w) micro emulsions upon minimal agitation as indicated by dilution in aqueous solutions. SMEDDS droplets with sizes between 300 and 500 nm, or even significantly smaller than 500 nm,can form. Lipophilic medications with dissolution rate-limited absorption may also offer repeatable blood-time profiles andan increase in absorption volume and rate [14].

The medicine is present in the oil in the soluble form in the SMEDDS approach, and due to self-emulsification, it forms fine globules when taken orally. The system's interfacial surface tension is decreased by the surfactant and cosurfactant. In the LSC method, the medication is dissolved in the solvent that isn't volatile. Therefore, the solubility of water insoluble medications may be enhanced by these established methods. [7]. However, it's crucial to create improved pharmacodynamic effects and oral bioavailability. There is a tendency to focus on creating an effective tablet dosage form by concurrently utilizing the methods of each SMEDDS-associated liquid-solid formulation methodology since the in-vivo performance of those two systems should be greater (PK and PD impacts). The disadvantages of this approach are addressed by combining the advantages of liquid SMEDDS with those of solid formulations in a solid dosage form. With this objective, The simplest composition in terms of drug dissolving qualities can be chosen by using an experimental design technique to optimize a SMEDDS formulation of the tablet [6].

SMEDDS

SMEDDS are described as isotropic blends of solid or liquid surfactants, natural or synthetic oils, or, alternatively, one or more hydrophilic solvents and co surfactants and solvents have the special capacity to create fine oil-in-water (o/w) microemulsions when mildly agitated and then diluted in aqueous media, such GI fluids.11 SMEDDS distribute easily throughout the GI tract, and the intestines' and stomach's digesting motility creates the agitation required for self-emulsification [2].

The primary distinction between self-emulsifying oil formulation and self-emulsifying drug delivery systems (SEDDS) (SEOF) and SMEDDS are different in that SMEDDS usually creates clear micro emulsions with droplets smaller than 100 nm and an oil content of less than 20%, whereas SEDDS usually produces opaque emulsions with droplets between 100 and 300 nm. In contrast to emulsions, which are delicate and metastable dispersed forms, SMEDDS are formulations that are straightforward to create and physically stable. Therefore, these systems may provide an improvement in the rate and extent of absorption and lead to more repeatable blood-time profiles for lipophilic medicinal molecules that display dissolution rate-limited absorption [3, 4].

Finding an appropriate oil surfactant mixture that can dissolve the medication at the necessary therapeutic concentration is the crucial first step. The composition of SMEDDS can be packed in gelatin capsules, either soft or hard. Typically, SMEDDS formulations include oils, surfactants, and antioxidants if necessary. Co-surfactants and co-solvents are frequently added to formulations to enhance their properties. [5].

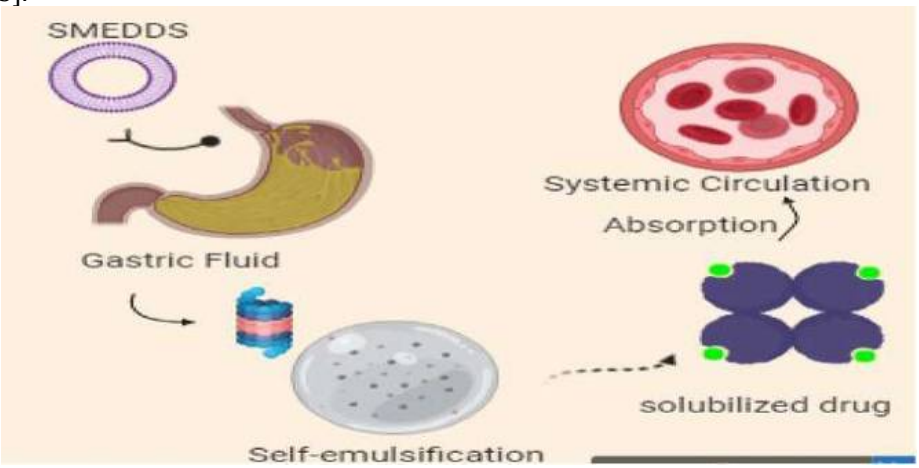

Fig 1:-Self emulsification and drug solubilization

Table 1: Use of SMEDDS belonging to multitudinous BCS class drugs

BCS Classification	Aqueous solubility	Membrane permeability	Hurdles overcome by SMEDDS
I	High	High	Enzymatic declination, Gut wall efflux
II	Low	High	Solubilization, Bioavailability
III	High	Low	Enzymatic declination Gut wall efflux, Bioavailability
IV	Low	Low	Solubilization, Enzymatic declination, Gut wall efflux, Bioavailability

Lipid formulation classification system - system This classification helps to better understand the fate of various lipid formulation in vivo it also helps to use systematic and rational formulation approach avoid trial and error. this system was established by Pouton in 2000 [17] and recently updated Based on the type of components divided in 4 types .this shows possible effect of dilution and digestion on their ability to prevent drug precipitation. [18].

