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SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM (SMEDDS) FOR INCREASING DRUG SOLUBILITY AND DISSOLUTION – A COMPREHENSIVE REVIEW

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ABSTRACT

Self-microemulsifying drug delivery systems (SMEDDS) have become a promising approachfor enhancing the bioavailability of poorly water-soluble drugs. SMEDDS offer several advantages, including improved solubility, enhanced absorption, and increased bioavailability, which can lead to reduced drug dosages and more consistent therapeutic outcomes. Unlike conventional emulsions, SMEDDS spontaneously form fine oil-in-water microemulsions upon mild agitation in the gastrointestinal tract, eliminating the need for high-energy input and ensuring uniform and stable formulations. However, SMEDDS also present challenges, such as the need for precise selection and optimization of their components to ensure compatibility and stability, and potential gastrointestinal side effects due to surfactants and co-surfactants. Characterization of SMEDDS typically includes assessing droplet size, polydispersity index, zeta potential, and drug loading efficiency, using techniques such as dynamic light scattering, transmission electron microscopy, and differential scanning calorimetry. SMEDDS have wide-ranging applications, notably in improving the oral bioavailability of hydrophobic drugs and enabling the delivery of drugs with challenging physicochemical properties, across various therapeutic areas including cardiovascular, oncology, and infectious diseases. In summary, SMEDDS offer a versatile and effective approach for drug delivery, overcoming manylimitations of traditional systems and paving the way for enhanced therapeutic efficacy.

KEYWORDS: Unlike conventional emulsions, SMEDDS spontaneously form fine oil-in-

water microemulsions uponmild agitation in the gastrointestinal tract, eliminating the need for high-energy input and ensuring uniform and stable formulations.

INTRODUCTION

The oral route of administration is preferred for persistent drug therapy. Scientists were facing many problems in finding the techniques to improve the bioavailability of poorly aqueous soluble drugs. Since a drug has to be dissolved in gastrointestinal tract (GIT) before passing through gastrointestinal mucosa, poor water solubility can lead to incomplete and irregular absorption.[1]

The issues of low oral bioavailability afflict several therapeutic molecules including lipophilic drugs. Improvement in their bio-availability and simultaneous prevention of the oral degradation of the susceptible molecules seems to be challenging.[2],[3]

Approximately 40 % of modern drug applicants have poor water solubility and hurdles to their successful oral delivery due to a complex web of physical, chemical, physiological, and anatomical factors that act independently and in concert to limit drug bioavailability Numerous techniques are suggested to elucidate these problems, such as the use of surfactants, cyclodextrin, nanoparticles, strong dispersions, lipids complexes, and permeation enhancers. Particulate drug transport systems, consisting of nanoparticles and microspheres, were studied considerably for 10 years (3). But the toxicity of the synthetic polymeric substances consistingof alkyl cyno-acrylate, poly (lactic acid), Methyl methacrylate, etc. have been regularly used. The feasible accumulation and their poisonous metabolite product have also been studied.[4]

Microemulsions are being investigated as a capable new colloidal provider for lipophilic drugs. Microemulsions provide benefits like amazing thermodynamic stability, excessive drug solubilization capacity, progressed oral bioavailability and safety in opposition to enzymatic hydrolysis. The best hassle with microemulsion is terrible palatability because of the excessive lipid content which affect patient compliance. Moreover, because of their water content material, microemulsions can't be encapsulated in hard gelatin and soft gelatin drugs subsequently, there may be a need for anhydrous Self Emulsifying Drug Delivery system.[5] Thus, Self-Micro emulsifying Drug Delivery System (SMEDDS) is a lipid-based system designed to enhance oral bioavailability of lipophilic drugs. Few researchers have stated enhancement in bioavailability of poorly soluble capsules while formulated as SMEDDS.

