Letters in Applied NanoBioScience
Open-Access Journal (ISSN: 2284-6808)

*Article*
**Volume 13, Issue 1, 2024, 30**
https://doi.org/10.33263/LIANBS131.030

# Self-Nanoemulsifying Drug Delivery System of Loratidine for Improved Solubility: Physicochemical Characterization and *In vitro* Study

**Popat Mohite [1,*], Rohini Nangare [2], Ramdas Pandhare [2], Anil Pawar [2]**

[1] A.E.T.'s St. John Institute of Pharmacy and Research Palghar, Maharashtra-401404, India; mohitepb@gmail.com
[2] Mula Education Society's College of Pharmacy, Sonai, Tal- Newasa, Dist-Ahmednagar, Maharashtra-414105; rohininangare@gmail.com, ramdaspandhare@gmail.com, anilpharma123@gmail.com
* Correspondence: mohitepb@gmailmail.com (P.M.);

Scopus Author ID 6508240516
**Received: 3.01.2023; Accepted: 9.02.2023; Published: 13.08.2023**

**Abstract:** The primary goal of this study was to investigate whether or not a self-nanoemulsified drug delivery system (SNEDDS) could enhance the oral bioavailability of Loratidine. The solubility experiments were used to choose the excipients used to create SNEDDS, all of which had a high solubilizing capacity for the active ingredient Loratidine.It has a basic pKa of 3.83 and is a BCS class 2b compound with minimal solubility and oral bioavailability. Its solubility and dissolving properties were improved with the development of the Loratadine SNEDDS. The self-emulsifying zone was identified by developing a ternary phase diagram. The best self-nanoemulsified and solubilization-capable formulations included Isopropyl myristate, PEG-400, and Propylene glycol. The phosphate buffer pH 6.8 was used for the drug release investigation of SNEDDS and was contrasted with the commercial tablet. Compared to the tablet currently on the market, the LS4 formulation release was considerably boosted. Findings suggest that SNEDDS might be used to enhance Loratadine's solubility and dissolving properties.

**Keywords:** Loratadine; SNEDDS; solubility; surfactant; cosurfactant.

© 2023 by the authors. This article is an open-access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

## 1. Introduction

Most new drug candidates in current research and development pipelines have poor water solubility [1]. Most medications have excellent clinical therapeutic effects but low bioavailability because they are less soluble in water and absorb more slowly. Various techniques are being studied, including salt production, complex formation, particle size reduction, cosolvents, or surface active agents. Self-nano-emulsifying drug delivery systems (SNEDDS) have been receiving much attention recently because of their potential to increase medication solubility and bioavailability [2]. Unfortunately, many medicinal peptides and proteins cannot be delivered orally. The GI tract's enzymatic and absorption membrane limitations have led to technological research into ways to get around these problems [3]. Researchers are increasingly interested in developing nanoformulations to improve the solubility and efficacy of pharmacologically active compounds. A self-nano-emulsifying drug delivery system (SNEDDS) is one of the most effective systems for enhancing poorly soluble drug efficacy. SNEDDS is a combination of drug, oil, surfactant, and co-surfactant. SNEDDS comes into contact with water and spontaneously forms oil in water nanoemulsion (droplet size

50–250 nm) [4-6]. Due to their low solubility or lack of disintegration in water, hydrophobic medicines are evidence of poor gastrointestinal absorption when taken orally. Because of this, the bio-availability is low, and the variance is high [7]. As a result, the expected experimental utility is occasionally not realized even when the active agent has strong therapeutic effects. Therefore, there have been increased efforts in developing products with greater oral bioavailability of poorly soluble compounds [8,9].

With or without water, SNEDDS comprises lipids, surface-active compounds, and cosurfactants. When mixed with a reasonable amount of water, the SNEDDS can create an o/w nanoemulsion. Due to the G.I. tract's digestive motility caused by the movement of the stomach and intestines, shaking is required to produce self-emulsion [10,11]. Poor solubility and lower permeability are the leading causes of poorer oral bioavailability. The right amount of medicine must be dissolved in the bloodstream to have the desired therapeutic effect. When taken orally, a hydrophobic medication frequently requires high dosages to reach therapeutic plasma concentrations. Overall, SNEDDS can be employed to improve oral bioavailability and water solubility [12-14].

Loratadine is a B.C.S. Class 2b medication easily soluble in chloroform and methanol but insoluble in aqueous media [15,16]. There is limited oral absorption of Loratadine. There are 53 bonds among the Loratadine in total. 30 non-H bonds, 14 multiple bonds, 2 rotatable bonds, 2 double bonds, 12 aromatic bonds, 3 six-membered rings, 1 seven-membered ring, 2 eleven-member rings, 1 (thio-) carbamate(s) (aliphatic), and 1 pyridine are present. Ethyl 4-(8-Chloro-5, 6-dihydro-11H-benzo [5, 6] cyclohepta [1, 2-b] pyridin-11-ylidene)-1-piperidinecarboxylate is the chemical name for Loratadine (Figure 1). Loratadine is metabolized by isoenzymes of the cytochrome P450 system, including CYP3A4, CYP2D6, and to a lesser extent, numerous others. It is delivered orally, and the G.I. tract and metabolism are favorable. About 97–99% of the Loratadine in plasma is linked to plasma proteins. In 1.4–3.6 hours, the maximum blood concentration is reached [17].

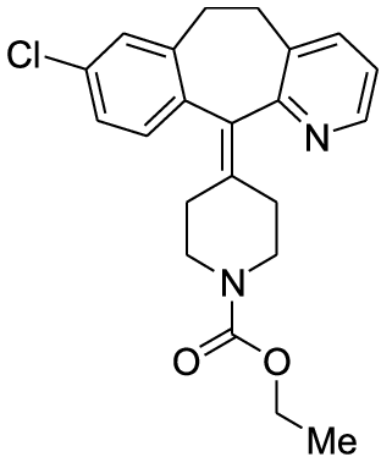


**Figure 1.** Structure of Loratadine.

The traditional antihistamine, Loratadine, and a neutraceutical chemical, sulforaphane (S.F.N.), showed synergistic chemopreventive activity for the first time when delivered using a self-micro emulsifying drug delivery system (S.M.E.D.D.S.). The improved solubility of the B.C.S. class II medication L.O.R. with the S.M.E.D.D.S. formulation was confirmed by an improved in vitro dissolution profile [18]. Colloidal silicon dioxide was used as an emulsifier and solid carrier in a novel lipid-based formulation to increase the oral bioavailability of Loratadine [19]. Solubility, solution, and gastrointestinal permeability limit medication bioavailability and absorption. A drug's water solubility is required for oral absorption. Drug

solubility is the rate at which the drug molecule or dose form dissolves in solution; it's essential when dissolving time is limited. Bioavailability depends on solubility, dissolution rate, drug permeability, efflux susceptibility, and first-pass metabolism ."Solubility" is the amount of solute in a solvent. Quantity is the solute concentration in a saturated solution at a temperature.

