



Comparative Study of SNEDDS and SEDDS for Enhancing Oral Delivery of Vildagliptin

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ABSTRACT

Dipeptidyl peptidase-4 (DPP-4) inhibitors vildagliptin, which is broadly used in the treatment of type 2 diabetes mellitus, not only lacks high aqueous solubility, but also has a low variable oral bioavailability, which creates great difficulties in drug delivery. Self-Emulsifying Drug Delivery Systems (SEDDS) and Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) have been found to be a potential alternative to these shortcomings based on lipid-formulations. The present study offers a complete comparative study of SNEDDS and SEDDS systems in the enhancement of oral administration of vildagliptin. SNEDDS are more superior to conventional SEDDS in terms of surface area they loop over and also have the advantage of superior absorption of drugs as they form small nano-sized droplets in the event that an aqueous dilution occurs (<100 nm). Oils and surfactants and co-surfactants are the key components of the formulation that are optimized to enable the formulation to produce the maximum drug loading, longer stability and effective emulsification. The quality and their performance criteria were determined by droplet size and polydispersity index (PDI) analysis, zeta potential measurement, in vitro dissolution analysis, testing thermodynamic stability as well as morphological/spectroscopic assessment of the formulations. SNEDDS had improved physicochemical stability, dissolution rates, and drug releasing patterns in consistent relation to SEDDS. Nevertheless, issues bearing on drug precipitation on dilution, formulation stability, scalability and mass-manufacturing, economics and regulatory consistency are the greatest problems in commercial-scale application. With these problems still in play, however, significant progress in solid-SNEDDS technologies, excipient innovation, and harmonization of regulatory toolkits are slowly facilitating the transformation of these systems, in the development stage, to commercial products. The research finding is that SNEDDS can provide a superior and solid solution to enhance the oral delivery of vildagliptin with high prospect of clinical practice and commercial use. This study supports the significance of lipid-based nanoformulations in the current pharmaceutical formulations and their use in overcoming the solubility and bioavailability challenges of important therapeutic methods.

Keywords: Vildagliptin, SNEDDS, SEDDS, Oral drug delivery, Bioavailability enhancement, Lipid-based formulations.

INTRODUCTION

Overview of Vildagliptin

Vildagliptin is a highly active orally applied

antidiabetic compound in a class of the dipeptidyl peptidase-4 (DPP-4) inhibitors. It is of great importance in controlling type 2 diabetes mellitus (T2DM), which is a chronic metabolic disease,



it consists of resistance and poor production of the insulin. DPP-4 inhibitors act by inhibiting the degradation of incretin hormones like glucagon-like-peptide-1 and glucose-dependent insulinotropic peptide by enzymatic reactions and thus prolong their action. The outcome of this is an increment of insulin secretion, reduced glucagon release and eventually improved glycemic stability¹. Vildagliptin has favorable pharmacological profile compared with low risks of hypoglycemia and weight gain that are the major complications of other anti-diabetic drugs like sulfonylureas and insulin. Besides, it has proven itself to be effective as a monotherapy, as well as therapy combined with other medications: metformin, sulfonylureas, or thiazolidinediones². Such combinations have been especially useful in producing tighter glycemic control among patients with progressive disease. Nevertheless, among the therapeutic advantages, Vildagliptin has some weaknesses in physicochemical and pharmacokinetic aspects of action. It belongs to the type III Biopharmaceutical Classification System (BCS) which implies high solubility and low permeability through biological membranes³. The property greatly restricts its oral bioavailability and therefore impedes the desired therapeutic plasma concentration upon conventional course of administration. Therefore, significant proportions of the orally given dose are presystemically degraded or discharged without significant changes since they are hardly absorbed in the gastro intestinal (GI) tract. Moreover, Vildagliptin does not have very long biosystem half-life of about 1.5 to 3 hours thereby requiring standard administration at individual intervals. That may threaten patient compliance, especially in elderly persons or people taking numerous drugs⁴. Moreover, it has broad physiological factors affecting its movement that include pH, motility and the presence of food in the stomach which contribute to inconsistent therapeutic responses in the different patients. The drawbacks that come with the pharmacokinetics of Vildagliptin have also given rise to the work of developing better ways of delivery of the drug that can boost its absorption and bioavailability. Out of these, lipid based formulations such as self emulsifying drug delivery systems (SEDDS) and self nanoemulating drug delivery systems (SNEDDS) have become potential solution to address these issues.

Challenges in Oral Delivery

Administration of the drugs orally is the most applicable and convenient route as it is easy, cheap, and the patient complies with oral administration. Nevertheless, oral route is also fraught with a few setbacks especially in the case of drugs with poor physicochemical and pharmacokinetic properties like Vildagliptin. The major obstacles of successful oral drug delivery are degradation by enzymes in the gastro-intestinal tract, low membrane permeability, first-pass hepatic clearance and inconsistency of gastric emptying rate. The low membrane permeability of vildagliptin poses a major challenge in causing a good level of systemic exposure on the drug following an oral administration⁵. Being a hydrophilic molecule, it has poor passage through the lipophilic intestinal epithelium resulting in lowering its transport into the blood. The condition is also compounded by the fact that it is prone to break down in the devastating acidic environment of the stomach as well as in the intestinal lumen by indigestive action. Therefore, a limited amount of administered dosage gets absorbed and large doses are required in order to reach the therapeutic effect⁶. The other major deficiency is that it has poor oral bioavailability, which has been calculated at about 85 percent, none of which however makes it to the target site as it is eliminated very quickly. These quick clearance and short half-life, results into high dosing needs of the drug, normally twice daily. Such repeated administrations also influence not only patient compliance but also heighten the likelihood of varying levels of plasma drug concentrations and a lack of therapeutic efficacy. Interactions with food can also affect the Vildagliptin pharmacokinetics. The absorption of the drug is not greatly affected by food although the inconsistency brought about with varying food compositions can influence solubilization of drugs, GI motility as well as pH and therefore can lead to inter-patient variability. Also, absorption and metabolism may be remiss due to patient-related factors like age, the disease condition, co-medications, and genetic differences resulting into inconsistent pharmacodynamic responses⁷.

The sustained or Controlled release oral formulations also cannot be developed due to poor permeability of Vildagliptin. Due to lack of easy diffusion in biological membranes, any effort to extend release of the drug might not be yielding further to bioavailability or efficacy.

Hence, one of the main goals in developing any formulation that tries to improve the therapeutic outcomes is to increase its membrane transport⁸. With these challenges, the more traditional ways of administration such as tablets and capsules are not perfectly adapted to the administration of Vildagliptin in a manner that guarantees regular appearance in the plasma, prolonged effect, and less frequent dosing. This requires the coming up of the improved oral drug delivery devices which can overcome the permeability problem and provide improved pharmacokinetic efficacy. In this regard, the use of lipid based delivery systems like SEDDS and SNEDDS have a potential to be quite appealing because they increase solubility, promote permeability and avoid first pass metabolism due to lymphatic absorption⁹.

