A SYSTEMATIC REVIEW ON SELF MICRO EMULSIFYING DRUG DELIVERY SYSTEM

Akiladevi. D*, Lashman. S. L, Manigandan. S

Department of Pharmaceutics, School of Pharmaceutical Sciences,

Vels Institute ofScience, Technology, and Advanced Studies,

Pallavaram, Chennai, Tamil Nadu, India.

Corresponding author **Akiladevi. D**

Email: **akilaajcp@gmail.com**

Abstract

Self-micro emulsifying drug delivery system (SMEDDS) is a novel formulation approach that has emerged as an effective method for enhancing the oral bioavailability of poorly water-soluble drugs. This system is based on the principle of the microemulsion, which is a thermodynamically stable isotropic mixture of oil, surfactant, and co-surfactant that forms spontaneously upon mild agitation.

SMEDDS comprises oil, surfactant, co-surfactant, and drug, formulated into a single-phase mixture. Upon dilution with gastrointestinal fluids, SMEDDS spontaneously forms a fine oil-in-water (o/w) microemulsion, which enhances the solubility and permeability of the drug, resulting in improved oral bioavailability. SMEDDS have gained popularity in recent years as they offer numerous advantages over conventional drug delivery systems, such as improved solubility, dissolution, absorption, and stability of drugs, which in turn lead to enhanced therapeutic efficacy.

The selection of appropriate excipients is critical in the formulation of SMEDDS. Oils with low viscosity and high lipid solubility are preferred for SMEDDS formulation, as they help in the formation of fine droplets upon dilution with GI fluids. Surfactants and co-surfactants are selected based on their ability to form stable microemulsions and their compatibility with the drug and other excipients. The ratio of oil, surfactant, and co-surfactant is optimized to achieve maximum drug solubility and microemulsion stability.

SMEDDS have been successfully used for a wide range of drugs, including poorly water-soluble drugs, peptides, and proteins. They have been demonstrated to improve the oral bioavailability of several drugs, such as cyclosporine, fenofibrate, and paclitaxel. Furthermore, SMEDDS can be easily formulated into various dosage forms, such as capsules, tablets, and granules, making them highly versatile for different drug delivery applications.

Keywords: SMEDDS, Bioavailability, Drug delivery, Droplet size, solubility

Introduction:

Self-Micro emulsifying drug delivery system

Self-micro emulsifying drug delivery system (SMEDDS) is a novel drug delivery technology that is gaining increasing attention in the pharmaceutical industry. It is a formulation that is

designed to improve the bioavailability and therapeutic efficacy of poorly soluble drugs. This technology utilizes the principles of microemulsions, which are thermodynamically stable, optically transparent, and isotropic mixtures of oil, water, and surfactants.

The SMEDDS formulation typically consists of an oil phase, a surfactant, and a co-surfactant emulsified in water to form a microemulsion. The microemulsion droplets generally are 10 to 100 nanometres in diameter, providing a large interfacial area between the drug and the surrounding aqueous environment. This increased surface area facilitates drug absorption and bioavailability.

One of the significant advantages of SMEDDS is that it enhances the solubility and dissolution rate of poorly soluble drugs, which can lead to improved drug absorption and bioavailability. This is especially important for drugs with low oral bioavailability, which can limit their therapeutic efficacy. In addition, SMEDDS can also improve the stability and shelf-life of drugs by protecting them from degradation and oxidation.

SMEDDS has been successfully used to improve the delivery of a wide range of drugs, including lipophilic drugs, peptides, and proteins. This technology has also been used to enhance the delivery of drugs to specific target sites, such as the brain, due to its ability to cross the blood-brain barrier.

In conclusion, SMEDDS is a promising drug delivery technology that offers numerous advantages over traditional drug delivery systems. It can potentially improve the bioavailability and therapeutic efficacy of poorly soluble drugs and has been shown to be effective for a wide range of drugs. With continued research and Development, SMEDDS could become a valuable tool in the pharmaceutical industry for improving the delivery of drugs.

Micro Emulsions

Microemulsions are liquid mixtures composed of oil, water, surfactants, and sometimes co-surfactants that are clear, thermodynamically stable, and isotropic. They are extensively used in various fields, including pharmaceuticals, cosmetics, and chemical engineering. Their stability, transparency, and droplet sizes ranging from 10 to 100 nanometres, make them highly desirable for drug delivery applications.

Microemulsion formation is initiated by the free energy of mixing between the different components and facilitated by the presence of surfactants and co-surfactants. The surfactants are molecules with both hydrophilic and hydrophobic properties, reducing the interfacial tension between the oil and water phases and stabilizing the microemulsion. On the other hand, co-surfactants are utilized to increase the solubility of the oil phase in the microemulsion.

A significant advantage of microemulsions is their ability to solubilize both hydrophobic and hydrophilic drugs, which can improve bioavailability and therapeutic efficacy. Furthermore, microemulsions can target specific tissues or organs as they can cross biological barriers such as the blood-brain barrier.