Solubility is expressed as parts, %, molality, molarity, volume fraction, and mole fraction. Solubility is a spontaneous molecular partnership between two substances. A saturated solution has a solute-solvent equilibrium [20]. The formulated SNEDDS were evaluated for FT-IR spectroscopy, Zeta potential, solubility, and Differential scanning colorimetry [21].

With the aid of oil, surface active agents, and cosurfactants, Loratadine SNEDDS. were successfully generated in the current work, and the physical & chemical properties were assessed in-vitro. Loratadine's water solubility in various additives was examined. Lipid, surfactant, cosurfactant, and water ternary phase diagrams were plotted, and the nanoemulsion area was displayed. We looked into zeta potential, droplet size, size distribution, and stability. To advance water solubility for the delivery of Loratadine, SNEDDS demonstrated excellent potential.

## 2. Materials and Methods

The source of the Loratadine was Shreya Life Science in Aurangabad. Harmon Finochem Ltd. donated the polymers and excipients like isopropyl myristate, Tween 80, and PEG-400. The supplier of Polyethylene Glycol 400 (PEG 400) was Lobachem, Pvt. Ltd. in Mumbai, India.

### *2.1. Solubility of Loratadine in different excipients.*

The solubility of Loratadine in various oils, cosurfactants, and surfactants was examined. A saturated amount of Loratadine combined with 2mL of additives stirred the mixture for 24 hours at 25°C on a magnetic stirrer (Remilab, FHMS-3491). Each vial was centrifuged at 300 rpm for up to 15 minutes once equilibrium was established at room temperature (Sigma 3K15, U.S.A.). Filtration was used to remove the solid Loratadine using a membrane filter (0.45mm). After the required dilution with methanol, the amount of Loratadine was measured using a U.V. spectrophotometer (Jasco, V630, Japan). The solubility of Loratadine was then calculated (mg/ml).

### *2.2. Phase diagrams for pseudo-ternary systems.*

Plotting the pseudo-ternary phase diagrams allowed us to pinpoint the nanoemulsion region[22]. The mixture included distilled water. Analysis was done to determine the proper ratio of excipients to one another in SNEDDS. Figures 2 and 3 display the pseudo-ternary phase diagrams of Labrafil, Isopropyl Myristate, Tween 80, PEG 400, and Propylene Glycol. The existing area of the o/w nanoemulsion was seen in the dark area. When comparing the nanoemulsion's area in diagrams, it was discovered that the self-nano emulsification efficiency increases with size. The phase diagrams also determined the ideal additive concentration for SNEDDS. When Km was 1, the nanoemulsion area had the largest size.

*2.3. Preparation of Loratadine SNEDDS.*

Based on Loratadine solubility, the best surfactant, cosurfactant, and oils were selected. The SNEDDS. was created by combining Loratadine with cosurfactant or Smix in a container, heating it to 37°C, and then stirring. The required amount of oil was added to the vial while continuously mixing to create a clear, transparent liquid. This transparent fluid was put into capsules until utilized and kept at 25°C.

**Table 1.** Composition of Loratidiene SNEDDS.

| Contents | LS1 | LS2 | LS3 | LS4 | LS5 | LS6 |
|---|---|---|---|---|---|---|
| Loratadine (mg) | 5 | 5 | 5 | 5 | 5 | 5 |
| Labrafil (mg) | 300 | 300 | 300 | - | - | - |
| Isopropyl Myristate (mg) | - | - | - | 300 | 300 | 300 |
| Tween 80 (mg) | - | 150 | - | 150 | - | 150 |
| PEG-400 (mg) | 150 | - | 150 | - | 150 | - |
| Propylene Glycol | 300 | 300 | 300 | 300 | 300 | 300 |

*2.4. In-vitro effectiveness of self-nanoemulsification.*

A solvent was used to dilute SNEDDS before visualization. The moderate stirring and dropwise addition of 20 mL of filtered water to 0.2 mL of SNEDDS. in a dissolution device (Electrolab TDT 08L) at 37°C. When equilibrium is reached, self-nano emulsification time, dispersibility, and appearance are measured and ranked according to the five classes shown in Table 2.

**Table 2.** Type of formulation depends upon visual observation.

| Sr. No. | Dispersibility And Appearance | Grade | Time of S.E. (Min) |
|---|---|---|---|
| 1 | They were rapidly forming (less than 1 min) nanoemulsions, having a Transparent or bluish appearance. | A | Within 30 sec |
| 2 | Rapidly forming, slightly less transparent emulsion, having a bluish-white appearance. | B | Within 1 min |
| 3 | It is a whitish milky emulsion that is formed within 2 min. | C | Within 2 min |
| 4 | The soft, greyish-white emulsion has a slightly oily appearance that is slow to emulsification. | D | Within or Longer than 3 min |
| 5 | Formulation, exhibiting either less or minimal emulsification with large oil globules on the Surface. | E | Longer than 3 min |

*2.5. Determination of Zeta potential.*

In a volumetric flask set at $37^0$C, distilled water (20mL) was used to dilute the Loratadine SNEDDS. (0.2mL). The DelsaTM Nano Zeta Potential and Submicron Particle Size Analyzer were used to calculate the zeta potential [23].

*2.6. Measurement of cloud point.*

The chosen SNEDDS was diluted 100 times with distilled water before being placed in a water bath that gradually heated. The cloud point was defined as the temperature at which muddiness suddenly formed. The sample was heated and cooled once the cloud point was exceeded to assure repeatability [24].

