



Recent Developments in Self Emulsifying Drug Delivery System

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ABSTRACT

Lipophilic drugs comprise of majority of the active pharmaceutical ingredients which shows the lower oral bioavailability. Many methods have been used to enhance the bioavailability, especially the lipid-based formulations have gained a lot of attention of the researchers, one among the lipid-based formulation approach is the self-emulsifying drug delivery system (SEDDS). SEDDS basically is an isotropic mixture of oils, surfactants and co-surfactants or co-solvents, which after reaching the gastro intestinal tract (GIT) emulsifies itself to emulsion upon mild agitation in the stomach. Solid self-emulsifying drug delivery system (S-SEDDS) is one of advancements in the self-emulsifying systems, which uses the adsorbents where the liquid self-emulsifying system adsorbs and converts itself in to solid, which overcomes the disadvantages of the liquid SEDDS. Various S-SEDDS have been developed in recent years and few of them are, tablets, pellets, microbeads, suppositories, nanoparticles, patches, microspheres etc, without any compromise in the drug release kinetics. These formulations are the cost-effective means of enhancing the bioavailability of the lipophilic drugs.

Keywords: Self-emulsifying drug delivery system (SEDDS), solid Self-emulsifying drug delivery system (S-SEDDS), self-double emulsifying drug delivery system (SDEDDS), Self-emulsifying implants.

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INTRODUCTION

Self-emulsifying systems were coined in 1960s where the water insoluble insecticides and other lipophilic compounds were mixed with lipidic and hydrophilic excipients to increase their effectiveness. Pouton revealed the discovery of SEDDS, a strategy for overcoming the many obstacles faced by lipophilic drugs, for the first time in 1985. Enormous research was carried out since 1960s to enhance the bioavailability of the drugs and technology transfer from investigative laboratory to the industrial scale and finally to the clinics¹.

Chemical active moieties with the therapeutic activity available nowadays are lipophilic in nature. Up to 30-40% of all available drug molecules are lipophilic in nature, that imparts low water solubility and completely reduced bioavailability. This problem acts as a hurdle in delivery of drug, so many approaches have been used to overcome these problems. Permeation enhancement, micronization, salt formation, cyclodextrin complex formation, nanoparticle and solid dispersions (SDs), surfactant use, and self-emulsifying drug-delivery systems are only a few of the techniques (SEDDSs). Lipophilic drugs' oral

bioavailability can be enhanced while the dosage is reduced by using a self-emulsifying drug delivery system².

When introduced in the aqueous phase under modest agitation, isotropic oil-surfactant mixtures spontaneously emulsify into fine oil-in-water emulsions. Modern SEDDS formulations contain non-ionic surfactants, which are less toxic than ionic surfactants. These devices work by forming fine emulsions (or micro-emulsions) in the gastrointestinal system as a result of the little agitation caused by gastric movement (GIT)³.

SEDDS have been tried as solid dosage forms, as well as adding large amounts of solidifying excipients (adsorbents and polymers) to them. Because of their stellar meritorious visages, such as a remarkable increase in dissolution efficiency, solubility, and penetrability, diminished gut wall metabolism by CYP450 group of enzymes, circumnavigation of extensive hepatic first-pass effect, and limited P-gp efflux, lipid-based self-emulsifying drug delivery systems (SEDDS) have been investigated for lowering intra-/inter-subject inconsistencies in gastrointestinal (GI) absorption⁴.

Liquid SEDDSs can be powdered to form solid SEDDSs. This granulated form can subsequently be utilised to produce solid-dosage products like SE pellets (SEPs), SE tablets, and other SEDDS formulations. Solid SEDDSs, as opposed to liquid SEDDSs, have no stability difficulties. SEDDSs are being utilised to deliver hydrophobic medicines, according to reports⁵.



Advantages of SEDDS over other emulsions

- Irritating responses are commonly found as a result of extended exposure among active moieties as well as an inner surface of the GI tract, but this may be avoided by using SMEDDS preparations, which facilitate the transportation of active molecules from small globules through the GI tract.
- These preparations form small globules with a large interfacial area after dispersion in the aqueous phase, which generally facilitate drug partitioning from oil to aqueous phase. In the case of oil-soluble lipophilic medications, however, this does not occur.
- When it comes to stability, SMEDDSs are superior than traditional emulsions owing to the integration of less energy and the production process, which typically does not include any challenging phases. SMEDDS are also easier to prepare than emulsions since they use simple mixing instruments and take less time to make.
- The drugs that have a lower solubility in water have rate limited absorption that is generally dependent on the dissolving rate. SMEDDS might be successfully absorbed in this situation, with a following constant plasma time profile.
- SMEDDS is made up of emulsifying agents such as Spans, Tween 80, Cremophor EL, and Pluronics that have been found to block efflux transporters, hence enhancing the bioavailability of active chemicals that are often a substrate for efflux pumps.
- The SMEDDS might protect drug molecules that are prone to being damaged by chemical substances, as well as enzymes in the GI tract, while the active agents are delivered throughout the body by embedding them in the oil globules.
- In terms of spreading active moieties via liquid packed in soft gelatin capsules, microemulsion preconcentrate outperforms other typical microemulsion formulations.
- SMEDDSs are discovered to be less reliant on bile salts for globule production, with an increased rate of absorption for the active molecules⁶.

