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Development of Solid Self Micro-emulsifying Drug Delivery Systems of Lovastatin Using Neusilin US 2

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Abstract

The aim of the work is to enhance the solubility, dissolution rate and then the bioavailability of a poorly water soluble Lovastatin, by formulating it as self-micro emulsifying drug delivery system. Solubility of lovastatin in various oils was determined to select the oily phase. Various surfactants and co-surfactants were screened for their ability to emulsify the selected oily phase. The SMEDDS formulation was optimized by Heating cooling cycles, Percent Transmittance, droplet size and zeta potential tests. The optimized L-SMEDDS formulation containing Lovastatin, Capryol PGMC, Cremophor RH 40 and Labrafil M 2125 was further evaluated for TEM analysis, Drug content and In-vitro drug release studies. L-SMEDDS was further converted into S-SMEDDS by Adsorption technique using Neusilin US 2 as adsorbing agent and the S-SMEDDS were evaluated for various flow properties and SEM analysis. The L-SMEDDS and S-SMEDDS showed enhanced in vitro dissolution profile as of Plain drug. Hence, the results from both L-SMEDDS and S-SMEDDS suggest the potential use of SMEDDS to improve the solubility and further the bioavailability of BCS Class II drug lovastatin.

Keywords: Lovastatin, poor water solubility,SMEDDS, Neusilin US 2, Solid SMEDDS

INTRODUCTION

For the long-term management of many disorders, the oral route has been the predominant drug delivery method. The most economical drug delivery method is oral, and it dominates the global market. However, in the current environment, oral drug delivery is continually exploring new channels because 40 percent of new drug candidates have poor water solubility and/or absorption, high intra- and inter-subject variability, rapid metabolism, high fluctuation in the drug plasma level, variability due to food effect, and lack of dose proportionality, which are all significantly contributing to the disappointing in vivo results that are leading to the failure of drug formulations. The use of complexing agents such cyclodextrin, solid dispersion (suspension), co-precipitation, micronization, salt creation, emulsion, micelle utilisation, and co-grinding have all been described as innovative ways to increase solubility and bioavailability.[1] Recently, lipid solutions, emulsions, and emulsion pre-concentrates have received a lot of attention since they can be created as physically stable formulations suited for encapsulating such poorly soluble drugs. Emulsion systems have their own unique set of complications, such as manufacturing issues and stability issues related to their commercial production one formulation approach which may provide a suitable solution to these issues is the use of self-emulsification systems. These methods may give an improvement in the rate and amount of absorption and lead to more repeatable blood-time profiles for lipophilic drug molecules that show dissolution rate-limited absorption. Finding an appropriate oil surfactant mixture that can dissolve the medicine at the desired therapeutic concentration is the critical step. In a typical SMEDDS formulation, oils,

surfactants, and, if needed, antioxidants are included. Co-surfactants and co-solvents are frequently added to formulations to enhance their properties. [2, 3]

The first statin used in clinical settings is lovastatin, which belongs to the class of medications used to decrease cholesterol. It is a prodrug that works by temporarily inhibiting the enzyme 3-

hydroxy-3-methylglutaryl coenzyme A reductase, which is essential for the manufacture of cholesterol. Although it is offered in both standard and extended release tablets, its low aqueous solubility (1.3µ g/mL in water) ultimately leads to its limited oral bioavailability (less than 5 percent). Additionally, it goes through a lot of first pass metabolism, which results in hepatic extraction and a low and unstable availability in the general circulation. Therefore, the primary goal is to increase Lovastatin's solubility in water.Lovastatin is a Biopharmaceutical Classification System (BCS) Class II drug with its low daily oral dose (10–40 mg) and high log P (octanol/water) of 4.3 providing strong justification to develop SMEDDS. [4,5]

The main objective of the study is to develop and evaluate an optimal SMEDDS formulation containing Lovastatin by using Capryol PGMC as oil and Cremophor RH 40 as surfactant and Labrafil M 2125 as a co-surfactant and then converting the liquid SMEDDS form into the solid SMEDDS by using Neusilin US 2 as adsorbing agent

MATERIAL AND METHODS

Materials

Lovastatin API was a generous gift from Alembic limited (Vadodara, Gujrat) Capmul MCM C8, Captex 200, Captex 300, Captex 355 obtained as a gift sample from Abitec ltd. Cremophor EL, Cremophor RH 40, Labrafil M1944 cs, Labrafil M2125 cs, Capryol PGMC, Capryol 90, Lauroglycol 90, Transcutol P, Transcutol HP was obtained as a gift sample from Gattefosse (Mumbai, Maharashtra, India). NEUSILIN US2 was obtained from Fuji Chemicals (Japan). All the excipients and reagents were of analytical grade, and distilled water was freshly prepared whenever required throughout the study.

Solubility Study[6,7]

1) Visual observation for estimating solubility: A suitable amount of lovastatin was added to a vial containing 1gm of prewarmed vehicles, and the solutions were vortexed using a cyclomixer for 4-5 min to facilitate uniform mixing. To ascertain the degree of the drug's solubility in the first aliquot, mixes in vials were visually inspected. The second portion was added to vehicles where the first portion of the drug had completely dissolved it, and the same procedure was repeated numerous times until the vehicles became completely saturated with the drug. The entire amount of medication added to completely saturate the vehicles was reported. Only a small number of potential vehicles that were effective in solubilizing drug in large quantities were chosen.

2) UV-Visible Estimation: Each vial containing prewarmed 5gm of the chosen vehicles to which an excess amount (more than the approximate solubility) of the lovastatin was added. The vials were shaken for 48 hours in an incubator orbital shaker kept at 37°C. The mixtures were then centrifuged for 15 minutes at 5000 rpm to remove any extra insoluble lovastatin by filtering. Drug assay was carried out after diluting the aliquots of supernatant

Emulsification efficiency study [8,9]

Emulsification efficiency of various surfactants was screened using shake flask method. 300mg of selected oil and 300mg of pre warmed surfactant was taken in a vial, cyclomixed for 5mins and Heated at 40-50°C. 50mg from above solution was taken in a beaker & 50ml of DDW was added then it was Shaken slowly and transfered into an Iodometric Flask Flask inversions were performed and the number of inversions required to obtain transparent or slight bluish colour solution is noted down, The flask was kept at standing for 2hrs, observed for phase separation; if none observe %Transmittance at 638.2nm against DDW by UV-160A double beam spectrophotometer (Shimadzu, Japan) using double distilled water as blank.