*2.7. Measurement of percentage transmittance.*

In a volumetric flask, SNEDDS. (1 mL) was diluted with 100 mL of distilled water. As soon as nanoemulsions formed, the absorbance of each solution was measured at 200–400 nm

using a U.V. spectrophotometer (Jasco, V630, Japan). Using Abbe's Refractometer, the optical clarity of a few SNEDDS was evaluated in terms of the Refractive Index.

*2.8. Determination of Drug content estimation.*

Using a sonication process, Loratadine was removed from SNEDDS. by solvent extraction and dissolved in methanol. Through Whatman filter paper, these solutions were filtered. The resulting extract's drug content was examined using a U.V. spectrophotometer at 275 nm.

*2.9. Differential scanning calorimetry.*

DSC. Q 20 (T.A. Instruments, New Castle, Delaware, U.S.A.) was utilized to do the DSC. of SNEDDS. In the Tzero pan, 5 mg of sample was inserted, and the lid was heated at a rate of 10°C/min from 60 °C. to 175°C with nitrogen gas flowing at a rate of 50 mL/min [25].

*2.10. Drug: excipient compatibility.*

The I.R. spectra of Loratadine in the isotropic mixture of excipient were obtained using an FT-IR 4600 spectrophotometer (Jasco, Japan) with A.T.R. Every sample was dried before the spectra were obtained. The frequency range covered by the spectrum was 4000-650 $cm^{-1}$, with a resolution of 4 $cm^{-1}$.

*2.11. In vitro drug release study of drugs.*

The U.S.P. Dissolution Apparatus II was used for the Loratadine SNEDDS. in vitro drug release study. The amount of Loratadine per capsule is equivalent to the standard control commercial tablet (10 mg). Hard gelatin Capsules (Size-00) containing Loratadine SNEDDS. were filled and put in the dissolution vessel. At 37°C, the paddles were rotating at 100 rpm. As a dissolving medium (900ml), a phosphate buffer of pH 6.8 was employed. A 5 mL sample was taken at regular intervals, and the concentration of Loratadine in the filtrate was evaluated using a U.V. spectrophotometer at 275 nm. New dissolution media was added to the volume that had been withdrawn. Compare Loratadine SNEDDS's *in vitro* drug release to the commercially available traditional tablet (Loratia, 10mg).

*2.12. Stability study.*

The chosen Loratadine SNEDDS. were placed in capsules and tightly sealed for 90 days of storage at room temperature (25°C). Then, at regular intervals, Loratadine's medication content was assessed.

## 3. Results and Discussion

*3.1. Solubility of Loratadine in different excipients.*

Using a U.V. spectrophotometer, the solubility of Loratadine in various excipients at room temperature (25°C) was determined and shown in Table 3. When making SNEDDS., the Loratadine needs to be soluble. Isopropyl myristate, Tween 80, and PEG 400 have higher levels of Loratadine solubility than other excipients. Because of this, these excipients were chosen to make Loratadine SNEDDS.

**Table 3.** Solubility of Loratadine in different oils, surfactants, and cosurfactants.

| Sr. No. | Oil | Water Solubility (mg/ml) | Surfactant | Water Solubility (mg/ml) | Cosurfactant | Water Solubility (mg/ml) |
|---|---|---|---|---|---|---|
| 1 | Sunflower oil | 25.69±2.53 | Tween 80 | 72.96±2.80 | Transcutol P | 59.96±2.58 |
| 2 | Soya oil | 30.47±1.62 | Tween 20 | 57.48±3.25 | Propylene Glycol | 68.68±1.45 |
| 3 | Liquid Paraffin | 38.46±3.15 | Span 80 | 46.66±1.66 | | |
| 4 | Coconut oil | 68.66±2.55 | Labrafil | 48.86±2.65 | | |
| 5 | Castor oil | 10.155±3.69 | Span 20 | 60.28±3.33 | | |
| 6 | Isopropyl Myristate | 77.82±2.75 | PEG-400 | 75.84±3.10 | | |

Mean ±SD, n=3

*3.2. Investigation of the excipients used in SNEDDS formulations.*

Small molecular weight lipids may penetrate the cosurfactant and the surfactant similarly. The most often utilized lipids are medium or long-chain glycerides. When making a nanoemulsion, the interfacial tension is taken into account, and as the number of alkyl chains increases, the polarity of the lipids decreases. For nanoemulsion, more polar lipid molecules work best. The HLB number of the surfactant affects how well a substance is self-emulsified. Surfactant with an HLB value between 12 and 15 is suitable for nanoemulsion. The surfactants were picked based on their biocompatibility and safety. The alteration in cosurfactant chain length also interfered with nanoemulsification's efficacy. The SNEDDS., which include Isopropyl myristate as a lipid, Tween 80, PEG 400 (a surfactant), and propylene glycol as a cosurfactant, were selected for further study because they had the best nano emulsification efficiency [26].

*3.3. Determination of self-nano emulsification efficiency.*

Tween 80, PEG 400, propylene glycol, and isopropyl myristate were chosen as surfactants, cosurfactants, and lipids after research on ternary phase diagrams and nanoemulsions. Table 1 lists the ingredients of the SNEDDS formulations from LS1 to LS6. Self-nanoemulsification time, zeta potential, dispersibility, stability, and self-nano emulsification efficiency were used to evaluate SNEDDS. in vitro [27]. The zeta potential represents the static electric repulsion.

By dispersing SNEDDS with distilled water, the impact of the dispersion medium on zeta potential was evaluated. Propylene glycol, Tween 80, and isopropyl myristate formulations exhibited good self-nano emulsification.

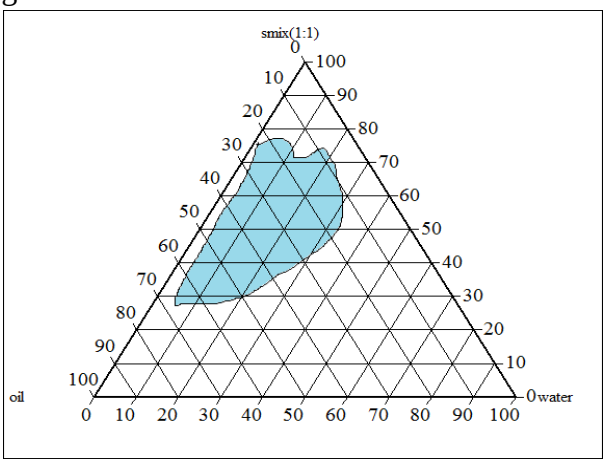


**Figure 2.** Ternary phase diagrams with a 1:1 ratio between oil (Isopropyl myristate), (Smix: Tween 80 & Propylene glycol), and water.

