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Desloratadine Microemulsion Based Solid Lipid Nanoparticles

Varsha Dute[1], Vijay Mahajan[2], Amol Deshmukh[3]

[1, 2, 3]Department of Pharmaceutics, S.M.B.T. College of Pharmacy Nandi hills Dhamangaon, Igatpuri. Dist. Nashik, India

Abstract: ***In this study, novel and main objective of this research work was to formulate and evaluate the Microemulsion Based Solid lipid Nanoparticles. Desloratadine o/w microemulsion based SLN was prepared to enhanced solubility. Desloratadine saturated solubility determined in different oils, Surfactants and co-surfactants. Sunflower oil, as oily phase and Tween 80 as surfactants and co-surfactants Propylene glycol used for pseudo ternary phase diagrams was constructed to identify the microemulsion regions. Evaluation Drug content, Drug release, Emulsification time, Visual inspection. pH, Particle size. Solid SLN – DSC, XRD, SEM, FT-IR, Refractive index, Drug Release.***

Keywords: Solid lipid Nanoparticles, Microemulsion, SEM, XRD, Spray drying

1. Introduction[1,2]

Desloratadine is a potent and selective antagonist of the histamine H1 receptor, which has been widely used to treat allergic symptoms and allergic reaction most preventing inflammatory disorders of upper respiratory tract is allergic rhinitis which is characterized by a specific immunoglobin E-mediated hypersensitivity reaction. Desloratadine (DL) is the major active metabolite of the parent drug loratadine. it acts by inhibiting the release of pro inflammatory mediators from human mast cells/ basophil.

Microemulsion Based Solid Lipid Nanoparticles[3,4,5]

Gasco and co-workers were the 1st to develop SLN based on the dilution of microemulsion. Microemulsion are thermodynamically stable, clear and isotropic mixtures usually composed of an oil or lipid emulsifier or co-emulsifier and water.

Solid lipid Nanoparticles are colloidal developed at the beginning of the 1990s as alternative novel carriers' system to liposomes, emulsions and polymeric nanoparticles. Mostly, they are made of solid hydrophobic core having a monolayer of phospholipids coating. The solid core contains the drug dissolved or dispersed in the solid high melting heavy matrix. Nanoparticles, entrapped and / or which the active principal is adsorbed. The different methods solid lipid nanoparticles are at forefront of the fast-developing field of nanotechnology with several potential applications in the drug delivery, clinical medicine and research as well as other varied sciences. In system consists of spherical solid lipid nanoparticles in the nanometers ranges, which are dispersed in water or on aqueous surfactant solution. It is identical to an oil-in water emulsion for parenteral nutrition but the lipid (oil) of the emulsion has been replaced by a solid lipid i.e. solid lipid nanoparticle. SLN are sub- micron colloidal carrier 50-1000 nm size range which lipid dispersed in water or in an aqueous surfactant solution. They have potential to transfer lipophilic or hydrophilic drugs or diagnostic. Lipid particulate DDS are depending on their architecture and particle size. Due to the hugequantity of administration routes available, these delivery systemsmake differently depending on the formulation type and route of administration. SLN offer unique properties such as smaller size, larger surface area, interaction pf phases at the interfaces, and these are attractive of their ability to improve performance of nutraceuticals, pharmaceuticals and other materials. The lipid used in SLNs melting point must highest body temperature. This is one most popular approach to improve the oral bioavailability of poorly water -soluble drug.

Principal of Microemulsion based SLN

The principal of this method is to add a warm oil-in-water microemulsion into a large amount of cold water which leads to precipitation of the lipid phase forming fine called Solid lipid nanoparticles. Therefore, this technique is easily processed at laboratory scale since microemulsion, the key intermediate product of this SLN preparation at laboratory scale since microemulsion forms spontaneously. Microemulsion are optically transparent, of low viscosity and thermodymically stable dispersion of oil and water stabilized by an interfacial film of a surfactant, typically in combination with a co-surfactant. Surfactant reduces the interfacial tension between oil and aqueous phases in order to decrease the free energy of the system while a co-surfactant enhances the flexibility of the interfacial film by penetrating into interface. Microemulsion are spontaneously formed when suitable ratios of all components i.e. oil or melted lipid, water, surfactant and co-surfactant are simply mixed. No specific technique or high energy input is required. The preparation of SLN via microemulsion technique is processing different lipid composition should be investigating to obtain the optimal SLN formulation.

Advantages of Microemulsion based SLN

- Low mechanical energy input.
- Theoretical stability.
- Lab scale possible.

Disadvantages of Microemulsion Based SLN

- Extremely sensitive to change.
- Labor intensive formulation work.
- Low nanoparticle concentrations.

2. Materials and Methods

Desloratadine was gifted from Amsal Pharmaceutical company (Mumbai) Pvt.Ltd. Sunflower oil purchase from Research Lab Fine Chem Industries. Propylene glycol and Tween 80, 20 were purchased from. Research Lab Fine Chemical Industries. All added chemicals and solvents were analytical grade and used without further purification.

Solubility Studies [5]

Stability is the amount of a solute that can dissolved in a specific solvent under given conditions. The dissolved substance is called the solute and the dissolving fluid is fluid is called the solvent which together from a solution. The solubility of Desloratadine in different solvent such as distilled water, 0.1NHcl. Methanol and chloroform were determined using shake flask method. An excess amount of Desloratadine was added in the solvent and vortexed for 48 hr at room temperature. Mixture was then centrifuge at 3000rpm for 10 min and filtered through 0.5µ filter paper. Filtrate was further diluted with methanol to obtain suitable concentration. The solubility of Desloratadine was determined by analyzing UV spectra at max 245nm. The results of solubility study are displayed in Table.

The solubility studies of DL in different oils (Sunflower oil, Clove oil, Caster oil, Groundnut, Caproyl 90, Isopropyl myristate). Surfactants and Co-surfactants (Tween 20, Tween 80, Span 80, Labrasol, Cremophore RH, Transcutol and Propylene Glycol). Was determined by adding an excess amount of the drug to 1ml of the selected vehicle in a centrifugal tube, followed by mixing at 3000 rpm in a centrifuge and kept for 48 hrs. Excess DL removed after centrifuge for 10 min. The supernatant was measured spectrophotometrically at λmax 245 nm.

Construction of Pseudoternary Phase Diagrams[6,7,8,9]

To investigate concentration range of components for the existing boundary of Microemulsion, pseudo-ternary phase diagrams were constructed using the water titration method. Based on the results of the solubility studies, the oil and surfactant and co-surfactant in the present study were sunflower oil and Tween 80, Propylene glycol.

Preparation of Microemulsion Based Solid lipid Nanoparticles[10, 11]

- A series of SLN formulation was prepared using sunflower oil, Tween 80 as surfactant and propylene glycol as co-surfactant.
- Preparation of solid lipid Nanoparticles via microemulsion method was performed at a temperature above melting point.
- Appropriate quantities of oil, surfactant, co-surfactant was weighed and mixed at a temperature 10℃ and melt above the melting point 70℃ the lipid in water bath.
- Water was heated to the same temperature as the lipid phase and added drop wise under mild stirring to the lipid melt.
- The hot microemulsion is dispersed in cold water (2-3℃) under continuous magnetic stirring and addition of drug sample desloratadine and vortexing for 10 seconds.
- Visualized for clarity when turbidity that did not disappear after vortexing was observed the sample were sonicated for 5 min at a temperature above the melting point of the lipid. The ratio of microemulsion to aqueous medium 1:20.
- SLN dispersion can be used as granulation fluid for transforming in to solid product. This dispersion was then observed visually for 5 days at interval of 24 hrs. for any phase separation.