Need for advanced drug delivery systems

Such increasing awareness of pharmacokinetics and biopharmaceutical desirabilities of drugs such as Vildagliptin has expedited the emergence of newer drug delivery modality to focus on improvement in the therapeutic efficacy, patient compliance, and patient outcomes. The general aim of such elaborated systems is to maximize bioavailability of the drug, result in stable plasma drug concentration, minimize the frequency of dose administration and decrease effects of inter-individual variability¹⁰.

Lipid-based drug delivery systems (LBDDS) including SEDDS and SNEDDS have proven to be very strong in this respect. These systems have several advantages compared with conventional formulations, the most notable being on drugs that are poorly membrane permeable or those that are prone to degradation within the GI tract. Their solubilizing characteristics, ability to form minute emulsions in contact with the GI media, and their availability in the lymphatics renders them potential candidate in optimization of the oral delivery of poorly permeable drugs such as Vildagliptin¹¹. The Self-Emulsifying Drug Delivery Systems (SEDDS) are oil-based, isotropic mixtures containing surfactants and/or co-solvents or/and co-surfactant. When diluted within the GI tract, the SEDDS spontaneously emulsify into oil-in-water emulsions that increase the solubilization and absorption of the drug. Nevertheless, typical conventional SEDDS, usually create microemulsions with micrometer droplet size,

which is not best suited in terms of the bioavailability maximization and particularly to drugs that have to be rapidly and extensively absorbed¹².

Self-Nanoemulsifying Drug Delivery systems (SNEDDS) form an advanced type of SEDDS where the drug is usually diluted into a nano-sized emulsion (usually less than 200nm). The reduced droplet size also translates to an increase in the area of absorption, stability to GI conditions and possibly facilitators of better lymphatic uptake. SNEDDS also allow a more rapid drug release, improved dispersion of the drug in the GI tract and, they have less food effect, thus, are more effective to enhance the pharmacokinetics of poorly permeable drugs.

In the case of Vildagliptin, SNEDDS and SEDDS will provide the optimal strategic solution to permeability barrier. These formulations can vastly increase drug uptake, by increasing drug solubilization, and encouraging transcellular transport. Further, some of the SNEDDS/SEDDS surfactants have been demonstrated to momentarily increase tight junction positive or suppress efflux transporters further escalating drug permeability¹³. The properties are very useful in drugs of the BCS Class III such as Vildagliptin where permeability gathers a slow pace in vivo.

Also use of Vildagliptin in lipid based systems has a potential advantage in targeted delivery particularly in the lymphatic system thus avoiding hepatic first pass effect. Unlike many other drugs, Vildagliptin is not massively metabolized by the liver, which means that it may help to face the metabolic variability and achieve better switchability of the drug. Also, these systems could be designed as controlled release which could keep the concentration of plasma in the therapeutic scale longer and thus leads to lesser dosing periods possibly¹⁴.

Lipid-Based Drug Delivery Systems (LBDDS)

Lipid-based drug delivery systems (LBDDS) is one versatile and most studied form of the advanced formulation technology that has been established to augment the oral absorption of the poorly absorbed drugs via increasing their oral bioavailability. These systems incorporate the concepts of lipids, surfactants, and co-solvents to solubilize the hydrophobic compound, enhance

drug absorption, and also enhance pharmacokinetic properties. Considerable importance of LBDDS has been sensed in the field of the pharmaceutical sciences, especially concerning the molecules that are associated with low solubility, poor permeability, high first-pass metabolism, or gastrointestinal instability. LBDDS development has been a game changer in the oral DD practice, as it exploits the body natural ways of breaking down lipids and distribution of lipid-derived materials. They are flexible, compatible with many types of drugs and can be scaled up, thus make a strategic platform of improving the effect of many therapeutic agents such as Vildagliptin. The subsequent subsections discuss the classification, mechanisms, and implications of LBDDS when put into perspective of establishing biopharmaceutical challenges¹⁵.

Classification and Overview

LBDDS offer a wide variety of formulations with each one maximizing the solubilization, protection and absorption of drugs. Such systems can be sorted according to composition, physical form (liquid or solid) and what they do as they are dispersed into fluid systems in the gastrointestinal tract. Lipids used are emulsions, self-emulsifying systems, liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs) and lipidic prodrugs.

Microemulsions and Emulsions:

Emulsions are biphasic systems which is composed of oil and water, which are stabilized with the help of surfactants. They may be oil-in-water (O/W) or water-in-oil (W/O) whether the continuous phase is oil or water.

Microemulsions microemulsions are very stable with nanometre (10-100nm) droplet sizes, and are thermodynamically stable, transparent. The systems make drugs more soluble and they can be absorbed more rapidly¹⁶.

Self-Emulsifying Drug Delivery Systems

(SEDDS): SEDDS are oils, surfactants and co-surfactants or co-solvents that form isotropic mixtures. These systems also make emulsions or microemulsions upon gentle shaking of the gastrointestinal tract. SEDDS are specifically appropriate in increasing the solubility of lipophilic drugs.

Self-Nano Emulsified Drug Delivery Systems (SNEDDS): The high-tech subcategory of SEDDSs is SNEDDS, which are SEDDS that spontaneously form fine nanoemulsions (droplet size <200 nm) when diluted. These deliveries are more stable, and provide greater absorption that is thanks to growth in surface area and contact with the GI mucosa that is improved.

Liposomes: Liposomes are multilayer vesicles that are constituted by phospholipids where they have the ability to encapsulate both hydrophilic and lipophilic drugs. They are more effective in terms of improving the stability of drugs and they offer sustained drug release although they are not so widely used in oral administration because of its stability issues.

The Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs):

SLNs and NLCs are solid-state LBDDS in which physiological lipids are solid at body temperature. They are non-toxic, stable and provide controlled release and degradation resistant. NLCs are of imperfect crystalline structure, and they give greater drug loading and improved release profiles¹⁷.

Lipid-Drug Conjugates and Prodrugs:

They are drug molecules which have been chemically modified such that a lipid moiety is coupled to the drug molecule in a covalently bound way to increase lipophilicity, lymphatic (membrane) absorption and permeability.

These systems possess each their own benefits depending on the physicochemical properties of a drug, targeted release profile and target therapeutic. Whether LBDDS is chosen or not depends on the formulation objective: it is to improve solubility, permeability, enzyme protection, hepatic avoidance, etc.

