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Original Article

Solid Self-Nanoemulsifying Drug Delivery System of Meclizine HCl: *In vitro* Dissolution and *ex vivo* Intestinal Permeation Study for Oral Delivery

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ABSTRACT

Background: Meclizine hydrochloride Solid Self-Nanoemulsifying Drug Delivery System S-SNEDDS) was formulated and optimized to improve solubility and intestinal absorption. **Objectives:** Solubility studies identified Transcutol HP (25 ± 1.2 mg/mL), Tween 80 (30 ± 2 mg/mL), and Capryol 90 (30 ± 1.5 mg/mL) as ideal excipients. **Materials and Methods:** A Surfactant-cosurfactant mixture ratio of 1:2 yielded a broad nanoemulsion zone with stable Grade A emulsions. Thermodynamic stability was confirmed through stress tests. The optimized SNEDDS had a droplet size of 130.4 nm, PDI of 0.442, and -14.1 mV of zeta potential. X-ray Diffraction confirmed the drug's amorphous state, while Fourier Transfer Infrared Spectroscopy revealed no drug-excipient interaction. **Results:** Scanning Electron Microscope images showed successful solidification with Neusilin US2, and excellent flow properties were observed. **Conclusion:** *In vitro* drug release exceeded 95% within 30 min compared to 55.96% for the pure drug. *Ex vivo* studies demonstrated enhanced permeability through the intestinal membrane (SNEDDS: 98.45%, S-SNEDDS: 96.15%) vs. pure drug (60.1%), suggesting improved oral bioavailability.

Keywords: Bioavailability, *Ex vivo* Permeation Study, Meclizine Hydrochloride, Nano emulsion, S-SNEDDS, Weakly Water-Soluble Drugs.

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INTRODUCTION

The most often recommended method of drug administration for systemic action is the oral route due to its ease of consumption, patient comfortness, non-invasiveness, acceptance, and adaptability. About 60% of all formulations are solid dosage forms.[1]

It is the easiest way of administration; oral delivery is restricted by needing to transit via the Gastrointestinal (GI) tract's various hurdles.[2] Drug absorption requires the drug to be soluble in the GI tract because inadequate drug dissolution can result in low bioavailability, significant variability after oral delivery, and incomplete absorption. According to the BCS Class II and IV pharmaceuticals make up the most of the medications that have been identified thus far.[3]

The low aqueous solubility and bioavailability of pharmaceuticals can be greatly improved by using delivery systems that contain SEDDS, SMEDDS, and SNEDDS.[4] These systems are isotropic mixtures of oil, surfactant, and co-surfactants or cosolvents.[5] Oils that are natural, synthetic, or semi-synthetic can be used to formulate these systems.[6] In SEDDS, oils serve as inactive components (lipophilic solubility enhancers), boosting the load of medications that have a low water solubility.[7]

A drug's ability to dissolve as much as possible in the oil phase is essential for maintaining its dissolved state and avoiding precipitation in the intestinal lumen during the dissolution process. Lowering the amount of oil required for formulation is also aided by the medication's improved ability to dissolve in the selected oil. As a result, less excipients will be required to sufficiently emulsify the oil droplets containing the medication.[8] Non-ionic surfactants are widely suitable for oral administration and generally thought to be safer than their charged relatives.[9] Surfactants have a major role in self-emulsification mechanisms and droplet size determination; the cosurfactant contributes to dissolving the medicine in the oil and acts as a surfactant support to keep the oil mixture stable. A poor choice of oil, surfactant, or cosurfactant may cause the formulation to fail and reduce the effectiveness of the SNEDDS.[10]

Therefore the present aim of this study is to develop and evaluate S-SNEDDS of meclizine hydrochloride to improve its solubility, dissolution and intestinal permeability.

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MATERIALS AND METHODS

Materials

Capryol 90, Transcutol HP, Labrasol AlF, Maisine CC, Geloil CC, and Peceol were donated by Gattefosse, France. Acconon AKG-6, Acconon MC8-2, Captex 8000, Caprol PGE 860, Capmul MCM and Capmul MCM C-8 were supplied by Abitec Corporation (USA), Tween 80 from SDFCL, S. D. Fine-Chem Limited, Mumbai; Neusilin US2, Micro labs Ltd., Bangalore, India.

Methods

Analysis of Meclizine Hydrochloride Solubility in Various Oils and Surfactants

The meclizine hydrochloride solubility equilibrium in oils and surfactants can be applied to examine excipients through the shake flask technique. 2 mL of each chosen oil and surfactant sample were mixed with meclizine hydrochloride in a glass test tube. The medicine was then manually blended with the oil and surfactant using a glass rod for 30 min.[11]

Compatibility test

The FITR (Cary 630 FTIR, UV Agilent Technology) was used to analyse the medicine and physical combination of drug and excipient in order to describe any possible structural changes that might have been created. As a result, the collected material was stored in the sample holder for analysis after being tested in the 4000-400 cm^{-1} value range.[12]

Pseudo ternary Phase Diagram

The Pseudo-ternary phase diagrams were solved with water titration technique for nanoemulsion regions. At room temperature, mixtures of oil, surfactant, and co-surfactant were gradually mixed with distilled water. Based on solubility tests, Transcutol HP, Capryol 90, and Tween 80 were chosen as co-surfactant, oil, and surfactant, respectively. Clear and homogenous mixes were created at various Smix ratios. Diagrams were constructed for Smix ratios of 1:0, 1:1, 1:2, 1:3, 1:4, 2:1, 3:1, and 4:1.[8]