Selection of Co-surfactant[9]

The best co-surfactant was selected using the turbidimetric approach from a large pool of co-surfactants. This method was also utilised to assess the relative effectiveness of the co-surfactant to improve the surfactants' ability of micro-emulsification. Mixing 300 mg of oil, 200 mg of surfactant, and 100 mg of co-surfactant, the mixture then homogenised using mild heat (45–60 °C). 50 milligrammes were accurately weighed and diluted with 50 ml of double-distilled water to create a fine emulsion. Researchers could see how easily an emulsion is made thanks to the low number of flask inversions required to create one. The relative turbidity of the produced emulsions was evaluated visually.

Preparation of liquid SMEDDS

Different ratios of oil, surfactant, and co-surfactant were used to create a series of SMEDDS formulations. All formulations contained a single (10 mg) dose of lovastatin. The formulations were made by combining the surfactant and co-surfactant in glass vials after the lovastatin had been dissolved in oil. To produce an isotropic, homogeneous mixture, the resulting mixtures were vortex mixed continuously for a short period of time. The transmittance value of these various oil, surfactant, and co-surfactant systems was assessed. Prior to usage, the SMEDDS formulations were kept at room temperature.

Optimization of formulation

Stage 1) % Transmittance

The SMEDDS were reconstituted with distilled water, and the resulting microemulsions were observed visually for any turbidity. Thereafter, its % transmittance was measured at 638.2nm using the UV-160A double beam spectrophotometer (Shimadzu, Japan) against distilled water as the blank. The studies were conducted after 100 times dilution.

Stage 2) Freeze Thaw Cycle [10]

The formulations were subjected to freezing at – 4°C for 24 hours followed by thawing at 40°C for 24 hours. Three alternate cycles were performed, and the formulations were visually observed for any sign of phase separation and/or precipitation of drug.

Stage 3) Globule size, zeta potential, polydispersibility index

The formulation taken and diluted with double distilled water and visual observations were done for its emulsification efficiency. Glouble size, zeta potential and polydispersibility index were determined using Horiba zeta-sizer.

Evaluation of optimized L-SMEDDS

Thermodynamic Stability Studies: In order to determine the thermodynamic stability of the synthesised SMEDDS, Freeze Thaw Cycle , and centrifugation tests were performed.

A) Freeze Thaw Cycle

Three alternate cycles were performed, and the formulations were visually observed for any sign of phase separation and/or precipitation of drug.

B) Centrifugation Test

Centrifugation is then applied to the batches. The mixture is centrifuged at 4000 rpm for 15 minutes, and any phase separations or drug precipitation is again checked for.

In-vitro dissolution

In order to assess the impact of pH on in-vitro dissolution, the In-vitro release profile of L-SMEDDS was investigated using USP apparatus II (Paddle type) at 37 ±0.5 ºC with a rotating speed of 50 rpm in the dissolution media, specifically 0.1N HCl and 6.8pH buffer. Throughout the investigation, 5 ml of aliquot was taken out of the dissolution medium and replaced with new buffer at predetermined intervals of 0, 5, 10, 20, 30, 45, and 60. A UV spectrophotometer with a maximum wavelength of 238 nm was used to measure the amount of lovastatin dissolved in the dissolving media.

Transmission electron microscopy

The resulting SMEDDS morphology was studied using transmission electron microscopy.

Conversion of L-SMEDDS to S-SMEDDS

Proportions of the lovastatin-containing liquid SMEDDS were adsorbed onto MCC, Aerosil, and Neusilin US2[10]. Neusilin US2 was chosen over these agents because it displayed improved flow characteristics The addition of the liquid formulation onto carriers by mixing in a blender represents the only step in the simple adsorption process. The resulting powder can then be compressed into tablets or alternatively combined with appropriate excipients before filling directly into capsules

Evaluation of S-SMEDDS

Micromeritic properties of S-SMEDDS

Micromeritic characteristics of the prepared S-SMEDDS were assessed, comprising angle of repose, bulk and tapped density, compressibility index, and Hausner ratio.

Globule size, PDI, Zeta Potential

Globule size, PDI, and Zeta potential were also characterised for reconstituted S-SMEDDS in accordance with the procedures for liquid SMEDDS

Determination of drug content[11]

Drug content was calculated using drug isolation from L-SMEDDS and S-SMEDDS. It was, in a nutshell, sufficiently dissolved in methanol. To extract lovastatin from the solution to methanol, it was sonicated for 10-15 minutes and then filtered. The UV- Visible Spectrophotometer was used to measure the filtrate's absorbance at 238 nm. Using the Beer-lamberts equation of the drug's standard curve in methanol, the amount of lovastatin was determined.

Scanning electron microscopy

SEM analysis of lovastatin and the prepared S-SMEDDS was carried out using Scanning electron microscope to study surface topography.

Differential scanning calorimetry

A differential scanning calorimeter was used to characterise the physical state of lovastatin in S-SMEDDS. Utilizing a differential scanning calorimeter, the following thermograms were obtained: Lovastatin, Neusilin US2, and S-SMEDDS

X-ray powder diffraction studies

With an X-ray diffractometer, measurements of the Lovastatin's X-ray powder scattering and that of solid self-microemulsifying powder were made.

In-vitro dissolution study[11]

With the aid of a USP-type-II dissolution test apparatus, an in-vitro dissolution study of S-SMEDDS and plain drug was conducted at 37°C with a 50 rpm rotating speed in buffer solutions with a pH of 1.2 and 6.8. Using a Whatmann filter, 5 mL samples were taken at regular intervals of 0, 5, 10, 15, 30, and 60. To maintain the sink condition, an equal volume of each dissolution media was introduced. The sample's drug content was examined using a UV spectrophotometer at 238 nm.