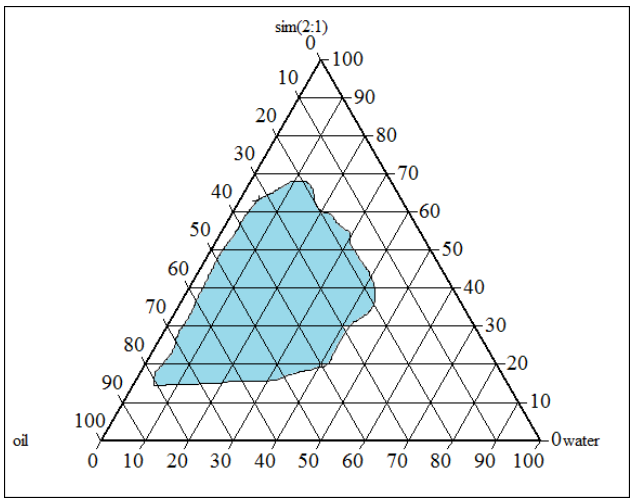


**Figure 3.** Ternary phase diagrams with a 2:1 ratio between oil (Isopropyl myristate), (Smix: Tween 80 & Propylene glycol), and water.

**Table 4.** Dispersibility, appearance, and self-emulsification time of SNEDDS.

| Sr. No. | Dispersibility and Appearance | Grade | Time in SE(Min) |
|---|---|---|---|
| LS1 | Clear dispersion | A | Within 1 |
| LS2 | Milky white | C | Within 2:00 |
| LS3 | Bluish white | B | Within1 |
| LS4 | Milky white | C | Within1:30 |
| LS5 | Clear | A | Within 1 |
| LS6 | Milky white | C | Within 1:45 |

**Table 5.** Zeta potential of SNEDDS.

| Sr. No. | Formulation code | Zeta potential (Mv ) |
|---|---|---|
| 1 | LS1 | 21.9±0.92 |
| 2 | LS2 | 23.94±1.25 |
| 3 | LS3 | 21.89±1.30 |
| 4 | LS4 | 25.71±0.89 |
| 5 | LS5 | 23.45±2.10 |
| 6 | LS6 | 24.04±1.75 |

Mean ±SD, n=3

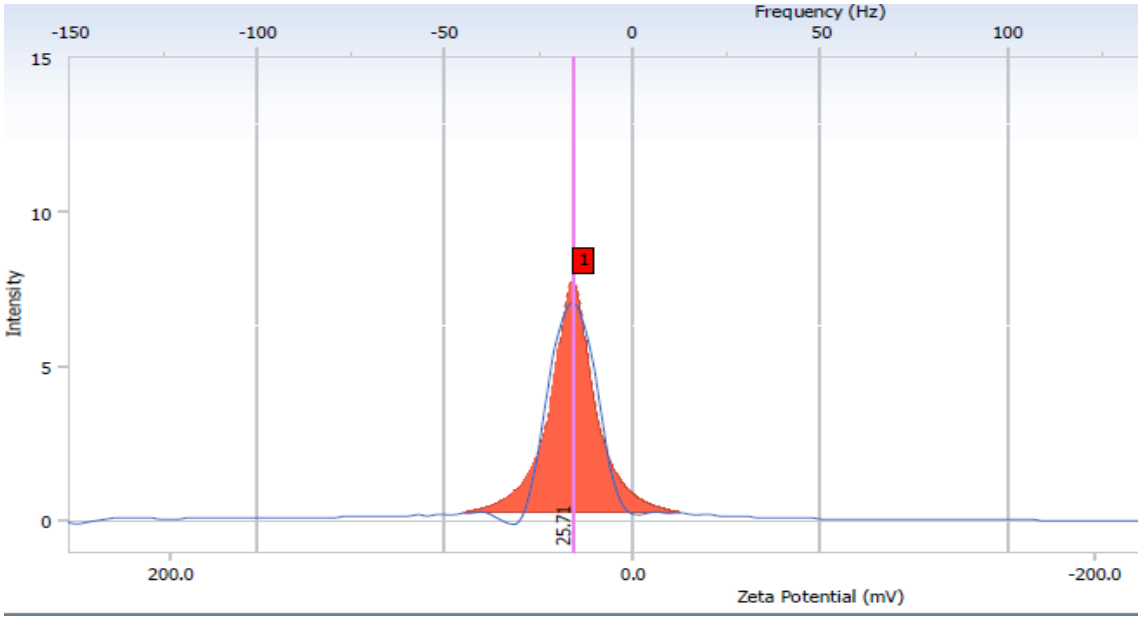


**Figure 4.** Zeta potential of SNEDDS. (LS4).

*3.4. Measurement of percentage transmittance and cloud point.*

Transmittance provides information about the formulation's clarity, transparency, and phase separation[28]. Formulations with more than 99% transmittance are said to be clear and transparent. The LS4 and LS6 SNEDDS chosen for further study displayed transmittance values greater than 99%, indicating transparent and precise formulation (Table 6).

**Table 6.** Percent Transmittance and Clouding Point of SNEDDS.

| Sr. No. | Formulation code | % Transmittance | Clouding point ($^0$C) |
|---|---|---|---|
| 1 | LS1 | 93.43 | 81 |
| 2 | LS2 | 95.41 | 76 |
| 3. | LS3 | 96.15 | 79 |
| 4. | LS4 | 99.87 | 83 |
| 5. | LS5 | 95.85 | 85 |
| 6. | LS6 | 99.20 | 83 |

*3.5. Estimation of drug content.*

Since the medication was evenly distributed across all SNEDDS formulations, the drug content was established at more than 90%. (Table 7).

