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"Review on: Self Micro-Emulsifying Drug Delivery System for Poorly Water Soluble Drug"

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ABSTRACT

Oral route is the most convenient route of drug administration in many diseases and till today it is the first way investigated in the development of new dosage forms. The major problem in oral drug formulations is low and erratic bioavailability, which mainly results from poor aqueous solubility, thereby pretense problems in their formulation. More than 40% of potential drug products suffer from poor water solubility. For the therapeutic delivery of lipophilic active moieties (biopharmaceutical classification system Class II drugs), lipid-based formulations are inviting increasing attention. Currently, a number of technologies are available to deal with the poor solubility, dissolution rate, and bioavailability of insoluble drugs. One of the promising techniques is self-microemulsifying drug delivery systems (SMEDDS). SMEDDS have gained exposure for their ability to increase solubility and bioavailability of poorly soluble drugs. SMEDDS, which are isotropic mixtures of oils, surfactants, solvents, and co-solvents/surfactants can be used for the design of formulations to improve the oral absorption of highly lipophilic drug compounds. Conventional SMEDDS are mostly prepared in a liquid form, which can have some disadvantages. SMEDDS can be orally administered in soft or hard gelatin capsules and form fine relatively stable oil-in-water emulsions. Solid-SMEDDS are prepared by solidification of liquid/semisolid self-micron emulsifying ingredients into powders, have gained popularity. This article gives a complete overview of SMEDDS, but special attention has been paid to formulation, design, evaluation, and little emphasis on application of SMEDDS. Keywords: Self-microemulsifying drug delivery system, Surfactant, Oil, Co-surfactant, Bioavailability, Lipophilic, Biopharmaceutical classification system Class II drugs.</p. Approximately 40% of all lipophilic medications

are administered orally. Because of their poor water solubility, new chemical entities discovered during drug discovery programs (i.e. BCS Class II Drugs) present the biggest hurdle.4 the number of inferior water-soluble therapeutic candidate molecules has steadily increased because of current drug development strategies, and more than 50% of newly discovered chemical compounds with pharmacological activity have low water solubility and are lipophilic.

Key Words: Biopharmaceutical, Co-surfactant, Bioavailability, SMEDDS, lipophilic, ETC.

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1. INTRODUCTION:

The comprehensive review on Self Micro Emulsifying Drug Delivery Systems (SMEDDS). In this article, we will delve into the intricacies of SMEDDS, a revolutionary approach in the field of pharmaceuticals.(1) With its potential to improve drug solubility, bioavailability, and therapeutic efficacy, SMEDDS has garnered significant attention from researchers and pharmaceutical companies alike. In this review, we will explore the underlying principles, benefits, and challenges associated with SMEDDS, and how it has the potential to revolutionize drug delivery systems.(2) So, let's begin our journey into the world of SMEDDS! Among the different drug administration methods, the oral route is thought to be the most practical and patient-favored. One of the major factors affecting a medicine's oral bioavailability is its solubility because a pharmacological ingredient must dissolve in the GI tract's aqueous environment before it can be absorbed.(3) Approximately 40% of all lipophilic medications are administered orally. Because of their poor water solubility, new chemical entities discovered during drug discovery programs (i.e. BCS Class II Drugs) present the biggest hurdle.4 the number of inferior water-soluble therapeutic candidate molecules has steadily increased because of current drug development strategies, and more than 50% of newly discovered chemical compounds with pharmacological activity have low water solubility and are lipophilic. bioavailability, and therapeutic efficacy, SMEDDS has garnered significant attention from researchers and pharmaceutical companies alike.(4,5)In this review, we will explore the underlying principles, benefits, and challenges associated with SMEDDS, and how it has the potential to revolutionize drug delivery systems. So, let's begin our journey into the world of SMEDDS! Among the different drug administration methods, the oral route is thought to be the most practical and patient-favored.(4,6) One of the major factors affecting a medicine's oral bioavailability is its solubility because a pharmacological ingredient must dissolve in the GI tract's aqueous environment before it can be absorbed.1 2 3 Approximately 40% of all lipophilic medications are administered orally.(5,7) Because of their poor water solubility, new chemical entities discovered during discovery programs (i.e. BCS Class II Drugs) present the biggest hurdle. improve the oral absorption of highly lipophilic drug compounds. Conventional SMEDDS are mostly prepared in a liquid form, which can have some disadvantages. SMEDDS can be orally administered in soft or hard gelatin capsules and form fine relatively stable oil-in-water emulsions. Solid-SMEDDS are prepared by solidification of liquid/semisolid self-micron emulsifying ingredients into powders, have gained popularity. This article gives a complete overview of SMEDDS, but special attention has been paid to formulation, design, evaluation, and little emphasis on application of SMEDDS. Keywords: Self-microemulsifying drug delivery system, Surfactant, Oil, Co-surfactant, Bioavailability, Lipophilic, Biopharmaceutical classification system Class II drugs.</p. the number of inferior water-soluble therapeutic candidate molecules has steadily increased because of current drug development strategies, and more than 50% of newly discovered chemical compounds with pharmacological activity have low water solubility and are lipophilic.