Figure 1: Aqueous Dispersion of Microemulsion Based SLN

Evaluation of Microemulsion Based Solid lipid Nanoparticles[13,14,15,16,17,18,19,20]

- **Visual Inspection:** [10, 12]
  The prepared Microemulsion based aqueous SLN were examined for clarity, and Phase separation.
- **pH Measurements:**
  The pH of 10% w/w aqueous solution was measured by pH meter. The solutions were prepared by dissolving in 9 g of distilled water.
- **Viscosity Measurements:**
  The viscosity of microemulsion was measured at room temperature (Brookfield Viscometer) using spindle no 40-speed started at 5 rpm gradually increased until reached 100 rpm at constant time interval of 30 seconds.
- **Precipitation Assessment:**
  Aqueous SLN formulation was diluted up to 100 times with distilled water continuous stirring on magnetic stirrer to form microemulsion precipitation was evaluated by visual inspection of resultant microemulsion after 24 hours. The preparations were then considered as clear transparent, non-clear (turbid), stable (no precipitation at end of 24 hrs.) or unstable (showing precipitation within 24 hours)
- **Self-emulsification time:**
  Approximately 1 ml of liquid SLN was added to 250 ml of purified water stirred gently and checked for clarity of solution. Self-emulsification time of preparation was determined using USP II dissolution apparatus. 1 ml of formulation was added drop wise to 250 ml of purified water at 37℃. Gentle agitation was provided by dissolution paddle rotating at 75 rpm. Time reserved for formation of clear solution was noted as self - emulsification time.
- **Drug Content determination:**
  Amount of Drug in the aqueous SLN formulations was determined by UV spectrometric method. Weighed Accurate quantity of Liquid SLN formulation Equivalent to 10 mg of drug (Desloratadine) in 100ml volumetric

flask and was diluted with methanol to make up volume Upto 100ml. further 1 ml of the solution was diluted to 10 ml using methanol to make 10µg/ml solutions. The drug content was analyzed by taking UV absorbance at 245 nm.

- **Refractive Index:** [21]
  Refractive index proved the transparency of formulation. The refractive index of the system is measured by Abbe Refractometer by placing drop of solution on slide and recording the refractive index. Refractive index of Sunflower oil, Tween 80, propylene glycol was noted.
- **Drug Release Study**
  The in- vitro dissolution study of aqueous SLN and plain were carried out using dissolution test apparatus no. II as per USP. Parameters used for drug release study of aqueous SLN is displayed in table.Quantity equivalent to 10 mg of aqueous SLN formulation was added to dissolution media. Samples of 5ml at 5 min interval were withdrawn at regular time 5 min to 60 min and filtered using Whatman filter paper. An equal volume of respective dissolution medium was added to maintain the volume constant Drug release was analyzed using UV-spectrophotometer at 245 nm.

Table 1: Parameters for Drug Release study of aqueous SLN and plain

Sr. No	Parameters	Specification
1	Dissolution Apparatus	USP Apparatus NO II
2	Dissolution Medium	900 ml 0.1N HCl
3	Speed	50 rpm
4	Time	60 minutes
5	Temperature	37±0.5°C

In the SLN formulation the free energy required to form a microemulsion is very low, as there is continuous and spontaneous formation of an interface between the oil droplet and water. The oil/ surfactant / co-surfactant and water phase swell this results in decrease in oil droplet size and this eventually increase the drug release rate. Hence, this technique is used for the solubility enhancement of the poorly water-soluble drug.

Solidification Of Aqueous Dispersion of SLN

Solidification can be done by spray drying technique. Colloidal silicon dioxide (Aerosil 200) was used as the carrier for the conversion of liquid SLN to solid SLN. Aerosil 200 (5gm) was dissolved in 150 ml methanol by magnetic stirring. The liquid SLN (10gm) was then added with constant stirring and the solution was kept 50°C for 10 min to obtain a good o/w microemulsion. Parameters of spray drier are displayed in table 2.

Table 2: Process Parameters for spray Drying

Sr. No	Parameters	Optimized value
1	Solvent	Methanol
2	Inlet Temperature	48°C
3	Outlet temperature	34°C
4	Aspiration speed	35
5	Compressed air flow rate	2.5 Bar
6	Feeding Rate	2ml/min

After the completion of drying process, fraction pf dried SLN were collected from different parts of spray dryer, i.e. drying chamber, first cyclone separator and collector attached to it. These fractions were then mixed in polybag for 15 min to ensure the uniform mixing of blend. shows preparation of solidification of SLN by spray drier.

Figure 2: Preparation of Solid SLN by spray Drier

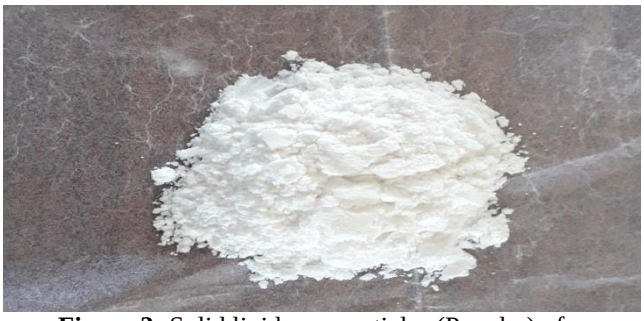

Figure 3: Solid lipid nanoparticles (Powder) of Desloratadine

Characterization of Solid SLN[22]

- **Yield of spray Dried Product**

The percentage yield of Solid SLN was calculated by using following formula

$$\% \text{ Yield} = \frac{\text{Material recovered from spray dryer}}{\text{Weight of Liquid SLN + Weight of Aerosil 200}} \times 100$$

$$= \frac{11.80}{10+5} \times 100$$

= 78.66%

The percentage yield of spray dried S-SLN product was found to be 78.66 % w/w. The S-SLN obtained with set parameter like inlet, outlet temperature, feed rate etc. Was satisfactory considering the small batch.

- **Powder Flow Properties**

Spray dried product was evaluated for bulk density, tapped density, cars compressibility index, Hausner ratio, angle of repose.

- **Particle Size:** [23, 24]

Particle size of microemulsion was determined by laser scattering technique using Malvern Zetasizer Ver.6.20 serial Number: MAL1051945 Malvern Ltd) All measurements were performed at a 25±2°C.
Parameters of particle size are as follows

Table 3: Parameters of Particle Size determination

Measurement type	Particle size
Scattering Angle	90˚
temperature of holder	25℃
Viscosity of the dispersion media	0.88872 (cP)
Form of distribution	Standard
Representation of result	Scattering light Intensity
Count rate	90.4 (kcps)

Result of particle size are displayed in **Table 17.** and **figure 12.**

- **Zeta potential measurement:** [24,25,26,27]

Solid SLN formulation containing 10 mg Desloratadine SLN was diluted to 20 ml with distilled water in flask and was mixed gently by inverting the flask. The particle size so formed was determined by dynamic light scattering (DLS) technique using Zetasizer (Nano ZS, Malvern Instruments, UK). With the zeta potential Electrophoretic mobility was also determined.