Microemulsions can be easily prepared using simple techniques such as high-energy mixing, making them scalable for commercial production. Additionally, they can be modified by altering the composition of oil, surfactant, and co-surfactant components, which enables the formulation of a broad range of products with varying physicochemical properties.

Components of Micro Emulsion

a. Oil Phase

The oil phase in microemulsions refers to the component that provides the necessary solubility and compatibility with the desired drug or active ingredient. It is typically a nonpolar liquid or a mixture of nonpolar liquids with low water solubility. The oil phase plays a crucial role in determining the physical and chemical properties of the microemulsion, such as droplet size, stability, and drug release kinetics. The choice of oil phase depends on the specific application and the desired properties of the final product.

b. Surfactants

Surfactants in microemulsions are molecules with both hydrophilic and hydrophobic properties. They are essential in stabilizing the mixture of oil and water phases by reducing the interfacial tension. Surfactants also play a vital role in determining the droplet size and stability of the microemulsion. The selection of the surfactant is dependent on the type of oil phase and the intended application of the final product. Additionally, the surfactant concentration affects the microemulsion's viscosity and drug release kinetics.

c. Co-Surfactants

Co-surfactants in microemulsions are used to increase the solubility of the oil phase in the mixture, which improves the overall stability and drug delivery properties. They are typically small molecules with amphiphilic properties, similar to surfactants. Co-surfactants reduce the interfacial tension and help to form a monolayer at the oil-water interface. They also play a role in determining the microemulsion's droplet size, viscosity, and drug release kinetics. The selection of the co-surfactant is dependent on the surfactant and oil phase used, as well as the intended application of the final product.

d. Solvents

Solvents play a crucial role in the formation of microemulsions, which are thermodynamically stable mixtures of oil, water, and surfactant. They help to solubilize the oil phase and facilitate the formation of tiny droplets that remain dispersed in the water phase. The choice of solvent can have a significant impact on the properties of the resulting microemulsion, such as its stability, viscosity, and ability to solubilize certain types of oils. Common solvents used in microemulsion systems include alcohols, glycols, and hydrocarbons.

e. Drug

In microemulsion drug delivery systems, the drug is typically incorporated into the oil phase of the formulation. The small droplet size and large interfacial area of the microemulsion provide a high surface area for drug release, which can lead to improved drug absorption and bioavailability. The drug can be either hydrophilic or lipophilic as long as it can be solubilized in the oil phase of the microemulsion. The choice of surfactant and co-surfactant can also influence the drug phase behaviour and release kinetics in the microemulsion system.

Mechanism of Self Micro Emulsifying Drug Delivery System

The following equation can describe the free energy of the emulsion:

$$\Delta G = \sum N\Pi r2\sigma.$$

$\Delta G$is the free energy, $N$is the number of droplets, $\gamma$is the radius of droplets, $\sigma$and is the interfacial energy.

- It is clear from this equation that the free energy decreases as the interfacial energy increases.
- Self-emulsification happens when the energy required for droplet formation is greater than the energy involved in the dispersion.
- A traditional emulsion has a very high free energy because it takes much energy to create a new surface between two immiscible phases, such as water and oil. High free energy can make an emulsion unstable and cause the two phases to split. However, in the case of SMEDDS, emulsion formation takes place immediately since the system's free energy is extremely low and occasionally even negative due to the existence of a flexible interface.
- An interface between two phases is created when oil, water, and a surfactant/cosurfactant mixture are combined. Once inside the oil phase, the aqueous phase permeates the interface and solubilizes until it reaches the solubilization limit. Dispersed liquid crystalline phase forms as a result of increased water penetration.
- The concentration of the surfactant affects the amount of liquid crystalline phase. When SMEDDS are lightly shaken, water penetration happens quickly, disrupting the contact and causing droplets to form.

- Even though there is a constant interchange of matter between the various phases, equilibrium exists in the system because microemulsions are thermodynamically stable. The two main ways that matter exchanges hands are through the fission of bigger droplets into smaller ones and the fusion of smaller droplets that then coagulate with other droplets.

Preparation of Micro Emulsion

There are two methods to prepare microemulsion:

a. Phase Titration Method

b. Phase Inversion Method

Phase Titration Method

Phase titration method is a technique to determine the required amounts of surfactant and co-surfactant to form a microemulsion.

- Dilution of an oil-surfactant mixture with water. (w/o)
- Dilution of a water-surfactant mixture with oil. (o/w)

Phase Inversion Method

- The phase inversion method is a technique to form a stable microemulsion by changing the composition of the system.
- The method involves adding water or oil to the initial mixture until the system undergoes a phase inversion, resulting in the formation of a microemulsion.
- The principle of the method is to change the ratio of oil to water, surfactant to oil, and co-surfactant to oil until the phase inversion point is reached.
- The phase inversion point is the point where the system becomes more water- or oil-loving, leading to the formation of a stable microemulsion.
- The resulting microemulsion is stable and can be used for various applications such as drug delivery, cosmetics, and the food industry.
- The phase inversion method is a simple and efficient technique for producing microemulsions, and it has been widely used in the pharmaceutical industry.