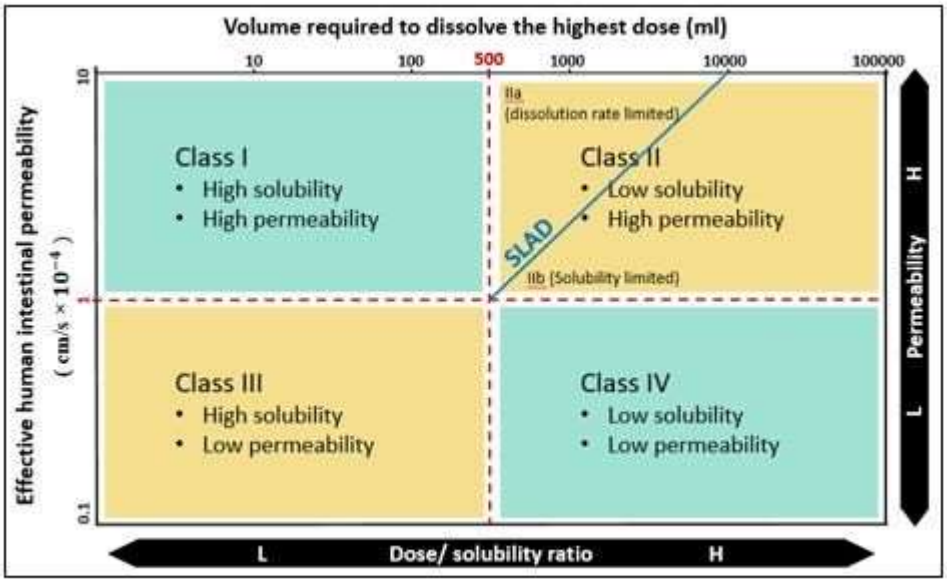


Figure 1: Illustration of various drug classes of developability classification system.

The number of inferior water-soluble therapeutic candidate molecules has steadily increased because of current drug development strategies, and more than 50% of newly discovered chemical compounds with pharmacological activity have low water solubility and are lipophilic.(8,9)Particle size reduction (micronation) is one method that has been thoroughly researched to increase the oral bioavailability of such medications. Salt generation, solubilization based on cosolvents, surfactants, or nanosizing), complexation with cyclodextrins, etc.(7,8) The dissolving rate of a medicine can be increased by altering its physicochemical qualities, such as via salt production and particle size reduction, however these techniques are not always feasible, for instance, it is impossible to make salts of neutral chemicals. Additionally, weak acid and basic salts may revert to their original acid or base forms and cause aggregation in the digestive system. (2) Particle size reduction may cause static charges to accumulate, provide handling challenges, and is not always beneficial. favored in situations where very fine particles have inadequate wettability.(10) Other formulation options,

including the use of cyclodextrins, nanoparticles, solid dispersions, and permeation enhancers, have been used in an effort to get around these restrictions. Indeed, these methods have worked in a few carefully chosen instances.(11) Lipid-based formulations have attracted great deal of attention to improve the oral bioavailability of poorly water soluble drugs. In fact, the most favored approach is to incorporate lipophilic drugs into inert lipid vehicles such as oils, surfactant dispersions, micro emulsions, self-emulsifying formulations, self-micro emulsifying formulations, and liposomes.(10) This could lead to increased solubilization with concomitant modification of their pharmacokinetic profiles, leading to increase in therapeutic efficacy. Solutions, suspensions, solid dispersions, and self-micro emulsifying drug delivery systems (SMEDDS) are just a few of the formulations available in lipid-based formulations.1formulations, which are isotropic combinations of natural or synthetic oils with lipophilic or hydrophilic surfactants and co-solvents, spontaneously emulsify to produce an oil-in-water emulsion or micro emulsion.(11)SMEDDS are a type of emulsion that has drawn interest specifically because it can improve the oral bioavailability of medications that aren't well absorbed.(7) These systems are essentially co-surfactants that produce emulsions when mixed with water while requiring minimal energy input. Despite having potential pharmacodynamic efficacy, many drug candidates fail to reach the market due to poor water solubility.(6,8) additionally, to obtain the appropriate plasma level, weakly aqueous soluble drugs now on the market are delivered at substantially greater individual dosages than intended. Due to the toxicity issues caused by this, the advantages of therapy, patient comfort, and patient adherence.(4) (12)

