



A REVIEW ON SELF EMULSIFYING DRUG DELIVERY SYSTEM

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ABSTRACT

The most practical and easiest way to administer medication is orally. The most economical and dominant in the global drug delivery industry are oral medication delivery systems. Low and irregular bioavailability, primarily due to inadequate water solubility, is the main issue with oral medication formulations. High levels of variability between and between subjects, a lack of dose proportionality, and treatment failure could result from this. According to estimates, 40% of active ingredients are inherently water insoluble or weakly soluble in water. Enhancing the bioavailability of medications possessing such attributes is a formidable task in drug formulation. The literature reports on a number of technological approaches, such as solid dispersions, the production of cyclodextrine complexes or micronization, and other drug delivery system technologies.

With these methods included, self-emulsifying drug delivery systems (SEDDS) have drawn increased interest in order to improve oral bioavailability while lowering dosage. Isotropic blends of oil, surfactants, solvents, and co-solvents/surfactants are known as SEDDS. The main feature of these systems is their capacity to dilute by an aqueous phase and then, upon gentle agitation, form fine oil-in-water (o/w) emulsions or microemulsions. SEDDS could be a useful tactic to increase the pace and extent of oral absorption for lipophilic medications, whose absorption is limited by their dissolution rate.

This review article describes how poorly soluble drugs can become more soluble and more bioavailable through the use of self-emulsifying drug delivery devices.

KEY-WORDS: Self-Emulsifying Drug Delivery System, Lipophilic, Bioavailability, Soluble, Isotropic.

1. INTRODUCTION

Self-emulsifying drug delivery systems (SEDDSs) have gained exposure for their ability to increase solubility and bioavailability of poorly soluble drugs. SEDDS are isotropic mixtures of oils and surfactants; sometimes it contains co-solvents, and it can be used for the design of formulations in order to improve the oral absorption of highly lipophilic compounds.^[2] The oral route is the most used route for chronic and newly diagnosed diseases due to ease of administration and patient compliance.^[1] According to published research, forty percent of newly discovered chemical entities have low water solubility, in situ emulsification or self-emulsification, the release of SEDDS formulation into the gastrointestinal tract lumen results in the formation of a fine emulsion (micro/nano) with GI fluid. This process further solubilizes the drug, enabling it to be absorbed by lymphatic pathways without going through the hepatic first-pass effect. Many in vivo characteristics of the lipid formulations have been linked to this bioavailability-enhancing feature, including:

1. Creation of micellar suspensions and fine dispersions to stop the medication compound from precipitating and re-crystallizing.
2. The potential of specific lipid molecules and their metabolites to cause alterations in the gastrointestinal fluid that promote better medication absorption.
3. Inhibition of the cellular efflux systems that prevent medicines from entering the bloodstream.
4. Reducing the impact of first-pass drug metabolism, certain lipid excipients are linked to selective drug absorption into the lymphatic transport system.^[2]

2. MECHANISM OF SELF-EMULSIFICATION

Reiss states that self-emulsification happens when the energy needed to expand the dispersion's surface area is less than the entropy shift that favors dispersion. The typical emulsion's free energy can be expressed by the following equation, which is a direct function of the energy needed to form a new surface between the water and oil phases: The associated free energy (AG) in the emulsification process is provided by the following equation:^[6]

$$\Delta G = \sigma \Delta A - \Delta n R T \ln \frac{V_o}{V_w}$$

where N is the number of droplets with radius r , σ is the interfacial energy, and ΔG is the process free energy (ignoring the mixing free energy). Over time, the two phases of the emulsion tend to separate and diminish the interfacial area. Emulsifying agents then stabilize the emulsion by forming a monolayer of emulsion droplets, which lowers the interfacial energy and acts as a barrier to prevent coalescence.