Physiochemical Properties of Self Micro Emulsifying Drug Delivery System

- Lipid type and composition: The type and composition of the lipids used in SMEDDS can significantly influence their physicochemical properties, including their droplet size, stability, and drug solubilization capacity.
- Surfactant type and concentration: The type and concentration of the surfactants used in SMEDDS can affect their ability to form stable emulsions, as well as their compatibility with different drugs and biological fluids.
- Co-solvent type and concentration: Co-solvents are often added to SMEDDS to enhance drug solubility and aid in the formation of microemulsions. The type and concentration of co-solvent can impact the drug solubilization capacity, as well as the stability and viscosity of the SMEDDS.
- Droplet size and distribution: The droplet size and distribution of SMEDDS can affect their stability and bioavailability. Small droplet sizes (<100 nm) and narrow size distributions are generally preferred to ensure rapid drug release and absorption.

- Zeta potential: The zeta potential of SMEDDS is an essential indicator of their stability and propensity for aggregation. SMEDDS with high zeta potentials (i.e., > 30 mV) are typically more stable and less prone to aggregation.
- pH and temperature sensitivity: Some SMEDDS may be sensitive to changes in pH or temperature, which can affect their physicochemical properties and drug release characteristics.

Latest advancements for Self-Micro Emulsifying Drug Delivery System

Self-micro emulsifying drug delivery systems (SMEDDS) have gained attention as a promising drug delivery system due to their ability to enhance drug solubility and bioavailability. Recent advancements in SMEDDS include:

- Nanoparticles: Incorporation of nanoparticles in SMEDDS has been shown to enhance drug loading and stability. Nanoparticles can also provide sustained drug release and targeted drug delivery.
- Co-solvents: Co-solvents such as ethanol, propylene glycol, and polyethylene glycol have been used to improve drug solubility in SMEDDS. However, their use can lead to toxicity and formulation instability.
- Solid SMEDDS: Solid SMEDDS have been developed to overcome the stability issues associated with liquid SMEDDS. Solid SMEDDS can be prepared as tablets or capsules, and they offer improved stability, ease of handling, and dosing accuracy.
- Stimuli-responsive SMEDDS: Stimuli-responsive SMEDDS can release the drug in response to a specific trigger such as pH, temperature, or enzymes. This technology offers targeted drug delivery and reduces side effects.
- Natural oils: Natural oils such as olive oil, coconut oil, and fish oil have been used in SMEDDS due to their biocompatibility and low toxicity. These oils can also enhance drug solubility and bioavailability.

Importance of Self Micro Emulsifying Drug Delivery System

- The irritation caused by prolonged contact between the drug and the wall of the GIT can be alleviated by the formulation of SMEDDS. The microscopic droplets that are formed help in the wide distribution of the drug along the GIT, and these are transported quickly from the stomach. This alleviates the irritation caused by prolonged contact between the drug and the wall of the GIT.
- Upon dispersion in water, these formulations produce fine droplets with an enormous interfacial area, which makes it possible for the easy partition of the drug from the oil phase into the aqueous phase. This is something that cannot be expected in the case of oily solutions of lipophilic drugs.
- SMEDDS are advantageous over emulsions in terms of stability because of the low energy consumption, and the manufacturing process does not include any critical steps. The formulation of SMEDDS only requires simple mixing equipment, and the amount of time necessary for preparation is significantly less than that of emulsions.

- Microemulsion functions as a super-solvent for medications, and it has the capacity to solubilize both hydrophilic and lipophilic pharmaceuticals. • Due to the very small droplet size, there is an increased rate of absorption and an increased bioavailability of the drug.

Factors affecting Self Micro Emulsifying Drug Delivery System

- **Lipid phase composition:**
  The lipid phase of SMEDDS typically consists of oils, such as medium-chain triglycerides (MCTs), long-chain triglycerides (LCTs), or vegetable oils. The type and concentration of the lipids used in the formulation can affect the microemulsion's size, stability, and drug solubilization capacity. For example, using unsaturated oils may increase the susceptibility of the microemulsion to oxidation. In contrast, using saturated oils can lead to increased viscosity and reduced drug solubilization.
- **Surfactant and co-surfactant selection:**
  Surfactants and co-surfactants are essential components of SMEDDS that help to stabilize the microemulsion and facilitate the solubilization of the drug. The selection of surfactant and co-surfactant can significantly influence the formation and stability of the microemulsion. For instance, the use of non-ionic surfactants, such as polysorbate 80, can improve the stability of the microemulsion. In contrast, the use of anionic surfactants, such as sodium lauryl sulphate, can destabilize the microemulsion.

- **Drug solubility:**
  The solubility of the drug in the lipid phase can affect its distribution within the microemulsion and, therefore, its bioavailability. The use of lipophilic drugs in SMEDDS is preferred because they can be easily solubilized in the lipid phase. However, the solubility of hydrophilic drugs in the microemulsion can be enhanced by the addition of co-solvents or co-surfactants.

- **pH and ionic strength:**
  The pH and ionic strength of the surrounding medium can affect the stability of the microemulsion and the solubility of the drug. For example, the solubility of weakly acidic or basic drugs can be pH-dependent, and changes in pH can affect the stability of the microemulsion.