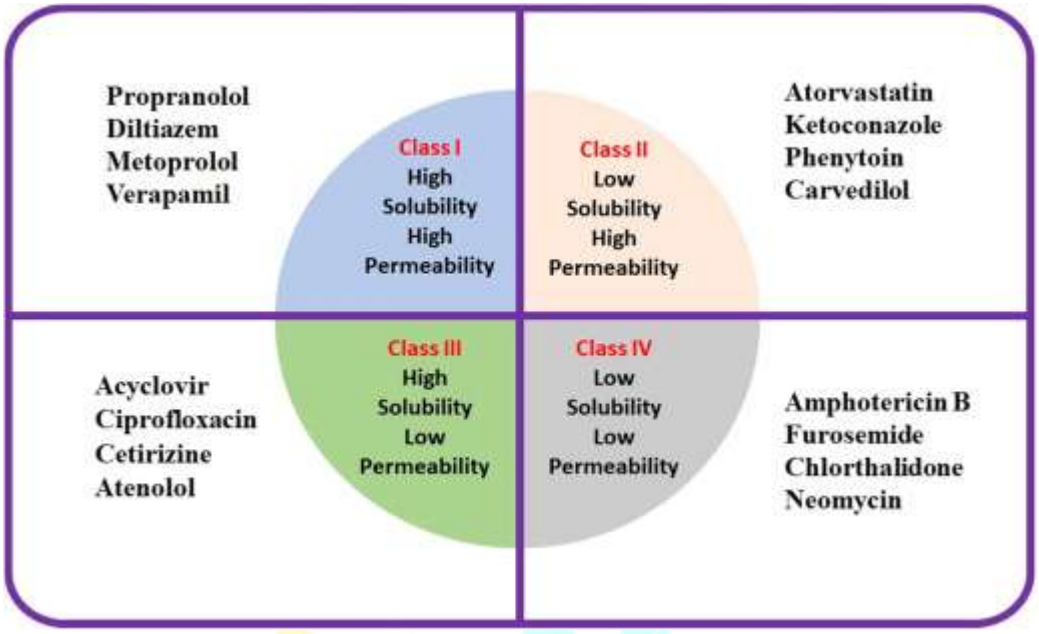


Fig. 2. Biopharmaceutical Classification

1.1.Advantages:

• SMEDDS can significantly improve the solubility of poorly water-soluble drugs, thereby increasing their bioavailability and therapeutic efficacy. (13)

• The microemulsion formulation allows for better drug absorption due to its ability to bypass the dissolution step, leading to faster and more consistent drug release. (14)

• SMEDDS can reduce the variability in drug absorption caused by food effects or other physiological factors, ensuring more predictable drug delivery. (13)

• By forming a stable microemulsion, SMEDDS can protect the drug from degradation and improve its shelf life. (13)

• SMEDDS offer the advantage of adjusting the drug dosage by simply changing the formulation's composition, making it easier to customize treatments for individual patients.(15)

• SMEDDS are more stable than emulsions due to their low energy consumption and the absence of certain steps in their manufacturing process. Crucial actions. SMEDDS can be created using only basic mixing tools, and preparation time is shorter than it is for emulsions.

• The formulation of SMEDDS allows for efficient absorption of poorly water-soluble medicines with dissolution rate-limited absorption, with stable time-profile of the plasma he

presentation of the poorly soluble drug in dissolved form, which skips the crucial phase in drug absorption known as dissolution, may be the cause of the drug's constant plasma levels.(16)

• The formulation of SMEDDS can protect drugs from being degraded in the GIT by chemical and enzymatic mechanisms because the medicine will be administered to the body as oil droplets.(16)

• Pre-concentrated microemulsion is preferable to microemulsion when dispensing in the form of liquid-filled soft gelatin capsules. SMEDDS are preferable to SEDDS because the former is less dependent on bile salts for the creation of droplets, which is believed to result in better medication absorption compared to SEDDS.(16)

1.2 Disadvantages:

• Designing SMEDDS requires expertise and can be challenging due to the need for a careful balance of surfactants, co-solvents, and oils to form a stable microemulsion. (17)

• Scaling up the production of SMEDDS may present difficulties and require specialized equipment.

