RESEARCH PAPER

Formulation and In-Vitro Evaluation of Vildagliptin-Loaded Self-Nanoemulsifying Drug Delivery System

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ABSTRACT

Vildagliptin, a dipeptidyl peptidase-4 inhibitor used for type 2 diabetes mellitus, exhibits pharmacokinetic limitations including variable absorption, rapid metabolism, and only moderate oral bioavailability (~85%), motivating formulation approaches that can maintain the drug in a solubilized state in the gastrointestinal tract. This study aimed to develop and optimize a vildagliptin-loaded self-nanoemulsifying drug delivery system (SNEDDS) and convert it into a solid SNEDDS (s-SNEDDS) suitable for oral administration, followed by in vitro characterization and stability evaluation. Solubility screening (UV spectrophotometry, 210 nm) identified isopropyl myristate (8.45±0.25 mg/mL), Tween 20 (21.45±0.19 mg/mL), and propylene glycol (28.45±0.30 mg/mL) as optimal oil, surfactant, and co-surfactant, respectively; these were used to construct pseudo-ternary phase diagrams, which indicated stable nanoemulsion formation up to 60% w/w oil and poor emulsification below 45% w/w surfactant. A 3-level factorial response surface design (9 runs) evaluated oil and Smix (Tween 20:propylene glycol) as independent variables with droplet size, PDI, and % transmittance as responses; droplet size (60–150 nm; quadratic model, F=78.25, R^2=0.97), PDI (0.196–0.538; F=16.85, R^2=0.94), and transmittance (88.76–99.26%; F=14.92, R^2=0.93) supported robust optimization. The optimal formulation (Run 6; low oil/high Smix) achieved 60 nm droplet size, PDI 0.206, and 99.26% transmittance, with characterized ranges of 60–70 nm, 0.20–0.27, and 98–99%, respectively, for both liquid SNEDDS and s-SNEDDS. The s-SNEDDS showed zeta potential −13.5±0.87 mV, drug content 86.15±0.57%, spherical porous morphology without visible drug crystals (SEM), spherical droplets (~100 nm; TEM), and disappearance of the crystalline drug peak (DSC), indicating amorphization and uniform dispersion. Under accelerated storage (40±5°C/75±5% RH, 6 months), no major changes were observed, with minor degradation (93.548±4.21% drug remaining at 180 days) and an estimated shelf life of 192 days, supporting SNEDDS-based solidification as a stable platform for oral vildagliptin delivery.

Keywords: Vildagliptin, Self-Nanoemulsifying Drug Delivery System (SNEDDS), Bioavailability, Solubility, Nanoemulsion, Type 2 diabetes, Dipeptidyl peptidase-4 (DPP-4) inhibitor

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1. Introduction

Vildagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor used primarily in the treatment of type 2 diabetes mellitus to improve glycemic control by enhancing incretin hormone activity. Chemically, it is identified as (S)-1-[N-(3-hydroxy-1-adamantyl)glycyl]pyrrolidine-2-carbonitrile with a molecular formula of $C_{17}H_{25}N_3O_2$ and a molecular weight of 303.40 g/mol. It appears as a white to off-white crystalline powder, freely soluble in water and methanol, with a melting point of approximately 149°C. Pharmacokinetically, Vildagliptin is rapidly absorbed after oral administration, achieving peak plasma concentration within 1 to 1.5 hours, and exhibits an oral bioavailability of about 85%. It is metabolized primarily by hydrolysis to an inactive metabolite and is mainly excreted via the renal route. The drug acts by inhibiting DPP-4, thereby increasing active incretin levels, which results in enhanced insulin secretion, decreased glucagon release, and improved blood glucose regulation. It is indicated for monotherapy or combination therapy in type 2 diabetes patients inadequately controlled by diet and exercise. (1-3)

Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) are isotropic mixtures composed of oils,

surfactants, co-surfactants, and sometimes co-solvents that spontaneously form fine oil-in-water nanoemulsions upon gentle agitation in aqueous environments such as the gastrointestinal tract. SNEDDS are designed to enhance the oral bioavailability of poorly water-soluble and lipophilic drugs by improving their solubility, dissolution rate, and absorption. The nano-sized droplets (typically 20–200 nm) provide a large interfacial surface area, facilitating rapid drug release and improved permeation across biological membranes. Compared to conventional emulsions, SNEDDS offer superior physical and chemical stability, ease of manufacturing, and better patient compliance due to their suitability for encapsulation in soft or hard gelatin capsules. The formulation components, particularly the oil phase and surfactant/co-surfactant system, are critical in determining the efficiency of nanoemulsion formation, drug solubilization, and stability. SNEDDS also reduce variability in drug absorption by minimizing dependence on bile salts and dietary conditions. This delivery system is especially advantageous for drugs like Vildagliptin, which have solubility and bioavailability limitations, enabling enhanced therapeutic efficacy through improved oral delivery. (4,5)

The rationale for selecting Vildagliptin as the drug is based on its therapeutic significance and inherent pharmacokinetic limitations. Vildagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor widely used for managing type 2 diabetes mellitus by improving glycemic control through incretin hormone activity. However, despite its clinical efficacy, Vildagliptin exhibits challenges such as variable absorption, rapid metabolism, and moderate bioavailability (~85%). These factors limit consistent therapeutic outcomes and necessitate advanced delivery strategies to enhance its oral bioavailability and efficacy.