**Table 7.** Percent drug content of SNEDDS.

| Sr. No. | Formulation code | % drug content |
|---|---|---|
| 1 | LS1 | 94.27±0.96 |
| 2 | LS2 | 96.22±1.26 |
| 3 | LS3 | 96.79±2.10 |
| 4 | LS4 | 98.46±1.85 |
| 5 | LS5 | 95.51±0.87 |
| 6 | LS6 | 92.12±1.24 |

Mean ±SD, n=3

*3.6. Differential scanning calorimetry.*

Endothermic reactions, including melting, phase change, and chemical deterioration, are frequently studied using DSC. It can explore the morphology and interactions between drugs and excipients. Figure 5 displays the thermogram of Loratadine, while Figure 6 shows the thermogram for LS4 formulation. The endothermic peak of the Loratadine thermogram appears at 134°C, indicating the compound's melting point and confirming its crystalline form (Figure 5). The thermogram for LS4 formulation showed no inherent peak, which suggests that the Loratadine was present in SNEDDS in a dissolved state (Figure 6).

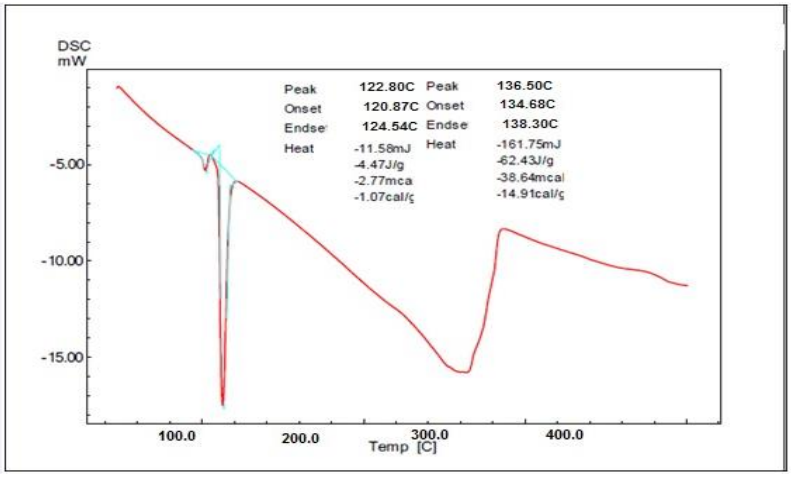


**Figure 5.** DSC thermogram of Loratadine.

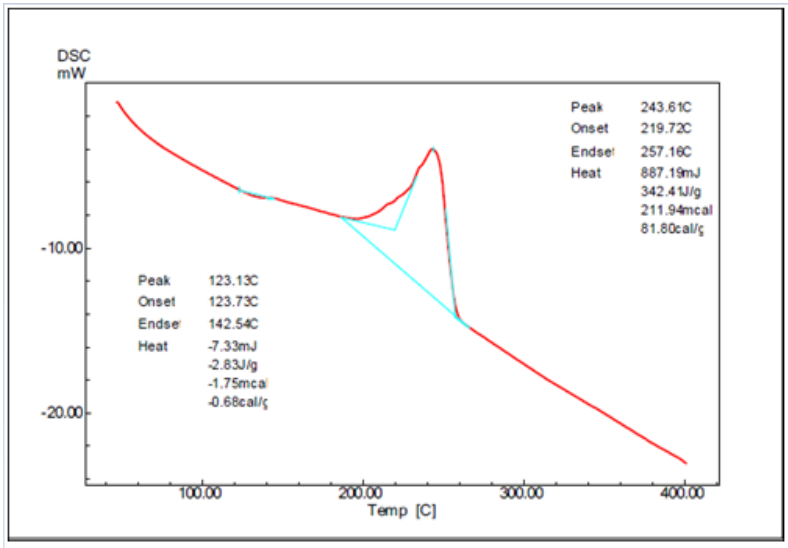


**Figure 6.** DSC thermogram of SNEDDS formulation (LS4).

*3.7. Drug: Excipient compatibility.*

The FTIR spectra of Loratidine and SNEDD formulation (LS4) are shown in Figures 7 and 8. At 2867.63 $cm^{-1}$ (C-H stretching), 2360.44 $cm^{-1}$ (-C=C stretching), 1733.69 $cm^{-1}$ (-C=O bending), and 1069.58 $cm^{-1}$ (-C-O stretching), the Loratadine created distinctive bands (Figure 7). These specific bands (2867.63, 2360.44, 1733.69, and 1059.58) can also be found in FTIR spectra from the LS4 formulation. (Figure 8). No bands shifted or formed, showing no alteration in the bond formation between Loratadine and the excipients.