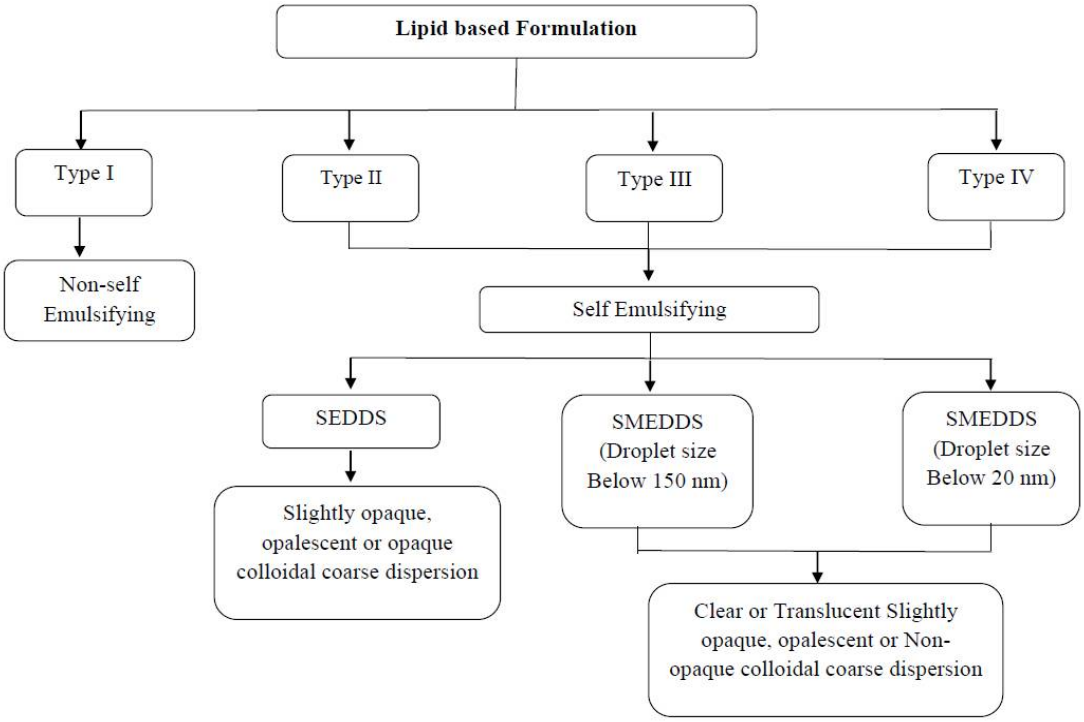

Fig 1: Liquid base Formulation

Type I: This lipid easy formulation it consists highly lipophilic compounds in which oil are present without surfactant such as, example is glyceride. Which are non-dispersing required digestion, this is generally safe but, formulation has poor solvent capacity [9, 12].
Type II: This lipid formulation consist SEDDs. which consist of oils and water with insoluble surfactant dispersion drug absorption without digestion. Further classified in two types;1) type III A 2) type IIIB to identify more this SEDDS formed without water soluble components.it gives benefits to overcoming the slow dissolving rate seen in solid dosage form which are unlikely to lose solvent capacity on dispersion but, it is turbid o/w dispersion (particle size 0.25-2µm) [11,5].
Type III: Lipid based formulation commonly for SMEDDS.it consist of oil, surfactant /cosurfactant are water soluble. which clear or almost clear hydrophilicity. Type IIIB formulation has greater dispersion when compared with type IIIA [14].
Type IV: This formulation content predominantly hydrophilic surfactant and co surfactant which not contain any natural lipid. contain water soluble surfactant and co solvents (no oil). formulation disperse typically to form micellar solution having good solvent capacity for many drugs [3, 4].

The history of Micronemulsions: In 1943, Hoar and Shulman, chemistry professors at Cambridge University, coined the word "microemulsion"[2].