The choice of the Self-Nanoemulsifying Drug Delivery System (SNEDDS) as the delivery platform is justified by its ability to address the solubility and bioavailability issues associated with poorly water-soluble and lipophilic drugs like Vildagliptin. SNEDDS spontaneously form fine oil-in-water nanoemulsions upon contact with gastrointestinal fluids, improving drug solubilization, dissolution rate, and absorption. The nanoscale droplets provide a large interfacial surface area, facilitating rapid and consistent drug release and permeation. Additionally, SNEDDS reduce variability in drug absorption by minimizing dependence on bile salts and dietary conditions. (6)

Moreover, SNEDDS offer advantages such as improved physical and chemical stability, ease of manufacturing, patient compliance through suitable capsule encapsulation, and potential for targeted and controlled drug delivery. This delivery system effectively maintains the drug in a solubilized state throughout the GI tract, enhancing lymphatic uptake and reducing first-pass metabolism, which is particularly beneficial for Vildagliptin's pharmacokinetic profile. (7)

2. Materials and methods

2.1 Materials

Vildagliptin was procured from Century Pharmaceuticals Ltd. (Vadodara). Isopropyl myristate (IPM) was procured from Loba Chemie, Mumbai, India. Tween 20 and propylene glycol were purchased from Hi Media Labs, Mumbai, India. Neusilin US2 was supplied by Gangwal Chemicals Ltd, Mumbai, India. All other chemicals and reagents used in the study were of analytical grade and used as received.

2.2 Solubility studies

Solubility studies were performed by adding an excess amount of Vildagliptin to 2 mL of various oils, surfactants, or co-surfactants. The mixtures were vortexed and sonicated for 30 minutes, followed by shaking at 37 °C for 48 hours using a water bath shaker (Remi, Mumbai, India). After equilibration, the mixtures were allowed to stand at room temperature for 24 hours and then centrifuged at 3000 rpm for 15 minutes using a 12C-micro centrifuge (Remi, Mumbai, India). The clear supernatant was carefully collected, appropriately diluted with methanol, and analyzed for drug concentration spectrophotometrically at the λmax of 210 nm using a UV-Visible spectrophotometer (Shimadzu 1800, Japan). (8)

2.3 Construction of ternary phase diagram

Different mixtures with varying concentrations of surfactant (Tween 20), co-surfactant (propylene glycol), and oil (isopropyl myristate) were prepared. The concentration ranges of surfactant, co-surfactant, and oil were varied systematically to cover the formulation space. Each mixture was then diluted 100 times with deionized water, gently mixed, and allowed to equilibrate for 2 hours. The resulting dispersions were evaluated for nanoemulsion formation by measuring the percentage transmittance using a UV-Visible spectrophotometer (Shimadzu 1800, Japan) at 510 nm and the droplet size using a particle size analyzer (Malvern Zetasizer, UK). Dispersions

exhibiting droplet sizes of 200 nm or below and high transmittance values were considered suitable nanoemulsions. The data obtained were plotted on pseudo-ternary phase diagrams to delineate the nanoemulsion region and to identify the optimal ratios of surfactant, co-surfactant, and oil for SNEDDS formulation. (9)

2.4 Formulation and optimization of SNEDDS using 3^2 full factorial design

Design of Experiments (DOE) was employed to investigate the quadratic response surface and to develop a polynomial model using Design-Expert software (Trial Version 7.0.2, Stat-Ease Inc.). To optimize a Self-nanoemulsifying Drug Delivery System (SNEDDS) through the DoE method, key formulation parameters such as oil, surfactant, and cosolvent ratios were systematically varied. The responses, including droplet size, PDI and % transmittance, were then analyzed to identify the optimal formulation. For the optimization process, trial formulations of SNEDDS were prepared, considering oil (A or X1) and S_{mix} (B or X2) as independent variables, while droplet size (Y1 or R1), PDI (R2 or Y2), and percentage transmittance (R3 or Y3) were chosen as dependent variables. Consequently, the values were assessed to determine the impact of each response and to evaluate the statistical significance of each term in the regression model. (10)