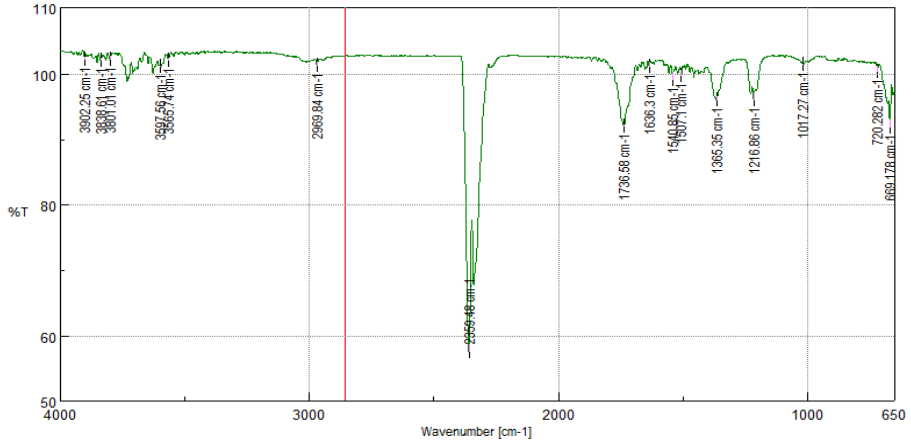


**Figure 7.** FTIR spectra of Loratadine.

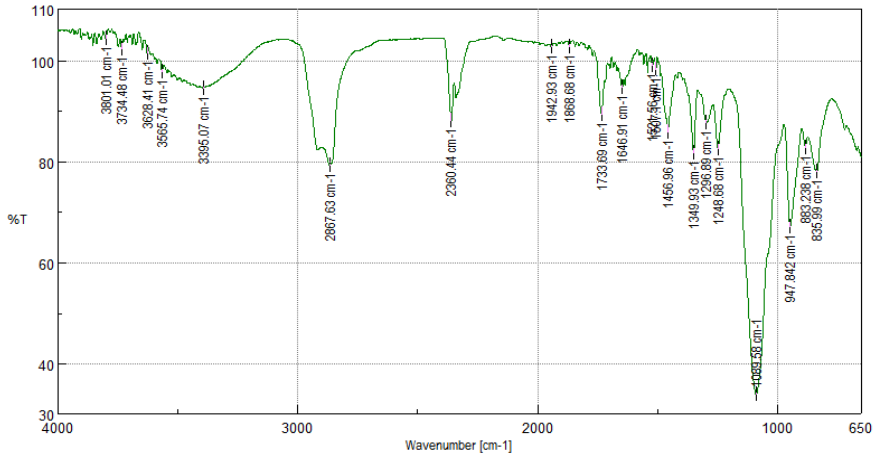


**Figure 8.** FTIR spectra of Loratidine SNEDDS (LS4).

*3.8. Study of in vitro dissolution.*

Utilizing U.S.P. dissolution equipment, SNEDDS and brand-name tablets underwent *in vitro* dissolution (Electrolab, TDT-08L). More drugs were released through SNEDDS. (LS4) (98.88%) than through other SNEDDS as well as commercial tablets (58.65%) after 60 min. Due to the small droplet size, complete dissolution of the drug in SNEDDS., and conversion of the drug into an amorphous state, there was a slight variation in the drug release patterns of other SNEDDS., and the maximal drug release was seen when compared to marketed tablets. These findings suggested that SNEDDS might help improve the dissolving properties of Loratidine (Table 8). The cumulative drug release of marketed formulation and formulation LS1 to LS6 is shown in Figure 9.

**Table 8.** % Cumulative release of drug through SNEDDS and marketed tablet.

| | % Cumulative release of drug | | | | | | |
|---|---|---|---|---|---|---|---|
| **Time (min)** | **LS1** | **LS2** | **LS3** | **LS4** | **LS5** | **LS6** | **Marketed tablet** |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | 16.25±1.27 | 13.25±0.08 | 12.3±0.07 | 18.56±0.90 | 14.98±0.86 | 15.99±0.55 | 9.56±1.35 |
| 10 | 23.65±0.95 | 21.56±0.93 | 22.88±0.69 | 23.65±1.23 | 25.65±2.11 | 22.35±1.85 | 13.52±2.35 |
| 15 | 39.85±2.22 | 38.74±1.52 | 30.25±1.59 | 39.45±2.22 | 31.54±2.45 | 38.45±1.75 | 19.65±2.36 |
| 20 | 36.23±1.36 | 42.56±1.66 | 45.25±1.85 | 42.87±2.35 | 37.65±1.33 | 46.98±2.75 | 23.54±3.36 |
| 25 | 44.89±0.92 | 52.65±2.34 | 58.62±2.15 | 57.89±1.85 | 49.85±2.55 | 58.32±2.66 | 27.56±3.42 |
| 30 | 51.23±0.06 | 59.68±2.58 | 62.58±3.25 | 62.11±1.65 | 56.87±1.65 | 62.52±1.87 | 31.47±4.05 |
| 35 | 69.89±1.32 | 65.32±3.56 | 69.36±2.22 | 70.12±2.85 | 64.58±1.85 | 69.56±1.96 | 38.99±2.53 |
| 40 | 78.45±2.35 | 72.85±4.02 | 75.56±2.53 | 84.45±3.55 | 71.56±2.15 | 72.63±1.62 | 41.87±4.63 |
| 45 | 81.25±2.96 | 79.35±2.21 | 83.45±1.78 | 89.56±4.01 | 88.66±2.35 | 81.58±2.55 | 46.12±3.87 |
| 50 | 88.96±2.10 | 87.36±1.35 | 93.56±1.65 | 95.15±2.55 | 91.56±2.56 | 90.88±2.15 | 50.1±2.65 |
| 60 | 90.25±3.42 | 93.58±1.35 | 97.58±3.20 | 98.88±1.35 | 96.58±3.00 | 95.56±1.95 | 58.65±3.55 |

Mean ±SD, n=3

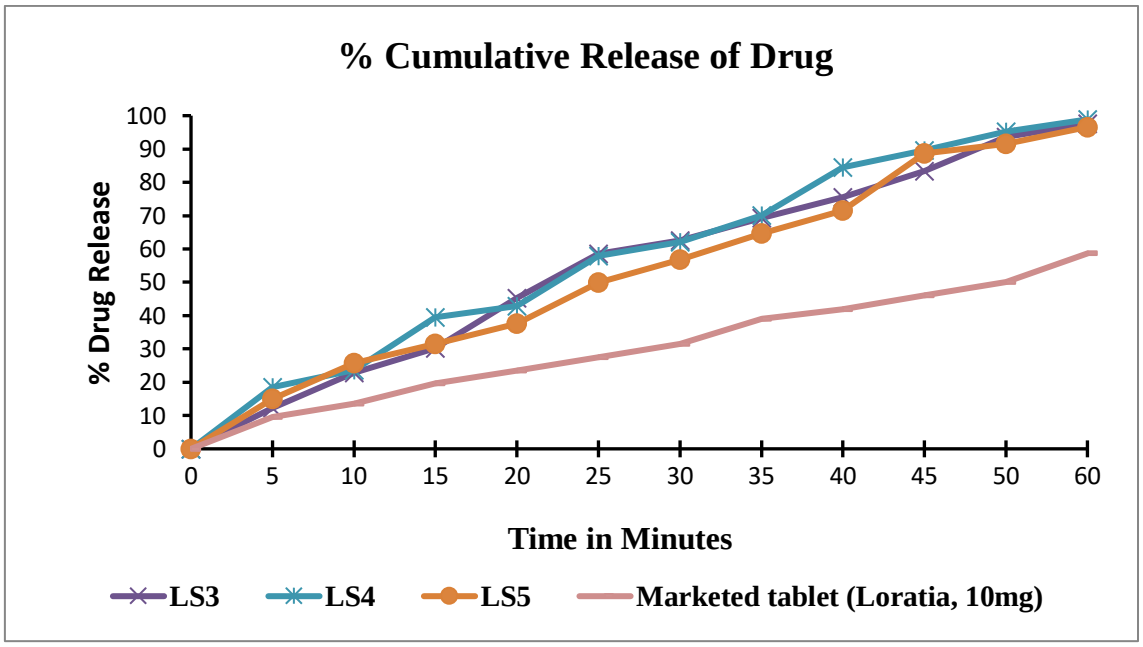


**Figure 9.** % Cumulative release of drug through selected SNEDDS and marketed tablet (Loratia, 10mg).

*3.9. Stability study.*

After 90 days of storage at room temperature (25°C), there were no significant changes in the drug concentration of SNEDDS. The results are shown in Table 9.