Table 4: Parameters used for determination of zeta potential

Measurement Type	Zeta Potential
Temperature	25℃
Viscosity of dispersed medium	0.8872 (cP)
Conductivity	0.579(mS/cm)

- **Drug content determination**

Drug content of solid -SLN was determined by adding sufficient amount of methanol to spray dried powder then the UV absorbance was measured at 245 nm. By the calculation 300 mg of Solid -SLN contain 10 mg of the drug, so for the drug content determination 300 mg of Solid- SLN were taken.
The result of the drug content is displayed in **Table 18.**

- **In-Vitro Dissolution Study**

The in -vitro dissolution study of SLN was carried out using dissolution test apparatus no II as Per USP. Parameters used for drug release study of SLN are displayed in **table 5.**Quantity equivalent to 10mg of SLN powder was added to dissolution media. Samples of 5 ml at specific time interval was with-drawn and filtered using 0.45µm filter paper. An equivalent volume of specific dissolution medium was added to keep the volume constant. Drug release from sample was analyzed using UV- spectrophotometer at 245nm. Results are displayed in **table 14. and figure 10.**

Table 5: Parameters for Drug Release study of Solid SLN

Sr. No	Parameters	Specification
1	Dissolution Apparatus	No. II
2	Dissolution Medium	0.1 N HCl
3	Speed	50
4	Time	60 minutes

Solid State Characterization of SLN Powder [19,20,23]

- **Differential Scanning Calorimetry:** [27]

The physical state of desloratadine in SLN was characterized by the differential scanning calorimetry (DSC instruments, METTLER, STAR SW 10.00). The samples were place in standard aluminum pans, and dry nitrogen was used as effluent gas. All samples were scanned at a temperature range speed of 5℃/min. The DSC thermograms of Desloratadine, SLN containing Desloratadine and Aerosil 200with each other. Results are displayed in **figure.14,15**

- **Scanning Electron Microscopy:** [27]

Surface topography of the Solid- SLN was investigated by Scanning electron microscopy (SEM).
Results are displayed in **Figure 16.**

- **Powder X-ray Diffraction**

X-ray powder diffraction pattern of the Desloratadine-SLN were recorded. Peaks present in the sample were measured. X- ray powder diffraction was recorded as shown in **figure.**Result strongest peak show in **Table**

- **Stability Study**

The determination stability testing is to deliver evidence on how excellence of drug substance or drug product varies with time under the influence of variety of environmental factors such as temperature, humidity and light, and enables recommended storage conditions, re-test periods and shelf lives to be established.

- **Stability study of liquid SLN**

a) Thermodynamic stability studies
The liquid SLN were filled in vials and was kept at different temperature condition to check the stability of the formulation. This study was performed for 3 months and any change in the formulation was reported. The sample were kept at various temperature condition like
25℃- room temperature
40℃- stability oven
The results of thermodynamic stability study are displayed in **table 21.**

b) Centrifugation test
Prepared liquid SLN was centrifuged at 3500 rpm speed for about 30 min. the phase separation after 30 min was observed. If the Liquid- SLN shows the phase separation then the formulation is unstable and if no phase separation is observed the formulation is stable and hence can be used for the further studies.

c) Drug content
Drug content was determined from initial level to 1 months. The sample kept at different temperature condition at every month were added to sufficient amount of methanol and the UV absorbance was measured at 245 nm. The result from initial level 1 month was compared. The result of drug content is displayed in **Table 22.**

d) In – vitro drug release study
The in-vitro dissolution study of solid SLN for stability was carried out using dissolution test apparatus no II as per USP in vitro drug release study. Parameters used for drug release study of solid SLN are displayed in **Table 6.** Quantity equivalent to 10 mg of solid SLN formulation was added to dissolution media. Samples of 5 ml at specific interval was with- drawn and filtered using 0.45µm filter paper. An equivalentcapacity of respective dissolution medium was added to maintain the volume constant. Drug release from sample was analyzed using UV-spectrophotometer at 245 nm. Results are displayed in **table 23** and **figure18.**

Table 6: Parameters for Drug Release study of solid SLN (stability study)

Sr. No	Parameter	Specification
1	Dissolution Apparatus	No. II
2	Dissolution Medium	0.1 N HCl
3	Speed	50 rpm
4	Time	60minutes

d) FT-IR Study

one-month stability study of solid – SLN at room temperature 25℃. 10 gm of solid SLN formulation was placed in glass vial and seal vial was placed at 25℃ temperature condition and sample is visually observed at interval of each week for any color change and after 1 months samples were analyzed by FT-IR. FT-IR of the solid SLN after 1 months was compared with the FT-IR of pure drug for identification of any change in the drug during stability study.

3. Results and Discussion

Solubility Studies

Solubility of the drug in the vehicle is one of the most important attributes in the successfulness of Microemulsion based SLN, as it would help to maintain the drug in the solubilized form. The solubility of DL in numerous vehicles is existing in chart form. The solubility of Desloratadine in Tween 80 was found to be the best among all the investigated surfactants. DL was more soluble in Propylene glycol.

Table 7: Solubility study of Drug

Sr. no	Solvent	Solubility (mg/ml)
1	Distilled water	1.22± 0.05
2	0.1 N HCl	6.41± 0.10
3	Methanol	7.59± 0.30
4	Chloroform	4.49± 0.40

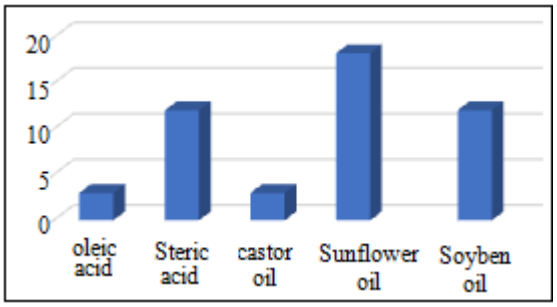

Figure 4: Solubility of Desloratadine in Different oils

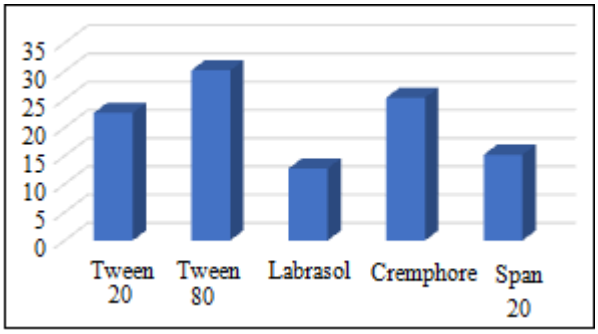

Figure 5: Solubility of Desloratadine in different Surfactant

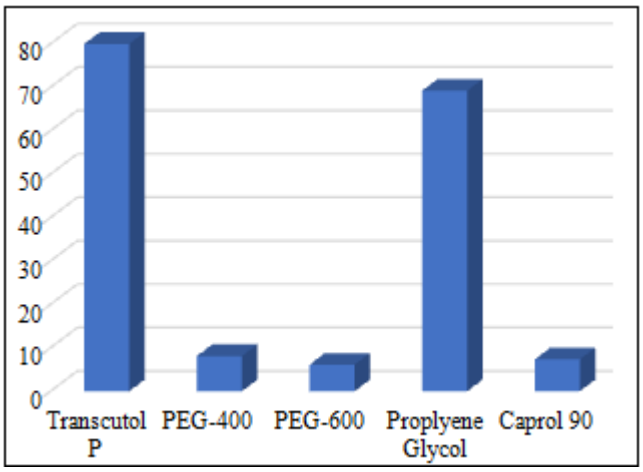

Figure 6: Solubility study in different co-surfactant

Incompatibility

Desloratadine and its compositions are prone to oxidation and decomposition by acidic excipients to form decomposition such as deschlorodesloratadine, dehydrodesloratadine and N-formyl desloratadine. The desloratadine undergoes extensive degradation in the presence of common excipients such as steric acid to form N-formyldesloratadine as a major degradation product. Various oils such oleic acid, castor oil, caproyl 90 incompatible with Desloratadine showing red coloration and various surfactants and co-surfactants shows incompatible with Desloratadine. DL more soluble in Transcutol then propylene glycol but it shows red blood coloration after 1 week.