Table 1: Various levels and constraints for the variables

Factors	Levels		
Independent Variables	**Low**	**Medium**	**High**
Oil (mL) = X1	0.4	0.5	0.6
S_{mix} (mL) = X2	1.8	1.9	2.0
Dependent Variables	**Constraints**		
Droplet size (nm) = Y1	Minimum		
PDI = Y2	Minimum		
Percentage transmittance = Y3	Minimum		

2.5 Characterization of SNEDDS

2.5.1. Dispersibility studies

Dispersibility studies were conducted to assess the self-emulsification time of the SNEDDS formulation. One milliliter of SNEDDS was added dropwise to 500 mL of 0.1 N HCl maintained at 37 ± 0.5 °C, with gentle agitation provided by a USP Type II (paddle) dissolution apparatus rotating at 50 rpm. The self-emulsification process was visually monitored to evaluate the rate and efficiency of nanoemulsion formation. Additionally, the resultant emulsion was observed after 24 hours of storage at room temperature to assess any precipitation or phase separation. (11)

2.5.2. Globule size, size distribution and zeta potential

Malvern Zetasizer (Malvern Instruments, UK) was employed to determine globule size, polydispersity index and zeta potential. Liquid SNEDDS or Solid SNEDDS were diluted 1000 times with distilled water and shaken gently to form a fine emulsion and the resultant emulsion was utilised for the further study. The values of z-average diameters were used. (12)

2.5.3. Comparative in vitro drug release studies

In vitro drug release studies of Vildagliptin-loaded liquid SNEDDS, solid SNEDDS, formulation-based, and pure drug were performed using a USP Type II dissolution apparatus (Model Disso 2000, Lab India). The dissolution medium consisted of 900 mL phosphate buffer (pH 7.4), maintained at 37 ± 0.5 °C, with a paddle rotation speed of 50 rpm. At predetermined time intervals (5, 10, 15, 20, 30, 45, 60, and 90 minutes), 5 mL aliquots were withdrawn, filtered, suitably diluted, and analyzed spectrophotometrically at the λmax of 210 nm using a UV-Visible spectrophotometer (UV-1800 Shimadzu, Japan). (13)

2.5.4. Transmission electron microscopy

The visual observation of the optimized SNEDDS batch was performed using transmission electron microscopy (TEM) (H-7000, Hitachi, Japan). A drop of the diluted SNEDDS formulation was placed onto a copper grid and stained with 1% w/v phosphotungstic acid solution for 5 minutes at room temperature. Imaging was conducted at an accelerated voltage of 100 kV to capture detailed morphology and droplet structure. (14)

2.6 Preparation of Solid-SNEDDS

The optimized liquid SNEDDS formulation was converted into solid, free-flowing granules by adsorption onto Neusilin US2 and Aerosil 200 as adsorbent materials. The appropriate quantities of these adsorbents required to transform the liquid SNEDDS into a compressible and free-flowing solid system were determined experimentally. The resulting solid formulations were passed through a #22 sieve to obtain

uniformly sized self-nanoemulsifying granules (SNEG).

2.7. Characterization of Solid-SNEDDS

2.7.1. Drug content estimation

Liquid SNEDDS, solid SNEDDS (s-SNEDDS), each equivalent to 50 mg of the drug, were accurately weighed and dispersed in a suitable volume of methanol. The mixtures were stirred thoroughly to ensure complete dissolution of the drug, followed by centrifugation at 3000 rpm for 15 minutes to separate any undissolved excipients. The clear supernatant was appropriately diluted with methanol and analyzed spectrophotometrically at the λmax of 210 nm using a UV-Visible spectrophotometer (UV-1800 Shimadzu, Japan) to determine the drug content. (15)

2.7.2 Differential Scanning Calorimetry Studies

Thermal analysis of the pure drug, optimized solid SNEDDS, physical mixture, and blank solid SNEDDS was performed using a Differential Scanning Calorimeter (DSC) (Shimadzu, DSC 60 TSW 60, Japan). The study was conducted over a temperature range of 50–200 °C at a scanning rate of 10 °C/min. An empty aluminum pan was used as the reference. (16)

2.7.3 Accelerated Stability Studies

The optimized solid SNEDDS (s-SNEDDS) were stored at 40° ± 5 °C and 75 ± 5% relative humidity (RH) for a period of 6 months. Samples were withdrawn at predetermined intervals of 0, 1, 2, 3, and 6 months and evaluated for self-emulsification time, globule size, and drug release at 15 minutes to assess their stability under accelerated conditions. (17)