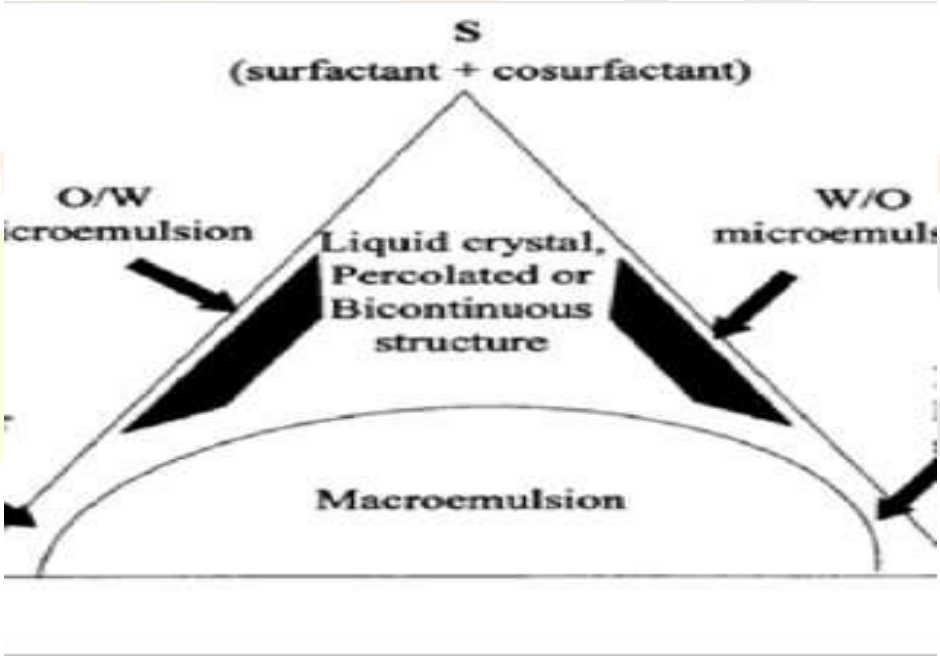
• SMEDDS might not be suitable for all drugs, as some may not be compatible with the chosen excipients or interact adversely with the formulation components. (17)

• Despite improved bioavailability in most cases, certain drugs may still exhibit variable absorption with SMEDDS due to individual physiological differences.(17)

• In some cases, the use of SMEDDS may lead to gastrointestinal irritation or adverse effects, which could limit their application.(17)

1.3. Mechanism of self-emulsification:

Self-emulsification is a process in which a water insoluble substance, such as an oil, spontaneously disperses into tiny droplets in the presence of water form a stable emulsion. This phenomenon occurs without the need for external energy input or the use of traditional emulsifying agents like surfactants.(6) The energy required for this process comes from the thermal motion of the molecules and is sufficient to overcome the interfacial tension, leading to the breakup of the bulk oil into droplets.



1.3.1. The mechanism of self-emulsification typically involves the following steps:

A.Surfactant-like Behavior: The substance to be emulsified (e.g., oil) possesses surfactantlike properties due to its chemical structure. A surfactant a molecule with a hydrophilic (water-attracting) head and a hydrophobic (water-repellent) tail. In self-emulsification, the substance's molecular structure allows it to align at the oil-water interface, reducing the interfacial tension between the two phases.(16)

B. Formation of Nano-emulsion: When the water insoluble substance is introduced into water, the surfactant-like molecules arrange themselves at the oil-water interface, forming a protective layer around the oil droplets. This layer stabilizes the droplets and prevents them from coalescing.(17) Spontaneous Dispersion: Due to the surfactant-like behavior, the water-insoluble substance disperses spontaneously into small droplets when mixed with water. The energy required for this process comes from the thermal motion of the molecules and is sufficient to overcome the interfacial tension, leading to the breakup of the bulk oil into droplets. (18)

C. Formation of Stable Emulsion: The small droplets formed during self-emulsification are stabilized by the surfactant-like molecules that continue to cover their surfaces. This ensures the emulsion remains stable over time, preventing phase separation or coalesce of droplets.(18) Self-emulsification is commonly utilized in pharmaceuticals, cosmetics, and food industries to enhance the solubility and bioavailability of poorly water-soluble substances, such as certain drugs or essential oils. The process offers several advantages, including ease of preparation, improved absorption, and better product stability.(18)However, the success of self-emulsification depends on the specific properties of the substances involved, including their molecular structure and compatibility with water Selfemulsification occurs when the entropy trade that favors dispersion is bigger than the power necessary to increase the dispersion's floor location. Hence For emulsification to take place, the interfacial form must be free of resistance to surface shearing.(19) The addition of a binary aggregation (oil/non-ionic surfactant) to water creates the interface between the oil and aqueous non-stop phases. As a result of aqueous penetration across the interface, this is followed by solubilization in the oil part. This occurs until the solubilization limit at the interphase is reached. the dispersed liquid crystal (LC) will form as a result of aqueous penetration.(4) The unfastened strength of a typical emulsion is an immediate element of thepower required to build a new surface between the water and oil phases, and it can be used to produce a new surface between the water and oil stages.(6) According to the aforementioned equation, the spontaneous creation of an interface between oil and aqueous phase is thermodynamically stable. elaborated on the spontaneous generation of emulsion, also known as self-emulsification, is measured in terms of the free energynecessary to produce the emulsion, which can be very low and positive or negative. Pouton proposed a link between the surfactant's emulsification properties and the system's phase inversion behavior.(20)For example, if the temperature of an oil-in-water system stabilized by non-ionic surfactant(s) is raised, the cloud point of the surfactant is reached, followed by phase inversion. Because the surfactant is highly mobile at the phase inversion temperature, the o/w interfacial energy is minimized, resulting in less energy required for emulsification.(8)