Construction of Pseudo ternary Phase Diagram.

Pseudo ternary phase diagram was constructed to investigate the effect of surfactant to co-surfactant ratio (km) on the area of microemulsion existence region. it is well known fact that km value has considerable effect on the area of microemulsion existence. The lipid mixture with different surfactant, co-surfactant and oil ratio leads to formation of SLN with different properties structure. In order to form self-emulsifying o/w and w/o microemulsion. oil, surfactant and aqueous phase were used. This four-component system can be best described by pseudo ternary phase diagram where a constant ratio of two of the components was used and other two were varied. To determine optimum concentration of oil, surfactant and co-surfactant for development of SLN formulation optimum ratio of excipients concentration established by means of phase diagram studies provided the area of the monophasic region. A pseudo ternary phase diagram of the investigated system. sunflower oil (oil), tween 80 (surfactant), Propylene glycol (co-surfactant) are shown in **figure 7, 8, 9.**

For the construction of pseudo ternary phase diagram different ratio of surfactant and co-surfactant are prepared (Smix). Ratios are prepared as follows-

- oil + Smix (1:1)
- oil + Smix (2:1)
- oil + Smix (3:1)

Water was added in a drop wise manner to each oily mixture under proper magnetic stirring at 37℃ until the mixture become clear at a certain point. the concentrations of the

components were recorded in order to complete the pseudo ternary phase diagrams, and then the contents of oil, surfactant, co-surfactant and water at appropriate ratios were selected based on these results. The boundaries of the self-micro emulsification regions in the phase diagrams were determined by connecting the points representing formation of the microemulsion.

Ternary phase diagram of different ratio is shown in figure no.

Phase Diagram indicated that the Smix ratio 2:1, 3:1, shows less self-emulsification region than the others therefore these ratios were rejected. in case of the phase diagram indicating the Smix ratio 3:1, 2:1there is slight difference in the self-emulsification region but the Smix ratio 1:1 shows larger self-emulsification region than 2:1. Therefore the Smix ratio 1:1 will be selected for further study.

Phase Diagram of (1:1) ratio

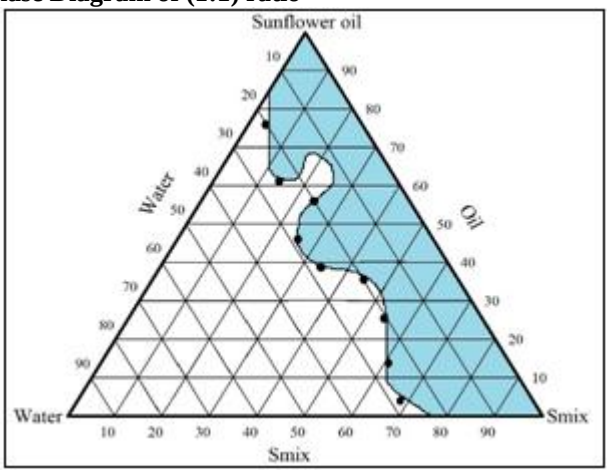

Figure 7: Phase Diagram of (1:1) ratio

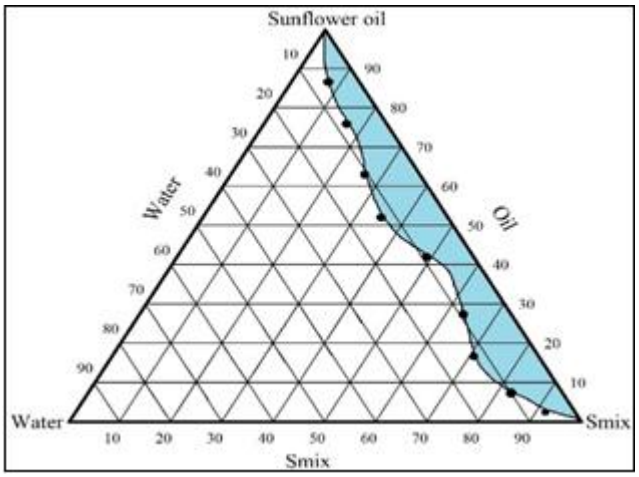

Figure 8: Phase Diagram (2:1) ratio

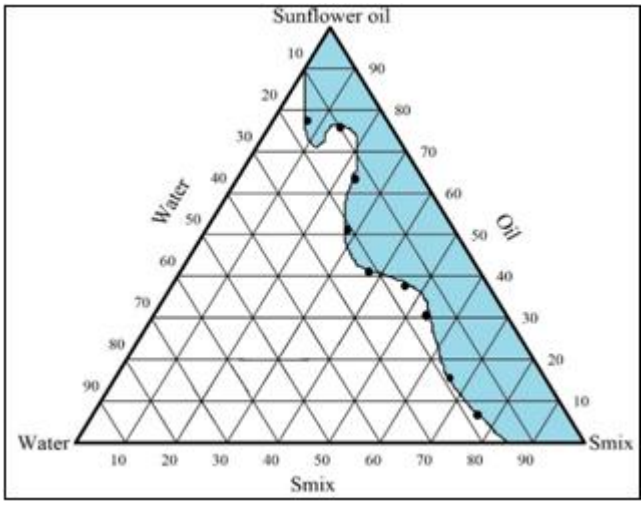

Figure 9: Phase Diagram (3:1) ratio

Visual Inspection

All the three formulation shows clear and no phase separation. Result show in table

Table 8: Visual Inspection

Sr.no	Formulation code	Visual Inspection
1	D1	Clear no phase separation
2	D2	Clear no phase separation
3	D3	Clear no phase separation

Table 9: Precipitation assessment of different liquid SLN formulation

Sr. no	Formulation code	Precipitation after 24 hrs.
1	D1	Transparent, clear microemulsion, no precipitation, stable
2	D2	Transparent, clear microemulsion, no precipitation, stable
3	D3	Precipitation observed after 24hrs.

From precipitation assessment D1and D2 formulation to be transparent, clear microemulsion with no precipitation and found to be stable. D3 formulation forms precipitate after 12 hr. Therefore, D3 formulation will rejected. D1 and D2 formulation will be selected for further study.

Drug content determination

Amount of drug present in the Liquid SLN formulation (table no) was determined by UV Spectrometric method.

Table 10: Drug content of different liquid SLN formulation

Sr.no	Formulation code	Drug content (% w/w)
1	D1	95.82 %
2	D2	96.06 %
3	D3	94.56 %

Self- emulsification time

The results obtained for self-emulsification time were noted in **table 11.**

Table 11: Self-emulsification time of SLN formulation.