3. Results and discussion

3.1. Solubility studies

Table 2: Solubility studies of Vildagliptin in various solvents

Solvents	Name	Solubility (mg/ml)
Oils	**Isopropyl myristate**	**8.45±0.25**
	Orange oil	3.26±0.14
	Soybean oil	2.41±0.16
	Groundnut oil	2.18±0.022
	Virgin coconut oil	3.12±0.32
	Olive oil	3.75±0.20
	Castor oil	4.86±0.41
	Ethyl oleate	6.72±0.21
Surfactants	Tween 80	19.36±0.42
	Span 80	9.82±0.32
	SLS (Sodium Lauryl Sulfate)	18.64±0.24
	Tween 20	**21.45±0.19**
	Span 20	10.75±0.13
	Cremophor RH40	20.18±0.18
	Labrasol	19.56±0.22
Co-surfactants	PEG 400	26.82±0.36
	PEG 200	24.7±0.21
	Propylene glycol	**28.45±0.30**
	Transcutol P	22.18±0.35
	Propanediol	21.56±0.26

Comparative solubility studies of Vildagliptin in various liquids are presented in Table 2. Among the oils, surfactants, and co-surfactants tested, Isopropyl myristate, Tween 20, and propylene glycol exhibited the highest solubility, respectively. These excipients were subsequently selected for the construction of the pseudo-ternary phase diagram to optimize the SNEDDS formulation.

3.2 Construction of ternary phase diagrams

The phase diagram for the system comprising isopropyl myristate as the oil phase, Tween 20 as the surfactant, and propylene glycol as the co-surfactant was constructed to delineate the concentration ranges conducive to nanoemulsion formation. All components were expressed in weight/weight percentages prior to diagram construction. The shaded region within the ternary phase diagram indicates the self-emulsifying zone where spontaneous nanoemulsion formation occurs. The incorporation of the surfactant and co-surfactant significantly enhanced emulsification efficiency, attributable to their increased hydrophilicity. Stable nanoemulsion systems were observed with oil concentrations up to 60% w/w. Furthermore, the presence of propylene glycol improved the self-emulsification properties of the system. It was also noted that formulations containing less than 45% w/w surfactant exhibited inefficient spontaneous emulsification, underscoring the critical role of adequate surfactant concentration in achieving stable nanoemulsions.

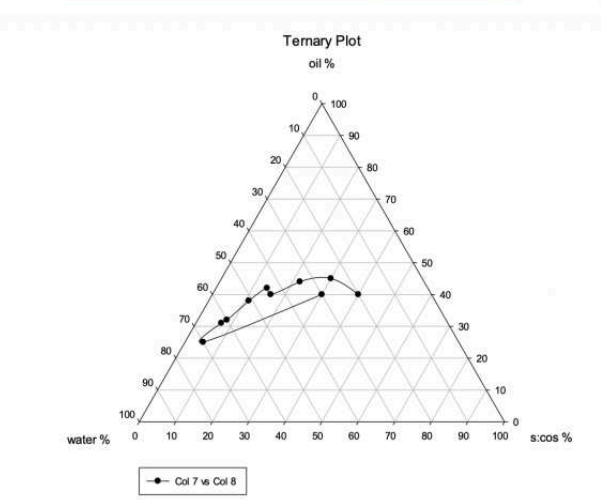

Figure 1: Ternary plot

3.3 Optimization of SNEDDS

To enhance the formulation and process parameters, the concentrations of three excipients—oil (Isopropyl Myristate) and Smix (a blend of surfactant-tween 20 and co-surfactant propylene glycol)—were chosen as independent variables. Experiments were carried out according to the design created using Design Expert® 11.0. The study focused on droplet size (Y1), PDI (Y2), and % transmittance (Y3) as dependent variables. An analysis of variance (ANOVA) was conducted to determine the appropriate model fit. Equations for each dependent variable were derived, and response surface plots were created to examine the interactions affecting each dependent variable. An overlay plot was also constructed to identify the optimal range of independent variables that would result in a robust product with the desired characteristics.

Table 3: Build Information

File Version	22.0.3.0		
Study Type	Response Surface	**Subtype**	Randomized
Design Type	3 Level Factorial	**Runs**	9
Design Model	Quadratic	**Blocks**	No Blocks
Build Time (ms)	20.00		

Table 4: Independent Factors

Factor	Name	Units	Type	Min.	Max.	Coded	Coded	Mean	Std
A	A (Oil)	%	Numeric	-1.0000	1.0000	-1 ↔ -1.00	+1 ↔ 1.00	0.0000	0.8660
B	B (Smix)	%	Numeric	-1.0000	1.0000	-1 ↔ -1.00	+1 ↔ 1.00	0.0000	0.8660