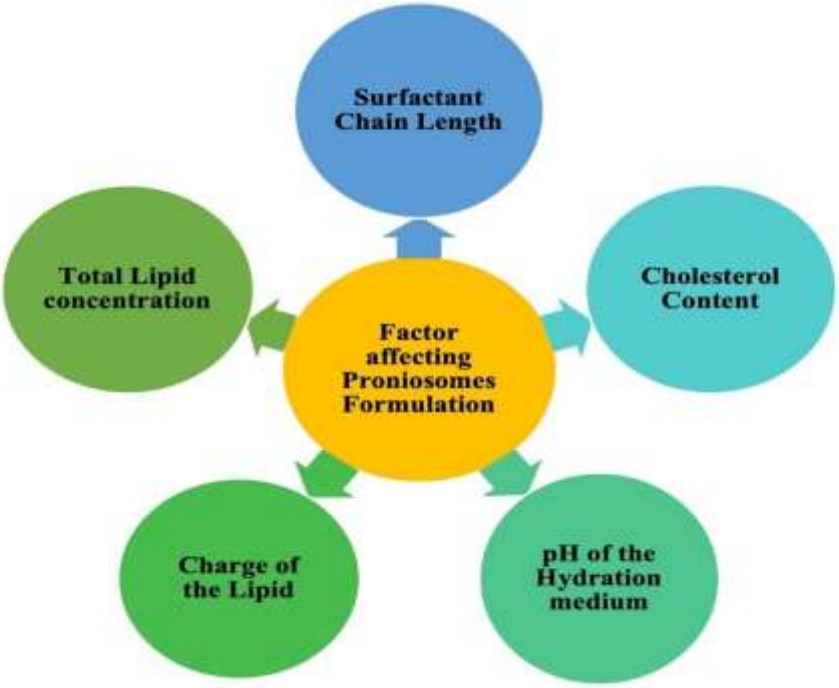


Fig.3. Factors affecting of SMEDDS.

2.Composition of SMEDDS:

The self- emulsification process is said to be particular to the nature of the oil surfactant pair. The process is based on

2.1. Oils.

2.2. The concentration of surfactants and the oil/surfactant ratio.

2.3. The temperature at which self-emulsion takes place.

2.4 Oils:

The oil is one of the most significant excipients in the SMEDDS formulation, not only because it can solubilize the appropriate amount of the lipophilic medication, but also because it is a natural lubricant.(21) It can increase the fraction of lipophilic medication delivered by the intestinal lymphatic system, hence enhancing absorption from the GI tract depending on the molecular composition of the triglyceride. Long and medium chain triglyceride (LCT and MCT) oils with varying degrees of saturation were employed to create self-emulsifying compositions.(21) Furthermore, due to their low ability to dissolve large amounts of lipophilic medicines, edible oils, which may be the obvious and preferred lipid excipient choice for the development of SMEDDS, are not usually used.(22)Vegetable oils that have been modified or hydrolyzed have been widely employed as excipients because they create good emulsification systems with a wide range of surfactants. Authorized for oral administration and display superior drug solubility qualities. They provide formulative and physiological benefits, and their breakdown products are similar to the natural end products of intestine digestion.(3) Novel semisynthetic medium chain derivatives, described as amphiphilic chemicals with surfactant characteristics, are gradually and efficiently replacing traditional medium chain triglyceride oils in the SMEDDS The oil grouping found in SMEDDS is approximately 40-80% altered and hydrolyzed vegetable oils, which have higher solubility and stability. excellent self-emulsifying ability.(2) Edible oils are not frequently used due to their inability to break down many lipophilic medicines. Altered or hydrolyzed vegetable oils have been widely used as excipients for good emulsification frameworks with a large number of surfactants recommended for oral organization and demonstrate enhanced medicine dissolvability features.(11)

2.1.Surfactant:

A variety of surfactant-containing mixtures could be used in the design of self-emulsifying frameworks, but because not all surfactants are suitable for ingestion, the decision is limited. Nonionic surfactants with a relatively high hydrophilic lipophilic equalization (HLB) are the most widely suggested.(23) When selecting a surfactant, safety is an important consideration. Surfactants have a limited ability to self-emulsify. Non-ionic surfactants are less toxic than ionic surfactants, although they may cause reversible changes in the environment(24). The gut lumen's permeability. Surfactant concentrations in the range of 30% to 60% w/w are often used to shape stable SMEDDS. It is critical to choose the surfactant concentration carefully because several surfactants might cause GI irritation. (25)

2.2.Co-surfactants/Co-solvents:

Usually, the formulation of a successful SMEDDS requires high concentrations of surfactant (up to 50%) and addition of co-surfactants aids in self-emulsification. Generally, cosurfactant of HLB value 10-14 is used with surfactant to decrease the oil-water interfacial tension, fluidize the hydrocarbon region of interfacial film, increase the drug loading to SMEDDS and allows the spontaneous formation of microemulsion.(11,23) Hence, surfactants (hydrophilic or lipophilic) and/or amphiphilic solubilizers are used for this purpose. (2,24)

The addition of the co-emulsifiers or solubilizers in SMEDDS may result in an expanding self-micro-emulsification region in the phase diagrams.The construction of an optimal SMEDDS necessitates somewhat high surfactant fixations (often greater than 30% w/w), yet this induces GI aggravation. As a result, co surfactant is used. Surfactant convergence is reduced.(12) The co-surfactant's and surfactant's job is to reduce interfacial strain to a minor, even temporary, negative value.(24) At this point, the interface would stretch to form fine distributed beads, adsorbing more surfactant and surfactant/co-surfactant until their mass condition is sufficiently depleted to make interfacial strain positive again.The method termed as' unconstrained emulsification' frames the micro emulsions. Natural solvents suitable for oral organization include ethanol, propylene glycol (PG), and water. Polyethylene glycol (PEG), for example, can aid in the dissolution of a large amount of either the hydrophilic surfactant or the medication in the lipid base and can operate as a cosurfactant in oneself emulsifying drug conveyance systems.(27) The method termed as' unconstrained emulsification' frames the micro emulsions. Natural solvents suitable for oral organization include ethanol, propylene glycol (PG), and water. Polyethylene glycol (PEG), for example, can aid in the dissolution of a large amount of either the hydrophilic surfactant or the medication in the lipid base and can operate as a cosurfactant in oneself emulsifying drug conveyance systems.(27) Organic solvents suitable for oral organization (ethanol, propylene glycol (PG), polyethylene glycol (PEG), and so on serve as co-solvents. may help with the dissolution of a significant amount of either the hydrophilic surfactant or the medication in the lipid base and can act as a co-surfactant in self-emulsifying drug conveyance frameworks, despite the fact that alcohol free self-emulsifying microemulsions have also been depicted in the writing. (1) When combined in case dose structures, such frameworks may exhibit a few focal points over previous definitions, because alcohol and other unpredictable co-solvents in ordinary selfemulsifying details are known to relocate into the shells of delicate gelatin or hard fixed gelatin containers, causing the precipitation of the lipophilic medication. (13,28)

3.Importance of SMEDDS:

To formulate a successful SMEDDS for maximum therapeutic effect, due consideration must be given to various factors such as physicochemical properties of the active moiety as well as excipients, the potential of drug excipient interaction (invitroor in vivo) and physiological factors that promote or inhibit the bioavailability(5). Further, other important factors such as regulatory status, solubilization capacity,

miscibility, the physical state of the excipients at room temperature, digestibility and compatibility with capsule shell, chemical stability and cost of the materials should also be considered during the formulation. Such a rationale approach not only helps in reducing the time involved in the formulation development and also reduces the cost of its developments(6, 8).

4.Types of SMEDDS:

According to Winsor, there are four types of microemulsion phases exists in an equilibrium, these phases are referred as Winsor phases.They are:

4.1. Winsor 1: with two phases, the lower (o/w): microemulsion phases in equilibrium with the upper excess oil.

4.2.Winsor 2: with two phases, the upper (w/o): microemulsion phases in equilibrium with lower excess water.

4.3.Winsor 3: with three phases, middle: microemulsion phases (o/w plus w/o, called bicontinuous) in equilibrium with upper excess oiland lowerexcess water.

4.4.Winsor 4:In single phases, with oil, water,and surfactant homogenously mixed.