Stability studies

The final Solid SMEDDS were placed at temperature 40±2°C/75±5%RH up to 3 months. At the end of 1st and 3rd month, powder was subjected to Globule size detection, Drug content or assay and *In-vitro* release studies performed in pH 6.8 and pH1.2

RESULTS AND DISCUSSION

Solubility studies

The goal of solubility investigations was to find an oily phase that would be ideal for the development of SMEDDS. To get the best drug loading, it's essential to use an oil that has the most solubilizing capability. Figure 1 shows the solubility of lovastatin in various oily phases. Capryol PGMC, the oil with the highest solubility out of all the oils examined, was chosen as the oily phase.

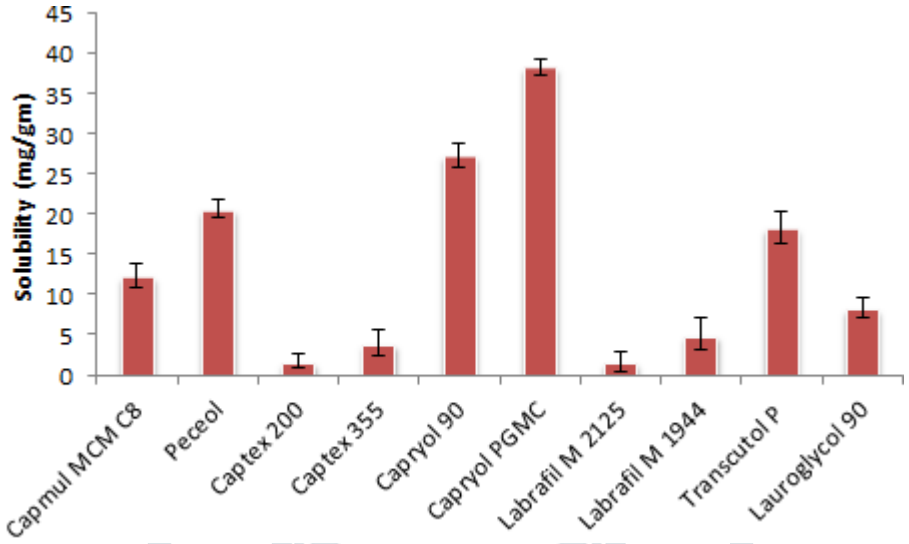

Fig.1: Solubility of lovastatin in various oils

Data is expressed as Mean ± Standard deviation of 3 replicates

Emulsification efficiency study

The surfactants were compared for their emulsification efficiencies for the selected oily phase Capryol PGMC. Cremophore RH40 showed good emulsification efficiency for the Selected oil. From Table1 it was observed that emulsification efficiency of Cremophor RH 40 was excellent compared to other surfactants, as resultant solution was clear and bluish with %T more than 95%, flask inversions less than 6 inversions. Hence, it was selected for Lovastatin and they were subjected to further selection of co-surfactant by spontaneity of emulsification ability.

Table 1: List of various surfactants used for screening

Surfactant	No of FI	%Transmittance	Appearance
Span 80	10	75	Turbid
Cremophor EL	7	98.3	Clear
Cremophor rh 40	5	99.5	Clear and Bluish
Tween 80	12	80.6	Colloidal
Labrasol ALF	12	81.5	Colloidal
Transcutol p	7	90.2	Colloidal
Labrafil M 2125	20	9.2	Very Turbid
Labrafil M 1944	17	15.3	Very Turbid

Screening of Co-surfactant

Cremophore RH 40 with Labrafil M 2125 CS displayed better transmittance of 99.5% with a lower number of flask inversions, it was discovered. Cr.RH40: Lab M 2125 was chosen as the pair to emulsify capryol PGMC oil because it show superior spontaneity of emulsion. As a result, the oil, surfactant, and co-surfactant capryol PGMC, Cremophore RH40, and Labrafil M2125CS were chosen

Table 2: List of various Co-surfactants used for screening

Co surfactant	No of FI	% Transmittance	Appearance
Labrafil M1944	4	96.7	Clear and bluish
Labrafil M2125	3	99.5	Clear and Transparent
Transcutol P	6	95.3	Colloidal
Transcutol HP	5	97.2	Clear and Transparent
Lauroglycol 90	5	96	Clear
Labrafac	6	95	Colloidal

Lauroglycol FCC	6	92.2	Colloidal
Labrasol ALF	5	97	Colloidal

Optimization of formulation

Percent Transmittance

The 12 different systems constructed by varying the concentrations of oil, Surfactant and co-surfactant from which 5 ratios were selected based on %Transmittance value(Table 3) and these batches are further subjected to freeze thaw cycle

Table 3: List of ratios selected for further studies

Batch	**LL1**	**LL2**	**LL3**	**LL4**	**LL5**
Lovastatin(mg)	10	10	10	10	10
Oil(mg)	250	250	250	250	250
surfactant(mg)	125	167	125	140.6	375
Cosurfactant (mg)	125	83	62.5	46.88	125
Total(mg)	510	510	447.5	447.5	510
%Transmittance	94	98	92.5	90.5	91.5

Freeze Thaw cycle

The selected batches were subjected to the Freeze Thaw cycle

Table 4:Results of Freeze Thaw cycle for selected ratios

Batch No	Phase separation	Precipitation	Results
LL1	Stable	Clear	Passes

LL2	Stable	Clear	Passes
LL3	Unstable	Precipitation	Fails
LL4	Unstable	Precipitation	Fails
LL5	Unstable	Precipitation	Fails

As seen in Table 4, LL 1 and LL 2 does not show any phase separation and precipitation hence selected for further study and subjected to particle size analysis

Globule size, zeta potential, polydispersibility index

Table5:Results of Globule size and polydispersibility index(PDI)

Batch (n=3)	**LL1**	**LL2**
Oil : SMix	1:1	1:1
S. : CoS	1:1	2:1
Globule size (nm) *	1891.33 ± 64.57	79.21 ± 3.10
PDI*	1.655±0.29	0.125±0.0045

* Values are expressed as Mean ± Standard deviation of 3 replicates

From the two batches LL1 and LL2, LL2 has shown the required particle size and PDI Hence it was Selected as the Final Optimised Batch

Evaluation of optimized L-SMEDDS

Thermodynamic Stability Studies

In order to evaluate the thermodynamic stability, L-SMEDDS were subjected to freeze thaw cycle, and centrifugation testing. It was discovered that there was no precipitation or phase separation seen, hence it was considered to be stable formulations.