Limitation of SEDDS

Traditional SEDDS, on the other hand, are usually made in liquid form and delivered orally in soft or hard gelatin capsules, resulting in various drawbacks like as⁶

- High production costs,
- Low drug incompatibility
- Stability,
- Drugs leakage
- Precipitation,
- Capsule ageing.

Challenges in SEDDS

- Lack of predictive invitro tests.
- Polymorphism of lipid excipients.
- Handling and storage issues.
- Precipitation of drug in vivo.
- Oxidation of lipid excipients.
- Limited lymphatic uptake.
- Encapsulation In to capsules⁶.

RECENT ADVANCES IN SELF-EMULSIFYING DRUG DELIVERY SYSTEM

This article will discuss about various newer approaches of solid self-emulsifying drug delivery system and all the works done on them by various candidates.

Self-Double Emulsifying Drug Delivery System

During last decade lipid-based formulation gained the prominence due to origination of various safe pharmacologically active hydrophobic ingredients. One among these lipid-based formulation is the multiple emulsion generally called as “emulsions of emulsions” which is a complex formulation. The much more basic among these numerous emulsions is the double emulsion⁷.

Double emulsions are mainly of two types: w/o/w emulsions, wherein the aqueous phase is distributed in large oil droplets that are then distributed into a continuous external aqueous phase. The aqueous phase will be contained by the oil membrane, which will operate as a storage chamber for the hydrophilic medicines. Oil-in-water-in-oil (o/w/o) emulsions consist of oil droplets distributed in water droplets, which are afterward emulsified into a continuous external oil phase. The internal phase, namely the oil phase, is encased in an aqueous membrane, which will serve as a storage chamber for hydrophobic medicines⁸.

Thermodynamically, double emulsions are more unstable than single emulsions because they have more surfaces. This difficulty can be solved by using SDEDDS instead of double emulsions. SDEDDS does not have an external water phase. In the aqueous gastrointestinal environment, SDEDDS creates water-in-oil-in-water (w/o/w) double emulsions containing drugs in the internal water phase⁹.

SDEDDS offer a lot of potential in terms of enhancing BCS class III drug oral bioavailability. SDEDDS are polydisperse system with droplets in the continuous phase's dispersed phase. It may be possible to simplify the administration and storage method by encapsulating or placing SDEDDS into soft or hard gelatine capsules right away¹⁰.

Advantages of SDEDDS

- As the drug's bioavailability rises, the dosage can be dropped.



- A formulation can be composed of a variety of oils and surfactants.
- Drugs that are both water soluble and insoluble can be captured and preserved.
- Drugs that specifically target the reticulo-endothelial system are conceivable to develop (RES).
- Drugs can be safeguarded against the stomach's unfriendly environment¹¹.

Disadvantages of SDEDDS

- Since it contains several components, it is difficult to formulate and validate.
- Bulky and prone to physical and chemical degradation.
- When drugs are diluted, their precipitation tendency may be increased due to the dilution impact of hydrophilic solvents.
- A scarcity of good in-vitro prediction models for evaluating formulations¹¹.

Hu. C et al., developed a drug delivery system comprising both epigallocatechin-3-gallate and α -lipoic acid was developed and characterised. They synthesised the SDEDDS for topical distribution utilising a modified two-step procedure, and they detailed it using confocal microscopy, invitro release, and antioxidant properties¹².

SELF EMULSIFYING FILMS

Self-Micro Emulsifying Mouth Dissolving Films (SMMDF)

Self-micro emulsifying mouth dissolving films are a recent advancement in the self-emulsifying drug delivery technology. SMMDF is formed with the integration of the self-emulsifying components upon the mouth dissolving film. SMMDF increases the absorption and solubility of hydrophobic pharmaceuticals when taken orally. Earlier they used to prepare a solid SMEDDS by incorporating the liquid SMEDDS in to the hard or soft gelatin capsules, which resembled as the solid dosage form. But the surfactants have the property of migration through the shells of capsules which led to the precipitation of the drugs through the shell. The most effective way to overcome this was to use self-microemulsifying mouth dissolving films. The SMMDF was discovered to have the property of retaining the liquid SMEDDS absorption properties.

Features of SMDDF

- Obstruction free delivery of the drug.
- It provides better mucoadhesion.
- Disintegration of the formulation is much faster (3-5 sec).
- Drug release is quicker.