Formulation code	0.1 N HCl		Distilled water	
	Time (sec)	Tendency	Time (sec)	Tendency
D1	15	Good	13	Good
D2	14	Good	13	Good

The D2 formulation requires less time for emulsification than the D1 formulation. Both formulations have good tendency for self-emulsification.

Conclusion: From all above characterization, it was found to that D2 formulation is better than D1 formulation. Therefore, D2 formulation considered to be the final formulation for next study.

Refractive Index

Refractive Index of the Sunflower oil, Surfactant, co-surfactant. Shown in **table 12.**

Table 12: Refractive index

Sr.no	Component	Refractive Index
1	Sunflower oil	1.4733
2	Tween 80	1.473
3	Propylene glycol	1.4324

Drug Release study

Table 14: In- vitro drug release study of Desloratadine Drug and Liquid SLN

Sr.no	Time (min)	% Drug Release		
		Plain Drug	D1	D2
1	5	0.970	41.703	41.903
2	10	3.750	52.624	58.171
3	15	9.343	69.424	69.632
4	30	15.38	76.462	76.941
5	45	20.76	89.462	90.284
6	60	22.17	95.814	96.601

In vitro drug release study was performed for plain Drug and Desloratadine SLN (liquid formulation). Results are shown **in table 10**

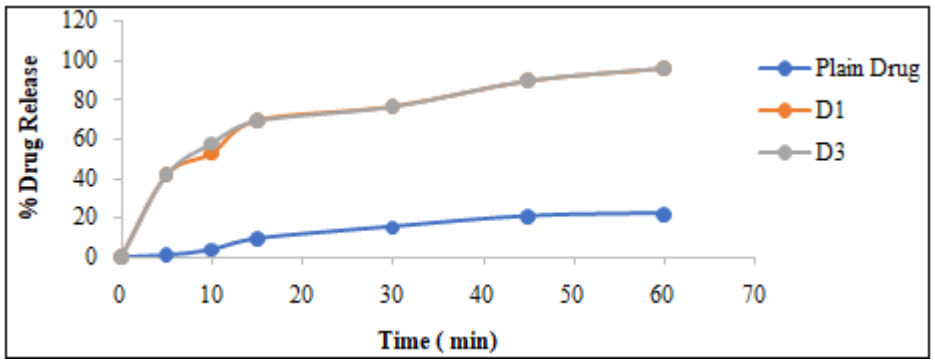

Figure 10: Comparison of dissolution profile of Plain Drug and liquid SLN (D1 and D2)

In vitro release study results revels that only 22.17 % w/w drug was released from plain Desloratadine filled in capsule in 60 min while 95.81% w/w and 96.60% w/w drug release from the liquid SLN D1 and D2 formulation respectively within 60 min.

Zeta Potential measurement

The zeta potential is used to identify the charge of the droplet. The value of zeta potential indicates the degree of electrostatic repulsion between particles in the dispersion. Zeta potential measurement is shown in following **Table 15.** and **figure 11.**

Table 15: Zeta potential measurement of liquid formulation

Formulation	Zeta potential	Conductivity (mS/cm)
Liquid Formulation	-19.3	0.579

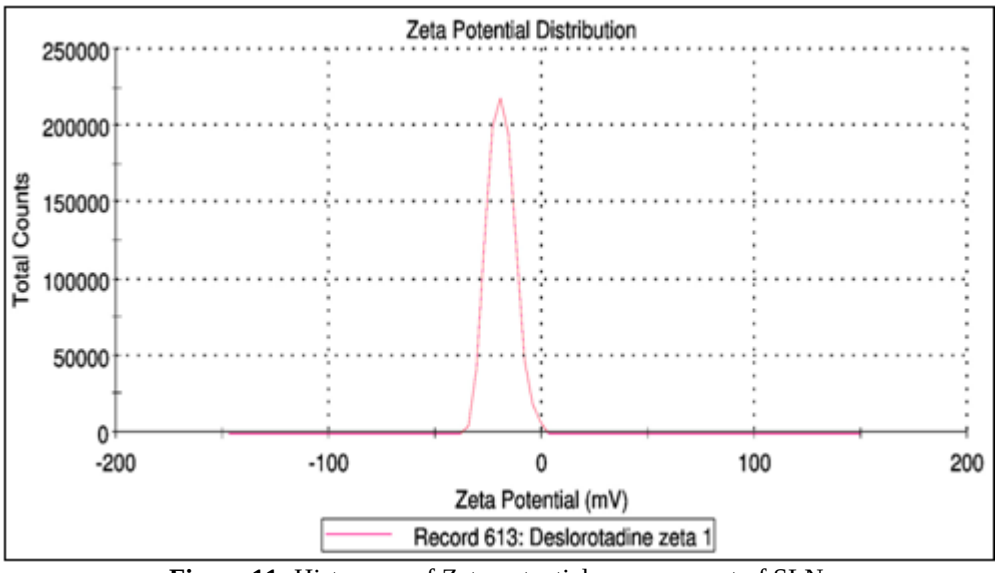

Figure 11: Histogram of Zeta potential measurement of SLN

Powder Flow Properties

Spray dried product was evaluated for bulk density, tapped density, cars compressibility index, Hausner ratio, angle of repose.

Table 16: Flow properties of Spray dried product

Sr.no	Parameter	Result	Inference
1	Bulk density	0.833 g/ml	-
2	Tapped density	1.1 g/ml	-
3	Carr's index	24.95	-
4	Hausner Ratio	1.33	Passable
5	Angle of Repose	19.65	Passable

The flow property of S- SLN was found to be passable because of floppy mass of Aerosil 200 and also it contains oil, surfactant, co-surfactant adsorbed on Aerosil 200

Visual Observation

Reconstitution property of S-SLN was determined by stirring S- SLN with distilled water for 5 min and observed visually. S- SLN showed rapid dispersion without any lump or agglomeration. this dispersion when observed visually after incubation for 60 min at room temperature was well dispersed without separation.