MECHANISM OF SELF-EMULSIFICATION

When the energy needed to expand the dispersion's surface area is less than the entropy change favoring dispersion, self-emulsification takes place. The energy needed to form a new surface between the water and oil phases directly determines the free energy of the typical emulsion, which is defined by the formula:

$\Delta G=\sum N i \pi r i^2 S$

where N is the number of droplets of radius r, S is the interfacial energy, and ΔG is the process's free energy (not including the free energy of mixing). Emulsification stabilizes the emulsion when the two phases of the emulsion tend to separate over time to decrease the interfacial area. agents that create an emulsion droplet monolayer, lowering the interfacial energy and acting asa barrier to stop coalescence (Maurya et al 2017). The aforementioned equation demonstrates the thermodynamic stability of the spontaneous development of the oil-aqueous phase interface. Reiss described self-emulsification, or the spontaneous development of an emulsion, in terms of the free energy needed to produce the emulsion, which can be either negative or very low and positive. Pouton has suggested a connection between the system's phase inversion behavior and the surfactant's emulsification characteristics. As an illustration, the When the temperature of the oil-in-water system is raised and stabilized by one or more non-ionic surfactants, the surfactant's cloud point is reached, and phase inversion occurs. Since the surfactant is very mobile at the temperature of phase inversion, the o/w interfacial energy is reduced, which lowers the energy required for emulsification [5, 7-8].

Advantages of SMEDDS: -

- **Enhanced oral bioavailability:-**One important factor limiting the bioavailability of many weakly water-soluble substances is dissolution rate-dependent absorption medications that dissolve. Improved bioavailability results from SMEDDS's capacity to deliver the medication to the gastrointestinal tract in a solubilized and microemulsified form (globule size ranging from 1 to 100 nm) and subsequently increase specific surface area, which facilitates more effective drug transport through the intestinal aqueous boundary layer and the absorptive membrane. For instance. Comparing the halofantrine formulation to tablet formulation, it was shown that the drug's bioavailability increased by about 6–8 times [15].
- **Manufacturing simplicity and scalability:-**One of the most significant benefits that sets SMEDDS apart is its ease of manufacturing and scaling up. in contrast to alternative drug delivery methods that deal with increasing bioavailability, such as solid dispersions, liposomes, nanoparticles, etc. For large-scale production, SMEDDS needs very basic and affordable manufacturing facilities, such as a basic mixer with an agitator and volumetric liquid filling apparatus. This explains why industry is interested in the SMEDDS [16, 8] .
- **decrease in dietary effects and intra- and inter-subject variability:-**Numerous medications have significant inter-subject and intra-subject heterogeneity in absorption, which results in patient noncompliance and a decline in drug performance. Food has a significant impact on how well a medication works in the body. Such medications benefit greatly from SMEDDS. There are numerous research studies that demonstrate that SMEDDS provides reproducibility of plasma profile and that its performance is independent of meals [6].
- **Capacity to transport peptides that are susceptible to GIT enzymatic hydrolysis:-**One special quality that sets SMEDDS apart is Their capacity to carry macromolecules such as peptides, hormones, enzyme substrates and inhibitors, and to provide protection against enzymatic hydrolysis sets them apart from conventional drug delivery systems. polysorbate 20 as an emulsifier in a microemulsion formulation can protect intestinal hydrolysis of the prodrug by cholinesterase. These systems work well with thermolabile medications like peptides since they are created naturally without the use of energy or heating [16].
- **No impact on the process of lipid digestion:-**In contrast to other lipid-based drug delivery systems, lipolysis has no effect on SMEDDS's performance. bile salt emulsification, pancreatic lipase activity, and mixed micelle production. Because SMEDDS present the medication in a micro-emulsified form that readily penetrates the mucin and water-unstirred layer, the drug is not necessarily digested before it is absorbed [11] .
- **Enhanced ability to load drugs:-** In addition, SMEDDS offer the benefit of greater drug loading capacity in contrast to traditional lipid solution because the solubility of weakly water-soluble

medications with an intermediate partition coefficient (24) is generally higher in amphilic surfactants, co-surfactants, and co-solvents and lower in natural lipids [12].