Thermodynamic stability

Centrifugation

Formulations selected from the nanoemulsion region at a suitable Smix ratio were subjected for centrifugation at 3500 rpm for 30 min, and any signs of phase separation or cracking were observed and reported. Those formulations that remained stable were then taken forward for H/C cycle.[13]

Heating-cooling Cycle

Heating-Cooling (H/C) cycles are performed for the stability of SNEDDS against temperature fluctuations. Each formulation were stressed for six successive cycles between 4°C and 45°C. Formulations demonstrating satisfactory stability under these conditions were subjected to F/T cycle.[13]

Freeze-Thaw Cycle (F/T cycle)

Each formulations underwent three F/T cycles, with a minimum hold time of 48 hr per cycles across a temperature range of -25 to +25°C. formulations that successfully passed this thermodynamic stability study were then subjected to dispersibility testing to determine their self-emulsification efficiency.[14,15]

Dispersibility test

The self-emulsification performance of oral nanoemulsion formulations was evaluated using standard USP XXII dissolution apparatus II. Testing involves dispersing 1 mL of each formulation in water of 0.5L at 37±0.5°C. Mild agitation was provided by the 50 RPM spinning stainless-steel dissolving paddle. Visual analysis is used to determine the emulsification time.[12]

Grade A: Rapid nanoemulsion, with clear or bluish appearance by 1 min.

Grade B: Rapidly forms nanoemulsion, a slightly less clear/ bluish-white emulsion in 1 min.

Grade C: Forms a milky or dull emulsion after 2 min.

Particle size measurement

To measure the mean globule size and PDI, the Horiba Scientific SZ-100 was used to the resulting nanoemulsions using photon correlation spectroscopy. Changes in the scattering of light caused by the particles' Brownian movement were noted. At a 90°C angle and 25.2°C, light scattering was observed.[16]

Zeta Potential Determination

To measure the zeta potential, Horiba Scientific SZ-100 was used for the SNEDDS formulation.[17]

Drug Release Studies

Dissolution Apparatus II used to analyze the drug release from SNEDDS using 0.9L (0.1N hydrogen chloride) with 50 rpm paddle speed at 37 ± 0.5°C. The medium was supplemented with a 25 mg drug equivalent. At regular time intervals, samples of 5 mL was taken out. After being diluted, the extracted samples were analyzed using UV spectroscopy at 232 nm. To maintain the volume sampled, fresh medium was provided.[15]

S-SNEDDS Formulation Preparation

Neusilin US2 (inert solid carrier) having high surface area and strong adsorption ability, was utilized to convert the improved L-SNEDDS formulation into a S-SNEDDS. The conversion was done by physical adsorption. Neusilin US2 was mixed with the improved L-SNEDDS formulation in moderate quantities on a petri dish to form a solid powder with free flow.[18]

Micromeritic Properties

Bulk density and tap density

Bulk density apparatus was employed to measure the bulk volume of the sample. The bulk density was subsequently calculated using the equation below:

$$\rho b = m / Vb$$

After two hundred taps on the cylinder, the tapped density was calculated using:

$$\rho t = m / Vt$$

Hausner's Ratio and Carr's Index (%CI):

The Hausner's ratio and Carr's index have been determined using ρ_b and ρ_t.

$$\text{Hausner's Ratio} = \rho t / \rho b$$

$$\% \text{ CI} = (\rho t - \rho b / \rho t) \times 100$$

Angel of Repose

The fixed funnel method was used to calculate the angle of repose of the powder pile.[19]

$$\theta = \tan -1 (h/r).$$

Scanning Electron Microscope

Photographs were collected on a scanning electron microscope Malvern, UK equipment (Nano series ZS 90), working at an accelerating voltage of 10 kV, to cast further light on the particle form and topology. A few µg of powder was put over a stub and adhered on a double-sided sticky carbon tape for better visibility.[12]

X-ray Diffraction Studies (XRD)

XRD analysis of meclizine hydrochloride SNEDDS was carried out. XRD analysis of meclizine hydrochloride SNEDDS was done using the Rigaku model Smart Lab 3KW Japan.[12]

In vitro Dissolution Study

Solid formulations of 25 mg drug equivalent (150 mg formulation) were formulated in hard gelatin capsules. A USP Dissolution equipment by paddle method (Type II) was used. For a guarantee adequate immersion, the capsules were placed in sinkers. At 50rpm the paddle rotates while the dissolution medium was 900 mL of 0.1N hydrogen chloride at 37.0°C ±0.5°C. 5 mL of the sample was taken out at the intervals indicated in the following table (5, 10, 15, 20, 30, 45, and 60 min). After diluting each of the extracted samples to the appropriate concentration, ultraviolet spectrophotometry was carried out at 232 nm. After each sampling, a volume of fresh 0.1N HCl was added to maintain a constant total volume.[20,14]

Ex vivo Intestinal Permeation Study By Franz Diffusion Cell

Diffusion of Meclizine Hydrochloride pure drug (API), SNEDDS and solid SNEDDS (S-SNEDDS) formulations was carried out *ex vivo* from goat intestinal membrane mounted on a Franz diffusion cell apparatus. Fresh intestine which was purchased from a local slaughter house was contaminated with cold normal saline, which is fed into a Franz diffusion cell system. All intestinal segments were vigorously cleaned with Phosphate-Buffered Saline (PBS, pH 6.8) in order to remove residual contents.