5.Factors Affecting:

5.1.Dose and nature of the drug:High dose of drugs are not suitable for SMEDDS if at least one of the component of SMMEDS not shows extremely good solubility, preferably lipophilic phase. In water and the lipids with log p-value of approximately two are most difficult to deliver by SMEDDS, which exhibit the limited solubility. The drug in solubilized form is affected by the solubility of the drug in oil.

5.2.The concentration of surfactants or co-surfactants: Risk of precipitation occurs if surfactant and co-surfactant conducive to the greater extent of drug solubilization. Lowering of the solvent capacity of the surfactant and co-surfactant is occurs as dilution of SMEDDS(16).

5.3.The polarity of lipophilic phase: Drugs release from the microemulsion is governed by one of the factors that arethe polarity of the lipid phase. HLB, the molecular weight of the micronized drug, the chain length and degree of unsaturation of fatty acid govern the polarity of the droplet.

5.4.Temperature: Increasing the temperature decreases the nucleation rate. At higher temperatures, the binding between drug and polymer is decreased, due to increased solubility of drug and weakening of intramolecular interactions.

5.5.Packing ratio:Type of microemulsion is determined by the HLB of surfactant by influencing the packing and film curvature for surfactant association's leading to the formation of the microemulsion.(13)

6.CHARACTERIZATION OF SMEDDS:

6.1. Differential scanning calorimetry

Differential scanning calorimetry for SMEDDS can be determined using DCS 60. Liquid and the solid sample should be placedin the aluminum pan and result can be recorded any chemical interaction shouldbe determined using DSC.

6.2. Fourier transport infrared spectroscopy

Fourier transport infrared for SMEDDS can be determined using FT-IR. The liquid sample should be placed in the liquid sample holder,andthe result can be recorded. Any chemical interaction should be determined.

6.3. Macroscopic evaluation

The macroscopic analysis was carried out to observe the homogeneity of microemulsion formulation. Any change in color and transparency or phase separation occurred during normal storage condition was observed inoptimizedmicroemulsion formulation(17).

6.4. Visual assessment

To assess the self-emulsificationproperties, the formulation was introduced into 100ml of water in a glass Erlenmeyer flask at 25°C,and the content was gently stirred manually.The tendency to spontaneously form a transparent emulsion was judged as good,and it was judgedbad when there was poor or no emulsion formation.

6.5. Determination of self-emulsificationtime

The emulsification time of SMEDDSwas determined according to USP 22, dissolution 2.300 mg of each formulation added dropwise to 500ml purification water at 37° C. Gentle agitation was provided by a standard stainless steel dissolution paddle rotating 50 rpm.Emulsification time was assessed visually.

6.6. Solubility studies

An unknown amount of selectedvehicle was added to each cup vial containing an excess of the drug.After sealing the mixture was heated at 40°C in a water bath to facilitate the solubilization.

6.7. Transmittance test

Stability of optimized microemulsion formulation concerning dilution was checked by measuring transmittance through U.V. spectrophotometer(18).

6.8. Zeta potential measurements

Zeta potential of microemulsion was determined using Zetaasizer HSA3000.The samplewas placedinclear disposable zeta cell,andthe resultwas recorded. Before putting the fresh sample, cuvettewas washed with the methanol using the sample to be measured for each experiment(17).

7.APPLICATIONS OF SMEDDS

7.1. Super Saturable SMEDDS (SS-SMEDDS)

The high surfactant level typically present in SMEDDS formulation can lead to GI side effects and a new class of supersaturable formulation including supersaturable SMEDDS. (S-SMEDDS) formulations have been designed and developed to reduce the surfactant side effects and achieve rapid absorption of poorly soluble drugs.

7.2. Solid SMEDDS

SMEDDS are normally prepared as liquid dosage form that can be administered in soft gelatine capsules, which has more disadvantages,especially in the manufacturing process. An alternative method is the incorporation of a liquid self-emulsifying ingredient into a powder to create solid dosage form (Tablet,

capsules). A pellet formulation of progesterone in SMEDDS has been prepared by extrusion/super-ionization to provide a good in-vitro drug release (100% within 15 min. T50% in 13 min.) (26)

7.3. Solubilization in SMEDDS

Owing to their frequently high content oil, as well as of surfactant, SMEDDS are usually efficient solubilizers of substances of a wide range of lipophilicity. Thus, the solubilizing capacity of a w/o Microemulsion for water-soluble drugs is typically higher than that of o/w Microemulsion, while the reverse is true for oil-solubledrugs. Furthermore, the solubilization depends on the SMEDDS composition.