Researchers have tried lipid-based delivery of lipophilic drugs like cyclosporine and concluded that cyclosporine is capable for such delivery.[6]

Self- micro emulsifying drug delivery systems (SMEDDS) are described as isotropic combinations of natural or synthetic oils, surfactants, and cosurfactants which have a completely unique capacity of forming splendid oil-in-water (o/w) micro emulsions upon slight agitation observed through dilution in aqueous media, together with GI fluids. Droplet sizes of SMEDDS ranging from 300-500 nm, even much less than 500 nm can also form. Lipophilic drugs showing dissolution rate limited absorption might additionally provide growth in rate and volume of absorption and reproducible blood-time profiles.[7],[8]

The SMEDDS can enhance the solubility and dissolution rate of the interfacial site for partitioning the medication among the oil and aqueous GI fluids. Generally, the conventional liquid SMEDDS (L-SMEDDS) are encapsulated in hard or soft gelatin capsules. However, the lipid technique may also interact with the capsules, ensuing both hardness and softness of the shell.[9]-[12]

L-SMEDDS promotes drug absorption via intestinal lymph by passing the first pass impact of drugs. Moreover, drug added with the aid of using L-SMEDDS can spontaneously shape micro- emulsion with a droplet size of dozens of nano-meters inside the gastrointestinal tract after oral administration and, therefore, enhances the absorption and bioavailability of poorly waters soluble drugs Despite many advantages, L-SMEDDS also have some significant drawbacks, including long-time stability issues, storage, transportation inconvenience, and irreversible drug precipitation. Liquid formulations may be converted to solid dosage forms through appropriate techniques to conquer these drawbacks. A form of therapeutic solidification techniques has been explored, extrusion roll technique, spray drying technique, solid carrier adsorption technique and so on. Nevertheless, those therapeutic techniques require harsh preparation conditions. For example, extrusion roll and spray drying techniques contain high temperatures, which can be infeasible for heat sensitive drugs. Also, high temperature impacts the drug loading capacity because of a low range of volatile surfactants in L-SMEDDS. On the other hand, solid carrier adsorption requires a massive quantity of adsorbent, which may cause high viscosity and low drug loading capacity. Thus, a more efficient technique for curing L- SMEDDS is urgently demanded. Liquid-solid compacts (LSC) are amongst the novel formulations for BCS category II medicine to extend the drug dissolution. In liquid-solid formulation, a non-volatile solvent may be used for solubilizing

the drug. Therefore, the resultant mixture adsorbs onto a carrier system to make dry and free-flowing powder.[13], [14]

In the SMEDDS technique, the drug is present in the soluble form inside the oil and ends up in fine globules when administered orally because of self -emulsification. The surfactant and cosurfactant reduce the interfacial surface tension of the system. In LSC technique, the drug is solubilized within the non-volatilizable solvent. Hence, these developed systems may improve the solubility of aqueous insoluble drugs. But, the development of good oral bioavailability and better pharmacodynamic effects are important. Out of those two systems, in-vivo performance should be superior (PK and PD effects) Therefore, there is a tendency to work on developing an efficient tablet dosage form by concurrent works exploiting the approaches of each SMEDDS-associated liquid-solid formulation technique. Incorporating liquid SMEDDS into a solid dosage form provides the benefit of SMEDDS with those of solid formulations and overcomes the drawbacks associated with this system. With this aim, an experimental design strategy to optimize a SMEDDS formulation of the tablet can be adopted, and the simplest composition in terms of drug dissolution properties can be selected.[15], [16]

Advantages

- The irritation caused by prolonged contact between the drug and the stomach wall canbe overcome with the SMEDDS formulation, as the micro-size droplets support the broad distribution of the drug along the GIT and are quickly transported through GIT.
- When dispersed in water, these formulations produce fine droplets with a large interface, as the active ingredient can easily be distributed from the oil phase to the aqueous phase, which is not to be expected with oily solutions having lipophilic activeingredients.
- Compared to emulsions, SMEDDS are advantageous in terms of stability due to their low energy consumption and simple manufacturing process. Simple mixing devices are sufficient for the formulation of SMEDDS, and the time required for preparation is lower than emulsions.
- The poor water-soluble drugs having dissolution rate absorption limited can be effectively formulated in the form of SMEDDS causing a stable plasma profile 36. The constant plasma levels of the poorly aqueous soluble medicament show the critical passage of drug absorption, i.e. dissolution.
- Microemulsion pre-concentrate is advantageous over microemulsions dispensed as liquid-

filled soft gelatin capsules.