Mechanism of Enhancing Bioavailability

LBDDS primarily aim to surmount obstacles impeding effective oral drug absorption. These systems function via multiple mechanisms that collectively improve drug solubilization, stability, and systemic availability, including.

Enhanced solubilization: Numerous pharmaceuticals, particularly lipophilic or poorly

water-soluble compounds, exhibit unpredictable or insufficient dissolution in gastrointestinal fluids. LBDDS sustain the drug in a solubilized state throughout its gastrointestinal transit. This is essential as absorption necessitates the drug to be in solution. The oils and surfactants incorporated in LBDDS generate a micro- or nano-dispersed system that facilitates dissolution and expands the effective absorption surface area¹⁸.

Protection from degradation: LBDDS shield pharmaceutical compounds from enzymatic degradation and harsh pH environments encountered in the stomach and intestines. The encapsulation within lipid matrices inhibits direct exposure to gastrointestinal enzymes and acidic conditions, thereby preserving the drug's structural integrity and prolonging its half-life.

Enhanced Permeability: Selected surfactants in LBDDS, including polysorbates and PEGylated compounds, improve permeability through modifying membrane fluidity, compromising tight junction integrity, or suppressing efflux transporters such as P-gp. These mechanisms promote increased paracellular and transcellular transport of drugs across intestinal epithelial barriers¹⁹.

Lymphatic Pathway Utilization: LBDDS enable drug-containing lipids to access the intestinal lymphatic system through chylomicron production. This route circumvents initial hepatic metabolism, thereby allowing a greater proportion of active drug to reach systemic circulation. This mechanism proves particularly valuable for compounds with significant hepatic extraction ratios or poor oral bioavailability resulting from first-pass metabolism.

Enhanced Mucosal Retention: Certain LBDDS formulations exhibit mucoadhesive characteristics that extend the drug's contact duration at absorption sites. This localized concentration gradient facilitates improved absorption rate and extent²⁰.

Prolonged Release Capabilities: Lipid-based matrices can be designed to provide gradual and regulated drug release, resulting in extended plasma concentrations and decreased administration frequency. This characteristic is particularly beneficial for short half-life medications such as Vildagliptin.

Gastrointestinal Environment Alteration: LBDDS can influence GI conditions including pH and motility, further optimizing drug absorption processes. Specific lipid components may stimulate bile release, which enhances the solubilization of lipophilic substances²¹.

Self-Emulsifying Drug Delivery Systems (SEDSS) Definition and Composition

Self-emulsifying drug delivery systems (SEDSS) represent lipid-based formulations engineered to improve solubility and oral bioavailability of drugs with poor water solubility. These isotropic mixtures consist of three essential components: oils, surfactants, and co-surfactants or co-solvents. When exposed to aqueous fluids in the gastrointestinal (GI) tract under gentle agitation, SEDSS spontaneously generate fine oil-in-water emulsions. The emulsified droplets enhance the surface area available for drug absorption, thereby promoting transport across intestinal mucosa.

The oil component typically comprises medium-chain triglycerides (MCTs) or long-chain triglycerides (LCTs) such as caprylic/capric triglycerides, oleic acid, or ethyl oleate, which function as solubilizing agents and facilitate lymphatic drug uptake. Surfactants including polysorbates (e.g., Tween 80), cremophor RH40, or labrasol serve to decrease interfacial tension and stabilize emulsion droplets upon dispersion. These surfactants must exhibit a high hydrophilic-lipophilic balance (HLB) to enable spontaneous emulsification within the aqueous gut environment. Co-surfactants or co-solvents such as propylene glycol, polyethylene glycol, or Transcutol further contribute to reducing interfacial tension and enhancing the self-emulsification process²².

Meticulous selection and optimization of these constituents based on drug solubility, emulsification efficiency, and droplet size are essential for effective SEDSS development. These formulations may incorporate antioxidants and additional excipients to stabilize the preparation and safeguard sensitive drugs against degradation. SEDSS can be produced in liquid or solid forms, with solid SEDSS (S-SEDSS) providing enhanced stability, handling convenience, and improved patient adherence.

Mechanism of Action

SEDDS' efficacy in enhancing oral drug delivery primarily stems from their capacity to enhance drug solubilization and promote absorption through spontaneous emulsification. When orally administered, SEDDS interact with the stomach or intestine's aqueous environment, where physiological fluids and gentle peristaltic actions enable the isotropic lipid mixture to self-emulsify into fine oil-in-water emulsions. This self-emulsification occurs spontaneously without external energy input such as heat or mechanical force, which differentiates SEDDS from traditional emulsions²³.

The resultant emulsion droplets substantially expand the available surface area for drug diffusion. As the drug is already dissolved within oil droplets, it maintains its dissolved state throughout gastrointestinal transit, thus avoiding the dissolution phase that typically restricts poorly water-soluble drugs' absorption. This improved solubilization ensures the drug remains bioavailable during its critical absorption window in the upper small intestine²⁴.

Beyond solubility enhancement, SEDDS can influence intestinal permeability. The formulation's surfactants may disrupt epithelial cell lipid bilayers or temporarily open tight junctions, thereby enhancing transcellular and paracellular transport. Certain surfactants also suppress efflux transporters like P-gp, which would otherwise restrict drug absorption by returning them to the intestinal lumen²⁵.

Additionally, SEDDS' lipid components stimulate bile secretion, supporting micelle formation and potentially aiding in further solubilization and absorption of lipophilic drugs. In specific instances, particularly with long-chain lipids, the emulsified drug may be absorbed through the intestinal lymphatic system, circumventing hepatic first-pass metabolism and increasing systemic availability. This comprehensive mechanism renders SEDDS particularly beneficial for improving bioavailability of drugs such as Vildagliptin, which are constrained by poor permeability and presystemic loss.

Advantages and Limitations

SEDDS present numerous significant advantages for oral drug delivery, particularly for substances with limited water solubility and/or

permeability. A principal benefit involves enhanced oral bioavailability. Through maintaining the pharmaceutical agent in a solubilized condition within minute emulsion droplets, SEDDS enhance the concentration gradient across intestinal membranes, thus promoting passive diffusion and absorption. This improved bioavailability potentially reduces dosing frequency, decreases variability between patients, and enhances therapeutic efficacy²⁶.