7.4. Sustain Release from SMEDDS

Due to a wide range of structures occurring in them, SMEDDS display a rich behavior regarding the release of solubilized material. Thus in case of O/W Micro emulsions, hydrophobic drugs solubilized mainly in the oil droplets, experience hindered diffusion and are therefore released further slowly (depending on the O/W partitioning of the substance). Water-soluble drugs, on the other hand, diffuse essentially without obstruction (depending on the volume fraction of dispersed phase) and are release fast. For Micro balanced emulsions, relatively fast diffusion and release occur for both water soluble and oil soluble drugs due to the bicontinuous nature of Micro emulsion "structure." Apart from the Micro emulsions structure, the Microemulsion composition is important for the drug release rate(23).

8.SOME DRUG DELIVERY SYSTEM USING SMEDDS

8.1. Oral delivery

Self-emulsifying capsule: After administration of capsules containing conventional liquids SE formulations, microemulsion droplets form and subsequently disperse in the GIT to reach the site of absorption. If irreversible phase separation of microemulsion occurs an improvement of drugs absorption can't be expected. For handling this problem, sodium dodecyl sulfate was added into the SE formulation(28).

Self-emulsifying sustained/controlled release: Combination of lipids and surfactant has presented great potential preparing SE tablets. SE tablets are of great utility in obviating adverse effect. The inclusion of indomethacin (or other hydrophobic NSAID) for example, into SE tablets, may increase its penetration efficacy through GI mucosal membrane potentially reducing GI bleeding.

Self-emulsifying sustained/control release pellets: Pellets, as a multiple unit dosage forms, possess many advantages over conventional solid dosage form, such as flexibility of manufacture, reducing intrasubject and inter-subject variability of plasma profile and minimizing GI irritation without lowering drug bioavailability.

Self-emulsifying solid dispersions: Solid dispersions could increase the dissolution rate and bioavailability of poorly water-soluble drugs, but still some manufacturing difficulties and stability problems existed.(3, 29)

8.2.Topical Delivery: Topical administration of drugs can have advantages over other methods for several reasons, one of which is the avoidance of hepatic first-pass metabolism of the drugs and related toxicity effects.

8.3.Oculars and Pulmonary delivery: For the treatment of eye disease, drugs are essentially delivered topically o/w microemulsion have been investigated for ocular administration, to dissolve poorly soluble drugs, to increase absorption and to attain prolong release profile.

8.4.Parenteral delivery: Parenteral administration of drugs with limited solubility is a major problem in the industry because of the extremely low amount of drug deliveredto the target site.

8.5.Ophthalmic delivery: In conventional ophthalmic dosage forms, water-soluble drugs are delivered in aqueous solution while water-insoluble drugs are formulated as suspensions or ointments. Low corneal bioavailability and lack of efficiency in the posterior segment of ocular tissue are some of the serious drawbacks of these systems. Recent research efforts have therefore focused on the development of new and more effective delivery systems. Microemulsion has emerged as a promising dosage form for ocular use.

8.6. Nasal delivery: Microemulsion is now being studied as a delivery system to enhance uptake across the nasal mucosa. Addition of a mucoadhesive polymer helps in prolonging the residence time on the mucosa. The nasal route for administration of diazepam might be a useful approach for the rapid onset of action during the emergency treatment of status epileptics.

8.7.Drug Targeting: Drug targeting to diseased cells can be achieved by exploiting the presence of various receptors, antigens/proteins on the cell membrane which may be uniquely expressed or overexpressed in these cells as compared to the normal cells. Specific antibodies to the surface proteins and ligands for the receptors can be used to target specific cells. The submicron size range of these systems confers excellent opportunities to overcome the physiological barriers and enables efficient cellular uptake followed by intracellular internalization.(21, 30)

9.CONCLUSION:

Self-microemulsifying drug delivery systems are the recent and effective approach for the augmentation of oral bioavailability of many poor water-soluble drugs provided that the drug should be potent with high lipid solubility. SMEDDS promotes lymphatic delivery of extremely hydrophobic drugs with good solubility in triglycerides. Faster and enhanced drug release can be attained with smaller droplets which in turn promotes bioavailability. The present review is involved in obtaining a robust and stable dosage form. Further research in developing SMEDDS with surfactants of low toxicity and to developin vitro methods to better understand the in vivo fate of these formulations can maximize the availability of SMEEDS in the market.In all, it was good to see that the students were propelled towards the said target and they have now known the basics of the publication process. Henceforth, this article will definitely prove to be a milestone in their future research carrier. Drug targeting to diseased cells can be achieved by exploiting the presence of various receptors, antigens/proteins on the cell membrane which may be uniquely expressed or overexpressed in these cells as compared to the normal cells. Specific antibodies to the surface proteins and ligands for the receptors can be used to target specific cells. The submicron size range of these systems confers excellent opportunities to overcome the physiological barriers and enables efficient cellular uptake followed by intracellular internalization.

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