The ease of emulsion may be increased by minimizing the phase inversion temperature, which is related to the specificity of surfactant combination needed to permit spontaneous emulsification. Phase studies are also required in self-emulsification for the creation of liquid crystals. These suggest that effective formulations typically operate in a zone of improved aqueous solubilization and close to a phase inversion region.

Mustafa and Groves devised a technique to measure the turbidity of the oil surfactant system in a water stream in order to quantitatively evaluate the emulsification using phosphated nonylphenoxyolate and phosphate fatty alcohol ethoxyolate in *n* hexane. They proposed that the ease with which water permeates the oil-water interface could be related to the emulsification process. With formation of liquid crystalline phase resulting in swelling at the interface, thereby leading to greater ease of emulsification. As a result, the scientists were able to connect the phase behavior to the spontaneity of emulsification, since the reduced equilibration periods suggest that liquid crystals tend to form emulsions more quickly. Poton has suggested that phase inversion behavior of the surfactant may be connected to its emulsification capabilities.^[16]

When one uses non-ionic surfactants to stabilize the temperature of the oil in a water system, for instance, phase inversion occurs once the surfactant reaches its cloud point. Because the surfactant is highly mobile at the phase inversion temperature, there is less o/w interfacial energy, which lowers the energy needed to cause emulsification.

These are the steps involved in the self-emulsification process, which has numerous applications, but in particular, it only improves permeability and bioavailability. It is occasionally also employed to increase solubility.

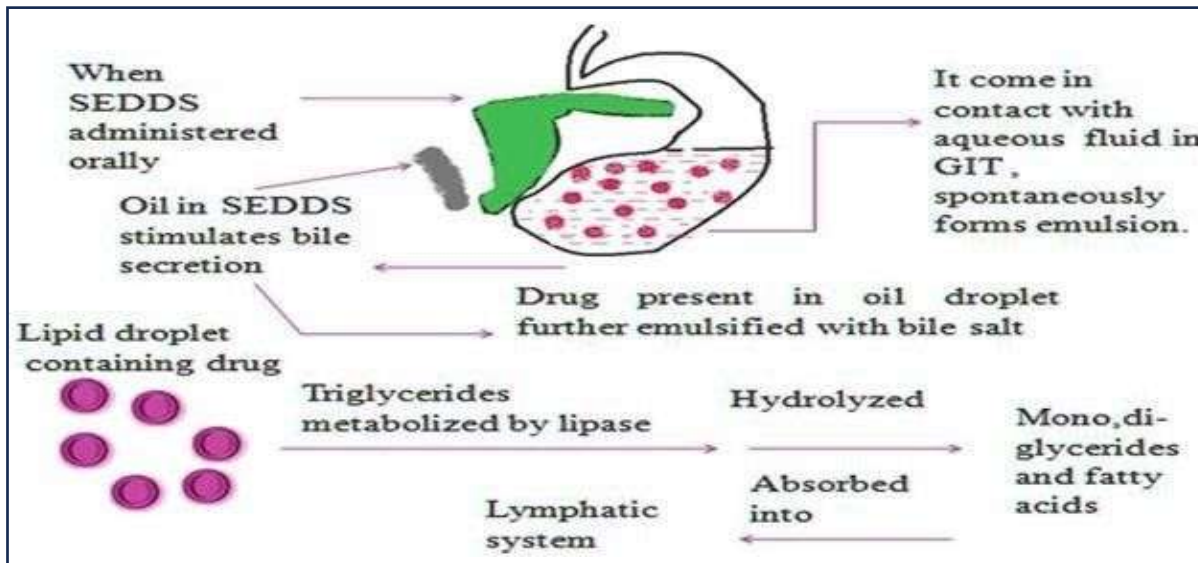


Fig.1 Mechanism of self-emulsification

3.COMPOSITION

[A] Surfactants

Tone-emulsifying systems can be made from a broad variety of composites with surfactant properties; however, there are very few surfactants that are appropriate for oral usage. Non-ionic surfactants are the ones that are most frequently advised since they have a higher hydrophilic-lipophilic balance (HLB) and a lower toxicity than ionic surfactants. However, they might result in transient modifications to the permeability of the intestinal lumen. Safety is a crucial factor to take into account while selecting a surfactant. Consequently, natural emulsifiers are preferred over synthetic surfactants but they have a limited potential to tone emulsify.