Determination of drug content

Drug content of optimized batch of L-SMEDDS was found to be as 101.8%±1.5% w/w where, the values are expressed as Mean ± Standard deviation of 3 replicates

Globule size, zeta potential, polydispersibility index

The outcomes showed that the L-SMEDDS generated a micro emulsion with a homogeneous particle size distribution with polydispersbiliity index value of 0.125±0.0045. As lower the value of polydispersity, the higher is the uniformity of the droplet size in the formulation A mean droplet size of 79.21 ± 3.10nm (Fig 2). The generated SMEDDS was found to have a negative Zeta potential value of - 34.2 mV(Fig2). The structure of the excipients employed includes fatty acids, which is why the surface charge of the droplet is typically negative[12,13]As a result, the results for Particle Size, PI, and Zeta Potential for Lovastatin were found to be acceptable.

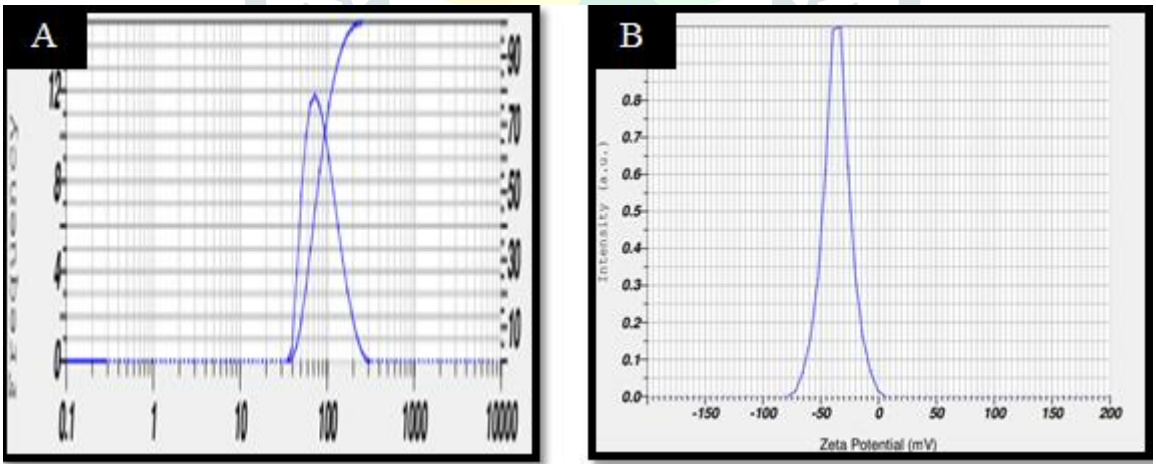

Fig.2: A)Globule size of optimised L-SMEDDS B) Zeta potential of optimised L-SMEDDS

In-vitro dissolution

The findings of optimised lovastatin L-SMEDDS and pure lovastatin *In vitro* dissolution profiles in dissolution media, 0.1 N HCL and Phosphate buffer pH 6.8, are shown in "Fig 3" and "Fig 4".

It was discovered that the release of pure lovastatin in 0.1 N HCL and phosphate buffer pH 6.8 was only about 35%. It is clear from the observation that L-SMEDDS significantly exceeded pure lovastatin in both of the dissolution media tested when compared to the in vitro dissolution profile. In 30 minutes with 0.1 N HCL and pH 6.8, L SMEDDS prove effective release (≥ 90%).