The mesenteric end of the intestine was cut open, and the mucosal side of the intestine was placed between the receptor and donor compartments of the Franz diffusion cell. PBS (pH 6.8) was added to the 50 mL receiver chamber, which was kept at 37°C ±0.5°C and agitated at 50 rotations per minute with a magnetic agitator.

Each formulation, containing the equivalent of 25 mg of drug was introduced into the donor compartment. To ensure sink conditions maintained during the study, 1 mL of aliquots was withdrawn from the receptor compartment at regular time intervals and immediately replaced with same volume of 6.8 pH PBS. The collected samples were filtered throughout a 0.45µm clarifier and the concentration of drug was measured using a verified UV-visible Spectrophotometry at 232nm.

Calculation of Flux and Permeability Coefficient

Flux (J) was calculated using the formula:

$$J = dQ / A \cdot dt$$

Where A is the area of the membrane, Q is the amount of drug that permeates through membrane, the time (t) is point at which stating point of contact the straight line of the cumulative permeation profile was used to estimate the steady-state flux.

The (P) permeability coefficient was calculated using:

$$P = J / C_0$$

Where J is the calculated flux value and C_0 refers to the drug's beginning concentration in the donor compartment. Calculations were performed using data from the early linear phase of drug permeation.[21,22]

Goat intestine tissue used for *ex vivo* permeation analysis were obtained through a licensed slaughterhouse after animal sacrifice for commercial food purpose. Therefore, no live animal experimentation was performed.

Statistical Analysis

All statistical evaluations were conducted using Microsoft Excel (Version 2021). Group comparison was made using one-way ANOVA, with Tukey's *post hoc* test used to identify significant differences among the mean values of *in vitro* dissolution and *ex*

vivo permeability data. Statistical significance was defined at a probability level of $p < 0.01$.[23]

RESULTS AND DISCUSSION

Study of Meclizine Hydrochloride Solubility in Various Oils and Surfactants

Meclizine hydrochloride solubility was highest in Capryol 90 (30 ± 1.5 mg/mL) among oils. Tween 80 exhibited the maximum solubility among surfactants (30 ± 2 mg/l) and co-surfactant Transcutol HP also showed solubility (25 ± 1.2 mg/mL) (Figure 1).

Compatibility test

Pure Meclizine Hydrochloride (MCZ), MCZ SNEDDS, and MCZ SNEDDS Powder all showed characteristic peaks that are highly preserved in pure formulations. In pure MCZ, we observed the characteristic peaks at 3267 cm^{-1} for (N-H stretching) and 2918.7cm^{-1} for (C-H stretching), 1707 cm^{-1} for (C=O stretching), and around 1340-1350 cm^{-1} (S=O stretching) (Figure 2). In all three cases, all the peaks showed no significant shifts in their positions, and the drug remains stable in both SNEDDS and SNEDDS powder formulations.

Pseudo ternary phase diagram

The nanoemulsion regions are identified on ternary phase diagram as Shown in the Figure 3.

The thermodynamic stability of the nanoemulsions

H/C: Heating-cooling; F/T: Freeze-thaw; Pass (+); Fail (-); Grade A: clear bluish nanoemulsion (optimal fine droplet dispersion); Grade B: slightly turbid with marginally larger droplets (acceptable but suboptimal).

Scanning electron microscope

The SEM images show aggregated particles with irregular shapes and rough surface morphology. Particles are not uniform in size, as seen in this study; that is, they appear to be distributed heterogeneously. In some larger aggregates, smaller particles were attached to the aggregate surface (Figure 4).

Micromeritic properties

The Hausner Ratio of the Solid SNEDDS formulation was found to be 1.068, which comes within the range of 1.00-1.11, demonstrated an excellent flowability characteristics. Carr's Index analysis revealed that the formulation exhibited a value of 6.3%, which falls within the range of 0-10, indicating excellent flowability. The Angle of Repose was found to be 21.06°, which lies in the range of <25°, indicating excellent flow property of the formulation.

Analysis of XRD

The XRD structure of pure Meclizine Hydrochloride (MCZ) and the solid SNEDDS formulation are presented in Figure 5. The pure drug exhibited sharp and intense peaks at 2θ values of 10.7°, 22.9°, 28.3°, and 28.5°, which are characteristic of its crystalline nature (Figure 5). These distinct peaks demonstrate the highly ordered crystalline structure of MCZ. In contrast, the XRD structure of the solid SNEDDS formulation found a dramatic reduction in the intensity of those characteristic peaks, and showed a broad diffuse halo pattern.

Evaluation of SNEDDS Formulation's Zeta Potential and Particle size

SNEDDS formulation of Capryol 90 (Oil), Tween 80 (surfactant) and Transcutol HP (co-surfactant) was analyzed to know zeta potential and globule size. Zeta potential was -14.1 mV, moderate colloidal stability due to electrostatic repulsion can be concluded. Z-average of 130.4 nm confirming nanoscale dimensions. 0.442