Table 5: Dependent Factors

Response	Name	Units	Observations	Min.	Max.	Mean	Std. Dev.	Ratio
R1	Y1 (Droplet size)	nm	9.00	60	150	116.67	31.62	2.50
R2	Y2 (PDI)	-	9.00	0.196	0.538	0.3788	0.1365	2.74
R3	Y3 (% transmittance)	%	9.00	88.76	99.26	95.53	4.10	1.12

Table 6: Variables selected for the optimization

Std	Run	Factor 1 A:A (Oil) %	Factor 2 B:B (Smix) %	Response 1 Y1 (Droplet size)
3	1	1	-1	120
6	2	1	0	110
1	3	-1	-1	130
5	4	0	0	130
4	5	-1	0	140
7	6	-1	1	60
8	7	0	1	70
2	8	0	-1	140
9	9	1	1	150

- **Effect of independent variables on droplet size (Y1)**

Droplet size is a critical parameter in nanoemulsion systems, as it directly influences drug release, absorption, and ultimately bioavailability. Smaller droplet sizes provide a larger surface area, which enhances drug dissolution and improves therapeutic efficacy.

In the present study, the droplet size for all experimental runs ranged from 60–150 nm, indicating successful formation of nanoemulsions within the desired nanometric range.

The obtained data were best fitted to a quadratic model, suggesting that both linear and interaction effects of independent variables significantly influenced droplet size. The model showed a significant effect with an F-value of 78.25 and an R^2 value of 0.97, indicating a strong correlation between the independent variables and the observed response.

The relationship between independent variables and response can be expressed by the following polynomial equation:

$$\text{Droplet size (Y1)} = +130 + 8.33A - 20.00B + 10.00AB + 6.67A^2 + 5.00B^2$$

- **Effect of independent variables on PDI (Y2)**

Polydispersity index (PDI) is an important parameter that indicates the uniformity and homogeneity of droplet size distribution in nanoemulsion systems. Lower PDI values represent a more uniform and stable formulation, while higher values indicate heterogeneity in particle distribution.

In the present study, the PDI values for all experimental runs ranged from 0.196 to 0.538, indicating an acceptable level of uniformity in the prepared nanoemulsions.

The experimental data were best fitted to a quadratic model, demonstrating that both individual and interaction effects of independent variables significantly influenced PDI. The model was found to be significant with an F-value of 16.85 and an R^2 value of 0.94, indicating a good correlation between the process variables and the obtained response.

The relationship between independent variables and response is expressed by the following polynomial equation:

$$\text{PDI (Y2)} = +0.532 - 0.028A - 0.065B + 0.022AB - 0.041A^2 - 0.023B^2$$

- **Effect of independent variables on percentage transmittance (Y3)**

Percentage transmittance is an important parameter that reflects the clarity and transparency of nanoemulsion systems. Higher transmittance values indicate the formation of transparent nanoemulsions with uniform droplet size, whereas lower values suggest turbidity and possible phase separation.

In the present study, the percentage transmittance across all experimental runs ranged from 88.76 to 99.26%, indicating that most of the formulations exhibited good transparency and homogeneity.

The experimental data were best fitted to a quadratic model, suggesting that both individual and interaction effects of independent variables significantly influenced the response. The model was found to be significant with an F-value of 14.92 and an R^2 value of 0.93, indicating a good correlation between the process variables and the observed response.

The relationship between the independent variables and percentage transmittance is expressed by the following polynomial equation:

$$\text{\% Transmittance (Y3)\} = +95.36 - 3.41A + 2.43B + 1.31AB - 1.12A^2 - 0.86B^2$$

The optimization of the nanoemulsion formulation was carried out by considering the desired criteria of minimum droplet size, minimum polydispersity index (PDI), and maximum percentage transmittance. Based on the experimental data obtained from the factorial design, Run 6 (Formulation 6) was selected as the optimized formulation.

Run 6 corresponded to low oil concentration (A = −1) and high Smix concentration (B = +1). This formulation exhibited the most desirable results with a minimum droplet size of 60 nm, low PDI of 0.206, and maximum percentage transmittance of 99.26%.

The selection of this formulation was based on its ability to simultaneously satisfy all optimization criteria. The smaller droplet size ensures enhanced surface area for drug release, the low PDI indicates uniform distribution of droplets, and the high transmittance confirms the formation of a clear and stable nanoemulsion system.

Although some formulations showed favorable individual responses, none provided an optimal balance of all three parameters. For instance, formulations with lower PDI exhibited larger droplet size or lower transmittance, making them less suitable. Therefore, Run 6 was considered as the optimized formulation, as it demonstrated the best overall performance with respect to droplet size, homogeneity,

and transparency. This confirms that a combination of low oil and high Smix concentration is ideal for developing a stable and efficient nanoemulsion system.