Table.1 Types of surfactants used in market as SEDDS^[6]

Surfactant	Drug	Product
Span 80, Tween 80	Cyclosporine	Gengraf soft gelatin capsule
Cremophor RH 40	Carmustine	BCNU self-emulsifying implant
Tween 20	Bexarotene	Targretin Hard gelatin Capsule

[B] Co-Solvents

As it is widely known that alcohol and other unpredictable cosolvents included in traditional tone. Emulsifying phrasings go into the shells of soft and hard gelatin capsules, causing the lipophilic substance to precipitate, these systems would not provide many advantages over earlier phrasings when added to capsule lozenge forms. ^[7]

Table 2: Types Óf Co-Solvents Used In Marketed SEDDS

Co surfactants	Marketed preparation
Glycerine	Sandimmune soft gelatin capsule.
Propylene Glycol	Neoral soft gelatin, Neoral oral solution, Gengraf hard gelatin, Lamprene soft gelatin capsule.
Ethanol	Neoral Soft gelatin & Neoral oral, Sandimmune soft gelatin & oral sol, Gengraf hard gelatin capsule.

[C] Oils

One of the most important excipients is oil painting because depending on the triglycerides molecular composition, it can help with tone

Emulsification, solubilize the required quantum of the lipophilic medication, and rise the likelihood that the medication will be transported through the intestinal lymphatic general, more attention from Cremophore Rh40 is required when using LCT t o create micro-emulsions than when using MCT.Cometible canvases are typically avoided because of their poor ability to dissolve sizable concentrations of lipophilic medicines Modified or hydrolyzed vegetable canvases are typically used as excipients because they provide efficient emulsification systems with several surfactants that are acceptable for oral administration and have higher rates of medication solubility. ^[6]

4. TYPES OF SEDDS ^[1,2]

A] Water soluble

These systems are formulated with hydrophilic surfactants (HLB > 12) and co-solvents (polyethylene glycols, ethanol, and propylene glycol). Type 3 Self emulsifying drug delivery system are also known as self-micro-emulsifying drug delivery systems, or SMEDDS. Type III formulations are also divided into type 3 A & type 3 B formulations in order to find more hydrophilic forms. In Type IIIB, there is a decrease in lipid content and an increase in hydrophilic surfactants and cosolvents.

B] Non-water-soluble

These are self-emulsifying isotropic mixes of lipids and lipophilic surfactants in an aqueous medium water emulsion, where the HLB value is less than 12. Self-emulsification happens when the surfactant content rises above 25% w/w. At a surfactant level of 50– 60% w/w, however, the emulsification process could be compromised if viscous liquid crystalline gels begin to develop at the oil/water interface. Type-II SEDDS (Lipid Formulation Classification System) is the name given to this system. By encasing poorly water-soluble medications in hard and soft gelatin capsules and adding them to SEDDS, it is feasible to produce handy single-unit dose forms.

Properties of SEDDS ^[17]

- 1.They have a high rate of self-emulsification in gastrointestinal fluids and produce a fine o/w emulsion when the gastro intestinal tract's peristaltic and other movements cause mild agitation
- 2.They are able to mix hydrophobic or hydrophilic drugs with oil surfactant mixtures
- 3.Both liquid and solid dose forms can be employed with them.
- 4.Compared to traditional dosage forms, they require a lesser dosage of the medication.

Advantages ^[18]

- 1.distribution throughout the GI tract and the stomach, and reducing the irritation that is frequently experienced during prolonged contact between the bulk drug substance and the gut wall.
- 2.SMEDDS are formulations that are physically stable, whereas emulsions are sensitive and metastable dispersed forms.
- 3.They offer a larger surface area for the medication to separate into oil and water compared to oily solutions.