Disadvantages of SMEDDS

- No reliable predictive in vitro models exist for evaluating the formulations;
- this in vitro model requires more refinement and verification prior to Its strength is measurable.
- Since future research will rely on correlations between in vitro and in vivo, various prototype lipid-based formulations must be created and evaluated in vivo using an appropriate animal model.
- Moreover, volatile cosolvents in the traditional self-microemulsifying formulations are known to migrate into the shells of soft or hard gelatin capsules, causing the precipitation of the lipophilic drugs.
- Chemical instabilities of drugs and high surfactant concentrations in formulations (roughly 30–60%) that irritate the GIT are another.

The hydrophilic solvent's dilution impact may increase the drug's precipitate tendency upon dilution [1-5].

FORMULATION COMPONENTS OF SMEDDS

- Active pharmaceutical ingredient
- Oil
- Surfactant
- Co-surfactant
- Co-solvents

- **Active pharmaceutical ingredient:** The drug's solubility in the oil phase affects SMEDDS's capacity to preserve the API in its solubilized state. Lipophilic medications, such cinnarizine are an excellent fit for SMEDDS if their log p is greater than 5 [3].
- **Oil:** Since it solubilizes the lipophilic medication in the necessary proportion, oil is the most crucial excipient in the formulation of SMEDDS. The drug's great solubility in the oil is the primary requirement for choosing it; this will reduce the formulation's volume and ensure an effective dosage is delivered.
- **Surfactant:**
  - **Anionic surfactants**, in which a negative charge is carried by the hydrophilic group. Examples include sodium lauryl sulfate and potassium laurate.
  - **Cationic surfactants**, which have a positive charge on the hydrophilic group. Quaternary ammonium halide is one example.
  - **Ampholytic surfactants**, also known as Zwitterionic surfactants, have a positive and a negative charge. Sulfobetaines, for instance.
- **Nonionic surfactants**, in which the highly polar groups give the hydrophilic group its water solubility despite the hydrophilic group having no charge. Examples include polysorbates (Tweens) and sorbitoan esters (Spans) [1].
- **Co-surfactant:** To produce an ideal SMEDDS, a high concentration of surfactant is needed to adequately lower interfacial tension, which can be hazardous. Co-surfactants are employed to lower the surfactant concentration. Co-surfactants with an HLB value of 10–14, such as ethanol, propylene glycol, and polyethylene glycol, are typically utilized [2].
- **Co-solvents:** Organic solvents enable the dissolution of large quantities of either the hydrophilic surfactant or the drug in oil phase. Examples: Ethanol, butanol, propylene glycol, etc., esters such as ethyl propionate, tributyl citrate and amides as 2-pyrolidine, caprolactum, and polyvinyl pyrollidine.
- **Other components:** Other components include pH adjusters, flavors, and antioxidants, consistency builder, enzyme inhibiter, polymers, etc [1].

Formulation design of SMEDDS

- **Oil Screening:** Using the shake flask method, the saturation solubility of API in various oils was examined in order to identify the right oil with a good solubilizing capacity of API.The vial that contained 0.5 g of each solvent had an excessive amount of API injected to it. To ensure that the API and the vehicles were properly mixed, the mixture was vortexed for ten minutes using a cyclomixer after sealing. After achieving equilibrium for 72 hours at room temperature, the mixtures were centrifuged for 15 minutes at an appropriate speed. After passing through a 0.45 µm membrane filter, aliquots of the supernatant were diluted with mobile phase. Using the high-

performance liquid chromatography (HPLC) technology, the drug content was directly measured [2].

- **Screening of Surfactant:** Following oil screening, the emulsifying ability of several surfactants with the screened oil was examined in order to identify the right surfactant with a good solubilizing capacity. To create an isotropic mixture, 0.3 g of surfactant and 0.3 g of oil phase were weighed, vortexed for two minutes, and then warmed for 30 seconds at 40–45°C. In a volumetric flask, 50 mg of the isotropic mixture was taken and diluted with double-distilled water that had been previously filtered using a 0.45 µm membrane filter. To create a transparent emulsion, several volumetric flask inversions were visually observed. Transmittance was measured at 638 nm after the resultant emulsions were let to stand for two hours. The surfactant that produces a transparent emulsion with a higher transmittance and fewer inversions was chosen.
- **Co-surfactant screening:** Following oil screening, the emulsifying potential of several co-surfactants with the screened oil was examined in order to identify a suitable co-surfactant with a good solubilizing capability. To create an isotropic mixture, 0.2 g of co-surfactant and 0.3 g of oil phase were weighed, vortexed for two minutes, and then warmed for 30 seconds at 40–45°C. In a volumetric flask, 50 mg of the isotropic mixture was taken and diluted with double-distilled water that had been previously filtered using a 0.45 µm membrane filter. Visually, the number of volumetric flask inversions that formed a clear emulsion was noted. Transmittance was measured at 638 nm after the resultant emulsions were let to stand for two hours. The co-surfactant that produces a transparent emulsion with a higher transmittance and fewer inversions was chosen [4].