Particle size determination

Particle size and polydispersity index of SLN is as follows-

Table 17: Particle size and polydispersity index of SLN

Formulation	Particle size (d. nm)	Polydispersity index
SLN	945.1	0.774

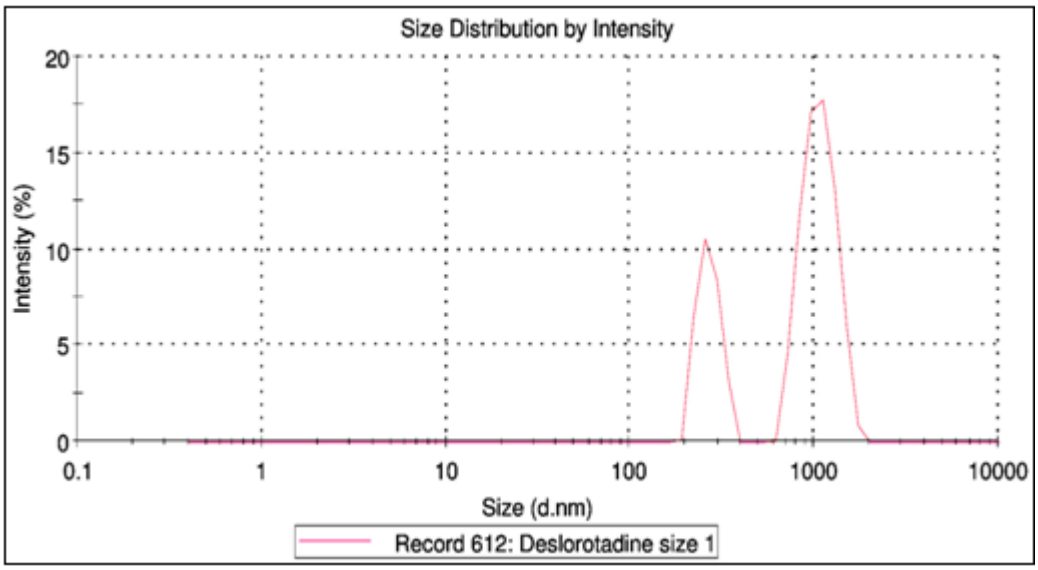

Figure 12: Histogram of particle size

Drug content determination

Table 18: Drug content in Solid - SLN

Sr.no	Formulation	% Drug content
1	Solid -SLN	96.60

In-vitro Dissolution Study

In vitro dissolution profile of plain drug, Liquid SLN and Solid SLN are compared together. In vitro study was performed. Solid SLN shows more % drug release than Liquid SLN and marketed formulation.

Table 19: In vitro dissolution data of plain drug, liquid formulation, SLN and Marketed formulation

Sr.no	Time (min)	% Drug Release			
		Plain Drug	Liquid -SLN	Solid -SLN	Marketed formulation
1	5	0.970	41.903	5.301	24.852
2	10	3.750	58.171	63.783	37.456
3	15	9.343	69.632	74.230	52.127
4	30	15.38	76.941	88.562	69.743
5	45	20.76	90.284	92.581	73.128
6	60	22.17	96.601	98.741	82.547

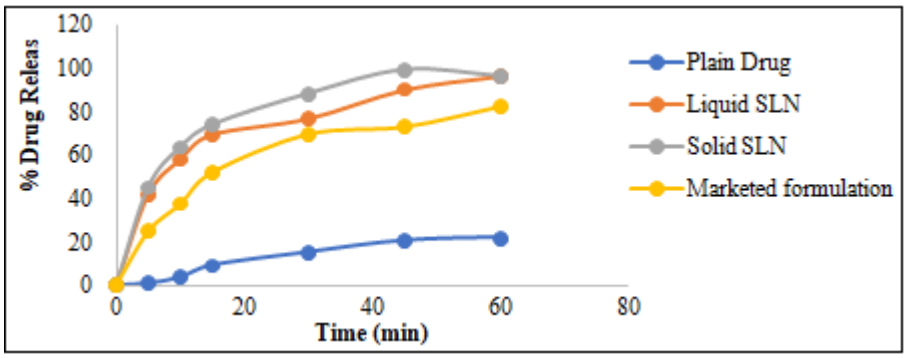

Figure 13: Comparison of dissolution profile of plain drug, Liquid- SLN, Solid-SLN and marketed formulation

- **Differential scanning Calorimetry**

DSC of Desloratadine (plain drug) and SLN were performed and results are shown in **Figure 14, 15.**

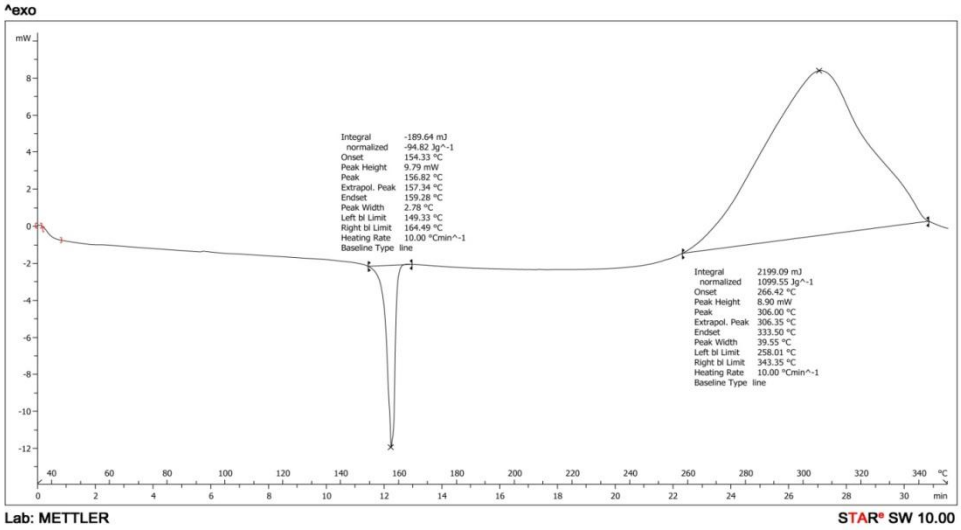

Figure 14: DSC of Desloratadine (plain drug)

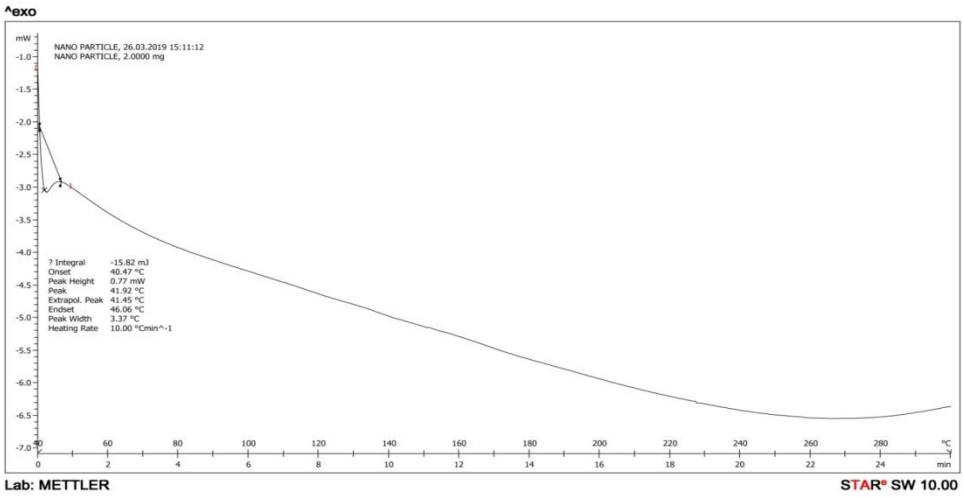

Figure 15: DSC of Desloratadine SLN

DSC of Desloratadine exhibits a sharp melting point at 151 to 158℃ with on set 154.33℃ and end set or recovery at 159.34 ℃. The DSC of nanoparticle does not show sharp peak. the absence of sharp melting point peak indicates that the lipids and Aerosil 200 inhibits the crystallization of drug i.e. is in amorphous from or in solubilized form in SLN.

- **Scanning Electron Microscopy**

Scanning Electron Microscopy (SEM) was used to determine the particle morphology of optimized SLN.Results of Desloratadine SLN was shown in Figure 16.