Advantages of SMDDF

- Avoids first pass metabolism.
- Faster dissolution and disintegration.
- Quicker onset of action compared to tablets.
- Doesn't require water for administration.
- It offers good stability.
- Better patient compliance.

Disadvantages of SMMDF

- Incorporation of only small amount drug.
- Dose uniformity varies.
- It absorbs moisture from atmosphere.

Seema Venkatrao Pattewar et al., concluded that the self microemulsifying mouth dissolving films are the most favourable approach for the drugs which have poor aqueous solubility, drugs with high molecular weight, drugs which undergo first pass metabolism, enzymatic degradable drugs, drugs having gastric irritation and finally the drugs having low dissolution and bioavailability. SMMDF provides instant onset of action as it keeps the drug in to the solubilized form which in turn improves dissolution characteristic of the low water-soluble drug. SMMDF is cost-effective because it only takes a little amount of drug and less complex machinery to manufacture. SMMDF is a novel strategy for overcoming lipophilic medicines' limited oral bioavailability. It is also an industrially viable technology. The study exposed various possibilities of incorporating wide range of plant actives as their scale up is economical and suitable¹³.

Self-Nano Emulsifying Loaded Sublingual Films

The lipid-based formulations known as self-nano emulsifying systems (SNES) are used to improve the bioavailability of hydrophobic medicines. Along with the medicine, these systems comprise clear mixes of oils, surfactants, co-surfactants, and co-solvents. The basic principle underlying these formulations is immediate emulsification in an aqueous solution to generate an O/W nano emulsion with a diameter of up to 100 nm. The great penetration of nano-sized globules through the sublingual mucosa, as well as the huge surface area of drug exposure they give, help to increase the pace and extent of drug absorption. Sublingual films are important because they are designed to dissolve within seconds upon contact with the tongue without the need for liquid intake or measuring devices, in addition to dose precision, discomfort avoidance, simplicity of handling, and convenient storage.

Advantages

- Faster onset of action.
- Enhances bioavailability of poorly soluble drugs.
- First pass metabolism and GIT can be bypassed.



- Drug have better permeability in to the systemic circulation.
- High dissolution rate.

Basant A. Habib et al., formulated optimized febuxostat self-nano emulsifying fast dissolving sublingual film which showed better dissolution rate and good mechanical properties. The drug was added to a fast-acting hydrated mix that released nano-sized globules. The sublingual mucosa is particularly permeable to these nano globules, enhancing medication absorption. The invitro study showed that these sublingual films had relative bioavailability of 240.64% compared to marketed febuxostat tablet. The SNFs were prepared by preliminary trials by using different film forming agents like HPMC, HMPC-E5, HPMC-K4, PVP and HEC were utilised at various quantities, however the film was ultimately prepared via a solvent casting process¹⁴.

Self-Nano Emulsifying Orodispersible Films

Orally disintegrating films (ODF) have lately acquired popularity due to their ease of administration, rapid disintegration, avoidance of the first pass effect, and high patient compliance. When compared to typical oral dosage forms like tablets and capsules, ODFs have shown to be very promising in terms of increasing medicine bioavailability while also having a speedy onset of action. Because of recent developments in numerous techniques to boost mucosal administration, self-nanoemulsifying drug delivery systems (SNEDDS) have shown enormous potential in enhancing the permeability of a hydrophilic medicine.

Sawani D et al., made a primary emulsion (W/O), a clear solution of captopril was added dropwise to the oil phase, which included Oleic acid and Span. After that, the primary emulsion was mixed with an external aqueous phase at different weight ratios. The external aqueous phase was made up of a film-forming polymer methocelms e15 (HPMC), a plasticizer (PEG 400), and DI water. The mean globule size, PDI, and zeta potential of the self-nanoemulsifying w/o/w systems were critical parameters since they indicated the quality of the produced films. The principal influence of tested film attribute, tensile strength, had a statistically significant favourable effect on permeability. In the developed formulations, improved permeability and pH-independent release patterns were found. Increased drug and film adhesion to the membrane may explain the beneficial effects of flux and tensile strength on permeability¹⁵.

Self-Nanoemulsifying Transdermal Films

Self-nanoemulsifying drug delivery systems (SNEDDS) may boost dissolution rates and absorption amounts because to the nano-sized droplets present, resulting in more predictable blood–time profiles. The use of SNEDDS can help to reduce the impact of pH variations on release performance. SNEDDS dispersion in aqueous medium in a fine emulsion with nanosized globules, keeping the drug in

solution and overcoming one of the most significant hurdles to drug absorption, the dissolution step. In addition, emulsifying SNEDDS in an aqueous gastrointestinal tract (GIT) medium enhanced the drug's permeability across the GIT membrane, hence enhancing its bioavailability. Pre-dissolving medicines in a mix of lipidic and emulsifying excipients reduces the possibility of disintegration/dissolution processes becoming rate-limiting factors for oral absorption of weakly water-soluble drugs. Solid SNEDDS is preferred to liquid SNEDDS for several reasons, including enhanced mobility, stability, drug loading, and, most importantly, patient compliance.