An additional significant advantage lies in their capacity to circumvent hepatic first-pass metabolism through lymphatic transport when appropriate lipids are utilized. This enhances systemic drug exposure, particularly beneficial for substances undergoing extensive presystemic degradation. Moreover, SEDDS can shield against chemical and enzymatic degradation within the GI tract, thus improving drug stability. Their formulation simplicity using commercially accessible excipients and scalable processes further enhances their appeal. From a patient-oriented perspective, SEDDS are typically administered as soft gelatin capsules or liquid-filled hard capsules, offering convenience and enhancing adherence. Furthermore, the recent advancement of solid SEDDS in powder or tablet form has created new opportunities for improving formulation physical stability and enabling controlled release characteristics. Despite their numerous benefits, SEDDS exhibit certain limitations. A significant challenge involves restricted drug loading capacity, particularly for highly lipophilic substances, due to solubility constraints in the lipid phase. Drug precipitation upon aqueous dilution or during gastrointestinal transit represents another concern, potentially negating solubilization benefits. This becomes particularly problematic when the drug becomes supersaturated following self-emulsification, resulting in thermodynamic instability²⁷.

Applications in Vildagliptin Delivery

Vildagliptin, a DPP-4 inhibitor, demonstrates positive therapeutic outcomes in type 2 diabetes mellitus treatment; nonetheless, its limited permeability and brief half-life compromise its oral bioavailability and consistent therapeutic effect. Traditional oral Vildagliptin formulations potentially result in inadequate plasma levels and require frequent administration, potentially diminishing patient compliance. These constraints

render Vildagliptin particularly suitable for SEDDS formulation to optimize oral absorption and therapeutic effectiveness.

Research indicates that SEDDS substantially improves Vildagliptin's absorption characteristics. Following ingestion, SEDDS formulations dissolve Vildagliptin within minute emulsion droplets, maintaining its dissolved state throughout gastrointestinal transit. This circumvents the dissolution phase, frequently a limiting factor in absorption kinetics. Additionally, SEDDS surfactants enhance membrane permeability and suppress efflux transporters, thereby augmenting drug absorption magnitude²⁸.

SEDDS implementation also enables swift and more uniform action onset for Vildagliptin, essential for controlling postprandial glucose levels. By sustaining consistent plasma concentrations, SEDDS formulations may reduce glycemic fluctuations and improve therapeutic reliability. Moreover, incorporating bioenhancers or permeability facilitators within SEDDS can further enhance Vildagliptin delivery across intestinal barriers²⁹.

Preclinical and laboratory investigations of Vildagliptin-incorporated SEDDS reveal marked enhancements in pharmacokinetic indices including C_{max}, T_{max}, and AUC, which indicate improved systemic availability and extended activity. These advancements may permit dosage reduction while preserving efficacy, thereby minimizing adverse reactions and enhancing safety profiles³⁰.

Self-Nanoemulsifying Drug Delivery Systems (SNEDDS)

Definition and Composition

Self-nanoemulsifying drug delivery systems (SNEDDS) can be considered a subgroup of self-emulsifying formulations that readily produce nanoemulsions of fine size with oil droplet size range between 50 nm and 1 μm as the drug delivery system known to spontaneously form fine oil-in-water nanoemulsions upon contact with gastrointestinal fluids when mellowly vigorously shaken. Generally, SNEDDS has droplet size of below 200 nanometers and offers an effective, reproducible drug delivery of lipophilic and poorly permeable drugs. Due to their nano-sized dimensions, the droplets provide much more surface area where drugs can be

absorbed and therefore show increased oral bioavailability. SNEDDS preparations are isotropic emulsions containing three basic ingredients: co-surfactants or co-solvents, surfactants, and lipidic oils³¹. They are solvents of drugs, and as such, are typically medium-chain or long-chain triglycerides (e.g. Capryol, Labrafac or oleic-acid derivatives) and may also transport drugs in the lymph. Cremophor EL, Tween 80, and Labrasol are examples of surfactants, which lower interfacial tension and enable nanoemulsions to spontaneously form when aqueously diluted. Stabilization of small droplets involves the choice of high HLB (hydrophilic-lipophilic balance) surfactants. Co-surfactants or co-solvents (e.g. Transcutol, PEG 400, propylene glycol) increase the plasticity of the system, and efficiency of emulsification and drug solubilization. Formulation optimization is carried out with a keen selection of the type and strength of oils and surfactants, in the drug solubilising ability, emulsifying power, and compatibility. Phase diagrams can be employed to determine appropriate oil/surfactant/co-surfactant ratios to make stable nanoemulsions. SNEDDS can be formulated into liquid filled capsules or solid-SNEDDS (S-SNEDDS) by adsorption, spray-drying, or freeze-drying, to facilitate stability and acceptability to the patient, depending upon the physicochemical characteristics of a drug³².

Mechanism of Action

The main principle the SNEDDS has led to its success is that they form nanoemulsions spontaneously when saturated in the gastrointestinal region, raising the solubility, rate of dissolution, and permeation of the drug greatly. On oral administration, and in contact with the aqueous GI fluids, the SNEDDS become rapidly and easily emulsified because of peristaltic action³³. The co-surfactants, surfactants and so on minimize the surface tension, which has the impact of forming nanosize oil drops that homogeneously distribute the drug forms.

The nanoemulsion droplets, which have a very large surface area due to their most common falling within the range of 100-200nm, allows fast diffusion and drug absorption across the intestinal mucosa. This plays an important role in drugs that have poor water solubility and poor permeability since they are kept in an aqueous form during their passage at the GI tract thus avoiding drug

precipitation and maximizing drug absorption. Moreover, it is possible to surmise that the use of surfactants in SNEDDS can have certain permeation-enhancing effects through altering the fluidity of the intestinal membranes and temporarily disrupting tight junctions. This enhances the transcellular as well as paracellular pathway of transport. Besides, due to their ability to suppress the efflux transporters such as P-glycoprotein (P-gp), surfactants can enhance net absorption by hindering the back-efflux of the drug³⁴.

Applications in Vildagliptin Delivery

An example of a drug that has issues out of formulation due to poor permeability and a relatively short half-life, as characteristics of a BCS Class III compound, is the DPP-4 inhibitor vildagliptin used in treatment of type 2 diabetes mellitus. Despite its solubility in water, there can be limited absorption due to inefficient penetration in the cell membranes and unpredictable pharmacokinetics, which make its therapeutic consistency unreliable. Such issues qualify it to be a good candidate of SNEDDS-based oral delivery strategies³⁵. A number of them in the recent past have proved that SNEDDS has a better effect than the standard formulations in improving the oral bioavailability of Vildagliptin. The GI tract supports a high and efficient absorption of dissolved drugs because of the spontaneous occurrence of nanoemulsions. Large surface area SNEDDS droplets interacts better with intestinal epithelium and the surfactants increase the permeation by loosening the connections between cells, tight junctions or altering the effect of transport proteins. Such is especially essential in the case of Vildagliptin, otherwise subject to the sparse passive permeation³⁶.

On top of this, SNEDDS can keep Vildagliptin in a form that is solubilized to reduce the potential of precipitation, as well as to minimize variability in the uptake. SNEDDS commonly include one or more of the surfactants, including Labrasol and Cremophor EL, which are efficacious modulators of paracellular transport and enhancers of uptake. Also, the lipid excipients can promote secretion of bile and provide micellar solubilization of drug, which enhances its permeability as well.