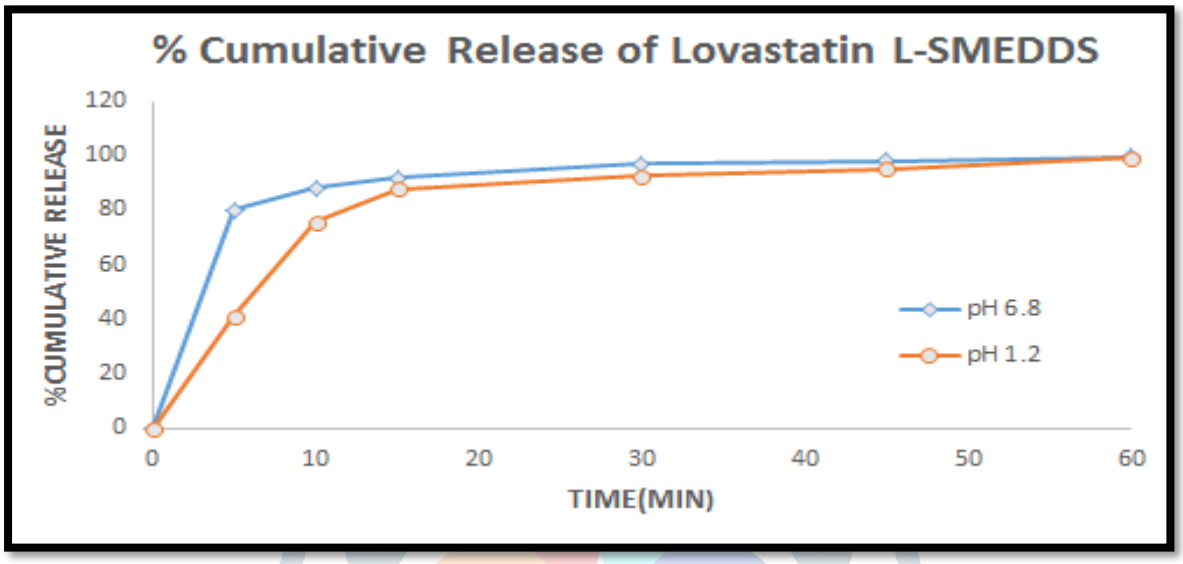

Fig.3: In-vitro dissolution profile of L-SMEDDS

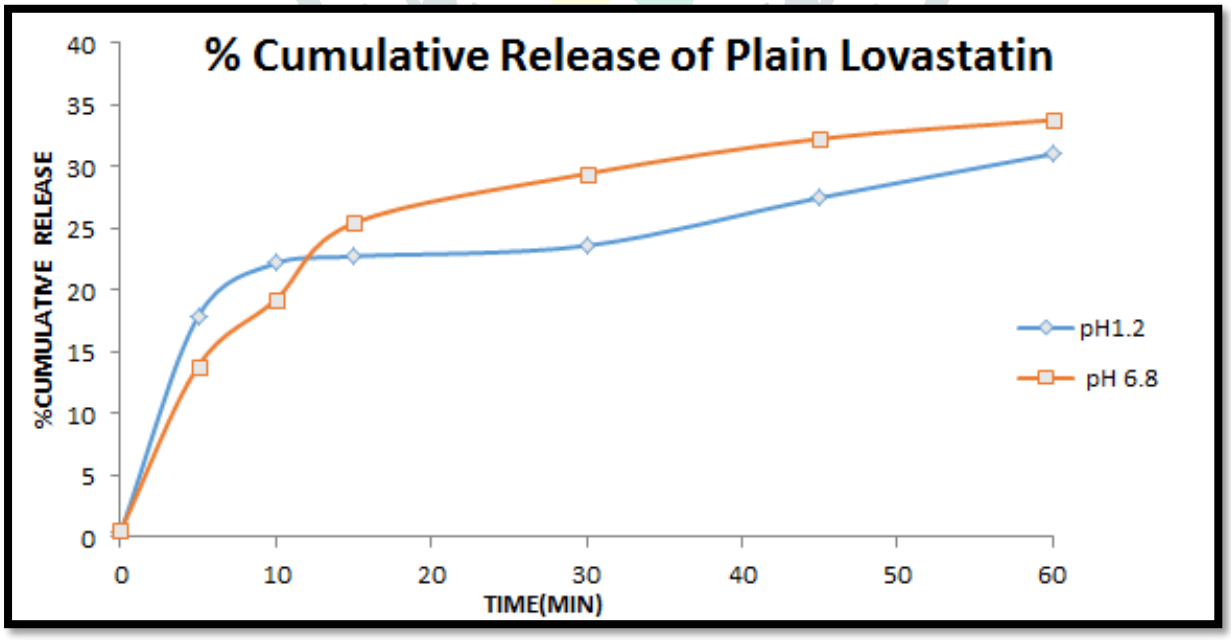

Fig.4: In-vitro dissolution profile of plain lovastatin

Transmission electron microscopy

As can be observed in Fig.5, the morphology of the reconstituted optimum formulation is depicted in electron microscopic images. The figures clearly show that all of the globules were of uniform shape, with the majority of them having globule sizes of less than 100 nm. The graphic clearly shows that there are no traces of coalescence, demonstrating the formulation's improved physical stability.

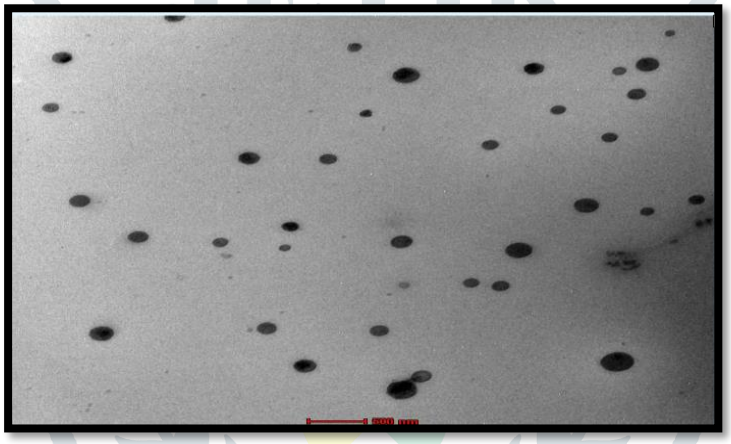

Fig.5: TEM image of lovastatin L-SMEDDS in Distilled water

Conversion of L-SMEDDS to S-SMEDDS

The current study used the adsorption technique to produce solid-SMEDDS, and Neusilin US2 was used as the carrier. Amorphous, ultra-lightweight, synthetic Neusilin US2 is made of magnesium aluminium metasilicate and is produced by spray drying. Neusilin has a highly porous structure, a significant surface area, and an effective ability to absorb oil.[14] The ratio of L-SMEDDS and Neusilin US2 taken were 1:0.5, 1:1, and 1:1.5. 1:0.5 was chosen from the preceding ratios because it produced good, free-flowing powder.

Evaluation of S-SMEDDS

Micromeritic properties of S-SMEDDS

Table 6: Flow properties of S-SMEDDS

Parameters	Results
Angle of Repose* (Degree)	26.23 ±0.06
Bulk density*(gm/ml)	0.2132±0.004
Tap density (gm/ml)	0.2412±0.008
Carr‟s Index *(%)	11.60±1.3
Hausner‟s Ratio*	1.13±0.02
Flow rate*	<1 sec

* Values are expressed as mean ± standard deviation of 3 observations

With a Carr's index between 11 and 15 and a Hausner's ratio less than 1.18, the solid-SMEDDS had good flow properties. Their angle of repose was also less than 30 degree. According to the observations, S- SMEDDS has exhibited promising flow characteristics.

Globule size, PDI, Zeta Potential

Table 7: Globule size, PDI, Zeta Potential of S-SMEDDS

Parameters	Results
Globule size (nm) *	101.8±3.41
PDI*	0.086±0.0004
Zeta potential	- 33.8Mv

Neusilin US2 particles were found in the sample, which is what caused the increase in globule size following conversion to S-SMEDDS. [16] The polydispersibility index value is less than 1, droplets are distributed uniformly throughout the formulation. Additionally, the Zeta potential value suggests that it is stable.