Khaled M Hosny worked on the self-emulsifying film with aim of loading a SQR SNEDDS formulation onto a polymeric PVA-based transdermal film using a two-step optimization approach to keep the process variables under control. The improved Saquinavir (SQR) SNEDDS was used to make transdermal films. SQR-SNEDDS and SNEDDS-loaded polymeric PVA transdermal films were successfully produced using a two-step optimization procedure. In comparison to pure SQR-loaded film, SNEDDS-loaded film had excellent folding durability and tensile strength. The findings provide a solid foundation for additional preclinical research, indicating that SNEDDS-loaded transdermal film might be a viable alternative to oral SQR administration, with better bioavailability, patient compliance, and reduced adverse effects¹⁶.

SELF EMULSIFYING IMPLANTS

The utility and application of solid self-emulsifying drug delivery system have been greatly influenced or enhanced by the research in to self-emulsifying implants. Carmustine a nitrosourea derivative that serves against the malignant tumors its potency was diminished due to its short half-life. In comparison to carmustine wafer implants made with PGLA (polyd,l-lactide-co-glycolide), a self-emulsifying system made with Labrafil 1944, tributyrin, and cremophor RH 40 was developed. Then, using compression modelling and a flat and smooth surface, self-emulsified carmustine wafers were created. With the use of a self-emulsified mechanism, carmustine's half-life was raised to 130 minutes. This formulation had a longer anticancer activity than other carmustine wafers without a self-emulsifying system, was less sensitive to hydrolysis, and had greater activity than other carmustine wafers without a self-emulsifying system¹⁷.

Gang soo chae et al., formulated carmustine wafer for the enhancement of the stability, which showed 4-fold enhancement of invitro half-life. According to the study conducted the cytotoxicity and the release rate pattern of the self-emulsifying carmustine loaded PGLA wafers was higher than that of the regular intact carmustine wafers¹⁸.

Loomis developed bioresorbable copolymers containing at least two cross-linkable functional groups per polymer chain and a hydrophilic region. Such copolymers have Self-Emulsifying capabilities even when no emulsifying agent is



used. These copolymers function effectively as sealants for prosthesis that have been implanted¹⁹.

Self-Emulsifying Drug Delivery System of Herbal

Herbal medicines have been utilised for thousands of years, although they were not widely employed in Western nations. Nearly 80% of the world's population consumes herbal remedies derived either directly or indirectly from plants. Because of their low water solubility and hydrophobic characteristics, most herbal medicines have a low bioavailability. This leads to the poor drug distribution, reduction in the efficacy of the drug and requirement of high and repeated dose for administration, hence SEDDS can be used to enhance the pharmacokinetics of hydrophobic phytoconstituents and other plant derived products. Self-emulsifying drug delivery for herbal drugs are the most looking forward approach to overcome the problem of low bioavailability of these drugs. There are considerable amount of research going on the SEDDS to target the herbal actives and to establish SEDDS as the novel delivery system for the lipophilic phytoconstituents²⁰.

Advantages:

- GI irritation is avoided
- Controlled and sustained release can be formulated.
- Bypasses the first pass metabolism

Disadvantages:

- High production cost.
- Lack of good invitro correlation models.
- Low stability.
- Precipitation of drug/ excipient.
- Large amount of surfactant is needed.

Ginkgo biloba extract (GBE) is a popular herbal medicine for improving cognition in the elderly. According to the research, quick self-emulsification and dispersion in absorption sites can increase the oral absorption of sparingly soluble compounds in GBE-loaded SEDDS. In vitro, the active components of the GBE-SEDDS form dissolved more faster than those of the GBE tablets. When fasting dogs were given 800 mg GBE as SEDDS or tablets, the relative bioavailability of SEDDS for bilabolide, ginkgolide A, and B was found to be 162.1%, 154.6%, and 155.8%, respectively, when compared to reference tablets²¹.

To improve the solubility and bioavailability of Fructus Schisandral Chinensis, SEDDS was developed. The dissolving rate of the active component of Fructus Schisandral Chinensis, SEDDS in vitro was substantially higher than the dissolution rate of commercial capsules. SEDDS demonstrated a relative bioavailability of 292.2 percent for schisandrin A and 205.8 percent for schisandrin

B when compared to commercial capsules. (Shao et al., 2010)²².

A SMEDDS of Glycyrrhetic acid was formulated for the oral administration by using almond oil as an oil phase. The permeability of Glycyrrhetic acid added into microemulsion systems was significantly higher than the plane formulation. These findings suggest that the microemulsion technology investigated is a viable method for enhancing Glycyrrhetic acid solubility and oral absorption²⁰.