- **Dilution rate:**
  Upon contact with gastrointestinal fluids, the microemulsion undergoes dilution, which can affect the release and absorption of the drug. The dilution rate can be influenced by the amount of food in the stomach and the gastric emptying rate. Slow dilution may lead to delayed drug release, while rapid dilution can lead to drug precipitation.

- **Temperature:**

The temperature can affect the stability of the microemulsion and the solubility of the drug. High temperatures can lead to the degradation of the lipid phase and the destabilization of the microemulsion. Conversely, low temperatures can increase the viscosity of the lipid phase, leading to reduced drug solubilization and delayed drug release.

Applications of Self Micro-emulsifying Drug Delivery System

Self-micro emulsifying drug delivery systems (SMEDDS) have found numerous applications in the field of pharmacy due to their ability to enhance the bioavailability of poorly soluble drugs. Here are some of the critical applications of SMEDDS in pharmacy:

- Improved drug solubility: SMEDDS can improve the solubility of poorly soluble drugs, which can lead to enhanced dissolution and absorption.
- Enhanced drug stability: SMEDDS can protect drugs from degradation, which can lead to improved stability and shelf-life of drug products.
- Targeted drug delivery: SMEDDS can be formulated to target specific areas of the body, such as the gastrointestinal tract, to improve drug absorption and efficacy.
- Reduced dose frequency: SMEDDS can reduce the frequency of drug administration, which can improve patient compliance and convenience.
- Formulation versatility: SMEDDS can be formulated into various dosage forms, such as capsules, tablets, and granules, making them highly versatile for different drug delivery applications.

Methods and Evaluation

a. **Pre-Formulation studies**
b. **Formulation of Dosage form**
c. **Formulation by High-Pressure Homogenizing method**
d. **Evaluation and Dissolution studies**

Pre-Formulation Studies

- FT-IR study and Development of standard calibration curve by UV Spectroscopic method.
- Screening of oils, surfactants, and cosurfactants by Equilibrium solubility studies.

Formulation of Micro Emulsion

Selection of Components: The components of microemulsion dosage forms play a crucial role in determining their physicochemical properties and drug delivery performance. The selection of components is based on their solubility, compatibility, and stability. The oil phase can be selected based on the solubility of the drug, and it can be a single oil or a mixture of oils. The surfactant and co-surfactant are selected based on their ability to form a stable microemulsion, and their HLB (Hydrophilic-Lipophilic Balance) value is an important

parameter to consider. The water phase can be selected based on the pH and ionic strength requirements of the drug.

Optimization Techniques: Optimization techniques are used to improve the physicochemical properties and drug delivery performance of microemulsion. These techniques include:

- Phase Diagram Construction: Phase diagrams are used to identify the region of microemulsion formation and to optimize the concentration of components.
- Use of Co-Solvents: Co-solvents such as ethanol or propylene glycol can be used to enhance the solubility of the drug in the microemulsion.
- Temperature and pH Optimization: The temperature and pH of the microemulsion can be optimized to improve the stability and solubilization capacity.
- Use of Nanoparticles: Nanoparticles such as liposomes, solid lipid nanoparticles, and polymeric nanoparticles can be incorporated into the microemulsion to improve drug delivery.
- In vitro Evaluation: The physicochemical properties and drug delivery performance of the microemulsion dosage form can be evaluated in vitro to optimize the formulation.

Screening of Oil for Micro Emulsion

- Screening oil for microemulsion involves selecting the most suitable oil to form a stable and effective microemulsion. The process involves testing various oils to determine their compatibility with the other components of the microemulsion, such as the surfactant and co-surfactant. The oil must dissolve the drug and be compatible with the other components to form a homogeneous and stable mixture.
- The selection of oil for microemulsion is based on several factors, including the solubility of the drug in the oil, the viscosity of the oil, and the ability of the oil to form a clear and transparent solution with the other components. The screening process typically involves testing several oils, either alone or in combination, to determine the most effective and stable mixture.

Screening of Surfactant and Co-Surfactants

- Screening of surfactants and co-surfactants is an important step in the formulation of the microemulsion. It involves identifying the surfactant and co-surfactant combination that can effectively form a stable microemulsion and maximize drug delivery. The screening process involves testing various surfactants and co-surfactants in different ratios to determine their compatibility and effectiveness.
- Surfactants are amphiphilic molecules that have both hydrophilic and hydrophobic properties, which enable them to stabilize the microemulsion by reducing the interfacial tension between the oil and water phases. Co-surfactants are small molecules that assist surfactants in reducing interfacial tension by increasing the solubility of the oil phase in the aqueous phase.

- The selection of surfactant and co-surfactant is based on several factors, including the HLB (Hydrophilic-Lipophilic Balance) value, the type and size of the oil phase, and the desired properties of the microemulsion, such as stability, droplet size, and drug solubilization capacity.