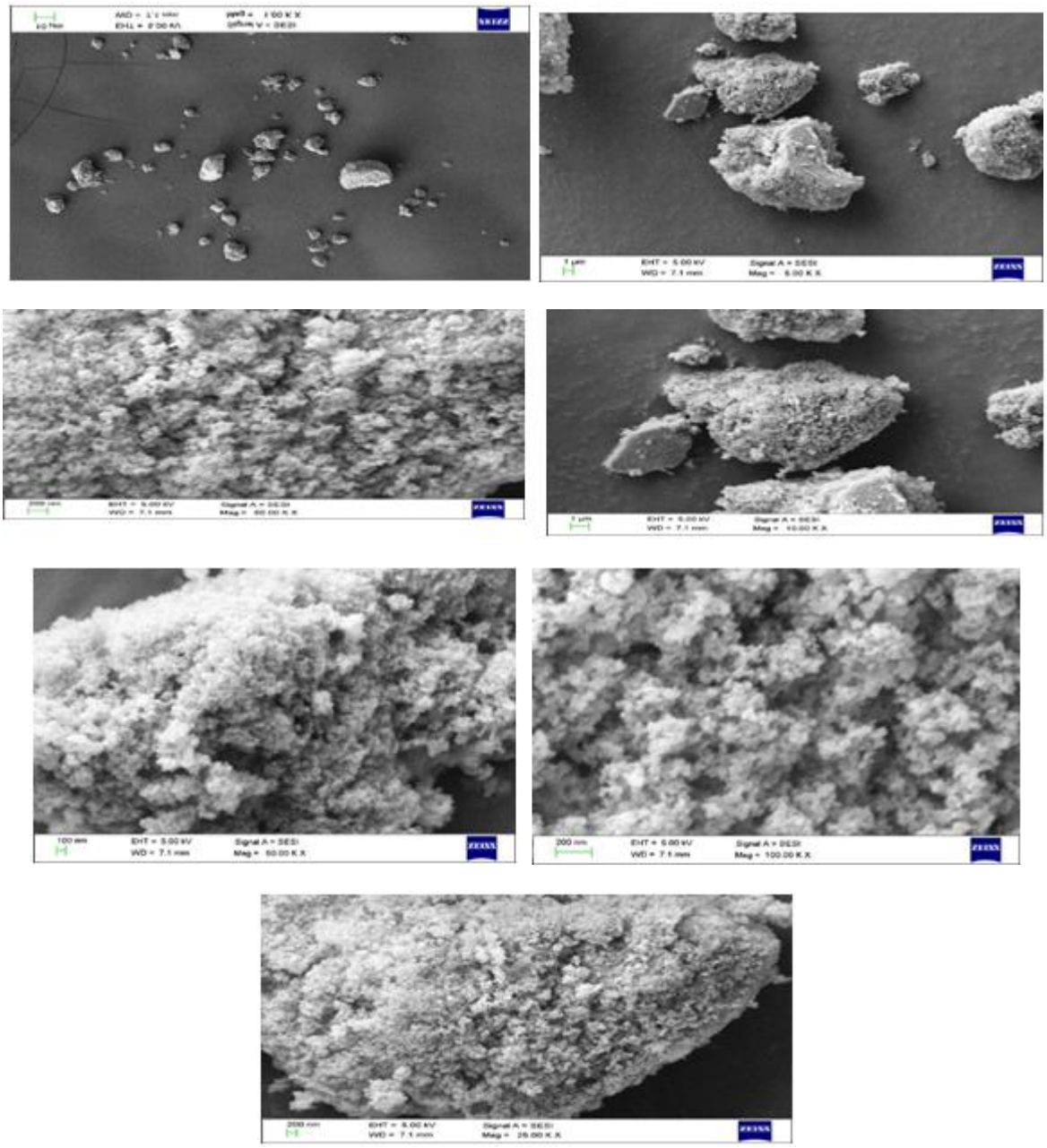

Figure 16: SEM images of Desloratadine SLN

Conclusion

Revels that the Desloratadine SLN shows irregular shape granular particle. The SEM of Desloratadine SLN does not show any rectangular crystals of drug on the surface of Aerosil 200 indicate that the drug present in the soluble form in lipid (SLN) formulation; which is adsorbed on the surface of Aerosil 200.

- **Powder X-ray Diffraction**

The Powder X-ray diffraction limits the symmetrical scattering of radiation from crystal planes within a solid allow the existences or absence of the former to be determined thus degree of crystallinity to be assessed.

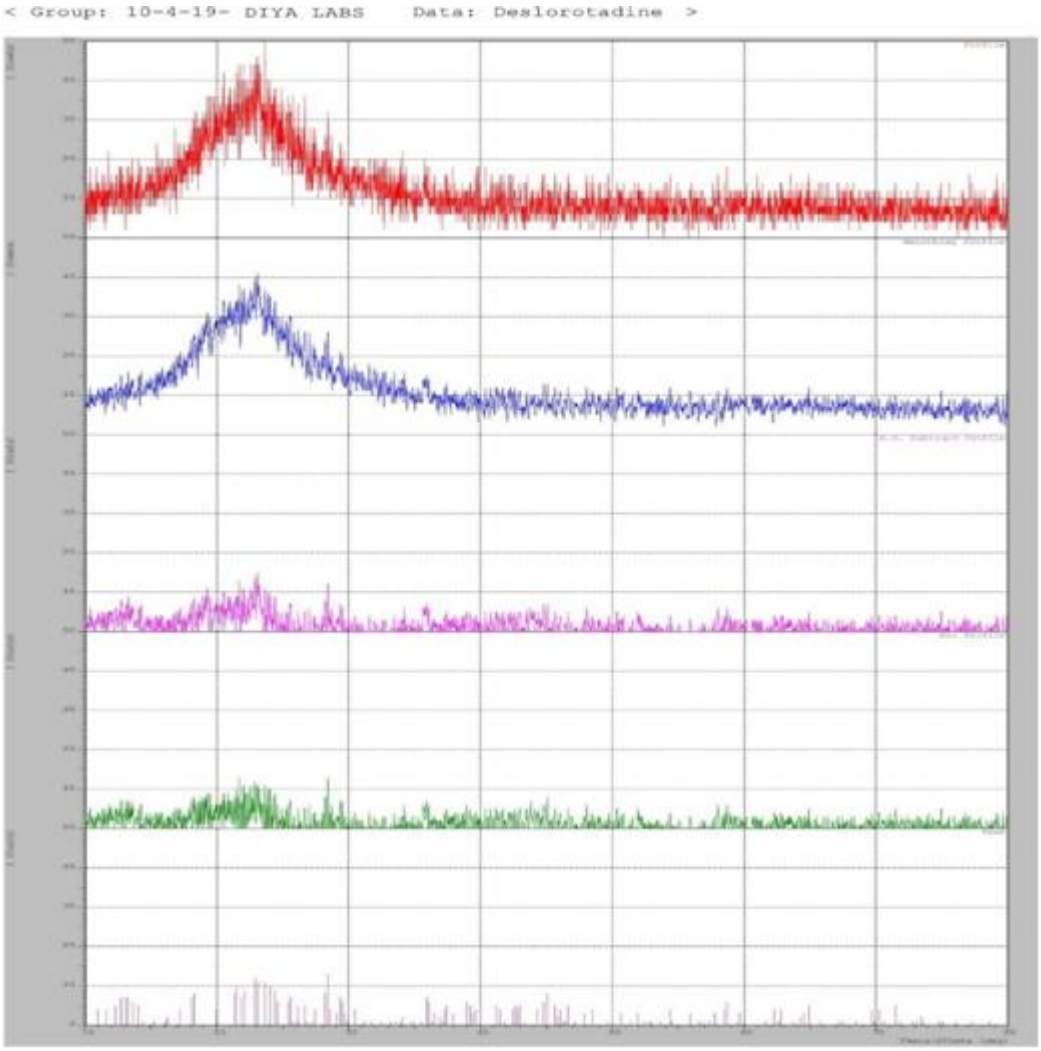

Figure 17: X-ray Diffraction

Conclusions

From X-ray powder Diffractograms, the internal physical state of Desloratadine in the SLN was verified. The Desloratadine showed sharp intense peaks representing crystalline structure of drug. Sharp peak appeared in Physical mixture but Spray dried powder of Desloratadine SLN did not show any peaks characteristics of desloratadine. This further confirms solubilization of drug in oil/ lipid.