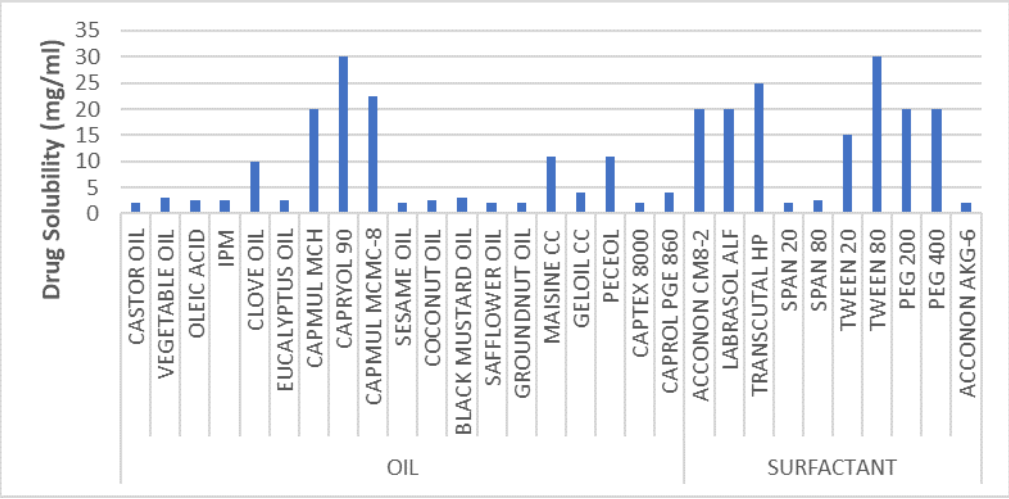

Figure 1: Solubility Profile of Meclizine Hydrochloride.

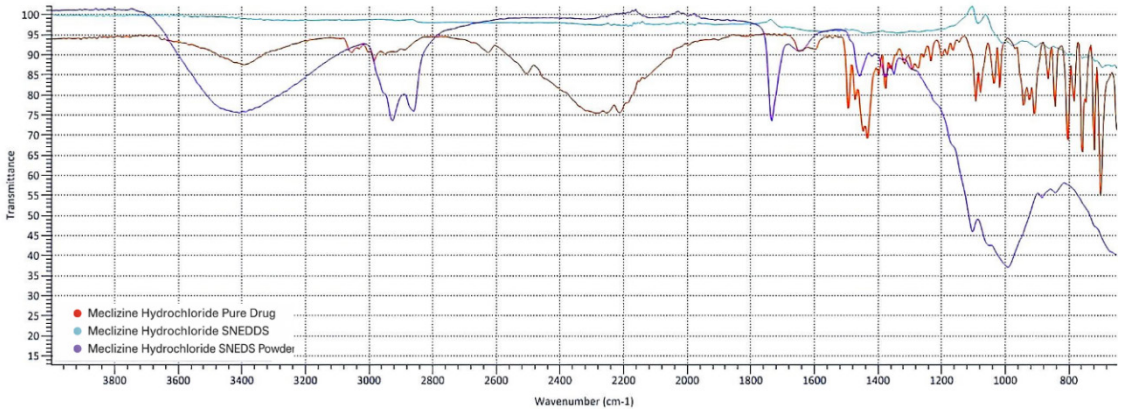

Figure 2: FTIR Spectra of Meclizine Hydrochloride API, Meclizine Hydrochloride SNEDDS and Meclizine Hydrochloride Solid SNEDDS.

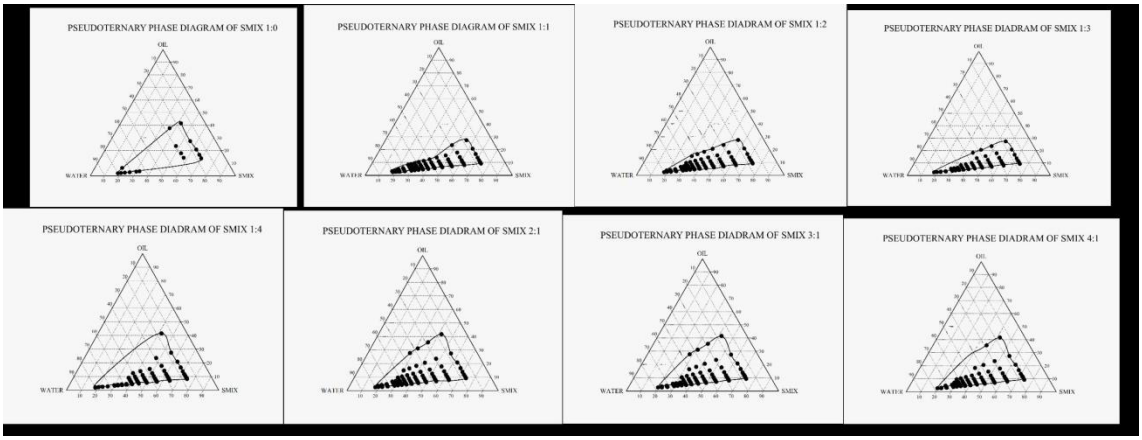

Figure 3: Pseudoternary phase diagram of various ratios.

Polydispersity Index (PDI) of droplet size distribution indicated moderate uniformity (Figure 6).

Drug Release Studies

Both pure Meclizine Hydrochloride and SNEDDS formulations (Smix 1:2, 1:3, 1:4, 2:1) release over 30 min showed *in situ* release only 12.159% at 5 min, 55% at 30 min and 96.978% at 30 min. Meanwhile SNEDDS formulations release enhanced over 30 min. SNEDDS release also followed the highest at 30 min with Smix 1:2 having the greatest (96.978%) free drug release followed by 2:1 (96.1108%), 1:4 (95.773%), and 1:3 (92.29%) (Figure 7).

Study of *In vitro* Dissolution

At 5 min, SNEDDS released 81.63% of the drug, while the S-SNEDDS loaded capsule delivered 28.01%. At 10 min, drug release was 85.62% for SNEDDS and 48.88% for the S-SNEDDS-loaded capsule. At 15 min, SNEDDS produced over 90% drug release, while the S-SNEDDS-loaded capsule achieved 80.97% drug release. At 20 min, drug release was 92.97% for SNEDDS and 90.52% for the S-SNEDDS-loaded capsule. Both formulations achieved more than 93% drug release at 25 min, and at 30 min virtually complete drug release (95%) was obtained for both formulations (Figure 8).