- SMEDDS are advantageous over SEDDS, as the former are less dependent on bile salts for droplet formation, so better active substance absorption is expected compared to SEDDS.
- Surfactants with a high HLB value, such as Tween 80, are said to increase the permeability of active ingredients when administered in conjunction with the formulation due to their loosening effect on tight junctions.[17]

Disadvantages

- One of the barriers to the development of SMEDDS and other lipid-based formulations is the lack of good in vitro predictive models for evaluating formulations.
- Conventional dissolution methods do not work as these formulations may depend on digestion before drug release.
- The drawback of this system includes chemical instabilities of the drugs and high surfactant concentrations in the formulations (approx. 30– 60%), which can irritate the gastrointestinal tract.
- It is known that volatile co-solvents in conventional SMEDDS formulations migrate into the shells of soft or hard gelatin capsules and cause precipitation of lipophilic drugs.
- Formulations with several components become more difficult to validate.
- High Production cost.
- Low drug compatibility.
- Due to drug leakage, it may allow fewer drug loading.[17]

Advantages of SMEDDS over Emulsion

SMEDDS not only offers the same advantages of emulsions of facilitating the solubility of hydrophobic drugs, but also overcomes the drawback of the creaming of emulsions after long time. SMEDDS can be easily stored since it belongs to a thermodynamically stable system. Microemulsions formed by the SMEDDS exhibit good thermodynamics stability and optical transparency. The major difference between the above microemulsions and common emulsions lies in the particle size of droplets.

The size of the droplets of common emulsion ranges between 0.2 and 10 µm, and that of the droplets of microemulsion formed by the SMEDDS generally ranges between 2 and 100 nm (such droplets are called droplets of nano particles). Since the particle size is small, the tot al surface area for absorption and dispersion is significantly larger than that of solid dosage form

and it can easily penetrate the gastrointestinal tract and be absorbed. The bioavailability of the drug is therefore improved. SMEDDS offer numerous delivery options like filled hard gelatin capsules or soft gelatin capsules or can be formulated in to tablets whereas emulsions can only be given as an oral solution.[17]

Composition of SMEDDS

The self emulsification process is reported to be specific to the nature of the oil surfactant pair. The procedure is based on

1. Oils.
2. The surfactant concentration and the oil / surfactant ratio.
3. Cosolvents

Some of the components used in SMEDDS are

Oils

Long-chain triglycerides (e. g. soybean oil) and medium-chain triglycerides (e. g. Capmul MCM) were used in the development of SMEDDS with different degrees of saturation. Due to their biocompatibility, oils significantly contributed to the success of the SMEDDS. Recently, medium chain triglycerides have been replaced with new medium-chain semi-synthetic triglycerides containing compounds like Gelucire. Other suitable oils and fats for SMEEDS formulation include olive oil, corn oil, soybean oil, and animal fats.[18]

Surfactants

A surfactant is required to take the property of self-emulsification by SMEDDS, which is the main method of forming a micro-emulsion and is also useful for solubilizing the hydrophobic drug; in turn, the dissolution rate can be improved. The solubilization behaviour of surfactants containing active ingredients gained popularity due to its inhibitory effect on the precipitation of actives in-vivo. The permeability barrier, i. e. the intestinal cell membrane, which consists of lipids, can be modified by the distribution of the surfactant; therefore, the potency can be improved. The opening of tight junctions by surfactants helps in improved permeability, as shown in the study by Sha et al. a greater permeability of the drug with the Labrasol surfactant was observed due to the opening of tight junctions. The inhibitory effect of surfactants on the p-glycoprotein helps to improve the overall bioavailability of many drug substrates for the p-glycoprotein transporter. Although natural surfactants are less toxic, the effectiveness of self-emulsification is limited. Surfactants must be carefully selected for spontaneous emulsification to achieve an extremely low interfacial tension.