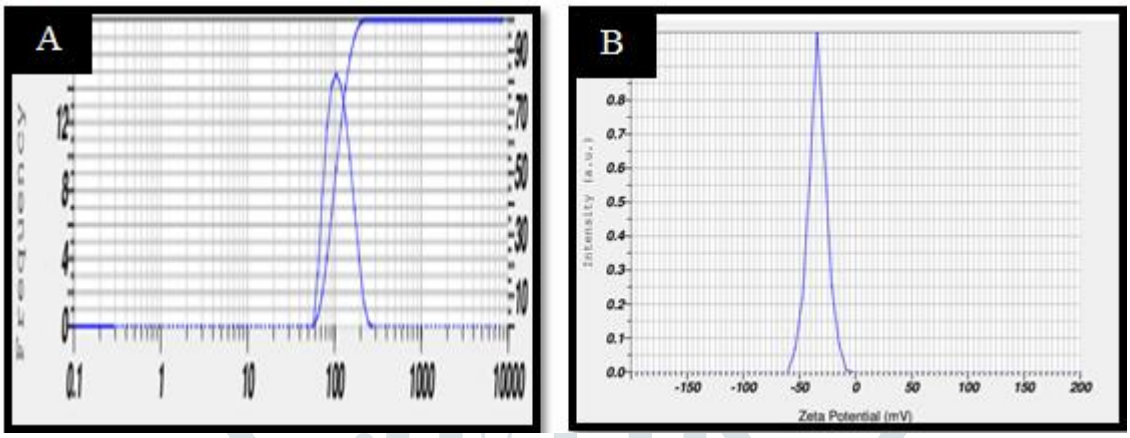

Fig.6: A) Globule size of S-SMEDDS B) Zeta potential of S-SMEDDS

Determination of drug content

Drug content of Solid SMEDDS was found to be 102.1%± 2.7% w/w, where the values are expressed as Mean ± Standard deviation of 3 replicates

Scanning electron microscopy

Micrographs of lovastatin seemed to be made of irregular crystalline structures Solid SMEDDS showed Smooth surfaced particles in S-SMEDDS micrographs, and liquid SMEDDS was shown adsorbed onto the spherical surface of Neusilin US2 particles. The lack of lovastatin's crystalline structural characteristics in S-SMEDDS micrographs suggests that the lovastatin is entirely dissolved in the Solid SMEDDS.

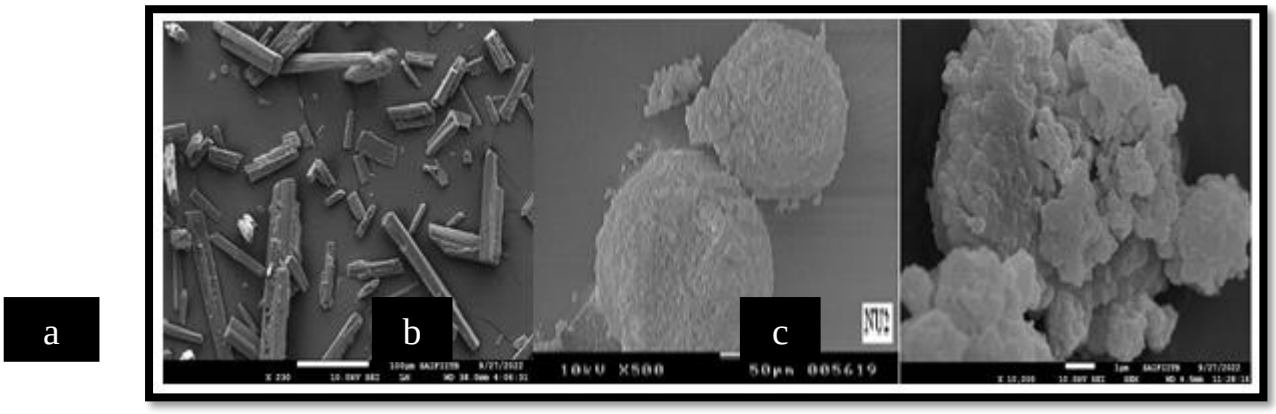

Fig.7: SEM micrographs of a) Lovastatin, b) Neusilin US2 and c) Solid SMEDDS

Differential scanning calorimetry

Figure 8 displays the DSC thermograms of three substances: Pure lovastatin, a physical mixture of lovastatin and Neusilin US2, and S-SMEDDS. The prominent endothermic peak for pure lovastatin at 172.14 °C indicates the substance is very crystalline. Due to the presence of crystalline lovastatin, the physical mixture including equal concentrations of Neusilin US2 and lovastatin displayed a less strong melting point peak at 170.64 °C. A change in the melting behaviour of lovastatin and a suppression of crystallisation after solubilization utilising lipid surfactants and physical mixing with a solid carrier, such as Neusilin US2, are shown by the absence of visible lovastatin peaks in the solid SMEDDS formulation.