High-Pressure Homogenizing Method

- High-pressure homogenization is a method for producing microemulsions by applying high pressure to the mixture: This method involves applying high pressure to the mixture, resulting in the formation of tiny droplets that are uniformly distributed in the mixture.
- The process involves multiple cycles of high-pressure pumping, which creates small droplets evenly distributed throughout the mixture: The method requires multiple cycles of high-pressure pumping, creating small droplets that are uniformly distributed in the mixture. This uniform distribution ensures that the microemulsion is stable and consistent.
- High-pressure homogenization is advantageous because it requires no special equipment or conditions and can be used to produce microemulsions on a large scale: This method is advantageous because it does not require any specialized equipment or conditions, making it cost-effective and accessible. Moreover, it can be used to produce microemulsions on a large scale, which is useful for industrial applications.
- High-pressure homogenization produces stable microemulsions with a small droplet size, which enhances the solubility and bioavailability of the drug: The method produces stable microemulsions with small droplet sizes that enhance the solubility andbioavailability of drugs. This ensures that drugs are delivered effectively and efficiently.
- This method is useful for the preparation of microemulsions in pharmaceuticals and cosmetic formulations. It offers numerous benefits for drug delivery systems: High-pressure homogenization is a valuable tool for the Development of effective and efficient drug delivery systems. It offers numerous benefits for drug delivery systems, including improved solubility, bioavailability, and stability, and is widely used in pharmaceuticals and cosmetic formulations.

Evaluations

- **Visual Evaluation**
- **pH Determination**
- **Thermodynamic stability studies**
- **Rheological Characterization**
- **Transmittance Test**
- **Drug Content Estimation**
- ***In Vitro* Drug Release Studies**

Visual Evaluation:

Visual evaluation is an important step in assessing the physical characteristics of microemulsion drug formulations. The appearance of a microemulsion can provide insight into its stability, homogeneity, and particle size. Visual evaluation can be done through techniques such as microscopy, turbidity measurements, or droplet size analysis. A thorough understanding of the visual characteristics of microemulsions can aid in the Development of stable and effective drug delivery systems.

pH Determination:

Accurate determination of pH is crucial in various scientific fields such as pharmaceuticals, food and beverage, environmental analysis, and biological research. pH can be determined using a pH meter or indicator, and proper sample preparation is essential for accurate readings. Understanding the principles of pH determination is important for researchers and practitioners in these fields.

Thermodynamic stability studies:

Thermodynamic stability study is a crucial aspect of the Development and characterization of microemulsion drug formulations. It involves determining the phase behavior and phase diagrams of the system under different conditions such as temperature, pressure, and composition. This study provides valuable information on the stability, miscibility, and performance of the formulation. A thorough understanding of the thermodynamic stability of microemulsion drugs can help in the optimization of the formulation and Development of effective drug delivery systems.

The thermodynamic stability of a microemulsion drug can be determined by calculating the free energy change of the system using the following formula:

$$\Delta G = \Delta H - T\Delta S$$

Where ΔG is the free energy change of the system, ΔH is the enthalpy change (i.e., heat absorbed or released) of the system, T is the temperature in Kelvin, and ΔS is the entropy change (i.e., the degree of disorder) of the system.

Rheological Characterization:

Rheological characterization is an important aspect of the Development and optimization of microemulsion drug formulations. It involves the study of the flow behavior, viscosity, and mechanical properties of the formulation. Rheological properties are important for predicting the stability, shelf-life, and ease of administration of the formulation. Understanding the rheological properties of microemulsion drugs can aid in the Development of formulations with optimized properties for effective drug delivery.

The rheological characterization of a microemulsion drug can be determined by measuring the viscosity of the system using the following formula:

$$\eta = \tau/\gamma$$

Where η is the viscosity of the microemulsion drug, τ is the shear stress applied to the system, and γ is the shear rate. The relationship between shear stress and shear rate can be plotted on a graph to generate a flow curve, which can provide information about the behavior of the microemulsion drug under different conditions.

Transmittance Test:

The transmittance test is a simple and useful method for evaluating the clarity and stability of microemulsion drug formulations. It involves measuring the amount of light that passes through the formulation, which indicates the level of turbidity or clarity. A decrease in transmittance can indicate the presence of larger droplets or instability in the formulation. The transmittance test is a quick and convenient method for evaluating the optical properties of microemulsion drugs and can provide valuable information on the formulation's stability and quality.

The transmittance test is used to determine the clarity and transparency of a microemulsion drug. It involves measuring the amount of light that passes through a drug sample at a specific wavelength. The transmittance is then calculated using the following formula:

$$T = (I/I0) \times 100$$

Where T is the transmittance expressed as a percentage, I is the intensity of light transmitted through the sample, and I0 is the intensity of the incident light.

The transmittance test is typically performed using a spectrophotometer, which measures the amount of light absorbed or transmitted by a sample at different wavelengths. A blank sample containing only the solvent and surfactants is used as a reference, and the transmittance of the drug sample is compared to that of the blank to determine its clarity and transparency.