The surfactant selection is based on HLB value. Surfactants with a high HLB value facilitate the formation of o/w microemulsions. Surfactants with a hydrophilic nature, i. e. HLB greater than 12, along with water-soluble co-solvents having relatively low octanol: water partition coefficient therefore to increase the solvent capacity of the formulation and the systems, very fine droplets size smaller than 100 nm at high surfactant concentrations is required. The lowertoxicity of non-ionic surfactants, such as oleates, polysorbates, polyoxyl, etc. compared to ionicsurfactants enables them to be used more frequently in the formulation of SMEDDS. Lipids commonly used in SMEDDS formulations, such as medium and long chain triglycerides and non-ionic surfactants such as HLB-11 oleates with unsaturated acyl side chains are more suitable excipients for effective self-emulsification.[19]

Co-Solvents

Co-solvent facilitates the dissolution of the surfactant and hydrophobic drug in the oil phase due to their ability to enable water to enter the formulation. These excipients play the role of co-surfactants in the micro-emulsion system. Short chain alcohols such as ethanol, n-butanol, propylene glycol, and polyethylene glycol are used as co-solvents. The addition of co-solvents such as short-chain alcohols give flexibility to the interface, which is useful for the free movement of the hydrophobic tails of the surfactant at the interface, which in turn gives micro- emulsions dynamic behavior. Alcoholic co-solvents with low molecular weight can cause drug precipitation when the formulation is filled into gelatin capsules, as they are absorbed into the capsule shells. In addition to nature, the co-surfactant concentration also influences drug precipitation. Due to their high polarity, they tend to migrate into the aqueous phase when dispersed in aqueous media, leading to the drug's precipitation. It is, therefore, advisable to formulate SMEDDS in minimal concentration. The selection of the suitable surfactant and cosurfactant should consider the effectiveness, irritation, changes in effect due to repeated administration of the formulation, the interaction with mucosal proteins and lipids, and the metabolic pathway followed.[20]

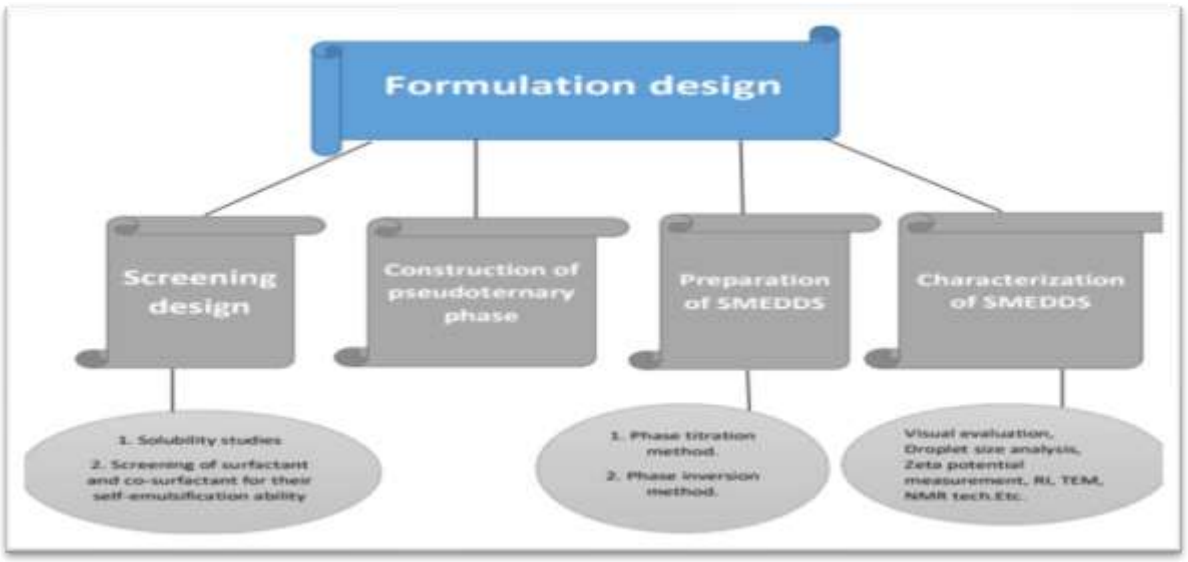

Figure 1: Formulation Design of SMEDDS.[17]

Screening of Excipients

Solubility study

The solubility of drug in various oils, surfactants and co-surfactants was determined by dissolving an excess amount of drug in each of selected oils, surfactants and co-surfactants in stoppered vials. The mixtures were continuously stirred using vortex mixer and kept at determined temperature in water bath shaker for some time to attain equilibrium. The equilibrated samples were centrifuged and supernatant was filtered through membrane filter and diluted with mobile phase. Drug content was quantified by using ultraviolet-visible (UV-VIS) spectrophotometer.[21],[22]