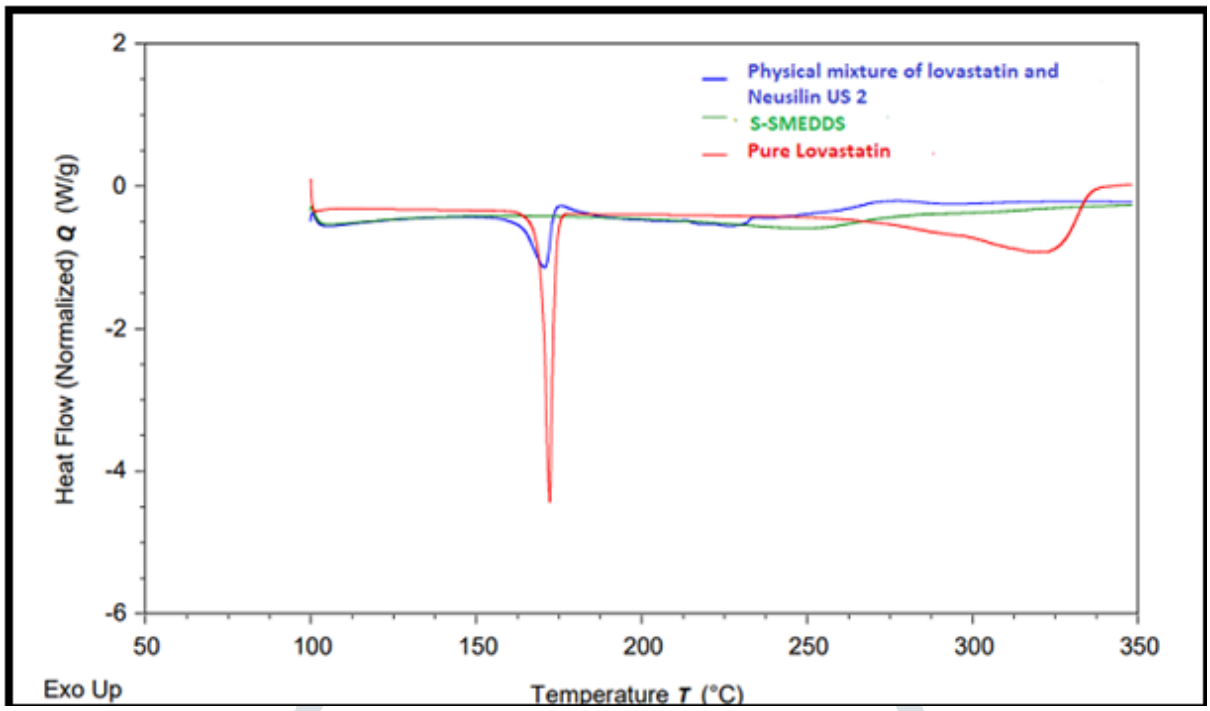

Fig.8: Overlay of Differential Scanning Calorimetric thermographs of lovastatin ,physical mixture of lovastatin and Neusilin And Solid SMEDDS

X-ray powder diffraction studies

Figure 9 illustrates the solid-SMEDDS and lovastatin X-ray powder diffraction pattern. High-intensity peaks at 2 theta values of 8.0904, 9.5684, 10.2995, 11.05, 12.8273, 15.3993, 15.8588, 16.8627, 17.3207, 18.0945, and 19.8111 were visible in the diffraction pattern of lovastatin. It's possible that the existence of the drug's crystalline form is what causes the sharp, strong peaks. While the S-SMEDDS graph revealed a lack of lovastatin constructive peaks, indicating that the drug had been changed from a crystalline to an amorphous state, it was also characterised by a diffuse peak, indicating that the drug had either been solubilized in the lipid excipients or had undergone this transformation.

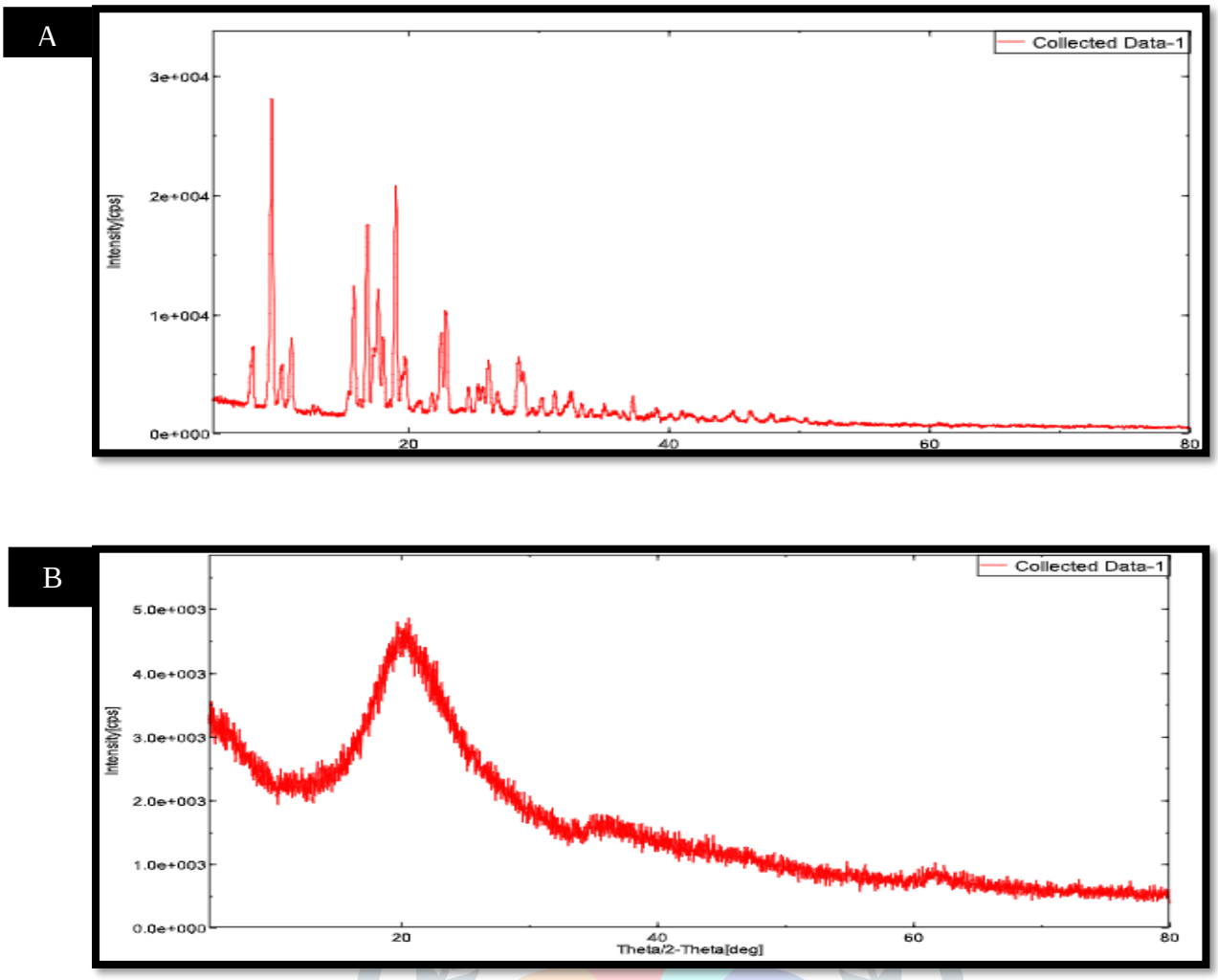

Fig.9: X-ray powder diffraction pattern of (A) pure Lovastatin and (B) Solid-SMEDDS

In-vitro dissolution study

More than 95% of the lovastatin was observed to have been released from the formulation in less than 30 minutes. It is clear by comparing the solubility of formulation and plain lovastatin in buffer pH 6.8 and 0.1 N HCl that the formulation has achieved its goal because there is an increase in drug release from formulation compared to release of plain drug in dissolution media.