4. These methods may provide improved oral bioavailability, more reliable drug absorption temporal patterns, and targeted drug delivery to a particular absorption site.

Disadvantages^[17]

1. The absence of reliable predictive in vitro models for formulation evaluation is one of the challenges facing the development of SMEDDS and other lipid-based formulations.
2. Since these formulations might be dependent on digestion before the medicine is released, traditional dissolving techniques are ineffective.
3. This system's shortcomings include the instabilities of the medications' chemical composition and the formulations' high surfactant concentrations (between 30 and 60%), which aggravate the gastrointestinal tract.
4. It is known that volatile co-solvents in traditional SMEDDS formulations move into the shells of soft or hard

5. DEVELOPMENT

Semisolid SEDDS to S - SEDDS include the following:

1. Capsule filling with liquid and circumfluous tone: Emulsifying phrasings: Capsule stuffing is regarded the most basic and extensively habituated way for recapitulating liquid and circumfluous SE phrasings for oral application. These four methods are involved: A) Raising the circumfluous excipient to a temperature at least 20 °C above melting point. B) The active ingredients are objectified. C) Filling the capsules with the melted mixture. D) Reducing its temperature to ambient^[10]

2. Adsorption to Solid Carriers: Liquid SE phrasings can be adsorbed onto solid carriers to create free-flowing maquillages. The adsorption is considered uncomplicated and merely involves the liquid expression transferring onto carriers through blending in a blender 30. Following that, the greasepaint is mixed with a p p l I appropriate excipients and then crushed into tablets or directly placed into capsules. One of the key benefits of the adsorption fashion is good content unity.^[11]

3. Melt Granulation

Greasepaint agglomeration systems such as Melt Granulation are accomplished by mixing in a binder that melts or softens at relatively low temperatures. Melt granulation, being a "one-step" process, gives many beneficial effects over typical wet granulation because it disregards the liquid objectification and subsequent drying phase. A few key variables that affect the granulation process are the density of the binder, the size of the binder flyspeck, the mixing duration, and the impellar speed. The melt granulation method was used to meet the need of adsorbing lipids, surfactants, and medications onto solid neutral carriers, particularly silica and magnesium aluminum silicate.^{[12][13]}

4. Melt Extrusion /Extrusion Spheronization

Melt extrusion is a solvent-free method that enables homogeneous content and high drug loading. Extrusion is a technique that creates products with consistent viscosity and shape by forcing a raw material with plastic rates through a bone at controlled temperatures, product flows, and pressure conditions. The extrusion-spheronization method is continuously used by the pharma companies to create uniformly sized squares (bullets). It involve below points:

A) The active ingredients and excipients are combined dry to create an invariant greasepaint; when the binder is concentrated, it is also wet. B) Extrusion into an extrudate that resembles spaghetti.

C) Spheronization of extrudate into homogeneous- sized squares.

D) Desiccating Sifting to obtain the appropriate size distribution and coating.^{[14][15][16]}

SEDDS enhances the oral Bioavailability and solubility of Herbal Medications^[18]

Due to their high hydrophobicity, herbal medications with low aqueous solubility provide a significant formulation difficulty in the majority of authorized solvents. Herbal medications are more thoroughly dissolved by the unique hydrophilic oils and surfactants found in SEDDS than by traditional vegetable oils. When the drug compound partitions into the intestinal fluids during droplet transit and disintegrates with the gastro intestinal tract, it is released from SEDDS. The efficient release of the medicinal ingredient from SEDDS was shown to be primarily determined by two factors: the polarity of the resultant oil droplets and the small particle size (Mandawgade et al., 2008; Shen et al., 2010). Elderly people can now utilize ginkgo biloba extract (GBE), a popular herbal medicine performance.