Self-Emulsifying Drug Delivery System in Nutraceuticals

"Nutraceuticals" is a term that combines the words "nutrition" and "pharmaceutics." A nutraceutical is a food or dietary component that provides pharmaceutical or health advantages, such as sickness prevention and treatment. Isolated nutrients, dietary supplements, genetically altered designer foods, herbal goods, and processed and functional foods are all examples of items that fall under this umbrella phrase²³.

These chemicals are weakly soluble in aqueous environments, making oral administration challenging to obtain appropriate and consistent bioavailability. SEDDS have been used to increase the solubility and hence bioavailability of prospective nutraceuticals such as quercetin (Tran et al. 2014), naringenin (Khan et al. 2015), and resveratrol (Khan et al. 2015). (Yen et al. 2017). As a result, the phrase "self-emulsifying nutraceutical delivery system" is more accurate.

Shailesh S. Chalikwar et al., prepared SMEDDS of hesperidin for improving its bio-absorption and its solubility. Utilizing innocuous solid carriers such as Neusilin US2 (aluminium-magnesium trisilicate) and Aerosil 200 (silicon dioxide), the optimised liquid SMEDDS-Hesperidin (HES) formulation was turned into a stable solid-state using spray drying and simple adsorption procedures, followed by solid-state characterisation. The generated solid SMEDDS-HES demonstrated good physical qualities, free-flowing ability, and stability. When compared to pure HES, the SMEDDS-HES formulation showed enhanced dissolving behaviour in in vitro drug release experiments. Solid SMEDDS-HES also showed improved therapeutic effectiveness in in vivo hypoglycaemic and histopathological tests.

Ankita shah et al., studied and developed self-micro-emulsifying drug delivery system for different poorly water-soluble bioactive nutraceuticals namely Vitamin K2, Vitamin A, Coenzyme Q₁₀, Quercetin and *trans*-resveratrol as they are hydrophobic in nature. Vitamin A palmitate is a fat-soluble vitamin that contains the biological activity of retinol and β -carotene, which are required for healthy development, eyesight, and immunological function. Vitamin K2 is a fat-soluble vitamin that has a role in blood clotting factor modulation. Coenzyme Q10 is thought to aid in the treatment of cardiovascular diseases such as congestive heart failure, as well as the maintenance of healthy cardiac and skeletal muscles. Quercetin has anti-



oxidant, anti-inflammatory, anti-cancer, and cardiovascular-protective properties. Trans-resveratrol has antioxidant, anticancer, cardioprotective, and anticarcinogenic properties. Both lipids and the surfactant displayed good solubilization capabilities for all of the nutraceuticals used. All SMEDDS formulations dispersed in minutes when exposed to wet surroundings²⁴.

Self-Emulsifying Microspheres

Many oily drugs, such as Vitamin E, Phytonadione, and Pennyroyal, are frequently employed in clinical practise due to their high therapeutic action. They are commonly created as emulsions or soft capsules containing oily medicines, due to their liquid state and low water solubility. Traditional self-emulsifying systems are included in soft capsules (SES). Following oral administration of SES containing the oily ingredient, the medication is quickly diffused and released from the droplets generated. As a result, a large portion of the medication is absorbed immediately after delivery, resulting in high plasma drug concentrations^{1,2}.

Jian You et al., designed a formulation of oily drug as sustained release. Self-emulsifying sustained-release microspheres containing zedoary turmeric oil were made using the quasi-emulsion–solvent-diffusion method (ZTO). The quantity of talc in the formulation impacts the self-emulsifying rate, and the polymer ratio can influence release behaviour. The stability and droplet size of the generated emulsions were similarly influenced by the polymer ratio in the formulation. When compared to the standard ZTO SES (self-emulsifying system), the microspheres' relative bioavailability was increased after oral administration, and plasma concentration–time profiles with superior sustained-release characteristics were obtained. Plasma concentration–time profiles with superior sustained-release characteristics were established after oral administration of the microspheres, with a bioavailability of 135.6 percent when compared to the traditional self-emulsifying formulation (a good strategy for improving the bioavailability of an oily drug)²⁵.

Self-Emulsifying Tablets

Great research has been carried out in the field of self-emulsifying drug delivery system with an aim of formulating a self-emulsified tablet, with combination of oils and surfactants. The main objective for this formulation is their stability. The major advantage of this system is they can be formulated as a sustained release or a controlled release formulation. Here the liquid self-emulsifying system is compressed or moulded as a tablet with the help of solid carriers. These tablets provide an advantage of getting melted at the body temperature, the propulsive movement of GIT hinders the melting point leading to the enhancement of the emulsification rate. In contrast to non-emulsified tablets the self-emulsified tablets have higher drug concentration in the blood²⁶.

Xiaole Q conducted research with the goal of developing a solid self-micro emulsified dispersible celastrol tablet with

a low dissolving rate and bioavailability. They ran a series of studies to screen and improve the Celastrol liquid SMEDDS. The liquid SMEDDS was then adsorbed onto microcrystalline cellulose KG 802 to convert it to solid SMEDDS, and subsequently dispersible tablets were made utilising the wet granulation compression process. When compared to the suspension, the relative bioavailability of Celastrol SMEDDS and Celastrol dispersible SMEDDS was 569 percent and 558 percent, respectively²⁷.