Drug Content Estimation:

Drug content estimation is an essential quality control parameter for microemulsion drug formulations. It involves measuring the amount of active pharmaceutical ingredient (API) present in the formulation. Accurate drug content estimation is critical for ensuring that the formulation contains the desired API amount and determining the appropriate dosing regimen. Various methods, such as high-performance liquid chromatography (HPLC) and UV spectrophotometry, can be used for drug content estimation in microemulsion drugs. A reliable drug content estimation method is necessary for maintaining the consistency and quality of the formulation.

The drug content of a microemulsion drug can be estimated by analyzing a sample of the drug to determine the amount of active pharmaceutical ingredient (API) present per unit volume or weight of the formulation. The drug content can be calculated using the following formula:

Drug content = (Amount of drug in sample / Total volume or weight of sample) x 100

Where the amount of drug in the sample is typically determined using a validated analytical method, such as high-performance liquid chromatography (HPLC) or UV spectrophotometry.

In Vitro Drug Release Studies:

In vitro drug release studies are essential for evaluating the performance of microemulsion drug formulations. These studies involve monitoring the release of the active pharmaceutical ingredient (API) from the formulation under controlled conditions. The results of in vitro drug release studies can be used to optimize the formulation, determine the release kinetics of the API, and assess the effect of various factors such as pH and temperature on drug release. Multiple methods, such as dialysis membrane diffusion and Franz diffusion cell, can be used in vitro drug release studies. Accurate in vitro drug release studies are critical for ensuring the efficacy and safety of the microemulsion drug formulation.

Conclusion

In conclusion, the self-micro emulsifying drug delivery system (SMEDDS) has been extensively researched and developed as a promising approach for enhancing the solubility and bioavailability of poorly soluble drugs. SMEDDS formulations are composed of oil, surfactant, and co-surfactant, which can form a thermodynamically stable microemulsion when mixed with water or gastrointestinal fluids. The microemulsion system can improve drug absorption by enhancing the surface area of drug particles and facilitating their dispersion in the gastrointestinal tract.

The Development of SMEDDS has provided numerous advantages, including ease of formulation, enhanced drug release, improved stability, reduced variability, increased patient compliance, and versatility for administration routes. However, there are still some challenges that need to be addressed, such as the potential for drug-drug interactions, toxicity concerns, and the need for appropriate excipients.

References

1. Mugwanya, Kenneth & John-Stewart, Grace & Baeten, Jared. (2017). Safety of oral tenofovir disoproxil fumarate-based HIV pre-exposure prophylaxis use in lactating HIV-uninfected women—Expert Opinion on Drug Safety.
2. Penjuri, S.C.B. & Damineni, S. & Ravouru, Nagaraju & Poreddy, S.R. (2017). Self-emulsifying drug delivery system (SEDDS) for ibuprofen administration: in vitro and in vivo evaluation of samples. Ceska a Slovenska farmacie: Journal of the Czech Pharmaceutical Society and the Slovak Pharmaceutical Society. 66. 23-34.
3. Bakhle SS, Avari JG. Development and Characterization of Solid Self-emulsifying Drug Delivery System of Cilnidipine. Chem Pharm Bull (Tokyo). 2015;63(6):408-17. doi: 10.1248/cpb.c14-00326.
4. Wong, Stephen & Lok, Anna. (2006). Tenofovir disoproxil fumarate: Role in hepatitis B treatment. Hepatology (Baltimore, Md.). 44. 309-13.
5. Gürsoy, R & Cevik, Ozge. (2013). Design, characterization and in vitro evaluation of SMEDDS containing an anticancer peptide, linear LyP-1. Pharmaceutical development and technology.
6. Pharmaceuticals dosage form: disperse system volume second = edition, revised and expanded edited by Hebert D. Liberman, Martine M. Rieger, and Gilbert S. banker page no 57-61
7. Pharmaceuticals dosage form: disperse system volume2nd, second edition, revised and expanded edited by Hebert D. Liberman, Martine M. Rieger and Gilbert S. bankar page no 49-51,67-74,95-96, 109.
8. The theory & practice of industrial pharmacy, Leon Lachman, Herbert a. Lieberman special edition 2009, CBS publisher & distributors pvt. Ltd page no 503-529
9. Alton pharmaceutics, the design, and mfg. of medicine by Michael Alton 3 Edition Churchill living store, Elsevier. Page no. 92-93, 391, 530-536,594.
10. Shaji Reddy, MS; Microemulsion as drug delivery system, Pharma Times 2004.pg.no:139-146.
11. Razdan, R., Devarajan. V.; Microemulsions Indian Drugs, 2003, pg.no: 139-146. omega college of pharmacy.
12. Weiner M, B Ernestine IL Advance Reaction to drug formulation Agents. New York; Marcel Dekker, Inc. 1989
13. Lawrence, M. J. and Rees, G. D. Microemulsion-based media as novel drug delivery systems. Adv. Drug Delivery Rev.; 2000; 45; 89-121
14. Kumar, P. and Mittal, K. L. Handbook of microemulsion: Science and Technology. Marcel Dekker, New York, Basel; 1999.
15. Nielloed F, Marti Mestres G. Pharmaceutical Suspensions and Emulsions. NY Marcel Deccar Inc, 2000.
16. Talegaonkar S, Azeem A, Ahmad FJ, Khar RK, Pathan SA, and Khan ZI.
17. Microemulsions: A Novel Approach to Enhanced Drug Delivery. Recent Patents on Drug Delivery & Formulation, 2, 2008, 238-257.
18. Martindale. The Complete Drug Reference. 33rd edition. London: Pharmaceutical Press, 2002, 642.