PHASE DIAGRAM CONSTRUCTION

To determine the percentage of components that can produce the largest microemulsion existence area, phase diagrams were created. Using the water titration method at room temperature, these diagrams were created using oil, surfactant/co-surfactant, and water. In order to create an isotropic mixture, the process involved making solutions with varying weight ratios of surfactant to co-surfactant, such as 1:1, 2:1, 3:1, etc. These solutions were then vortexed for five minutes and then heated to 50°C for one hour. The following weight ratios of oil and Smix (mixture of surfactant and co-surfactant) were then created using each of these solutions: At 1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2, and 9:1, and after 5 minutes of vortexing, bake for 1 hour at 50°C. After that, all of the mixes were let to stand at room temperature for a full day. Using a magnetic stirrer, water was added to each combination at intervals of 10 to 15 minutes, ranging from 5% to 95%. The mixtures were examined for appearance (turbid or clear) following each addition. A clear isotropic solution would suggest the creation of a microemulsion, while turbidity of the samples would suggest the formation of a coarse emulsion. A ternary phase diagram was created using the chosen percentages of oil, Smix, and water at which a clear mixture formed [3].

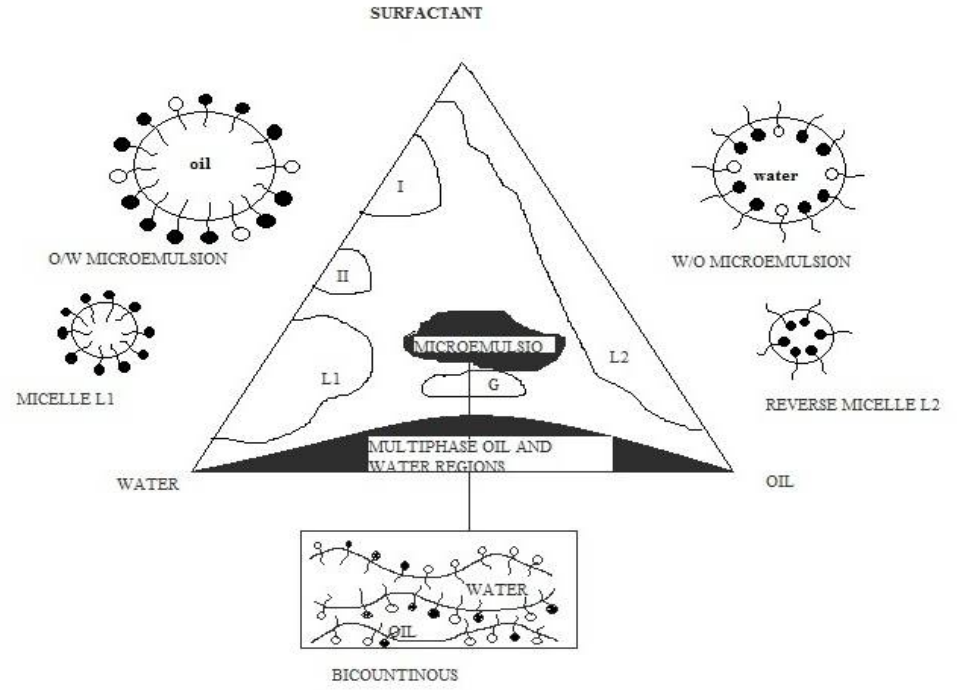

Fig 2:- Phase diagram

PREPARATION OF SMEDDS

The surfactant to co-surfactant diagram ratio was optimized from the ternary phase. Different formulations with and without the medication were then created by adjusting the oil to Smix ratio. First, the optimal ratio of Smix was created. Then, the surfactant and co-surfactant were precisely weighed and vortexed for five to ten minutes. Smix was then put in an oven set to 50°C for one hour. An isotropic mixture was created by adding oil to Smix in varying ratios, vortexing the mixture for five to ten minutes, and then baking it for one hour at 50°C. After the drug was introduced into these isotropic formulations, a vortex shaker was used to vortex the mixture until a clear solution was achieved.