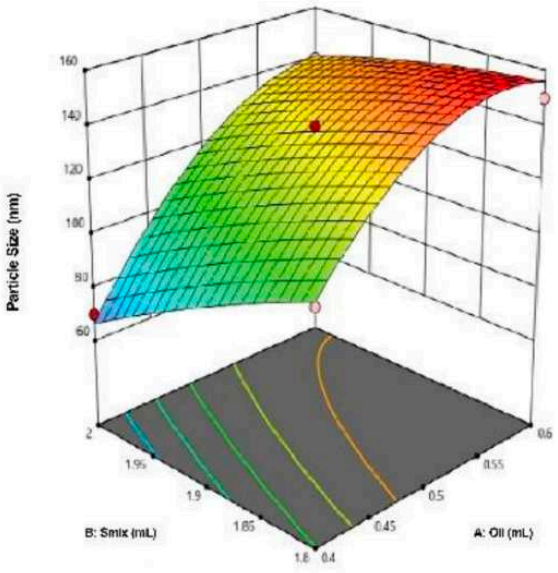

Figure 2 (a): The 3D surface response plot illustrates how the concentration of oil and Smix influences droplet size. As the oil concentration rises, the droplet size also increases, whereas a higher concentration of Smix leads to a reduction in droplet size.

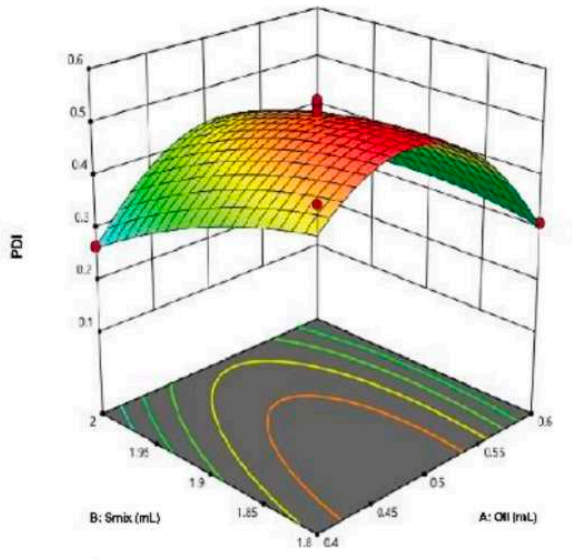

Figure 2 (b): The 3D surface response plot illustrates how the concentration of oil and Smix affects the PDI. As the oil concentration rises, the PDI decreases, whereas an increase in Smix concentration leads to a higher PDI. Nonetheless, a combination of oil and Smix concentrations results in improved homogeneity.

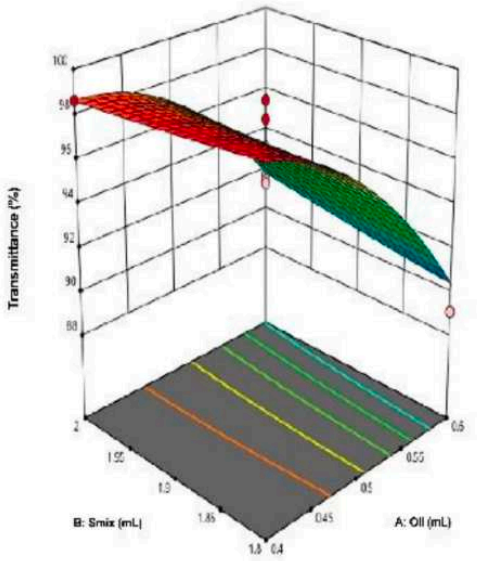

Figure 2 (c): The 3D surface response plot illustrates how the concentration of oil and Smix influences % Transmittance. A reduction in oil concentration coupled with an increase in Smix concentration leads to a rise in % Transmittance.

3.4 Characterization of SNEDDS

3.4.1 Droplet Size and PDI

The optimized nanoemulsion showed a droplet size of 60–70 nm and a PDI of 0.20–0.27, indicating a nano-sized system with uniform droplet distribution. The droplet size falls within the ideal range (50–200 nm), ensuring enhanced surface area, faster drug diffusion, and improved bioavailability. The low PDI values confirm narrow size distribution and good homogeneity, essential for formulation stability and consistent drug release.

3.4.2 Percentage Transmittance

The optimized formulation exhibited 98–99% transmittance, indicating excellent clarity and isotropic nature. High transmittance reflects small droplet size, uniform distribution, and minimal light scattering. These results support the formation of a stable nanoemulsion and correlate well with droplet size findings, confirming its suitability for efficient drug delivery.