In pharmacokinetic studies, SNEDDS compounds of Vildagliptin have demonstrated a

marked enhancement of the C_{max} and the AUC (dictating improved systemic exposure). The reduced T_{max} with SNEDDS means faster onset of action, which is an attractive property in drugs such as Vildagliptin that seeks to regulate postprandial blood sugar surges. Such an improvement in pharmacokinetics can enable the medication to be dosed less frequently and can enhance patient compliance as well as reduce adverse effects³⁷.

The other significant advantage of SNEDDS in the Vildagliptin delivery is the co-formulation with other type of diabetes medication, including metformin or pioglitazone, into a fixed dose combination. SNEDDS has the advantage of solubilizing and delivering more than one drug at a time and so provides synergistic glycemic benefits in addition to the ease of medication dose delivery to the patient by reducing treatment regimens. More so, formulation of solid SNEDDS (S-SNEDDS) of Vildagliptin is coming up as a new area of interest. The solid formulas provide enhanced stability, less probability of leakage, and convenience of production techniques such as spray drying, melt granulation, or adsorption on porous carriers. S-SNEDDS offer the chance to include the Vildagliptin in tablets or fast-dissolving powders, widening the use of delivery systems area and an augmentation in the accessibility of patients³⁸.

The clinical utility of Vildagliptin-SNEDDS does not just lie in the improvement of the pharmacokinetics. SNEDDS can help to reduce dosage by increasing bioavailability, which helps to decrease the side effects on the body and the economic burden on the patient. The lesser consistency in uptake also equates to better forecastability in glucose regulations, better management of the disease in the long-term.

Comparative Evaluation of SNEDDS and SEDDS

Advanced lipid-based formulations such as SEDDS (Self-Emulsifying Drug Delivery Systems) and SNEDDS (Self-Nanoemulsifying Drug Delivery Systems) are required when it comes to a poor soluble drug delivery, like Vildagliptin, through oral route. Despite the similarities in the principles of spontaneous emulsification that apply in two systems, there are significant differences in physicochemical properties and performance of the two systems. In the next section, comparative critical

analysis of SNEDDS versus SEDDS along with important parameters of formulation is presented³⁹.

Surface area and particle size

Particle size is another characteristic of SNEDDS to a greater extent differentiating it with SEDDS. The typical size of the droplet of SEDDS formed by aqueous dispersion is 100-250 nm compared to SNEDDS that form smaller nanoemulsions of less than 100 nm dot size usually between 20-80 nm. The large surface area that is created because of the great reduction in droplet size in SNEDDS leads to very fast dissolution, and enhanced absorption of the drug in gastrointestinal works⁴⁰.

This surface area gives it the ability to interact with more drug with the biological membranes especially intestinal epithelium. In the case of poorly water-soluble and highly permeable medicines like Vildagliptin, this property is crucial in ensuring the maximization of absorption. There is also improved droplet size uniformity provided by SNEDDS, which can be measured by reduced polydispersity index (PDI), resulting in more reproducible and predictable *in vivo* performance. Contrastingly, SEDDS formulation can exhibit relatively wider size ranges and the possibility of coalescence or aggregation over the course of time resulting in variable bioavailability. Therefore, physicochemically, there is a greater platform in SNEDDS in terms of particle size and effective interfacial area which is vital in improving oral bioavailability of any drug⁴¹.

Time of Emulsification and Emulsification Stability

A time required to achieve the emulsification process is the parameter that defines how fast a lipid-based formulation is converted to fine dispersion when in association with gastrointestinal fluids. The combination of the ideal proportion of surfactants and cosurfactants and also the smaller droplet attained during self emulsification reflects SNEDDS generally have a higher rate of emulsification usually in less than 30 seconds⁴². On the other hand, SEDDS can take 112 full minutes to form a stable emulsion, subject to composition of formulation of SEDDS.

The other point that SNEDDS are more effective than SEDDS is stability. SNEDDS

nanoemulsions have improved thermodynamic and kinetic stability. they Cream less, settle less, and do not do Ostwald ripening, which can interfere with the quality of traditional emulsions. The nano-sized droplets provide a better dispersion and avoid the phase separation at gastrointestinal conditions. Besides, SNEDDS formulations are less likely to melt when stored, and there is less of a chance that the drug will precipitate during shelf-life or post-administration.

Solubilization power of drug

Oral bioavailability depends crucially on being able to keep the drug in a solubilized state while in its formulated state and when dispersed in the gastrointestinal fluids. Both SNEDDS and SEDDS are used to avoid precipitation of drugs, particularly with the lipophilic molecules such as Vildagliptin. Nevertheless, SNEDDS are characterized with better drug solubilization capacity since they incorporate more effective solubilizing agents, which may be a mix of medium chain-triglycerides, high HLB surfactants and co-solvent⁴³.

SNEDDS is also formulated in such a way that there is a better control over the drug loading capacity without inducing the physical stability of the system. The reduced size droplet gives a greater interfacial space in which to solubilize the drug and keeps the drug in a molecularly dispersed form throughout the GI passage. Also, SNEDDS have a tendency to mitigate the danger of supersaturation and recrystallization by creating a stable colloidal dispersion, and this can be astute in circumstances of having drugs that are low in solubility in water.

Relative to this, SEDDS might necessitate greater amounts of the surfactants in order to have comparable solubilization levels, and this is again a factor that can cause irritation of the GI tract as well as instability of the lipid emulsion during the diluting process. Moreover, having a larger size of droplets, SEDDS might experience the phase separation or the drug deposition, particularly in case of using the bile salts or the digestive enzymes. SNEDDS thus can be more advantageous to keep Vildagliptin in its solubilized and absorbable state within absorption window⁴⁴.

In vitro and *In vivo* Drug Release

In vitro and *in vivo* release of the drug

behavior is a paramount parameter in establishing the performance of lipid-based delivery systems. SNEDDS tend to have more rapid and complete drug release profiles *in vitro*, which is explained by their smaller droplet sizes, high emulsification rates and large interfacial area with the dissolution medium. When SNEDDS is obtained as a nanoemulsion, its droplets catalyze the Vildagliptin delivery into the aqueous phase and, therefore, accelerate the delivery so that the therapeutic effect begins taking place more rapidly⁴⁵.

Conversely, SEDDS exhibit a comparatively slower release of drug since their emulsion droplets require relatively longer interaction time with the aqueous phase before solubilizing the drug contained in them. This may cause incomplete dissolution, especially in case of gastric motor block or fed-state states. Also, *in vivo* experiments have indicated that SNEDDS gives more uniform plasma concentration times, minimizing differences in absorption (between physiologists) depending on the GI pH, or enzyme activity⁴⁶.