19. Jaiswal P, Aggarwal G, Kaur A. Bioavailability enhancement of poorly soluble drugs by SMEDDS- A review. J Drug Deliv Ther. 2013; 3(1): 98-109
20. Shukla P, Prajapati SK, Sharma U, Shivhare S. A review on self-micro emulsifying drug delivery system: An approach to enhance the oral bioavailability of poorly water-soluble drugs. IRJP. 2012; 3(9): 16
21. Bansal AK, Sarpal K, Pawar YB. Self-emulsifying drug delivery systems: A strategy to improve oral bioavailability. CRIPS. 2010; 11(3): 4249
22. Gao P, et al. Development of a super saturable SEDDS (SSEDDS) formulation of paclitaxel with improved oral bioavailability. J Pharm Sci.2003; 92: 2386–2398.
23. Li P, et al. Development and characterization of a solid microemulsion preconcentrate system for oral delivery of poorly water-soluble drugs. Controlled Release Society Annual Meeting, Long Beach, CA, 2007; June.
24. Li P, et al. Novartis Pharmaceuticals Corp. Spontaneously dispersible pharmaceutical compositions. WO2006/050123.
25. Ito Y, et al. preparation and evaluation of solid oral heparin using emulsifier and adsorbent for in vitro and in vivo studies. Int J Pharm.2006; 317:114-119.
26. Schwarz J. Solid self-emulsifying dosage form for improved delivery of poorly soluble hydrophobic compounds and the process for preparation thereof. US Patent 20030072798. 2003; April 17.
27. Wei LL, et al. Investigations of a novel self-emulsifying osmotic pump tablet containing carvedilol. Drug Dev Ind Pharm.2007; 33:990-998.
28. Gandhi R, et al. Extrusion and spheronization in the Development of oral controlled-release dosage forms. PSTT 2, 1999; 160-170.
29. Serajuddin ATM. Solid dispersion of poorly water-soluble drugs. Early promises, subsequent problems, and recent breakthroughs. J Pharm Sci.1999; 88:1058-1066.
30. Vasanthavada M, Serajuddin ATM. Lipid-based self-emulsifying solid dispersions. In: Oral Lipid-Based Formulations: Enhancing Bioavailability of Poorly Water-Soluble Drugs (Hauss, D.J., ed.), Informa Healthcare, 2007; 149-184.
31. Serajuddin ATM, et al. effect of vehicle amphiphilicity on the dissolution and bioavailability of a poorly water-soluble drug from solid dispersions. J Pharm Sci.1988; 77: 414–417.
32. Khoo SM, et al. The formulation of halofantrine is either non-solubilizing PEG 6000 or solubilizing lipid-based solid dispersions. Physical stability and absolute bioavailability assessment. Int J Pharm.2000; 205:6578.
33. Kim JY, Ku YS. Enhanced absorption of indomethacin after oral or rectal administration of a self-emulsifying system containing indomethacin to rats. Int J Pharm.2000; 194: 81-89.
34. Chae GS, et al. enhancement of the stability of BCNU using self-emulsifying drug delivery systems (SEDDS) and in vitro antitumor activity of self-emulsified BCNU-loaded PLGA wafer. Int J Pharm.2005; 301:6-14
35. Dahan and A. Hoffman, "Rationalizing the selection of oral lipid based drug delivery systems by an in vitro dynamic lipolysis model for improved oral bioavailability of poorly water-soluble drugs," *Journal of Controlled Release*, vol. 129, no. 1, pp. 1–10, 2008.