**Table 9.** Stability study data of SNEDDS. (LS4).

| Parameter | Observations | | |
|---|---|---|---|
| **Time in days** | **30** | **60** | **90** |
| **% Drug content** | 98.10±1.62 | 98.23±2.01 | 98.75±1.85 |

Mean ±SD, n=3

## 4. Conclusions

In conclusion, to manufacture the Loratidine self-nanoemulsifying drug delivery system (SNEDDS), a self-nanoemulsifying drug delivery system made of isopropyl myristate, tween 80, PEG-400, and propylene glycol as a surfactant, cosurfactant was utilized. Because of the decrease in droplet size, the homogeneous breakdown of the medication, and the transformation into an amorphous state, the excipients that are utilized in SNEDDS.The findings of an in vitro dissolving research revealed that the dissolution rate of the created SNEDDS formulation LS4 in a variety of dissolution media was significantly faster than that of a commercial tablet. This was attributed to the formulation's small droplet size. In formulation LS4, the amount of medication discovered to be present was 98.85 %. Therefore, it is possible to conclude that the self-nanoemulsifying drug delivery system can potentially increase the solubility and oral bioavailability of Loratidine, which is poorly water-soluble.

## Funding

This research received no external funding.

## Acknowledgments

The authors thank the Principal, M.E.S.'s College of Pharmacy Sonai Maharashtra, for providing the research facilities.

## Conflicts of Interest

The authors declare no conflict of interest.

## References

1. Schmied, F.-P.; Bernhardt, A.; Engel, A.; Klein, S. A Customized Screening Tool Approach for the Development of a Self-Nanoemulsifying Drug Delivery System (SNEDDS). *AAPS PharmSciTech* **2021**, *23*, 39, https://doi.org/10.1208/s12249-021-02176-7.
2. Baloch, J.; Sohail, M.F.; Sarwar, H.S.; Kiani, M.H.; Khan, G.M.; Jahan, S.; Rafay, M.; Chaudhry, M.T.; Yasinzai, M.; Shahnaz, G. Self-Nanoemulsifying Drug Delivery System (SNEDDS) for Improved Oral Bioavailability of Chlorpromazine: In Vitro and In Vivo Evaluation. *Medicina* **2019**, *55*, https://doi.org/10.3390/medicina55050210.
3. Salawi, A. Self-emulsifying drug delivery systems: a novel approach to deliver drugs. *Drug Delivery* **2022**, *29*, 1811-1823, https://doi.org/10.1080/10717544.2022.2083724.
4. Zafar, A.; Yasir, M.; Alruwaili, N.K.; Imam, S.S.; Alsaidan, O.A.; Alshehri, S.; Ghoneim, M.M.; Alquraini, A.; Rawaf, A.; Ansari, M.J.; et al. Formulation of Self-Nanoemulsifying Drug Delivery System of Cephalexin: Physiochemical Characterization and Antibacterial Evaluation. *Polymers* **2022**, *14*, https://doi.org/10.3390/polym14051055.