Ex vivo Intestinal Permeation Study By Franz Diffusion Cell

The *ex vivo* membrane absorption study revealed that SNEDDS and S-SNEDDS significantly enhanced the intestinal absorption of Meclizine Hydrochloride compared to the pure drug. After 270 min, the cumulative drug permeation was highest for SNEDDS (98.45%), followed by S-SNEDDS (96.15%), while the pure drug showed only 60.1% (Figure 9). Meclizine hydrochloride's *ex vivo* flux (J) was highest for SNEDDS (91.96 μg/cm²·min), followed by S-SNEDDS (87.35 μg/cm²·min), and lowest for the pure drug (37.92 μg/cm²·min). The corresponding permeability coefficients (P) were 0.00368, 0.00349, and 0.00152 $min^{-1}·cm^{-1}$, respectively.

Statistical Analysis

One way ANOVA demonstrated statistically significant differences in dissolution ($F = 17.691$, $p = 0.000246$) and permeation ($F = 7.41$, $p = 0.002$) among the formulation, confirming the significant influence of formulation type on the drug performance. Tukey's HSD post hoc analysis showed that dissolution and permeation

were significantly greater for SNEDDS and S-SNEDDS when compared to the pure drug ($p < 0.01$ to 0.001), with S-SNEDDS further distinguishing itself from SNEDDS in terms of dissolution ($p = 0.0027$), whereas permeation showed no significant difference ($p = 0.952$) indicating that solidification process maintain permeation efficiency of the lipid-based systems. The data were represented as Mean ± SD ($n = 3$), confirming data reproducibility and reliability.[23,24]

DISCUSSION

Capryol 90 is a medium chain monoester with excellent solubilizing activity for lipophilic drugs, due to its amphiphilicity and moderate polarity; this factor increases affinity of the drug in the oil phase. By creating stable micelles, Tween 80, which belongs to the class of non-ionic surfactant and possesses a high HLB value[15], helps solubilize medications with poorly aqueous soluble. Transcutol HP is a hydrophilic co-surfactant with good solvent properties for both hydrophilic and lipophilic drugs enhancing fluidity of the interfacial surfaces and improving solubilization. Hence, they were selected for the SNEDDS formulation of meclizine hydrochloride.

Only those formulas at Smix ratios 1:2 (25% oil), 1:3 (5% oil), 1:4 (25% oil) and 2:1 (40% oil) passed all thermodynamic stress tests. The thermodynamically stable formulations (1:3 (5% oil), 1:4 (25% oil) and 2:1 (40% oil)) produced rapid, bluish-white and transparent emulsions (grade B), which suggest a slightly coarser droplet size and poorer optical clarity than the Grade A system. Overall, the 1:2 Smix ratio with 25% oil was designated as the best formulation for further development because of its high thermodynamic stability and desirable appearance.

The porous and uneven surface suggests a possible enhanced dissolution mechanism. This structure is typical of a solidified formulation or of a drug-loaded particle system.

Thus, the change in MCZ's composition from crystalline to amorphous or disordered crystalline state after incorporation into the SNEDDS matrix is clear, and the existence of significant degree of specific crystallinity in the solid SNEDDS strongly indicates good drug's molecular distribution through carrier matrix, and the mechanism could therefore help increase drug solubility and speed up its dissolution.

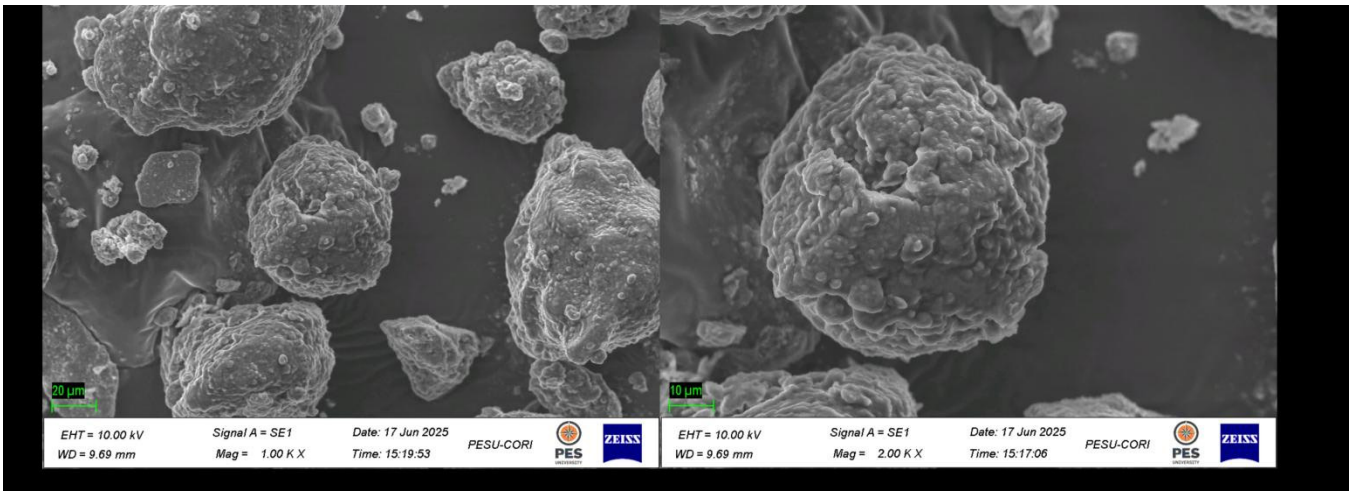

Figure 4: (1a-1b) Visualization of the morphology of surface and internal structure of Solid SNEDDS (S-SNEDDS) formulation at high magnification and resolution. The images provide detailed information about the shape, size, and surface characteristics of the S-SNEDDS formulation.