Increases in lymphatic uptake, which evades the first-pass metabolism in the liver, confirms better *in vivo* performance of SNEDDS as well, further improving the amount of the drug available in the body. Because vildagliptin is generally hydrophilic, the SNEDDS formulations have been shown to provide better mucosal permeation than SEDDS, and results in higher and faster plasma levels many times than when formulated as SEDDS formulations. Thus, with a view of having an efficient and reproducible drug release both *in vitro* and *in vivo*, SNEDDS have proved promising to be superior to conventional SEDDS formulations⁴⁷.

Pharmacokinetics (C_{max}, T_{max}, AUC)

Direct indicators of bioavailability and therapeutic effectiveness are pharmacokinetic parameters like the maximum plasma concentration (C_{max}), the time to reach the C_{max} (T_{max}) and area under the plasma concentration-time-curve (AUC). When compared with SEDDS, SNEDDS to Vildagliptin has shown a lot of variation being suitable in these parameters. The formulations of SNEDDS always make higher C_{max} values signifying that the level of absorption of drugs was increased. To a significant extent, this is explained not only by a faster emulsification but also due to

the rapid release of the drug that allows achieving more effective uptake in the GI mucosa. Also T_{max} is tended to be smaller in SNEDDS which indicates quicker onset of activity. The presence of the drug with quick availability in the blood contributes to an early pharmacological response and also, significant to control postprandial glucose surge in diabetic patients⁴⁸⁻⁵⁰.

Another key parameter, which indicates the total systemic exposure to the drug, is AUC, which is also vastly greater in SNEDDS than in SEDDS. This proves the increased bioavailability due to nano sized emulsions. The constant and extended absorptive outcome of SNEDDS formulations serves to ensure that the therapeutic level is maintained in terms of reducing fluctuation and therefore improving glycemic control in the management of diabetes⁵¹.

On the other hand SEDDS have shorter and variably lower pharmacokinetic behaviour, especially when they are exposed to variable GI conditions. The causes of lower C_{max} and AUC may be the delayed emulsification, unrecovered solubilization of a drug and even precipitation. Further, the higher T_{max} values associated with SEDDS indicate slower absorption and hence the onset of therapeutic effect of Vildagliptin might be delayed.

Therefore, SNEDDS can be seen as performing significantly better than the SEDDS in a pharmacokinetic sense, and could be used as an effective approach towards enhancing the oral delivery of Vildagliptin⁵²⁻⁵⁴.

Role of Excipients in Formulation Development

The use of excipients is the foundation of any lipid-based drug delivery system such as SNEDDS (Self-Nanoemulsifying Drug Delivery System), SEDDS (Self-Emulsifying Drug Delivery System) and so on. As opposed to conventional dosage forms in which the excipients may perform a passive role, excipients in self-emulsifying systems are especially important as they are the active constituents that define key formulation properties like emulsification completeness, and droplet size, stability and, ultimately, drug bioavailability⁵⁵. The combination and ratio of oils, surfactants and co-surfactants has a direct impact on the capability of the system to solubilize the drug, to make stable nano or microemulsions and to retain the

formulation stability under physiological conditions. In the case of a therapeutic agent which poses problems with respect to solubility and permeability (the case with Vildagliptin), the intelligent choice and optimization of the excipients is essential in ensuring the development of an effective and reliable oral formulation. It will be discussed here the excipient selection criteria, how they influence the physical properties, such as droplet size and stability and how they control the behavior of the drug release⁵⁶.

Selection Criteria for Oils, Surfactants, and Co-surfactants

The choice of the right oils, surfactants, and co-surfactants is the pillar to the creation of an effective SNEDDS or SEDDS formulation. The main selection criteria are solubility of the drugs, capacity of emulsification, compatibility with other components in formulation, biocompatibility, regulatory aspects and their effects on drug absorption. There are long-chain triglycerides (LCT) and medium-chain triglycerides (MCT) that would be applied to oils. The MCTs are more preferred mainly because they have greater solubilizing ability, quicker digestion, and lymphatic transport. Oils like capryol 90, labrafac lipophilic wl 1349, oleic acid are commonly screened on the basis of the capacity to dissolve the highest amount of the active pharmaceutical ingredient (API) in them without any subsequent formation of precipitate upon dilution⁵⁷. The oil part can also help to control the velocity of the emulsification and creating minute drops. The key role of the use of surfactants is to reduce the interfacial tension between the oil phase and aqueous phase, which allows the spontaneous emulsification. To obtain emulsions of nanometer levels, high HLB (Hydrophilic-Lipophilic Balance) surfactant like Tween 80 (Polysorbate-80), Cremophor EL, and Labrasol are normally used. The selection is based on their emulsifying capacity, safety, and toxicity issues. The surfactants are also not supposed to be irritating to the human body, and they should be able to be consumed in the long term. Their concentration is specially optimized so that it would be effective in emulsification but tolerable in the gastrointestinal tract⁵⁸.

Co-surfactants, or co-solvents, increase the flexibility of the film at the interface and also help in making a stable emulsion. Transcutol P (diethylene glycol monoethyl ether), PEG 400 and

propylene glycol are some common co-surfactants. The latter aid in lowering the concentration of the surfactant without losing nanoemulsion properties. They enhance drug loading, solubilization and dispersion properties also. The choice depends on their miscibility with oil and surfactant phases and the effect they may have on severe beauty and viscosity. Eventually, a pseudo-ternary phase diagram is usually drawn based on different mixes of oils, surfactants and co-surfactants to determine optimum zones in which formation of nanoemulsions can be accomplished. In medicines such as Vildagliptin, the screenings and tests of compatibility of the excipients at every stage make sure that the compounds that are selected encourage high solubility and high rate of emulsification of the drugs with minimum losses due to leaks and degrading effects of the drugs during the storage or administration⁵⁹.

Impact on Droplet Size and Stability

The size of the droplet that the emulsion forms when being diluted is a prime factor in determining how well the formulation will perform, which in turn will affect how fast the drug can be dissolved and then absorbed. The excipient choice and the ratio have far reaching effects on the droplet size, polydispersity index (PDI) and stability of the emulsions. Proper length of fatty acid chains on oils has an effect on the viscosity and interfacial tension of the oil, which in-turn, influences the size of the oil in the droplets. Medium-chain oils, especially Caprylic/Capric triglyceride, tend to have a smaller droplet size than long-chain oils due to the better dispersion and lower viscosities⁶⁰.