3.5 Characterization of s-SNEDDS

3.5.1 Droplet Size and PDI

The optimized s-SNEDDS showed a droplet size of 60–70 nm and PDI 0.20–0.27, indicating uniform, stable nano-sized droplets. The size lies within the ideal range (50–200 nm), ensuring enhanced permeability

and bioavailability, while low PDI confirms homogeneity.

3.5.2 Percentage Transmittance

The formulation exhibited 98–99% transmittance, indicating high clarity and formation of nano-sized droplets with minimal light scattering. This supports improved drug release and confirms system stability.

3.5.3 Zeta Potential

The zeta potential was −13.5 ± 0.87 mV, indicating moderate stability with no signs of aggregation or phase separation.

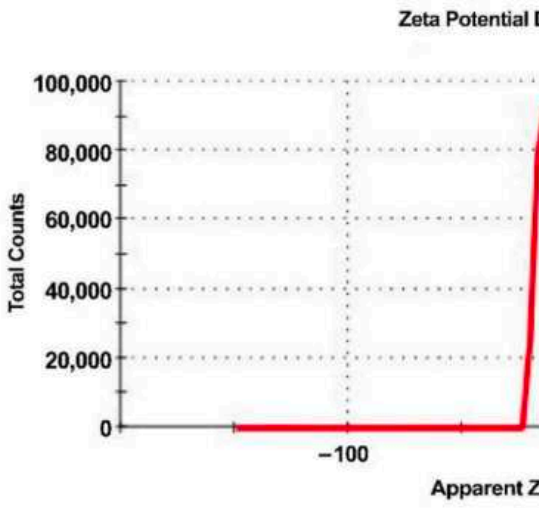

Figure 3: Zeta potential of Vildagliptin s-SNEDDS

3.5.4 Drug Content

Drug content was 86.15 ± 0.57%, confirming efficient drug loading due to optimized oil–Smix ratio.

3.5.5 Morphology (SEM & TEM)

SEM showed spherical, porous particles with no visible drug crystals, indicating complete encapsulation. TEM confirmed spherical droplets (~100 nm) with a stable interfacial layer.