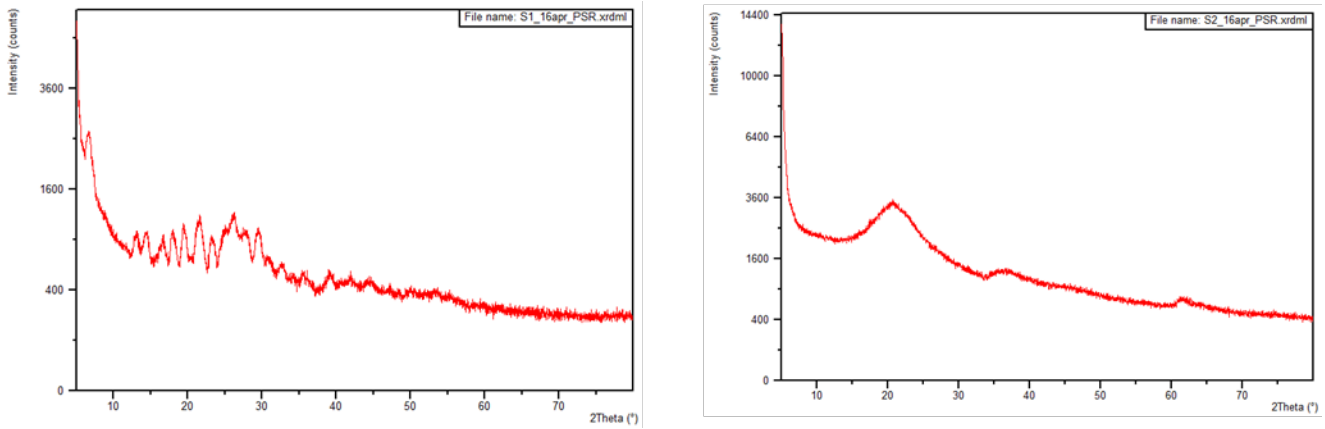

Figure 5: XRD of Meclizine Hydrochloride Pure Drug and Meclizine Hydrochloride Solid SNEDDS.

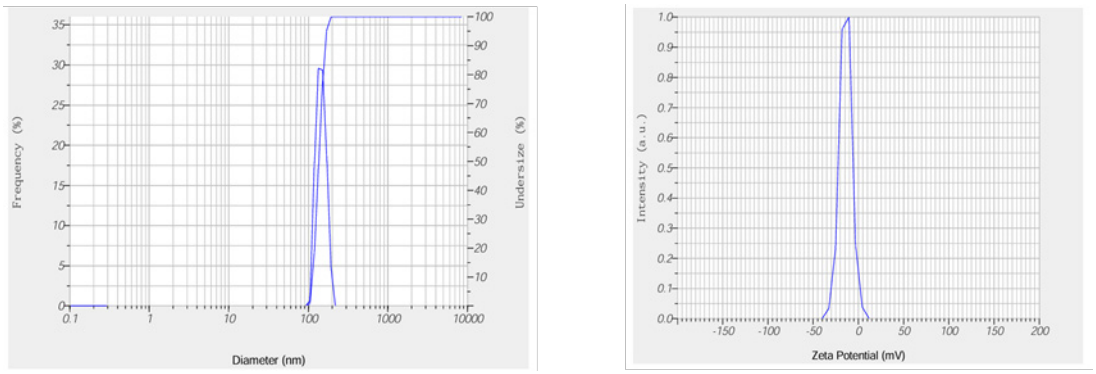

Figure 6: Globule Size and Zeta Potential of SNEDDS Formulation Respectively.

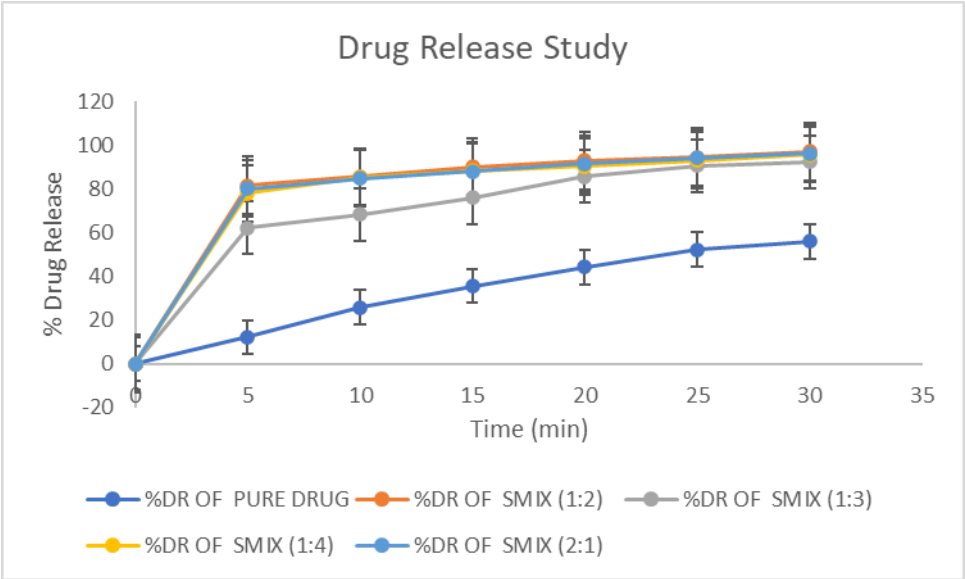

Figure 7: Drug Release of API, Smix 1:2, 1:3, 1:4 and 2:1.