Pseudo-ternary phase diagram

To facilitate the effective production of microemulsions, it is imperative to examine the ternary phase behaviour of possible oil, surfactant, and co-surfactant combinations. Based on the analysis from solubility studies, the maximum solubility containing oil, surfactant and cosurfactant were selected. For this reason, pseudo-ternary phase diagrams were created to identify the areas where microemulsion production occurs. Aqueous titration or the spontaneous emulsification method were used to generate the phase diagrams of ternary systems, which consist of an oil phase, a surfactant phase, and an aqueous phase. Glass vials were filled with optimised surfactant and allowed to dissolve in oil phase at room temperature in various ratios. Then, using a micropipette and distilled water, each ratio of surfactant to oil phase was constantly titrated drop by drop until it turned turbid. Minute details of each ternary system's phase behaviour during titration were noted. The observed data were plotted

on triangle coordinates to create phase diagrams, and the percentage composition of each component in each ternary system was calculated.[23]

Preparation of SMEDDS: Preparation involves adding the drug to the mixture of oil, surfactant, and cosurfactant, followed by vortexing. In some case the drug dissolve in one of the excipients and the remaining excipients are added to the drug solution. The solution must then be properly mixed and inspected for signs of cloudiness. After equilibrating for 48 hours at room temperature, the solution should be heated to a clear solution if necessary. Volume, the formulation should be stored in capsules of the appropriate size.[23]

Adsorption to solid carriers: Adsorption of liquid-SMEDDS onto solid carriers is one of the most commonly used techniques since it provides better uniformity of content, high level of adsorption (up to 75% w/v) on a suitable carrier (Bolko Seljak et al., 2018). This technique consists of simple mixing of liquid-SMEDDS with the solid adsorbent carrier in a kneader until liquid SMEDDS gets completely adsorbed. The further obtained mixture can be mixed with one or more solid carrier to get a uniform mixture. Selection of appropriate solid carrier is a fundamental requirement in the formulation of S-SMEDDS since it's the carrier assists in rendering tremendous potential for adsorption of liquids whether hydrophilic or lipophilic. Accordingly, the carrier having high porosity is preferable, popular examples of which includes Aeroperl 300 pharma, polyplasdone XL, Pharmacel 101, Lactochem, Starch 1500, Lycatab DSH, and also silica-based carriers.[24]

Characterization of SMEDDS

- **Visual Evaluation**: The self-emulsification can be assessed by visual assessment. After dilution of SMEDDS with water, an opaque and milky white appearance indicates the formation of a microemulsion. In contrast, a clear, isotropic, clear solution indicates the formation of a micro-emulsion. Precipitation of the drug in diluted SMEDDS is also possible by visual evaluation. Formulations can be considered stable if no precipitationof the drug is evident. Precipitation is common when the formulation contains water-soluble co-solvents and can be avoided by increasing the surfactant concentration.[25],[26]
- **Droplet Size Analysis:** The droplet size depends mainly on the type and concentrationof the surfactant. The micro-emulsion formed on dilution with water creates droplets ofvery narrow size and size distribution for efficient drug release, in vivo absorption, andstability. For droplet size analysis, spectroscopic techniques such as photon correlationspectroscopy

and microscopic techniques are used. Dynamic light scattering techniques with the zeta meter can also be used for droplet size analysis 88. Samples must be sufficiently diluted before size determination. Determining the polydispersity index (PDI) provides reasonable information about the size distribution.[26], [27]