The study discovered that through quick self-emulsification and subsequent dispersion in the absorption sites, GBE-loaded SEDDS could effectively increase oral absorption of the sparingly soluble medications. 10% 1,2-propanediol, 45% ethyl oleate, and 45% Tween 80-Cremophor EL35 (1:1, w/w) made up the ideal formulation for the bioavailability assessment. The GBE-SEDDS form's active ingredients dissolved far more quickly in vitro than they did in GBE tablets. After a single oral delivery of 800 mg GBE as SEDDS or tablets to fasting dogs, the relative bioavailability of SEDDS for bilabolide and ginkgo lide A and B was 162.1%, 154.6%, and 155.8% compared with the reference tablets, respectively (Tangetal., 2008).



To improve absorption and solubility, Fructus Schisandral Chinensis (Wurenchun), another herbal remedy, has also been developed as SEDDS.

The formulation that was optimized for bioavailability assessment comprised of 15% Transcutol P, 65% Tween 20, and 20% oleic acid. Diluted with a 1000-fold volume of distilled water, the optimized SEDDS had a mean droplet size distribution of 240 nm. The active ingredients of Wurenchun SEDDS dissolved far more quickly in vitro than they did in commercial capsules. When compared to reference capsules, Wurenchun's C_{max} and AUC have been significantly higher thanks to SEDDS (p<0.05). Furthermore, in comparison to commercial capsules, the relative bioavailability of SEDDS for schisandrin and schisandrin B was 292.2% and 205.8%, respectively.

Limitation ^[4]

The development of self-emulsifying drug delivery systems (SEEDS) and other lipid-based formulations is hampered by the lack of valid predictive in vitro models for formulation evaluation. Traditional dissolving techniques don't work with these formulations since the medicine may need to be digested before it can be released.

An in vitro model that replicates the duodenum's digestion processes has been created to emulate this. Before assessing the in vitro model's strength, more work and validation are required.

Different prototype lipid-based formulations must be created and tested in vivo in an appropriate animal model since future development will be predicated on correlations between in vitro and in vivo data. Subsequent research will focus on the creation in vitro model.

6.DOSAGE FORM

1.Self-Emulsifying Capsule

Micro-emulsion droplets form in the GIT and spread to the absorption area during delivery of capsules containing liquid solution SE preparations. It is not possible to anticipate a rise in drug absorption if the micro-emulsion's phase separation is permanent. Sodium dodecyl sulphate was added to the SE formulation as a solution to this issue.

2.Self-Emulsifying Sustained/Controlled Release

Lipids and surfactants have a lot of potential when it comes to creating SE tablets. Tablets containing SE are particularly helpful in preventing side effects. For instance, augmenting SE tablets with indomethacin may improve the drug's capacity to cross the GI mucosa and lessen GI hemorrhage. ^[13]

3.Controlled/Sustained Release Self-Emulsifying Pellets

Compared to conventional solid dose forms, pellets offer a number of advantages, including less intra- and inter-subject variability in plasma profiles, decreased GI distress without sacrificing medicine absorption, and production flexibility. Although self-emulsifying solid dispersions raise manufacturing and stability difficulties, they have the potential to increase the bioavailability and speed up the rate of dissolution of water-insoluble medications. ^{[12] [13]}

4.Semisolid SEDDS

Semisolid SEDDS is synthesized in situ using lipid components similar to those used in liquid SEDDS, but with a melting point higher than room temperature. Lipids and surfactants such as glycerides, cetyl alcohol, hydrogenated castor oil, lauryl macro-gel, and polyoxyethylene block polymer are typically utilized in the semisolid SEDDS production process. Compared to SEDDS, these preparations have a higher viscosity, which improves formulation stability and handling mobility.