Capryol 90 may contribute to surface charge mediated by free fatty acids and increase stability of emulsions. Non-ionic surfactants (Tween 80 and Transcutol hp) bind to droplets through steric hindrance rather than charge. The lower PDI value is preferable, but that is the acceptable value for oral nanoemulsion formulations. These physical parameters support the formulation's ability to deliver and absorb a stable dose of drug.

Overall Interpretation

This combination of a small droplet size and a moderate zeta potential indicates that the formulation of SNEDDS is physically stable and may be useful in improving oral bioavailability. It is concluded that the non-ionic nature of Tween 80 and Transcutol HP allows for neutral behaviour of the system which allows emulsification of the hydro forms and subsequent solubility. This balance between electrostatic and steric stabilization is essential in respect to preservation of the formulation chemical and physical properties during storage and dilution in gastrointestinal fluids.

The optimal Smix formulation (1:2 ratio) exhibited the largest nanoemulsion region in the pseudo-ternary phase diagram and successfully passed thermodynamic stability studies with Grade A emulsification. The optimized SNEDDS with 25% Caproyl 90 showed a globule size of 130.4nm, 0.442 of PDI and -14.1mV of zeta potential, indicating nanoscale dispersion with acceptable colloidal stability, Smix 1:2 showed the highest drug release at 30 min (96.98) compared with Smix 2;1 (96.11%), 1:4 (95.77%) and 1:3 (92.29%) representing ~697% enhancement over pure Meclizine HCl (~55%) attributed to increased interfacial surface area and improved solubilization by Tween 80 and Transcutol HP synergy.

Because the drug release profile of S-SNEDDS loaded capsule was slower initially, the gelatin shell negatively influenced the early drug release; however, the drug release from the capsule was very fast after disintegration, and in the end the S-SNEDDS-loaded capsule had a drug release profile comparable to that of the liquid SNEDDS formulation (Table 1).

The improved permeation from SNEDDS and S-SNEDDS is attributed to the nanosized droplets and presence of surfactants

like Tween 80 and Transcutol HP, which enhance solubilization and membrane permeability. SNEDDS exhibited slightly superior performance due to its liquid nature and faster release. S-SNEDDS also showed high permeation due to rapid reconstitution upon contact with aqueous fluids. The pure drug displayed limited permeation due to poor solubility and restricted membrane transport. The lipid-based systems likely improved drug flux and membrane interaction. Continuous stirring at 50 rpm and maintained physiological temperature supported consistent diffusion. These findings confirm the probability of SNEDDS and

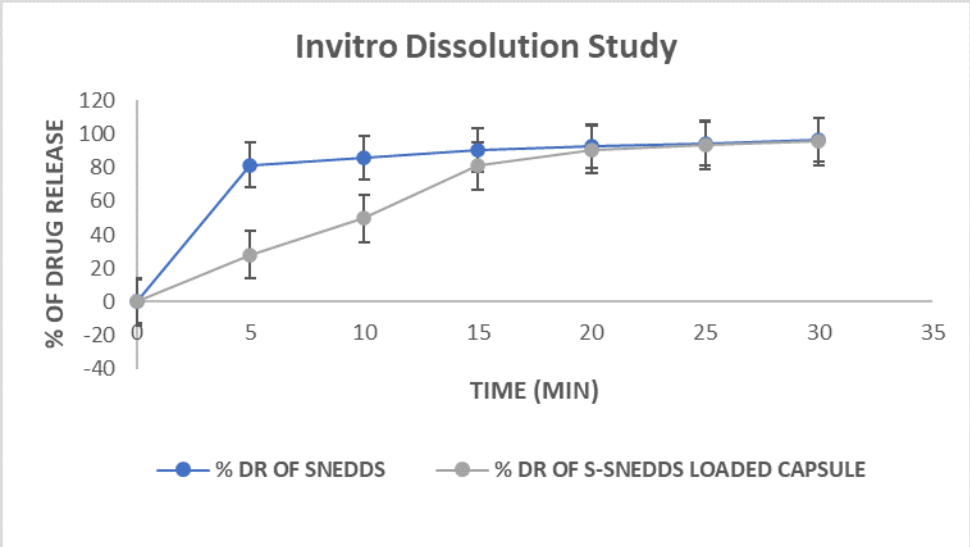

Figure 8: *In Vitro* Dissolution Study of SNEDDS and S-SNEDDS loaded Capsule.