Table 20: Strongest 3 Peaks

Sr.no	Peak	2 Theta (deg)	d (A)	I/II	FWHM (deg)	Intensity (Counts)	Integrated Int (Counts)
1	38	28.4212	3.13785	100	0.06250	13	44
2	21	22.8802	3.88367	92	0.07380	12	84
3	23	23.6430	3.76007	85	0.06600	11	61

Stability Study

1) Stability study of aqueous dispersion of SLN

a) Thermodynamic Stability studies

Thermodynamic study revel that there is no change in the formulation during the stability study of 3 moths. Results of stability study are displayed in **table. 21**

Table 21: Thermodynamic Stability studies

Formulation	Temperature	Time period			
		Initial	1month	2month	3month
Liquid SLN	25°C (Room Temp)	Clearand transparent liquid	Clear and transparent liquid	Clear and transparent liquid	Clear and transparent liquid
	40°C	Clear and transparent liquid	Clear and transparent liquid	Clear and transparent liquid	Clear and transparent liquid

b) Centrifugation test

Passed SLN was centrifuged at 3500 rpm for 30 min using centrifuge (Remi motors Ltd.) there was no phase separation found. This proves that the liquid SLN are stable when subjected to centrifugation test. Liquid SLN pass the stability the entire stability test.

c) Drug Content

Drug content of Solid – SLN was done after month for 1 months and result were shown in table no. The drug data shows that there is no change in drug content of solid SLN. This proves that the solid SLN are stable

Table 22: Drug content determination (stability study)

Formulation	Temperature	Time period	After 1 month
SLN Powder	-20°C	96.60 %	96.55%
	25°C	96.60 %	96.49%
	40°C	96.60%	95.40%

Table 23: In-vitro dissolution data of Solid SLN after 1 month

Sr. No	Time (min)	%Drug Release (%w/w)
		25°C
1	5	41.308
2	10	58.175
3	15	69.750
4	30	76.940
5	45	90.281
6	60	96.605

In vitro release study of solid SLN was done after 1 month in 0.1 N HCl solution. And result was noted in **Table. and figure.**

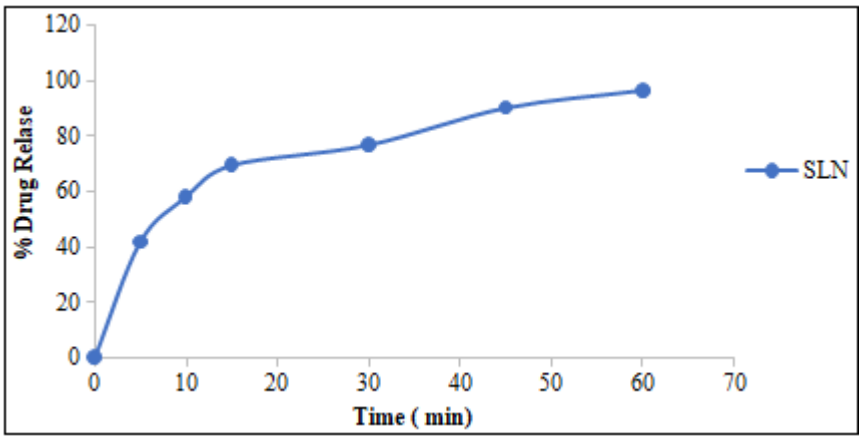

Figure 18: In vitro dissolution data of Solid SLN after 1 month

FTIR Study

FT-IR of solid SLN sample placed at temperature 25°C Was done after 1 month to determine any change in drug and result is shown in figure. The FT-IR of Solid SLN Shows that there is no change in the functional peaks of drug at temperature 25°C after 1 month.

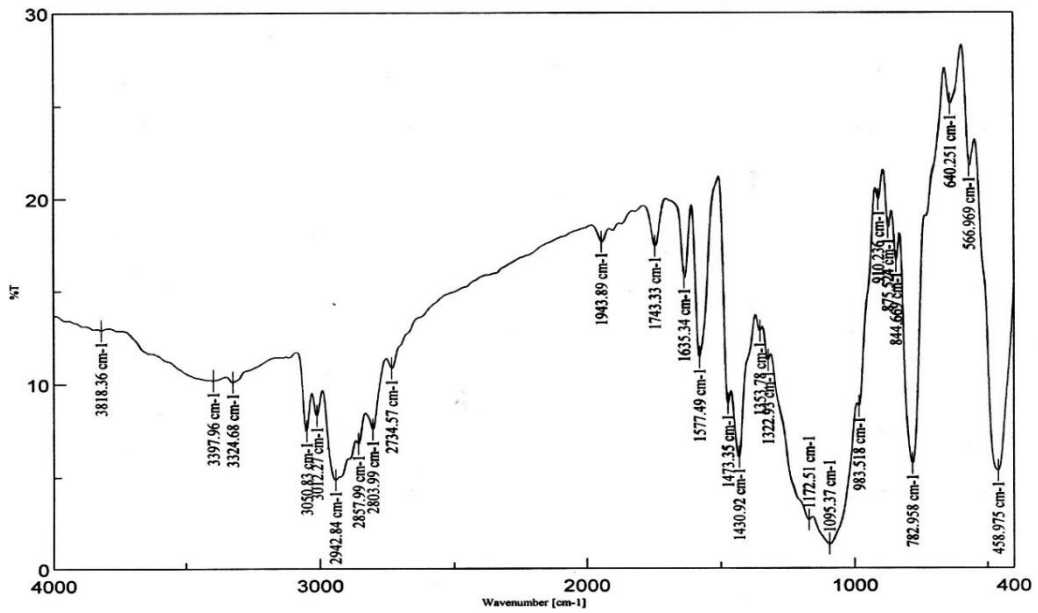

Figure 19: FT-IR Of SLN (25°C)

4. Conclusion

This study concludes that:

- Solubility study shows that sunflower oil as oil, tween 80 surfactant and propylene glycol as co-surfactant shows good solubilizing property for Desloratadine.
- The homogenous mixture of sunflower oil+ Tween 80+Propylne glycol shows good solubility.
- The phase diagram shows, increase in micro emulsifying region with increase in the ratio of surfactant to co-surfactant from 1:1, 2:1, and 3:1.
- Aerosil 200 can be used as adsorbent for converting aqueous SLN formulation to SLN, especially for spray drying purpose.
- In-vitro release study shows that SLN can be used as possible alternative to conventional oral formulation of poorly aqueous soluble drug such as Desloratadine, to improve its solubility and oral absorption.
- Scanning Electron Microscopy, Differential scanning calorimetry, and powder X-ray Diffraction confirmed that the presence of Desloratadine in a molecularly dissolved state in the SLN.
- Stability study was concluded that both liquid and SLN formulation are stable at all different temperature conditions.

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