5.Self-emulsifying controlled release tablets

Self-emulsifying controlled release tablets are the most current technology advancement around S-SEDDS for establishing a controlled drug release profile. AlphaRx Inc. (Markham, Canada) developed the patented proprietary platform technology known as SECRET which creates tablets by adsorbing liquid SE formulations onto the surface of rate-regulating polymers like HPC, HPMC, etc. ^[14]

Drug Content

Drug is extracted from pre-weighed SEEDS by dissolving 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]



7. EVALUATION ^[13]

1. Visual Evaluation

Tone-emulsification assessment is aided by visual observation. Rush or phase separation should not occur in the case of a stable expression. When SEDDS is diluted, a transparent result is obtained, which indicates the formation of micro-emulsions; in contrast, a solid, delicate white appearance is noticed, which shows the formation of macro-emulsions.

2. Analysis of Droplet Size

The size of the droplet is determined by the kind and concentration of the surfactant. For steady, in vivo absorption and efficient drug release in the micro-emulsion formed when SMEDDS is diluted with water, an exceptionally narrow droplet size distribution is necessary. Droplet size analysis is done with DLS techniques.

3. Emulsification Time

The oil painting and surfactant phase rate are used to determine how long it takes to emulsify an expression. Using a handbasket dissolving gear, this is ascertained by agitating the mixture after adding drops at a time to a handbasket filled with water until a distinct result appears.

4. Ball Point Determination

The temperature at which a homogenous product begins to gain translucency is its ball point. Above the ball point, the surfactant often loses all of its capacity to form micelles. Gradually adding the expression's temperature and utilizing spectrophotometry to gauge the turbidity help it become apparent. The ball point of a surfactant is the temperature at which its probability transmittance decreases. Phrasings need to be over 37.5 °C in order to continue with one-emulsification.

5. Density Measures

The density of the SMEDDS phrasings, which are micro-emulsions, is measured using a rheometer and a Brookfield viscometer, which has a cone and plate with a revolving spindle. 6. Liquefaction time: In this discussion, the melting time of S-SEDDS in a timebased GI landscape simulation is to be ascertained. The cure form is threaded onto the bulb of a thermometer and covered in a clear polyethylene film. After that, the thermometer must be maintained at 37 °C in an RBF that has 250 mL of disassembled stomach fluid free of pepsin. The timing of the liquefaction is then monitored and recorded.

7. Nuclear Glamorous Resonance (NMR) Studies

The kinetics and structure of micro-emulsions are studied using these methods. Toneprolixity evaluations that employ a variety of techniques—most commonly, radio labeling—provide information regarding the factors' medium and mobility. The gorgeous grade of the samples is used by the Fourier transfigure palpitated-grade spin-echo (FTPGSE) method to enable the quick and simultaneous estimation of the tone-prolixity sections of many components. The tone-prolixity measure $D = KT / 6\pi\eta r$ is deciphered using the Stokes-Einstein equation, where η stands for density, T for absolute temperature, K for Boltzmann constant, and r for the drop's compass.

8. APPLICATION

1. Improvement in Solubility and bioavailability

Drug solubility is increased when it is put into SEDDS because, in the case of Class-Ī drugs (low solubility/high permeability), the dissolving step is avoided. The preferred medication for prolonged release formulations, ketoprofen is a moderately hydrophobic (log P 0.979) NSAID with a considerable propensity for gastrointestinal discomfort when used long-term. Ketoprofen exhibits partial release from sustained release formulations due to its limited solubility. Vergote et al. reported total medication release from formulations with sustained release that contained nanocrystalline ketoprofen. Processing, stability, and financial issues may arise during the preparation and stabilization of nanocrystalline or enhanced solubility pharmacological forms. Ketoprofen can be successfully used in the SEDDS formulation to solve this issue. ^[19]