EVALUATION OF SMEDDS

- **Determination of droplet size/distribution and zeta-potential**: A zetasizer that can detect droplet size in the 10-5000 nm range is used in photon correlation spectroscopy, which analyzes variations in light scattering caused by the Brownian moment of particles. For precise droplet size assessment, this method can only be used at comparatively low dilutions. Because of the presence of certain groups, oil droplets have some charge on their surface. For example, traditional SMEDDS is negative because of the presence of free fatty acids; however, cationic SMEDDS can be produced by including cationic lipids at concentrations between 1% and 3%. As a result, the positive n-potential value of these systems is between 35 and 45 mV. After the medicinal molecules are incorporated, this positive n-potential value is maintained [19].
- **Rheological determination:** Rotational viscometer and Brookfield viscometer Rheomat 108 can be used to assess the microemulsion's rheological characteristics. This study verifies if the system is w/o or o/w. It ought to be carried out three times.
- **Polarity:** The HLB, chain length, degree of unsaturation of the fatty acids, molecular weight of the hydrophilic region, and emulsifier concentration are some of the parameters that control the polarity of an oil droplet. Polarity affects the drug's affinity for water and/or oil as well as the kinds of forces that are created. The formulation containing the oil phase with the highest polarity will yield the highest release [19].
- **Dispersibility test:** A standard USP XXII dissolution apparatus 2 is used to evaluate the effectiveness of oral nano- or microemulsion self-emulsification. At 37±10°C, 500 ml of water was mixed with one milliliter of each formulation. Gentle agitation is achieved by using a typical stainless steel dissolving paddle that rotates at 50 rpm. The following grading scheme is used to visually evaluate the formulations' in vitro performance:
    - **Grade A:** A transparent or bluish-looking nanoemulsion that forms quickly (within a minute).

• **Grade B:** A bluish-white, rapidly developing emulsion that is a little less transparent.
•**GradeC:** A fine, milky emulsion that developed in two minutes.
•**Grade D:** A dull, grayish white emulsion that takes longer than two minutes to emulsify and has a slightly greasy appearance.
• **Grade E:** Emulsification, with big oil globules visible on the surface and either poor or little emulsification.

- **Turbidimetric evaluation:** Nephelo turbidimetric evaluation can be used to track the growth of an emulsion. A turbidimeter is used to measure the increase in turbidity when a fixed amount of self-emulsifying system is added to a fixed quantity of an appropriate medium (0.1 N hydrochloric acid) on a magnetic plate at room temperature while being continuously stirred (50 rpm). However, the rate of change of turbidity (rate of emulsification) cannot be monitored because the time needed for full emulsification is too short.
- **Refractive index and transmittance percentage:** These two metrics demonstrate the formulation's transparency. A drop of solution is placed on a slide, and the refractive index is then measured using a refractive index meter by comparing it to water (1.333). A UV spectrophotometer is used to measure the system's transmittance percentage at a certain wavelength while using distilled water as a blank. A formulation is considered transparent if its refractive index is comparable to that of water (1.333) and its transmittance percentage is greater than 99% [3].
- **Electro conductivity test:** The purpose of this test is to measure the system's electroconductive character. An electro-conductometer is used to test the electroconductivity of the resulting system. Because free fatty acids are present in typical SMEDDSs, an oil droplet has a negative charge [4].
- **Drug content:** The drug is extracted from pre-weighed SMEDDS by dissolving it in an appropriate solvent. Using an appropriate analytical technique, the drug content in the solvent extract was compared to the drug's standard solvent solution [3].
- **In vitro dissolution testing:** The US Pharmacopoeia XXIV dissolution apparatus 2 is used to perform the quantitative in vitro release test. The paddles are set to revolve at 100 rpm, and the temperature is set to 37°C. The dissolution media is 900 ml of buffer with pH (as specified in the pharmacopoeia for the specific drug). The SMEDDS formulations are placed in firm gelatin capsules (size 00), and a 5 ml sample of the dissolving media must be removed for HPLC analysis during the drug release tests. Every time, 5 ml of new medium must be added to replace the withdrawn volume. To investigate how pH affects drug release, dissolution tests are also carried out in different media (buffers with varying pH) [6].