Mukund Maruti Gade et al., developed and tested an orlistat self-emulsifying tablet. At three levels, the impact of independent variables such as oil volume and surfactant/co-surfactant ratio on dependent variables such as globule size and emulsification time was investigated. After 60 minutes, the self-emulsifying tablet released 99.53 percent of the medication, compared to just 39 percent for the commercial version.

Self-Emulsifying Pellets

Pellets have a number of advantages as a multiple-unit dosage form, including increased flexibility in creating and producing solid dosage forms, reduced intra- and inter-subject variability in drug dissolution and plasma profiles, and thus improved medication safety and efficacy, as well as reduced GI irritation without affecting bioavailability. Extrusion/spheronization is a popular process for producing pellets in the pharmaceutical industry since it's simple to scale up and generates products with a spherical form, limited modal size distribution, good flow qualities, low friability, and homogenous packing features. SE pellets combine the advantages of both SEDDS and pellets in a single product. The SEDDS are entirely adsorbed onto a solid carrier, resulting in a finely flowable powder¹.

The solid self-emulsifying pellets of nitrendipine, a weakly water-soluble medication, were created and analysed by Zhiyuan Wang. The recent findings suggest that SE NTD pellets with 30% liquid SEDDS may be efficiently produced utilising the extrusion/spheronization method. The SE pellets that produced were uniform in size, spherical in shape, and hard enough. The pellets' self-emulsifying properties were also intact. After self-emulsification in water, the droplet size distribution of the SE pellets was nearly equal to that of the liquid SEDDS, and in vitro dissolving performance was comparable for the liquid SEDDS and SE pellets, both of which were significantly larger than typical tablets. When compared to liquid SEDDS, the oral bioavailability of NTD from SE pellets was much greater than that of regular tablets, with no apparent difference. As a consequence, the extrusion spheronization technique may be utilised to generate solid SE pellets from liquid SEDDS, which can aid oral absorption of poorly soluble medicines such as NTD.

Furthermore, the pellet compositions have a big impact on the development of SE pellets. In order to produce high-quality pellets, a compromise is struck between the least amount of MCC and the maximum amount of liquid SEDDS. The preparation procedure as well as the physical



properties of SE pellets will be greatly enhanced by using physical adsorbents to absorb liquid SEDDS before forming pellets. Physical adsorbents' retarding effect on liquid release from pellets, and hence oral absorption efficacy in vivo, should be taken into account²⁸.

Self-Emulsifying Nanoparticles

Self-emulsifying nanoparticles can be efficiently produced by using nanotechnology by using solvent injection method. In this method a mixture of surfactants, lipids and drugs are prepared in to a molten lipid mass. The melted lipid material is then combined with the nonsolvent system. After that, the nano-particles are filtered and dried, resulting in high drug loading efficiency nanoparticles^{1,2,4}.

By combining chitosan and glyceryl monooleate into a new nanoparticle system, W. J Trickler created a drug delivery method for a variety of therapies. The nanoparticles were made using several emulsions (O/W/O) and a solvent evaporation process. The study concluded that the nanoparticles of chitosan and glyceryl monooleate provided a better entrapment efficiency and sustained release characteristics along with remarkable mucoadhesive property, increased cellular association and presumably intercellular internalization, which have advantage of reducing the drug dose and increasing the therapeutic window and then ultimately reducing the adverse effects²⁹.

CONCLUSION

Therapeutic delivery systems that self-emulsify are a viable strategy for the formulation of drug molecules with low water solubility.

SEDDSs, which have been demonstrated to significantly enhance oral bioavailability, may be used to administer hydrophobic drugs orally. SEDDSs will continue to allow fresh applications in drug delivery and tackle challenges related with the delivery of poorly soluble medicines as this technology develops.

SEDDS significantly increased the solubility/dissolution, absorption, and bioavailability of weakly water-soluble medicines, according to several investigations. SSEDDS are better to traditional liquid SEDDS in terms of lowering manufacturing costs, simplifying industrial manufacture, and enhancing stability as well as patient compliance. Most notably, SSEDDS allow for the development of a wide range of solid dosage forms for oral and parenteral administration. Furthermore, GI discomfort may be avoided, and drug release can be regulated and maintained. However, there is still a long way to go before other reliable SE dosage forms hit the market. Because there are several domains of SEDDS that may be further explored, such as human bioavailability studies and in vitro/in vivo correlations. That is, SE implants, suppositories, and microspheres have not been researched as thoroughly as SE tablets, pellets, and capsules. It's also worth mentioning a few difficulties that

need special consideration, such as the physical aging phenomena linked to glycerides, the oxidation of vegetable oil, and drug-excipient interactions.