2. Controlling the release of drug

attain The preparation of matrix pellets of nano-crystalline ketoprofen, sustained release ketoprofen microparticles, floating oral ketoprofen systems, and transdermal ketoprofen systems are some of the formulation strategies that have been tried to increase the bioavailability, decrease the gastric irritation, and sustain release of ketoprofen. Processing, stability, and financial issues may arise during the preparation and stabilization of nanocrystalline or enhanced solubility pharmacological forms. Ketoprofen can be successfully used in the SEDDS formulation to solve this issue. This formulation reduces stomach irritation and increases medication solubility, which improves bioavailability. Additionally, the release of ketoprofen was maintained by the gelling agent incorporated into SEDDS. ^{[19] [20]}

3. Protection against Biodegradation

For medications whose low solubility and GI tract degradation both contribute to a low oral bioavailability, the self-emulsifying drug delivery system's capacity to decrease degradation and boost absorption may be particularly helpful. Numerous medications undergo physiological system degradation; the reasons for this can include the stomach's acidic pH, enzymatic or hydrolytic breakdown, etc. When these medications are administered as SEDDS, they can be effectively shielded from these degradation processes because the liquid crystalline phase of SEDDS may serve as a barrier between the medication and the environment that is



degrading. Acetylsalicylic acid (Mw=180, Log P = 1.2), a medication that breaks down in the gastrointestinal tract because an acidic environment easily hydrolyzes it to salicylic acid. When the medication was prepared using the Galacticles Oral Lipid Matrix System (SEDDS formulation) and compared to a commercial formulation, the comparison revealed a satisfactory plasma profile. When compared to the reference formulation, the Galacticles Oral Lipid Matrix System formulation increases the oral bioavailability of undegraded acetylsalicylic acid by 73%. This implies that the SEDDS formulation can shield medications from GI tract deterioration.

In order to prevent drug precipitation, supersaturable SEDDS are composed of a watersoluble cellulosic polymer (or other polymers) and a reduced quantity of surfactant. This allows the polymer to remain in a supersaturated condition in vivo. In comparison to the corresponding self-emulsifying drug delivery systems (SEDDS) formulation, the S-SEDDS formulations may lead to improved oral absorption, and the decreased surfactant levels may lessen gastrointestinal surfactant adverse effects. ^[20]

9.CONCLUSION

A technology that shows promise for the production of medication composites with low waterless solubility is the emulsifying medicine delivery system. New operations in medicine delivery systems will be made possible by the ongoing development of this SEDDS. Apart from augmenting the solubility of medicines that are not sufficiently answerable, SEDDS also enhances medicine bioavailability through multiple other potential pathways. These include bypassing the liver's first-pass impact, inhibiting P-gp import, and exhibiting resistance to the liver and gut metabolism of the cytochrome P450 family of enzymes. Before other solid SE lozenge forms (apart from SE capsules) arrive on the request, there is still a long way to go. Because there live some sectors of SEDDS to be further developed, similar as investigations about mortal bioavailability and the association of in vitro/in vivo. In other words, compared to SE tablets and capsules, suppositories microspheres have not undergone as much research. It's also worth pointing up several difficulties to which vital attention should be paid, for illustration physical aging miracle related with glyceride, oxidation of vegetable oil painting, and commerce between medicines and excipients. The primary chain involves the selection of appropriate excipients.