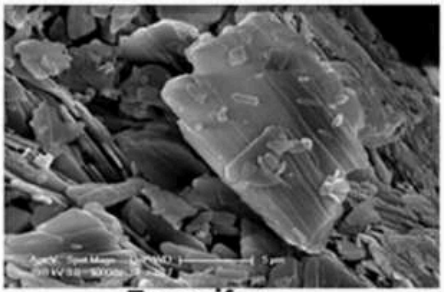

Figure 4 (a): Surface morphology of Vildagliptin

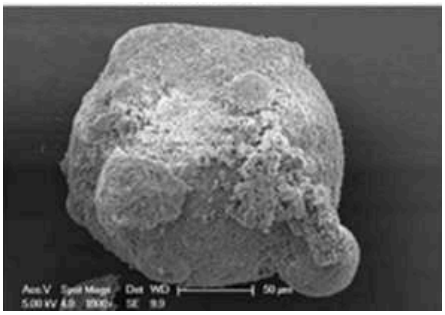

Figure 4 (b): Surface morphology of neusilin US2

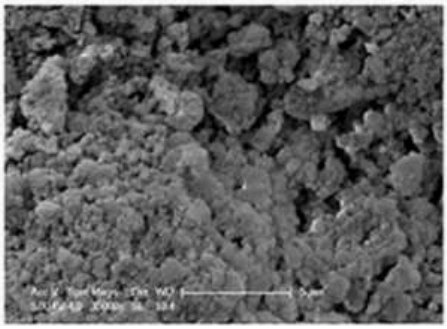

Figure 4 (c): Pores of neusilin US2

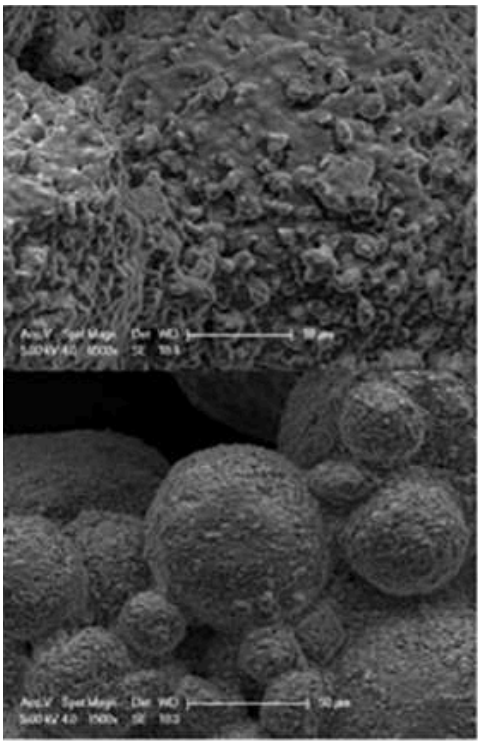

Figure 4 (d): Surface morphology of s-SNEDDS

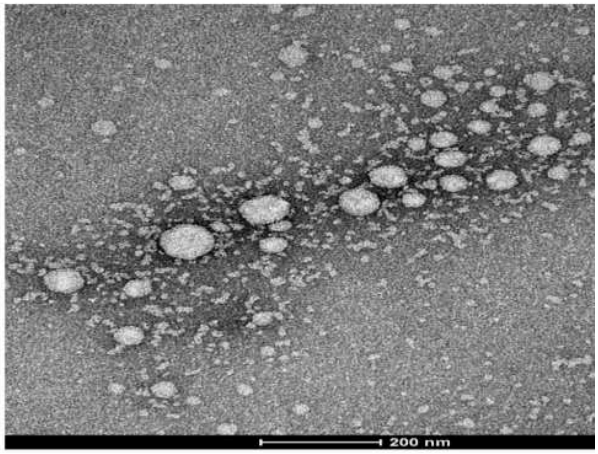

Figure 5: TEM images of SNEDDS illustrating the round form of the droplets

3.5.6 DSC Analysis

DSC revealed disappearance of the drug's crystalline peak, confirming its conversion to an amorphous form and uniform dispersion in the formulation.

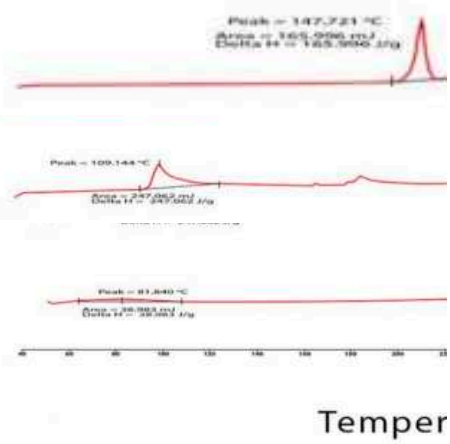

Figure 7.6: DSC curve

Accelerated stability tests were performed at 40° C / 75% RH for s-SNEDSS to assess various formulation parameters such as physical appearance, droplet size, percentage transmittance, reconstitution time, and drug content. After 180 days of storage, the physical appearance of s-SNEDDS remained unchanged from the initial day, with no signs of lump formation or color alteration. There were no significant changes in droplet size, PDI, or % transmittance of s-SNEDDS. The degradation results indicated a minor amount of degradation, with no notable difference in drug concentration from the first day to the last day, as shown in the table below. The shelf life of the developed s-SNEDDS was determined to be 192 days.

Table 7: Accelerated study data for optimized formulation

Time Point	Droplet Size (nm)	PDI	% Trans
Initial	86.526 ± 0.297	0.254 ± 0.017	99.60 ±
1st day	82.48 ± 0.886	0.255 ± 0.019	99.365
3rd day	80.96 ± 0.512	0.257 ± 0.014	100.96
7th day	81.323 ± 0.661	0.226 ± 0.012	99.566
14th day	78.930 ± 0.513	0.248 ± 0.015	98.216
28th day	84.301 ± 0.530	0.257 ± 0.013	99.09 ±
90th day	93.546 ± 2.57	0.375 ± 2.114	91.512
180th day	97.781 ± 5.411	0.361 ± 3.114	89.541

Conclusion

The study successfully developed and optimized a Vildagliptin-loaded Self-Nanoemulsifying Drug Delivery System (SNEDDS) to enhance the drug's solubility, dissolution, and oral bioavailability. Solubility screening identified isopropyl myristate, Tween 20, and propylene glycol as the most suitable oil, surfactant, and co-surfactant, respectively. The pseudo-ternary phase diagram and 3^2 full factorial design facilitated the identification of an optimal formulation (Run [illegible] Vildagliptin [illegible] oil and high Smix concentratio[illegible]ulsion with a droplet size around 60 nm, low polydispersity index, and high percentage transmittance.

Characterization of both liquid and solid SNEDDS confirmed uniform nano-sized droplets, high clarity, and moderate zeta potential indicating stability. Morphological studies and DSC analysis demonstrated complete drug encapsulation and conversion to an amorphous form, contributing to improved dissolution properties. Accelerated stability studies showed that the optimized solid SNEDDS maintained physical and chemical stability over six months with minimal degradation.

Overall, the developed Vildagliptin SNEDDS offers a promising delivery platform to overcome the drug's pharmacokinetic limitations by enhancing solubility, stability, and consistent drug release, potentially improving therapeutic efficacy in type 2 diabetes management.

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