The most difficult part of producing S SEDDS is deciding which excipients to use. As a result, these elements should constitute SSEDDS' primary future working directions. As a result, important breakthroughs are still necessary for good SEDDS development.

REFERENCES

1. Singh B, Beg S, Khurana R.K, Sandhu P.S, Kaur R, Katara O.P. Recent Advances in Self-Emulsifying Drug Delivery Systems (SEDDS). *Crit Rev Ther Drug Carr Syst* 2014;31(2):121-185. DOI: [10.1615/critrevtherdrugcarriersyst.2014008502](https://doi.org/10.1615/critrevtherdrugcarriersyst.2014008502); PMID: 24940626
2. Karwal R, Garg T, Rath G, Markandeywar T.S. Current Trends in Self-Emulsifying Drug Delivery Systems (SEDDSs) to Enhance the Bioavailability of Poorly Water-Soluble Drugs. *Crit Rev Ther Drug Carr Syst* 2016;33(1):1-39. DOI: [10.1615/CritRevTherDrugCarrierSyst.v33.i1.20](https://doi.org/10.1615/CritRevTherDrugCarrierSyst.v33.i1.20); PMID: 27279337.
3. Dey S, Jha S.K, Malakar J, Gangopadhyay A. Improvement of Bioavailability of Poorly Soluble Drugs through Self Emulsifying Drug Delivery. *J Pharm Sci Technol* 2012; 1(2): 6-11.
4. Kumar A, Sharma S, Kamble R. Self-Emulsifying Drug Delivery System (Sedds): Future Aspects. *Int J Pharm Pharm Sci.* 2010;2(4):7-13.
5. Nirosha M, Badarinath A.V, Hyndavi M, Prasad K, Naveen N, Kumar A.P. Recent advances in self-emulsifying drug delivery system. *Int J Rev Life Sci.* 2011; 1(4):206-214.
6. Rajpoot K, Tekade M, Pandey V, Nagaraja S.H, Sussane R, Tekade R.K. Self-microemulsifying drug-delivery system: ongoing challenges and future ahead. *Drug Deliv* 2020:393-454. DOI: <https://doi.org/10.1016/B978-0-12-814487-9.00009-0>.
7. Padole A, Bodhankar M. Self-Double Emulsifying Drug Delivery System (SDEDDS): a review. *Journal of drug delivery and Therapeutics* 2012;2(6):124-127. DOI: <https://doi.org/10.22270/jddt.v2i6.336>.
8. Bhattacharjee A, Chakraborty A, Mukhopadhyay G. Double Emulsions - a review with emphasis on updated stability enhancement perspective. *World J Pharm Pharm Sci.* 2018;7(6):475-493.
9. Bhattacharjee A, Verma S, Verma P.R.P, Singh S.K, Chakraborty A. Fabrication of liquid and solid self-double emulsifying drug delivery system of atenolol by response surface methodology. *J Drug Deliv Sci Technol.* 2017;41:45-57. DOI: <https://doi.org/10.1016/j.jddst.2017.06.014>
10. Qi X, Wang L, Zhu J, Hu Z, Zhang J. Self-double-emulsifying drug delivery system (SDEDDS): A new way for oral delivery of drugs with high solubility and low permeability. *Int J Pharm.* 2011;409:245–251. DOI: <https://doi.org/10.1016/j.ijpharm.2011.02.047>.
11. Chourasia J.K, Khutle N.M. Self-double emulsifying drug delivery system: a comprehensive review. *World J Pharm Pharm Sci.* 2015;4(5):433-447.