10.REFERENCES

1. Ajay Kumar , Surabhi Sharma, Ravindra Kamble. "Self-emulsifying drug delivery system (SEDDS): Future aspects". *International Journal of Pharmacy and Pharmaceutical Sciences* ISSN- 0975-1491 Vol 2, Suppl 4, 2010.
2. Meghana G and Prasanthi D. "Self-emulsifying drug delivery system: An approach to enhance solubility and permeability". *International journal of Current Advanced Research*, Volume 8, PAGE NO: 16931- 16938, October 2018.
3. Patel S.N.*, Patel D.M., Patel C.N., Patel T.D. Prajapati P. H. Parikh B.N. "Self-emulsifying drug delivery system". ISSN 0975 - 8542 *Journal of Global Pharma Technology*,
4. https://www.researchgate.net/publication/258026600_Self_Emulsifying_Drug_Delivery_System_A_nov_el_approach
5. Neha Tiwari, Himansu Chopra, Manoj Sagar and Ashok Kumar Sharma- "A Review on Self-emulsified Drug Delivery System: A Promising Approach for Drug Delivery of BCS Class II and drugs". *Journal of Pharmaceutical Research*: ISSN: 0973 7200.
6. Wakerly M.G. et al. Self-emulsification of vegetable oil non-ionic surfactant mixtures: *ACS Symp Ser.* 1986; 311: 242-255.
7. https://www.google.com/search?q=7.+%7Bhttps%3A%2F%2Fwww.ncbi.nlm.nih.gov%2Fpmc%2Farticles%2FPMC9176699%2F%7D&rlz=1C1VDKB_enIN1067IN1068&oq=7.%09%7Bhttps%3A%2F%2Fwww.ncbi.nlm.nih.gov%2Fpmc%2Farticles%2FPMC9176699%2F%7D&gs_lcrp=EgZjaHJvWUyBggAE EUYOdIBBzc3M2owajeoAgCwAgA&sourceid=chrome&ie=UTF-8
8. <https://pubmed.ncbi.nlm.nih.gov/9924128/>
9. Charman WN, Porter CJ, Mithani S, Dressman JB. "Physicochemical and physiological mechanisms for the effects of food on drug absorption: the role of lipids and pH.". 1997; 86: 269-82.
10. Fabio C, Elisabetta C. "Pharmaceutical composition comprising a water/oil/water double microemulsion incorporated in a solid support". WO2003/013421.
11. Gupta MK. Et.al. "Enhanced drug dissolution and bulk properties of solid dispersions granulated with a surface adsorbent". 2001; 6: 563-572.
12. Gupta MK et.al. "Hydrogen bonding with adsorbent during storage governs drug dissolution from solid-dispersion granules". *Pharm Res* 2002; 19: 1663-1672.
13. Jannin V. .et al. "Approaches for the development of solid and semi-solid lipid-based formulations". *Advance Drug Delivery Rev* 2008; 60: 734-746.
14. Verreck G., Brewster ME. "Melt extrusion-based dosage forms: excipients and processing conditions for pharmaceutical formulations". 2004; 97: 85-95.
15. Newton M.:The influence of formulation variables on the properties of pellets containing a self-emulsifying mixture". *J Pharm Sci* 2001; 90: 987-995.}
16. Gershanik T., Benita S. Self-dispersing lipid formulations for improving oral absorption of lipophilic drugs: *European Journal of Pharmaceutics and Biopharmaceutics*. 2000; 50:179- 188.



17. Sapraa K, et al: *Self Emulsifying Drug Delivery System: A Tool in Solubility Enhancement of Poorly Soluble Drugs*; *Indo Global Journal of Pharmaceutical Sciences* 2012; 2(3): 313-332. Sapraa K, et al: *Self Emulsifying Drug Delivery System: A Tool in Solubility Enhancement of Poorly Soluble Drugs*; *Indo Global Journal of Pharmaceutical Sciences* 2012; 2(3): 313-332.
18. Lin Zhang, lanying Zhang, Manhong Zhang, Yue Pang, Zhaoming Li, Aili Zhao & Jing Feng (2015) *Self-emulsifying drug delivery system and the applications in herbal drugs*, *Drug Delivery*, 22:4, 475-486.
19. El-Kamel AH, Sokar MS, Al Gamal SS.,Nagar VF . *Preparation and evaluation of ketoprofen floating oral delivery system*. *Int J Pharm.* 2001; 220:13-21.
20. Shah NH, Carvajal MT, Patel CI, Infeld MH, Malick AW. *Self-emulsifying drug delivery systems (SEDDS) with polyglycolized glycerides for improving in vitro dissolution and oral absorption of lipophilic drugs*. *Int J Pharm.*199