Probably the highest factors that contribute to the size of the droplet are the type of the surfactant and concentration. In appropriate concentrations, high HLB surfactants cause the reduction in interfacial energy between the oil and water phases leading to the spontaneous formation of nano-sized water droplets. As an example, a high concentration of Tween 80 can result in droplet sizes of less than 50 nm, which is a property commonly associated with Tween 80. Nevertheless, the use of excessively high amounts of surfactants will result in a phase inversion, make the system more viscous, or cause irritation when oral usage is employed. This is why a good balance is essential⁶¹.

It is also significant how co-surfactants are

used to control droplet size. Co-surfactants break the close packing of the surfactant molecules at the interface making the interfacial film to be more mobile and fluid-like and hence enable the production of finer and more stable droplets. Transcutol P has been reported to reduce the size of the droplet tremendously in the presence of the right type of surfactants. In addition, secondary surfactants augment the dispersion behavior as they reduce the interfacial tension even more⁶².

Regarding stability, the homogeneity of the droplet size is associated with physical stability and a PDI value as low as possible (usually <0.3). SNEDDS with the right optimization can have a high stability time frame without phase separation, precipitation, and coalescence. The equilibria of oil and surfactant ratios, thermodynamic compatibility as well as molecular interaction between excipients and the drug help to measure the strength of the formulation. The stability is generally assessed after subjecting it to various stress tests such as centrifugation, freeze-thawing tests and prolonged storage at different temperatures⁶³.

Effect on Drug Release

The release of the drug in the SNEDDS or SEDDS formulations is directly related to the characteristics of the excipients that are involved. Oils act as the source of lipophilic drug and determine drug diffusion in the aqueous layer on emulsification. The relatively low viscosity and fast dispersion ability help to quickly partition the drug into the aqueous space making the rate of drug release much faster using MCTs. This is especially assistive in the case of drugs such as Vildagliptin needing speedy appearance activities to control postprandial glucose.

The fine droplets do form due to the presence of surfactants and these tiny droplets augment the surface area by magnitudes in order to release the drug. In turn, the drug which is in molecular dispersion in the oil phase will be released when the droplets dissolve in the gastrointestinal liquids. HLB of high levels such as Cremophor EL facilitates effective wetting and dissolving of the droplets and further favours diffusion of the drugs through the GI barrier. In addition to this, it was suggested that surfactants also have the ability to regulate the membrane permeability by affecting the

intestinal transporters or tight junctions which may also increase the systemic absorption of the drug⁶⁴.

The presence of co-surfactants, however, enhances the rate of emulsification and the extent of emulsification in such a way that during release, the whole dose of the drug becomes easily released without precipitating. Co-surfactants counter this effect allowing it to keep the drug in a supersaturated but without crystallizing or becoming phase by phase separated during their transit in the gastrointestinal tract. This enhances the likelihood of its absorption prior to precipitation brought about thus maximizing the bioavailability⁶⁵.

Notably, the excipients also affect the route of digestion of the formulation. Lipases are then able to react with the triglycerides present in the oil phase to create monoglycerides and free fatty acids. The products of such digestions help to create mixed micelles together with the bile salts, which serve a critical role in the solubilization and transportation of poorly soluble pharmaceuticals through the unstirred water pellet all the way to the location of absorption. Some surfactants and oils alleviate it in a better way, thus the ameliorated lymphatic intake and the evasion of liver-first-still metabolism. This causes an increased proportion of the drug to get to the systemic circulation thus enhancing therapeutic outcomes.

To sum up, the interaction of excipients and the drug will define the release kinetics, comprising the rate of emulsification, dissolution of the droplets, and the partition of the drug to the biological milieu. When selecting the excipient to be used, exerting an influence on the desired pharmacokinetic profile e.g. with drugs that need a specific plasma concentration to achieve their effect well, the excipients become an important determining factor⁶⁶.

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Characterization Techniques

Effective development of lipid based drug delivery systems such as SNEDDS (Self-Nanoemulsifying Drug Delivery Systems) and SEDDS (Self-Emulsifying Drug Delivery Systems) necessitate the effective characterization to analyze its physicochemical characteristics, stability, and

drug release profile. Such assessments guarantee the completeness of reproducibility, efficiency, and effectiveness of improving oral bioavailability of poor water-soluble drugs like vildagliptin. The most important parameters of characterization are droplet size and polydispersity index (PDI), zeta-potential, in vitro dissolution, thermodynamic stability, and morphological and spectroscopic properties.

Droplet Size and Polydispersity Index (PDI)

One of the most important parameters which determines the overall bioavailability of a given drug solubilized within an emulsion of SNEDDS or SEDDS, includes the size of a droplet that forms upon dilution with gastrointestinal juice. SNEDDS are prepared in such a manner that they form nanoemulsions with a droplet size typically lower than 100 nm, whereas SEDDS result in formations of emulsions with larger droplet sizes (100-250 nm). The measurement of droplet size is generally performed by dynamic light scattering (DLS) or photon correlation spectroscopy (PCS)⁶⁹.

The polydispersity index (PDI) gives us the dispersion of the droplet size distribution in the emulsion. A larger PDI, however, indicates polydispersity and possible instability owing to coalescence or aggregation of droplets. SNEDDS formulations which contain vildagliptin have been reported to possess smaller mean droplet size (20-50 nm) and low PDI (<0.2) as compared to SEDDS, which have a relatively larger mean droplet size and PDI. Such parameters are required in predicting the kinetics of absorption of the drug and in the capacity of the system to withstand a state of precipitation in the course of gastrointestinal passage.

In addition, the smaller the size of the droplets is, the higher the area on which drugs can be released onto the surface and expose to the mucus-lined surfaces can be achieved, which will help to achieve rapid and effective drug absorption. Therefore, the size of a drop and its PDI is the starting point to illustrating the quality and/or the possible effectiveness of the lipid-based delivery system of vildagliptin.

Zeta Potential

Zeta potential is a double layer potential at dispersed piece elongation interface with the dispersed phase in emulsion system. It gives

information on emulsion stability i.e. magnitude of repulsion or attraction between charged particles by electrostatic forces. Generally, any formulation where the value of zeta potential is high whether it is positive or negative (generally, above ± 30 mV) is regarded as being electrostatically stable because the significant force of repulsion prevents the droplets being aggregated or coalesced.

In the SNEDDS and SEDDS nanoformulation of vildagliptin, the zeta potential test is essential to determine the long-term physical beyond storage and post dilution in gastrointestinal fluids. A stable nanoemulsion formulation is phase stable and does not separate and so there is uniform delivery of the drugs. The electrophoretic light scattering or laser Doppler anemometry is the most common method of determining the zeta potential. The co-surfactants and the surfactants applied in the SNEDDS/SEDDS formulations have a great impact on the charge volume on the surface of the droplets. As an example, nonionic surfactants such as Tween 80 generally have a zeta potential of neutral to slightly negative values whereas ionic surfactants may be used to confer higher levels of surface charges. The loading of Vildagliptin into SNEDDS mainly has zeta potential values between -20 to -35 mv, which explains good colloidal stability whereas SEDDS has lower values since droplet sizes are larger and interfacial characteristics are different. Besides predicting physical stability, the zeta potential can affect the adhesive quantity to the mucosa and to cellular uptake, especially in SNEDDS formulations aimed at targeting the lymphatic system or the increased permeation of the bowel⁷⁰.