- **Zeta Potential Measurement:** The zeta potential is generally measured with a zeta potential analyzer or a zeta meter system. The zeta potential value indicates the stabilityof the emulsion after sufficient dilution. A higher zeta potential indicates good formulation stability. In general, the zeta potential value is negative due to free fatty acids, but when cationic lipids such as oleyl-amine are used, the positive charge develops. Positively charged droplets have the property of efficiently interacting with the mucosal surface of the GIT. These interactions are electrostatic in nature, so strong adhesion with increased absorption can be expected.[28]
- **Cloud Point Determination:** The cloud point is generally determined by gradually increasing the temperature of the water bath into which the formulation is placed and measured spectrophotometrically. The point, at which the permeability in% decreases means the cloud point, which is the temperature above which the clear solution changesto a cloudy solution. The temperature is 37 °C; formulations must have a cloud point higher than body temperature to retain their self-emulsifying properties. Due to the susceptibility of the surfactant to dehydration, phase separation and reduced solubilization of the drug are often observed at temperatures above the cloud point. Thecloud point is influenced by the drug's lipophilicity and other formulation components.[29]
- **Viscosity Measurements:** The viscosity of the diluted SMEDDS formulation, which is a micro-emulsion, is generally determined with rheometers such as the Brookfield cone-plate rheometer with conical spindle or a Brookfield rotating spindle viscometer. During the titration, the initial increase in viscosity followed by a decrease, whereby the increase in water volume is due to the water percolation threshold, indicates the formation of an O / W micro-emulsion from a W / O micro-emulsion with an intermediate bi-continuous phase. The rheology of the micro-emulsion can be determined from the diagram between shear stress and shear rate. The behavior indicates the presence of small, spherical droplets.[30], [31]
- **Transmission Electron Microscopy (TEM) Study**: It is mainly used to study the structure and morphology of micro-emulsions formed by diluting SMEDDS. These studies arecarried out by combining bright-field images with increasing magnification and

diffraction modes.[31]

- **Differential Scanning Colorimetry (DSC) Study:** It is mainly used to characterize micro-emulsions formed by diluting SMEDDS with peaks corresponding to water. The peaks provide information about the state of the water as a bound or Free State. Pure water is used as a reference, showing a large, sharp peak at around -17 ° C, indicating the freezing point.[31]
- **Thermodynamic Stability Studies:** These studies are useful to assess the consequences of a temperature change in the formulation. The formulation is diluted with an aqueous phase and centrifuged for 15 min at 15,000 rpm 81 or 30 min at 3,500rpm. The sample in which phase separation is not observed is subjected to freezing andthawing cycles (-20 ° C and 40 °C temperature, respectively) and observed visually. Thermodynamically stable formulations show no change in the visual description.[31]
- **In-vitro Dissolution Profile:** The release of the drug from the formulation can be assessed after placing the formulation in a hard gelatin capsule with Apparatus I of USP XXIII at 100 rpm or Apparatus II of USP XXIII at 50 rpm or with the dialysis method.at 37 ± 0.5 °C. Samples should be taken from the medium at regular intervals and the active substance content estimated and compared with the control. The polarity of the oil droplet influences the active ingredient release from diluted SMEDDS. The higher the polarity, the faster the drug will be released from the oil droplet into the aqueous phase. The polarity depends mainly on the HLB of the surfactant, the molecular weight of the hydrophilic part of the surfactant, and its concentration, together with the degree of unsaturation of the fatty acid of the lipid phase.[17], [31], [32]

Applications

1. Self-micro emulsifying drug-delivery system in improving the solubility of poorly soluble drugs –The medication present in the conventional self-emulsified system may precipitate or crystallize in the GI tract, leading to discrepancies and unpredictable pharmacokinetics analysis results.

2. Solid self-emulsifying drug systems - In order to prepare tablets using this strategy, medications that are less soluble in water are added to liquid SEDDS. With solid dose forms like tablets and capsules, this method not only makes it easier to load around 70%of SEDDS but also exhibits good flowability, content consistency, and decent cohesiveproperties.

3. Self-micro emulsifying drug-delivery system in sustain release of Bioactive-The creation of S-SMEDDS provides bioactive delivery through a number of methods. The

lethargic release kinetics of these agents, which show poor water solubility characteristics, prevent the release of bioactive agents during gastric transit and maintain their solubilization throughout the gastrointestinal tract, making this system highly promising for the efficient transportation of these agents. Furthermore, depending on the process of diffusion or digestion, the release of bioactive compounds from this self-emulsified lipid system into the aqueous fluid is often rapid and Site- specific release While liquids and SMEDDS-based approaches can both be used to achieve controlled diffusion of drug molecules, the use of SMEDDS offers the potential to deliver bioactive molecules to achieve both controlled and a targeted release at the site of interest by using an appropriate solid carrier system.

4. **Self-micro emulsifying drug-delivery system in delivery of proteins-**Humulin, or human insulin, was originally used as a recombinant protein therapy in 1982, but since then, the application of protein has increased. The US Food and Drug Administration (USFDA) has currently authorized more than 130 different protein-based therapies for use in clinical settings. Though it is still in its early stages, protein therapy has emerged in every area of medicine.