12. Wang Q, Hu C, Quian A, Liu T, Zhang H, Zhang Y. Enhanced oral bioavailability of quercetin by a new non-aqueous self-double-emulsifying drug delivery system. *Eur J Lipid Sci Technol.* 2016;1:34.
13. Pattewar S.V, Kasture S.B, Pande V.V, Sharma S.K. A New Self Microemulsifying Mouth Dissolving Film. *Indian J Pharm Educ Res.* 2013;50(3):191-199.
DOI: 10.5530/ijper.50.3.29.
14. Habib B.A, Amina S, El-Samiae A, Boushra M. El-Houssieny Tag R. Formulation, characterization, optimization, and in-vivo performance of febusostat self-nanoemulsifying system loaded sublingual films. *Drug Deliv.* 2021;28(1):1321–1333. DOI: doi/full/10.1080/10717544.2021.1927247.
15. Talekar S.D, Haware R.V, Dave R.H. Evaluation of self-nanoemulsifying drug delivery systems using multivariate methods to optimize permeability of captopril oral films. *Eur J Pharm Sci.* 2019;130:215-224. DOI: [10.1016/j.ejps.2019.01.039](https://doi.org/10.1016/j.ejps.2019.01.039); PMID: 3071638.
16. Hosny K.M. Development of Saquinavir Mesylate Nanoemulsion-Loaded Transdermal Films: Two-Step Optimization of Permeation Parameters, Characterization, And Ex Vivo And In Vivo Evaluation. *Int J Nanomed.* 2019;14:8589-8601. DOI: <https://doi.org/10.2147/IJN.S230747>.
17. Gupta S, Kesarla R, Omri A. Formulation Strategies to Improve the Bioavailability of Poorly Absorbed Drugs with Special Emphasis on Self-Emulsifying Systems. *ISRN Pharm.* 2013:1-17. DOI: [10.1155/2013/848043](https://doi.org/10.1155/2013/848043); PMID: 24459591.
18. Chae G.S, Lee S.J, Kim S.M, Seo K.U, Kim M.S, Lee B.H. 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. *International Journal of Pharmaceutics* 2005;301:6–14. DOI: <https://doi.org/10.1016/j.ijpharm.2005.03.034>.
19. Tang B, Cheng G, Gu J, Xu C. Development of solid self-emulsifying drug delivery systems: preparation techniques and dosage forms. *Drug Discov.* 2008;13(13/14):606-612. DOI: <https://doi.org/10.1016/j.drudis.2008.04.006>
20. Chivate N, Chivate A, Wadkar K, Shah R. Design and Characterization of Self Emulsifying Drug Delivery System of Herbal Drug Compound. *Int J Pharm Sci.* 2020; 11(6): 2761-2766. DOI: 10.13040/IJPSR.0975-8232.11(6).2761-66
21. Zhang L, Zhang L, Zhang M, Pang Y, Li Z, Zhao A. Self-emulsifying drug delivery system and the applications in herbal drugs. *Drug Deliv.* 2015;22(4):475-86. DOI: [10.3109/10717544.2013.861659](https://doi.org/10.3109/10717544.2013.861659); PMID: 24321014
22. Chouhan N, Mittal V, Kaushik D, Khatkar A, Raina M. Self-Emulsifying Drug Delivery System (SEDDS) for Phytoconstituents: A Review. *Curr Drug Deliv.* 2015;12:1-10. DOI: [10.2174/1567201811666141021142606](https://doi.org/10.2174/1567201811666141021142606); PMID: 25335929
23. Chalikwar S.S, Surana S.J, Goyal S.N, Chaturvedi K.K, Dangre P.V. Solid self-microemulsifying nutraceutical delivery system for hesperidin using quality by design: Assessment of biopharmaceutical attributes and shelf-life. *J Microencapsul.* 2021;38(1):61-79. DOI: <https://doi.org/10.1080/02652048.2020.1851788>
24. Shah A.V, Desai H.H, Thool P, Dalrymple D, Sirajuddin A.T.M. Development of Self-microemulsifying Drug Delivery System for Oral Delivery of Poorly Watersoluble Nutraceuticals. *Drug Dev Ind Pharm.* 2018;44(6):895-90. DOI: [10.1080/03639045.2017.1419365](https://doi.org/10.1080/03639045.2017.1419365); PMID: 29254385
25. You J, Cui F, Han X, Wang Y, Yang L, Yu Y. Study of the preparation of sustained-release microspheres containing zedoary turmeric oil by the emulsion-solvent-diffusion method and evaluation of the self-emulsification and bioavailability of the oil. *Colloids Surf B Biointerfaces.* 2006;48(1):35–41. DOI: [10.1016/j.colsurfb.2005.12.011](https://doi.org/10.1016/j.colsurfb.2005.12.011); PMID: 16480856
26. Wagh M, Singh P.K, Chaudhari C.S, Khairnar D.A. Solid Self-Emulsifying Drug Delivery System: Preparation Techniques and Dosage Forms. *Int J Pharm.* 2014; 5(2): 101-108.
27. Qi X, Qin J, Ma N, Chou X, Wu Z. Solid self-microemulsifying dispersible tablets of celastrol: Formulation development, characterization and bioavailability evaluation. *Int J Pharm* 472 (2014) 40–47. DOI: [10.1016/j.ijpharm.2014.06.019](https://doi.org/10.1016/j.ijpharm.2014.06.019); PMID: 24929011.
28. Wang Z, Sun J, Wang Y, Liu X, Liu Y, Fu Q. Solid self-emulsifying nitrendipine pellets: Preparation and in vitro/in vivo evaluation. *Int J Pharm* 2010;383:1–6. DOI: [10.1016/j.ijpharm.2009.08.014](https://doi.org/10.1016/j.ijpharm.2009.08.014); PMID: 19698771
29. Trickler W.J, Nagvekar A.A, Dash A.K. A Novel Nanoparticle Formulation for Sustained Paclitaxel Delivery. *AAPS Pharm SciTech* 2018;9(2):486-493. DOI: [10.1208/s12249-008-9063-7](https://doi.org/10.1208/s12249-008-9063-7); PMID: 18431660

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