REFERENCES

1. Akula, S., Gurram, A. K., & Devireddy, S. R. (2014). Self-Microemulsifying Drug Delivery Systems: An Attractive Strategy for Enhanced Therapeutic Profile. International scholarly research notices, 2014(1), 964051.
2. Anand, S., Gupta, R., & Prajapati, S. K. (2016). Self-micro emulsifying drug delivery system. Asian J Pharm Clin Res, 9(2), 33-38.
3. Bashir, M. A., Khan, A., Shah, S. I., Ullah, M., Khuda, F., Abbas, M., ... & Ming, L. C. (2023). Development and evaluation of self-emulsifying drug-delivery system–based tablets for simvastatin, a BCS Class II Drug. Drug Design, Development and Therapy, 261-272.
4. Benival, D. M., & Devarajan, P. V. (2015). In situ lipidization as a new approach for the design of a self microemulsifying drug delivery system (SMEDDS) of doxorubicin hydrochloride for oral administration. Journal of Biomedical Nanotechnology, 11(5), 913-922.
5. Betageri, G. V. (2019). Self-emulsifying drug delivery systems and their marketed products: a review. Asian Journal of Pharmaceutics (AJP), 13(02).
6. Buya, A. B., Beloqui, A., Memvanga, P. B., &Préat, V. (2020). Self-nano-emulsifying drug-delivery systems: From the development to the current applications and challenges in oral drug delivery. Pharmaceutics, 12(12), 1194.
7. Cai, S., Shi, C. H., Zhang, X., Tang, X., Suo, H., Yang, L., & Zhao, Y. (2014). Self-microemulsifying drug-delivery system for improved oral bioavailability of 20 (S)-25-methoxyl-dammarane-3β, 12β, 20-triol: preparation and evaluation. *International Journal of Nanomedicine*, 913-920.
8. 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 tumor growth in mice. International Journal of Pharmaceutics, 579, 119134.
9. Dokania, S., & Joshi, A. K. (2015). Self-microemulsifying drug delivery system (SMEDDS)–challenges and road ahead. *Drug delivery*, *22*(6), 675-690.

10. Friedl, J. D., Jörgensen, A. M., Le-Vinh, B., Braun, D. E., Tribus, M., &Bernkop-Schnürch, A. (2021). Solidification of self-emulsifying drug delivery systems (SEDDS): Impact on storage stability of a therapeutic protein. Journal of Colloid and Interface Science, 584, 684-697.
11. Gershanik, T., & Benita, S. (2000). Self-dispersing lipid formulations for improving oral absorption of lipophilic drugs. European journal of pharmaceutics and biopharmaceutics, 50(1), 179-188.
12. Gursoy, R. N., & Benita, S. (2004). Self-emulsifying drug delivery systems (SEDDS) for improved oral delivery of lipophilic drugs. Biomedicine & pharmacotherapy, 58(3), 173-182.
13. Holm, R., Kuentz, M., Ilie-Spiridon, A. R., & Griffin, B. T. (2023). Lipid based formulations as supersaturating oral delivery systems: From current to future industrial applications. European Journal of Pharmaceutical Sciences, 189, 106556.
14. Jadhav Bharat, V., Tattu Arpita, B., Jadhav Supriya, B., & Bade Urmila, R. (2024). Review on self-micro emulsifying drug delivery system SMEDDS. Int. J. Pharm. Sci, 2(1).
15. 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.
16. Kalamkar, P., Pawar, K., Baddi, H., Thawkar, B., Yevale, R., & Kale, M. (2016). A Review on "Self Micro Emulsifying Drug Delivery System (SMEDDS). Indian Journal of Drug, 4(3), 361-373.
17. Pouton, C.W. (2000) Lipid Formulations for Oral Administration of Drugs: Non-Emulsifying, Self-Emulsifying and "Self-Microemulsifying" Drug Delivery Systems. European Journal of Pharmaceutical Sciences, 11, S93-S98.
18. Phuong Tran, Jeong-Sook Park,(2021). Application of supercritical fluid technology for solid dispersion to enhance solubility and bioavailability of poorly water-soluble drugs, International Journal of Pharmaceutics, Volume 610,121247,ISSN 0378-5173,https://doi.org/10.1016/j.ijpharm.2021.121247.
19. Lin, I. J., & Marszall, L. C. M. C. (1976). CMC, HLB, and effective chain length of surface-active anionic and cationic substances containing oxyethylene groups. Journal of Colloid and Interface Science, 57(1), 85-93.