5. Khalid, S.A.; Arafa, K.K.; El-Sherbiny, I.M. Chapter 4 - Self-nanoemulsifying systems for delivery of drugs. In *Systems of Nanovesicular Drug Delivery*, Nayak, A.K., Hasnain, M.S., Aminabhavi, T.M., Torchilin, V.P., Eds.; Academic Press: 2022; pp. 55-68, https://doi.org/10.1016/B978-0-323-91864-0.00014-0.
6. D, S.; J, L. A Literature Review on Self Nanoemulsifying Drug Delivery System (SNEDDS). *International Journal of Pharmaceutical Sciences Review and Research* **2021**, *70*, https://doi.org/10.47583/ijpsrr.2021.v70i01.011.
7. Vinarov, Z.; Abdallah, M.; Agundez, J.A.G.; Allegaert, K.; Basit, A.W.; Braeckmans, M.; Ceulemans, J.; Corsetti, M.; Griffin, B.T.; Grimm, M.; et al. Impact of gastrointestinal tract variability on oral drug absorption and pharmacokinetics: An UNGAP review. *European Journal of Pharmaceutical Sciences* **2021**, *162*, 105812, https://doi.org/10.1016/j.ejps.2021.105812.
8. Anwer, M.K.; Iqbal, M.; Aldawsari, M.F.; Alalaiwe, A.; Ahmed, M.M.; Muharram, M.M.; Ezzeldin, E.; Mahmoud, M.A.; Imam, F.; Ali, R. Improved antimicrobial activity and oral bioavailability of delafloxacin by self-nanoemulsifying drug delivery system (SNEDDS). *Journal of Drug Delivery Science and Technology* **2021**, *64*, 102572, https://doi.org/10.1016/j.jddst.2021.102572.
9. Zafar, A.; Imam, S.S.; Alruwaili, N.K.; Alsaidan, O.A.; Elkomy, M.H.; Ghoneim, M.M.; Alshehri, S.; Ali, A.M.A.; Alharbi, K.S.; Yasir, M.; et al. Development of Piperine-Loaded Solid Self-Nanoemulsifying Drug Delivery System: Optimization, In-Vitro, Ex-Vivo, and In-Vivo Evaluation. *Nanomaterials (Basel)* **2021**, *11*, https://doi.org/10.3390/nano11112920.
10. Schmied, F.-P.; Bernhardt, A.; Klein, S. Preparation of Solid Self-Nanoemulsifying Drug Delivery Systems (S-SNEDDS) by Co-Extrusion of Liquid SNEDDS and Polymeric Carriers—A New and Promising Formulation Approach to Improve the Solubility of Poorly Water-Soluble Drugs. *Pharmaceuticals* **2022**, *15*, https://doi.org/10.3390/ph15091135.
11. Reddy, M.R.; Gubbiyappa, K.S. Formulation development, optimization and characterization of Pemigatinib-loaded supersaturable self-nanoemulsifying drug delivery systems. *Future Journal of Pharmaceutical Sciences* **2022**, *8*, 45, https://doi.org/10.1186/s43094-022-00434-4.
12. Abushal, A.S.; Aleanizy, F.S.; Alqahtani, F.Y.; Shakeel, F.; Iqbal, M.; Haq, N.; Alsarra, I.A. Self-Nanoemulsifying Drug Delivery System (SNEDDS) of Apremilast: In Vitro Evaluation and Pharmacokinetics Studies. *Molecules* **2022**, *27*, https://doi.org/10.3390/molecules27103085.
13. Haddadzadegan, S.; Dorkoosh, F.; Bernkop-Schnürch, A. Oral delivery of therapeutic peptides and proteins: Technology landscape of lipid-based nanocarriers. *Advanced Drug Delivery Reviews* **2022**, *182*, 114097, https://doi.org/10.1016/j.addr.2021.114097.
14. Gupta, S.; Kesarla, R.; Omri, A. Formulation Strategies to Improve the Bioavailability of Poorly Absorbed Drugs with Special Emphasis on Self-Emulsifying Systems. *ISRN Pharmaceutics* **2013**, *2013*, 848043, https://doi.org/10.1155/2013/848043.
15. Nair, A.R.; Lakshman, Y.D.; Anand, V.S.K.; Sree, K.S.N.; Bhat, K.; Dengale, S.J. Overview of Extensively Employed Polymeric Carriers in Solid Dispersion Technology. *AAPS PharmSciTech* **2020**, *21*, 309, https://doi.org/10.1208/s12249-020-01849-z.
16. Hens, B.; Bermejo, M.; Augustijns, P.; Cristofoletti, R.; Amidon, G.E.; Amidon, G.L. Application of the Gastrointestinal Simulator (GIS) Coupled with In Silico Modeling to Measure the Impact of Coca-Cola® on the Luminal and Systemic Behavior of Loratadine (BCS Class 2b). *Pharmaceutics* **2020**, *12*, https://doi.org/10.3390/pharmaceutics12060566.
17. Sarheed, O.; Shouqair, D.; Ramesh, K.V.R.N.S.; Khaleel, T.; Amin, M.; Boateng, J.; Drechsler, M. Formation of stable nanoemulsions by ultrasound-assisted two-step emulsification process for topical drug delivery: Effect of oil phase composition and surfactant concentration and Loratadine as ripening inhibitor. *International Journal of Pharmaceutics* **2020**, *576*, 118952, https://doi.org/10.1016/j.ijpharm.2019.118952.
18. Desai, P.; Thakkar, A.; Ann, D.; Wang, J.; Prabhu, S. Loratadine self-microemulsifying drug delivery systems (SMEDDS) in combination with sulforaphane for the synergistic chemoprevention of pancreatic cancer. *Drug Delivery and Translational Research* **2019**, *9*, 641-651, https://doi.org/10.1007/s13346-019-00619-0.
19. Huang, R.; Tan, Y.; Shen, L.; Wang, T.; Quan, D. A Novel Surfactant-free Lipid-based Formulation for Improving Oral Bioavailability of Loratadine Using Colloidal Silicon Dioxide as Emulsifier and Solid Carrier. *Curr Pharm Biotechnol* **2018**, *19*, 217-223, https://doi.org/10.2174/1389201019666180509094812.
20. Bhalani, D.V.; Nutan, B.; Kumar, A.; Singh Chandel, A.K. Bioavailability Enhancement Techniques for Poorly Aqueous Soluble Drugs and Therapeutics. *Biomedicines* **2022**, *10*, https://doi.org/10.3390/biomedicines10092055.

21. Nazlı, H.; Mesut, B.; Özsoy, Y. In Vitro Evaluation of a Solid Supersaturated Self Nanoemulsifying Drug Delivery System (Super-SNEDDS) of Aprepitant for Enhanced Solubility. *Pharmaceuticals* **2021**, *14*, https://doi.org/10.3390/ph14111089.
22. Ternary Phase Diagram. In *Introduction to Phase Diagrams in Materials Science and Engineering*; world scientific: 2019; pp. 121-169.
23. Prieve, D.C.; Yezer, B.A.; Xu, K.; Khair, A.S.; Schneider, J.W.; Sides, P.J. Determination of the zeta potential of planar solids in nonpolar liquids. *Journal of Colloid and Interface Science* **2021**, *592*, 271-278, https://doi.org/10.1016/j.jcis.2021.02.044.
24. Daridon, J.-L. The Limitations of the Cloud Point Measurement Techniques and the Influence of the Oil Composition on Its Detection. *Petroleum Science and Technology* **2005**, *23*, 1113-1128, https://doi.org/10.1081/lft-200035541.
25. Green, S.P.; Wheelhouse, K.M.; Payne, A.D.; Hallett, J.P.; Miller, P.W.; Bull, J.A. On the Use of Differential Scanning Calorimetry for Thermal Hazard Assessment of New Chemistry: Avoiding Explosive Mistakes. *Angewandte Chemie International Edition* **2020**, *59*, 15798-15802, https://doi.org/10.1002/anie.202007028.
26. Nair, A.B.; Singh, B.; Shah, J.; Jacob, S.; Aldhubiab, B.; Sreeharsha, N.; Morsy, M.A.; Venugopala, K.N.; Attimarad, M.; Shinu, P. Formulation and Evaluation of Self-Nanoemulsifying Drug Delivery System Derived Tablet Containing Sertraline. *Pharmaceutics* **2022**, *14*, https://doi.org/10.3390/pharmaceutics14020336.
27. Obitte, N.C.; Ofokansi, K.C.; Kenechukwu, F.C. Development and Evaluation of Novel Self-Nanoemulsifying Drug Delivery Systems Based on a Homolipid from Capra hircus and Its Admixtures with Melon Oil for the Delivery of Indomethacin. *Journal of Pharmaceutics* **2014**, *2014*, 340486, https://doi.org/10.1155/2014/340486.
28. Avachat, A.M.; Patel, V.G. Self nanoemulsifying drug delivery system of stabilized ellagic acid–phospholipid complex with improved dissolution and permeability. *Saudi Pharmaceutical Journal* **2015**, *23*, 276-289, https://doi.org/10.1016/j.jsps.2014.11.001.