36. S. Chakraborty, D. Shukla, B. Mishra, and S. Singh, "Lipid—an emerging platform for oral delivery of drugs with poor bioavailability," *European Journal of Pharmaceutics and Biopharmaceutics*, vol. 73, no. 1, pp. 1–15, 2009.
37. R. N. Gursoy and S. Benita, "Self-emulsifying drug delivery systems (SEDDS) for improved oral delivery of lipophilic drugs," *Biomedicine and Pharmacotherapy*, vol. 58, no. 3, pp. 173–182, 2004.
38. C. W. Pouton and W. N. Charman, "The potential of oily formulations for drug delivery to the gastrointestinal tract: preface," *Advanced Drug Delivery Reviews*, vol. 25, no. 1, pp. 1–2, 1997.
39. J. Humberstone and W. N. Charman, "Lipid-based vehicles for the oral delivery of poorly water-soluble drugs," *Advanced Drug Delivery Reviews*, vol. 25, no. 1, pp. 103–128, 1997.
40. S. di Maio and R. L. Carrier, "Gastrointestinal contents in fasted state and post-lipid ingestion: *in vivo* measurements and *in vitro* models for studying oral drug delivery," *Journal of Controlled Release*, vol. 151, no. 2, pp. 110–122, 2011.
41. V. Jannin, J. Musakhanian, and D. Marchaud, "Approaches for the development of solid and semi-solid lipid-based formulations," *Advanced Drug Delivery Reviews*, vol. 60, no. 6, pp. 734–746, 2008.
42. J.-L. Tang, J. Sun, and Z.-G. He, "Self-emulsifying drug delivery systems: a strategy for improving oral delivery of poorly soluble drugs," *Current Drug Therapy*, vol. 2, no. 1, pp. 85–93, 2007.
43. S. Stegemann, F. Leveiller, D. Franchi, H. de Jong, and H. Lindén, "When poor solubility becomes an issue: from early stage to proof of concept," *European Journal of Pharmaceutical Sciences*, vol. 31, no. 5, pp. 249–261, 2007.
44. M. R. A. Alex, A. J. Chacko, S. Jose, and E. B. Souto, "Lopinavir loaded solid lipid nanoparticles (SLN) for intestinal lymphatic targeting," *European Journal of Pharmaceutical Sciences*, vol. 42, no. 1-2, pp. 11–18, 2011.
45. M. C. Gohel, R. K. Parikh, S. C. Modi, K. G. Vyas, and K. M. Sheth, "Novel drug delivery approaches to bypass P-glycoprotein efflux pump," *Pharmainfo.net*, vol. 9, no. 1, 2011.
46. P. P. Constantinides, J.-P. Scalart, C. Lancaster, et al., "Formulation and intestinal absorption enhancement evaluation of water-in-oil microemulsions incorporating medium-chain glycerides," *Pharmaceutical Research*, vol. 11, no. 10, pp. 1385–1390, 1994.
47. S. Narang, D. Delmarre, and D. Gao, "Stable drug encapsulation in micelles and microemulsions," *International Journal of Pharmaceutics*, vol. 345, no. 1-2, pp. 9–25, 2007.

48. T. Bansal, N. Akhtar, M. Jaggi, R. K. Khar, and S. Talegaonkar, "Novel formulation approaches for optimizing the delivery of anticancer drugs based on P-glycoprotein modulation," *Drug Discovery Today*, vol. 14, no. 21-22, pp. 1067–1074, 2009.
49. V. S. N. M. Dwibhashyam and J. Vijayaralna, "The permeability glycoprotein (P-GP)—a threat to effective drug therapy?" *Indian Drugs*, vol. 43, no. 8, pp. 609–615, 2006.
50. Gao, P., & Guy, R. H. (2008). Nanoparticle-based self-emulsifying drug delivery systems for poorly water-soluble drugs. Expert opinion on drug delivery, 5(1), 33-51.
51. Raval, A.,& Patel, J. (2019). Review on solid self-micro emulsifying drug delivery system (S-SMEDDS). Journal of Drug Delivery Science and Technology, 49, 413-423.
52. Sah, A. K., & Gupta, A. (2019). Self-emulsifying drug delivery system (SEDDS): A review. Journal of pharmaceutical research international, 27(4), 1-17.
53. Zhao, Y., Huang, Y., & Chen, Y. (2018). Co-solvents in self-micro emulsifying drug delivery systems for improving drug solubility and bioavailability. Expert Opinion on Drug Delivery, 15(11), 1127-1141.
54. Wu, W., & Mao, Y. (2021). Recent advances in self-micro emulsifying drug delivery systems. Asian Journal of Pharmaceutical Sciences, 16(4), 449-464.
55. Gupta, A., Rawat, M. K., & Vaidya, B. (2020). Stimuli-responsive self-micro emulsifying drug delivery systems: An overview of recent advances. Journal of Controlled Release, 328, 1053-1074.
56. Ha, E. S., Nho, Y. C., & Park, J. B. (2020). Solid self-emulsifying drug delivery systems: challenges and opportunities. Journal of Pharmaceutical Investigation, 50(4), 419-433.
57. Kaur, R., Sharma, G., & Kumar, A. (2019). Stimuli-responsive self-micro emulsifying drug delivery systems: A new paradigm in modern drug delivery. Drug Delivery and Translational Research, 9(4), 754-772.
58. Singh, S., Singh, J., & Singh, R. (2017). Natural oils based self-micro emulsifying drug delivery systems: An approach to enhance solubility and bioavailability of poorly water-soluble drugs. Journal of Drug Delivery Science and Technology, 39, 337-347.
59. Jaiswal, M., Dudhe, R., & Sharma, P. K. (2015). Nano emulsion: an advanced vehicle for efficient drug delivery system. Biotechnology Reports, 5, 71-77.
60. Khan, S. A., & Singh, S. K. (2020). Self-micro emulsifying drug delivery systems (SMEDDS): Future perspectives. Drug Delivery and Translational Research, 10(2), 323-336.

61. Shinde, R. L., Bharkad, V. B., & Devarajan, P. V. (2018). Self-micro emulsifying drug delivery systems (SMEDDS) for improving oral bioavailability of lipophilic drugs. Journal of Drug Delivery Science and Technology, 47, 93-101.