5. **Self-micro emulsifying drug-delivery system in gene delivery-** Oral gene therapy is an essential management strategy for GI disorders. For example, protein therapies maybe used to treat illnesses connected to the gastrointestinal tract or systemic diseases. Gene therapy, on the other hand, has the potential to significantly replace oral protein molecule delivery. This method provides a platform for both the absorption of protein molecules at the location of interest, or the site of sickness, and the synthesis of desirable proteins there.

6. **Self-micro emulsifying drug-delivery system in drug delivery-**Solvent injection has been used as a way to prepare self-emulsifying NPs. This method involves dissolving all of the excipients—lipid, emulsifying agent, and active molecules—together and then injecting the resulting mixture dropwise into a stirring media, which is typically a nonsolvent. Additionally, in a second method called sonication emulsion diffusion evaporation, two medications, 5-fluorouracil and antisense Human Epidermal Growth Factor receptor (EGFR) plasmids, were added simultaneously to the polymer, PLGA/OCMC. Furthermore, the combination of these two polymers promotes the system's self-emulsification, negating the need for the addition of an extra emulsifying agent. In the end, it was discovered that both medications contained almost the same amount of drug—94% and 95%, respectively.

7. **Self-micro emulsifying drug-delivery system in the enhancement of oral absorption of the drug-**When the globules travel and dissolve along the GI tract, the active molecules are released directly through the SMEDDS following their partitioning throughout the

intestinal tract fluids. Additionally, the drug's release is typically determined by two key elements, such as the particle's minuscule size and the polarity of the oil globules, which determine how well the active molecules are released through the SMEDDS. Nevertheless, since the drug molecules enter the capillaries that are housed inside the oil globules, the polarity of the globules does not have a major impact on O/W microemulsions.

8. Self-micro emulsifying drug-delivery system for increasing the bioavailability of the drug- Following loading in SMEDDS, there was an increase in the diffusion of lipophilic drug molecules in the systemic circulation. Furthermore, studies using non fasting dogs revealed three times the drug bioavailability of hydrophobic compounds that were combined with oral delivery of the SMEDDS and appropriately modified in naphthalene. Additional results indicated that there was an enhanced impact on both Cmax and AUC compared to products. Furthermore, employing lipid-based preparation, the results of another study on rats suggested increased blood circulation of Ontazolast, one of the anti-inflammatory compounds.

9. Self-micro emulsifying drug-delivery system for improving the lymphatic uptake of the drug. In a recent study, the medication huperzine-A was loaded into the SMEDDS and tested for its ability to increase lymphatic absorption. Additionally, it was indicated by the data that the blocking model's AUC and Cmax values were significantly lower than the control's (P,.05. Furthermore, compared to suspension, the percentage distribution of Huperzine-A in the lymph system from SMEDDS was nearly eight times greater, suggesting that the formulation of SMEDDS may significantly boost the transport of drug molecules via the intestinal lymphatic route.

10. Self-micro emulsifying drug-delivery system for enhanced liver uptake-GRAS excipients were used in the design of the SMEDDS. Following preparation, they were adsorbed at the Aerosil 200's surface. In addition, the optimized SMEDDS preparation was assessed in order to identify unique physicochemical factors. Furthermore, the pharmacodynamic effectiveness was evaluated using Peter's 4-Day suppressive research on the murine model. Additionally, flow cytometry research has been used in biodistribution studies. Moreover, these trials' biodistribution data showed enhanced absorption into the liver. Nonetheless, the research conducted on animals indicated that SMEDDS may have a promising future in enhancing drug absorption in the liver.

11. Self-micro emulsifying drug-delivery system in delivery of peptides-In a study, the impact of lipases on the octreotide leakage pattern through SNEDDS following oral administration was examined. Furthermore, by using different types of excipients, the results

clarified the potential of dual lipase-based degradable as well as nondegradable SNEDDS formulation. Furthermore, both formulations showed a reliable prolonged drug leakage for at least one day during the lipase deficiency. Nevertheless, in the caseof lipase, over 60% of the octreotide medication leaked through the preparations that were broken down by lipase.[24]

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