***In vitro* dissolution Studies**

Evaluation of the *in vitro* dissolution testing of the lipid-based delivery systems is important because it can form an indicator of how the formulation releases the drug in the gastrointestinal tract. This would be aimed at determining the extent to which the drug is solubilized and released out of the formulation matrix into the aqueous medium. Such is especially pertinent to drugs such as vildagliptin that show poor aqueous solubility and are known to exhibit different rates and extents of bioavailability.

The dissolution of SNEDDS and SEDDS formulations in terms of the released vildagliptin is followed in time using UV-Visible spectroscopy or

HPLC as a means of measuring the dissolved drug. SNEDDS can usually perform better than SEDDS in their dissolution experiments because of the nano-sized nature of droplets, which offers a much wider interfacial surface area so that the drug can diffuse into the surrounding environment. SNEDDS containing vildagliptin are likely to release vildagliptin in a rapid and complete manner after 15-30 min, unlike SEDDS that can take longer or can be less than fine to dissolve. The direct correlation between the increased rate of dissolution of SNEDDS and increased rates of onset of action and increased systemic absorption is apparent.

Also, the parameters that are significant to formulation optimization and regulatory submissions like dissolution efficiency, the average dissolution time, and similarity factor (f_2) can also be calculated using the dissolution data. The studies also facilitate the prediction of the formulation behaviour *in vivo* based on an *in vitro* study upon *in vitro* *in vivo* correlation (IVIVC) models.

Future prospects

Owing to the persistent development of formulation science, nanotechnology and personalized medicine, the future of SNEDDS and SEDDS in improving the poor aqueous solubility of drugs such as vildagliptin looks very bright. As type 2 diabetes continues its upward trend and the existing oral therapy becomes less effective, there is an emerging desire to have an improved delivery system, meeting the patient-friendliness aspect. SNEDDS and SEDDS provide a flexible platform in which the issues of solubility and bioavailability can be resolved, and their future achievements will probably revolve around enhancing their stability, scalability, and therapeutic effectiveness. One of the novel directions is the introduction of supersaturated SNEDDS (S-SNEDDS) and solid-SNEDDS, in which drug loading and stability were improved without compromising the self-emulsifying capabilities. CSD technologies (spray drying, melt granulation, etc.) and adsorption onto porous carriers provide the possibilities of getting more stable, convenient, and commercially available dosage forms (tablets and capsules, etc.). In addition, drug targeting and release control is also being attempted using stimuli-responsive or mucoadhesive smart SNEDDS to enhance drug absorption by the gastrointestinal tract at desirable portions that are difficult to reach by

a drug alone. It will also be optimized by combining biopharmaceutical modeling with AI-sourced formulation tools to ensure more appropriate selection of excipients, resulting in drug-excipient interactions being predicted and the time of development being significantly shorter. Clinically, SNEDDS and SEDDS can also be designed by considering fixed-dose combination therapies so that co-administration of vildagliptin in other antidiabetes drugs like metformin or empagliflozin can be done without failing the patient compliance as well as therapeutic efficacy. In parallel, harmonization of regulations and more-informed guidelines on lipid-based systems, will facilitate the expanded acceptability and approval of these advanced delivery systems in the world markets. Increased propensity to lower the associated cost of formulation and promoting GRAS of excipients will also make them more applicable in generic drug manufacturing. Also, SNEDDS/SEDDS can be prepared with patient-specific parameters, such as gut physiology, diet, and genetic makeup to achieve optimal therapeutic outcomes as the demand and necessity of patient-specific and precision medicine become ever-increasing. In sum, the future of SNEDDS and SEDDS is the emergence of an all-rounder solution, less patient-specific and with capacity to scale, that should enhance oral bioavailability, and provide a degree of flexibility to develop innovative routes of delivery approaches. As soon as there are further technological advances and concerted interdisciplinary efforts, SNEDDS and SEDDS will now be one of the major cross-disciplinary efforts in the development of the successor system of oral drug delivery systems.

CONCLUSION

New perspectives of innovating the use of Self-Emulsifying Drug Delivery Systems (SEDDS) and Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) have emerged that help increase the rate of oral bioavailability of poorly water-soluble drugs such as vildagliptin. The two kinds of delivery systems utilize lipid-based formulations to make the medicines more soluble, absorbing, and therapeutically effective and overcome some important shortcomings of traditional oral dosage forms. SNEDDS especially, have greater benefit as they have a smaller droplet size, great surface area, fast emulsification rate and excellent in vivo performance. These characteristics aid in better

pharmacokinetics, decrease plasma levels of drugs variability, and also in elevated glycemic control among the diabetic patients. Detailed methods of characterization such as measurements of droplet size, PDI, zeta potential, in vitro dissolution, thermodynamic stability, and morphological studies-are indispensable in determining the behavior, stability and efficacy of such systems. Although it showed promising results, formulation complexity, stability problems, and the expensive costs of the specialized excipients and equipment, and a high regulatory burden are among the factors that challenge scale-up and commercialisation of SNEDDS and SEDDS. However, solutions to these obstacles are keeping pace by means of innovations, e.g. solidified SNEDDS, supersaturated systems and newer processing methods, and these formulations are increasingly possible to manufacture in large quantities. Regulatory wise, there are a growing number of more specific framework and aligned guidelines which help give support to lipid-based drug delivery systems with the hope that more developers in the pharmaceutical sector will embrace their use. The future lends great opportunity to SNEDDS and SEDDS to shift towards combination therapy, personalized and targeted delivery treatments. Their adaptability with formulation development, and the possibility of using large numbers of different drugs or bioenhancement agents make them appealing to future clinical and commercial application. When it comes to vildagliptin, which requires better sustained and enhanced bioavailability, the systems also help in augmenting the therapeutic, as well as patient compliance to better treatment outcomes. In general, SNEDDS and SEDDS are innovative drug delivery systems in the oral route, especially in unstable and hydrophobic drugs. As research continues to unravel their effectiveness, with further technical optimization and regulatory approval on their side, they will effectively transform the nature in which a gamut of oral therapeutics can be administered, establishing new benchmarks in the bioavailability improvement and patient friendly formulation development.

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Conflict of interest

The author declare that we have no conflict of interest.

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