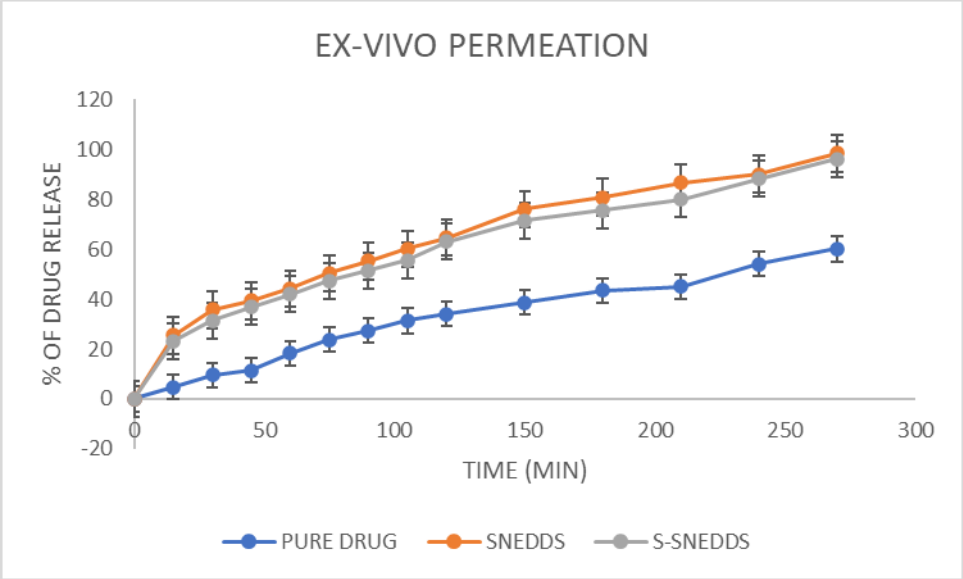

Figure 9: *Ex vivo* Permeation Study of API, SNEDDS and S-SNEDDS.

Table 1: Descriptive Table.

Smix	Oil %	Centrifugation	H/C cycle	F/T cycle	Grade	Inference
1:1	30	-	-	-	C	Fail
1:2	25	+	+	+	A	Pass
1:3	5	+	+	+	B	Pass
1:4	25	+	+	+	B	Pass
2:1	40	+	+	+	B	Pass
3:1	20	-	-	-	C	Fail

S-SNEDDS in enhancing oral bioavailability of poorly soluble drugs.

The rapid dissolution of SNEDDS and S-SNEDDS (>95% drug release within 30 min) and their significantly higher intestinal permeation, flux and permeability coefficients assessed against the pure drug indicate enhanced drug solubilization, also the membrane transport. The nanosized droplets along with Tween 80 and Transcutol HP enhanced interfacial surface area, wetting and intestinal diffusion, thereby promoting efficient absorption. These findings suggest that SNEDDS and S-SNEDDS may enhance *in vivo* absorption, increase plasma drug concentration and improve the oral bioavailability of Meclizine Hydrochloride.[25,26]

Due to its quick dispersion and instantaneous creation of nanosized droplets at the absorption site, SNEDDS demonstrated somewhat greater penetration than S-SNEDDS. The pure drug showed the lowest flow, also permeability due to its restricted membrane permeability and poor solubility. Overall, the study shows that intestinal drug transport is much improved by SNEDDS and S-SNEDDS when evaluated in relation to the unformulated drug.

CONCLUSION

The development and optimization of a S-SNEDDS of meclizine hydrochloride was carried out to increase the solubility, dissolution properties and intestinal permeability of this drug delivery system. Based on solubility screening, Transcutol HP (co-surfactant), Capryol 90 (oil), and Tween 80 (surfactant). The formula designed with a 1:2 ratio of Smix showed good thermodynamic stability and formed nanoparticles (130. 4 nm) that were acceptable in terms of colloidal stability (zeta potential -14. 1 mV; PDI - 0. 442). Lyophilization of stabilized liquid SNEDDS gave powders with good micromeritic characteristics and round morphology as evidenced by SEM. FTIR indicated no such significant interaction between the excipients and the drug. XRD analysis indicated that conversion of meclizine hydrochloride from crystalline to amorphous form promoted dissolution at lower temperatures. *In vitro* studies indicated significantly better SNEDDS/S-SNEDDS-loaded capsules in drug dissolution (>95% at 30 min) than purified drug (54.96% at 30 min). In addition, *ex vivo* permeation experiments with goat intestine and Franz diffusion cells revealed drastically improved permeation of SNEDDS (98.45%) and S-SNEDDS (96.15%) versus the pure drug (60.1%) over 270 min, ascertaining enhanced potential for intestinal absorption. These observations establish that SNEDDS formulations thus developed hold promise as a valid method to elevate the solubility, dissolution, and bioavailability of drugs with poorly aqueous solubility such as meclizine hydrochloride.

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ABBREVIATIONS

SNEDDS: Self-Nanoemulsifying Drug Delivery System; **S-SNEDDS:** Solid Self-Nanoemulsifying Drug Delivery System; **GI:** Gastrointestinal; **BCS:** Biopharmaceutics Classification System; **SEDDS:** Self-Emulsifying Drug Delivery System; **SMEDDS:** Self-Microemulsifying Drug Delivery System; **FTIR:** Fourier Transfer Infrared Spectroscopy; **XRD:** X-ray Diffraction; **SEM:** Scanning Electron Microscope; **PDI:** Polydispersity Index; **MCZ:** Meclizine Hydrochloride; **Smix:** Surfactant-cosurfactant mixture; **H/C:** Heating-cooling; **F/T:** Freeze-thaw; **USP:** United States Pharmacopeia; **PBS:** Phosphate-buffered saline; **API:** Active Pharmaceutical Ingredient; **ANOVA:** Analysis of Variance; **HLB:** Hydrophilic-Lipophilic Balance.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

Manjunatha G R: Data curation, Detailed Assessment, Exploration, Research Approach, Resources, Verification, Data presentation, Writing - original draft.

Panner Selvam R: Conceptualization, Formal analysis, Supervision, Review and Editing.

Prajwal B V: Writing, Methodology, Validation, Resources.

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