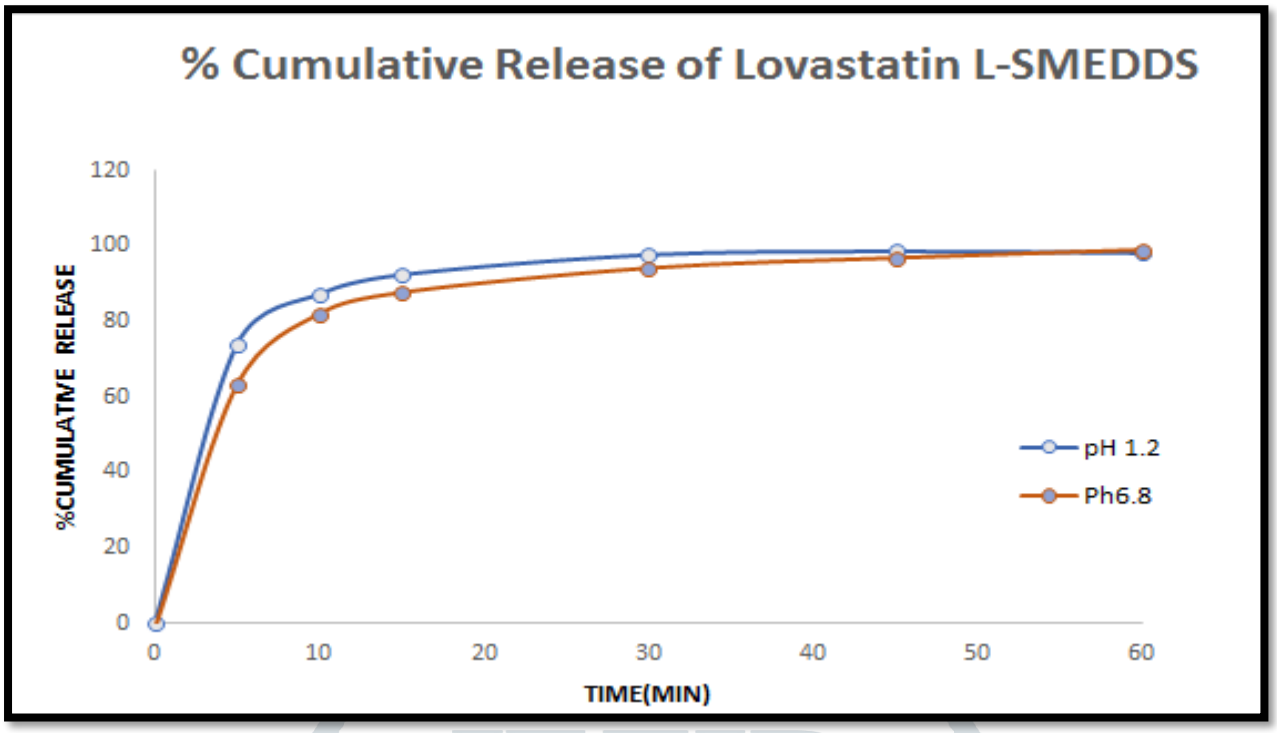

Fig.10: In-vitro dissolution profile of S-SMEDDS

Stability study

The stability studies were performed on the Solid SMEDDS at 40±2°C/75% RH ±5% RH up to 3 months .Parameters like flowability,particle size,zeta potential and the content of the formulation was assayed . *In-vitro* release performance of the formulation was analysed in both the media i.e PBS 6.8 and Ph 1.2.The results showed similarity factor F2 of more than 50 when compared against the initial results indicating the stability of formulations.

Table 8: Parameters evaluated for Stability Studies

PARAMETERS	0 DAYS	30 DAYS	90 DAYS
Flowability	Good	Good	Good
Particle size(nm)	100.3	105	109.2
Zeta potential(mV)	-32.8	-37.5	-36.4
Drug content(%)	100.80	99.60	97.89

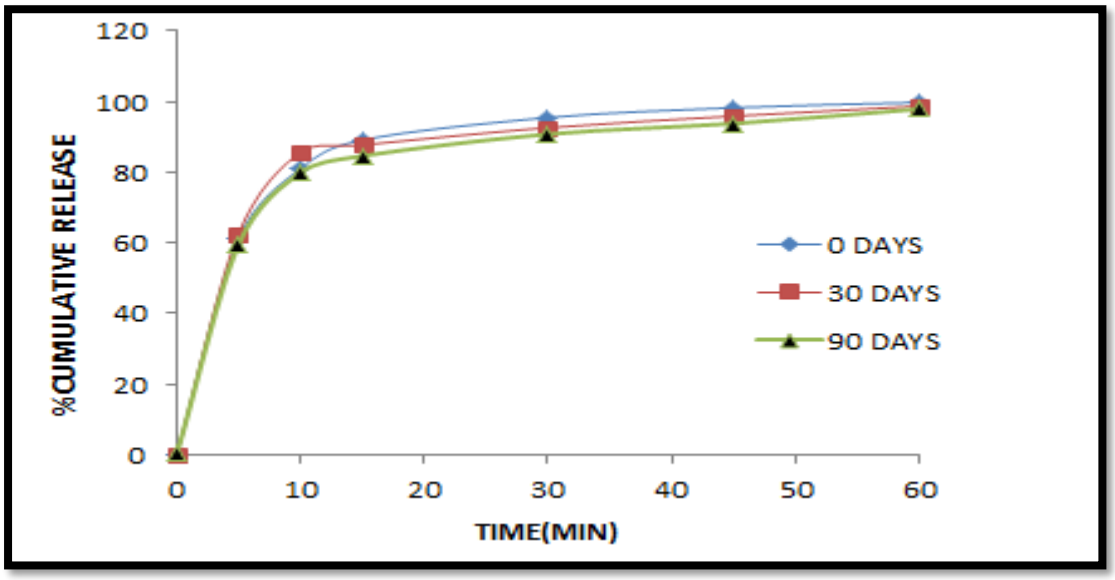

Fig.11: *In-Vitro* Dissolution Profile of Stability Studies in pH 6.8 PBS

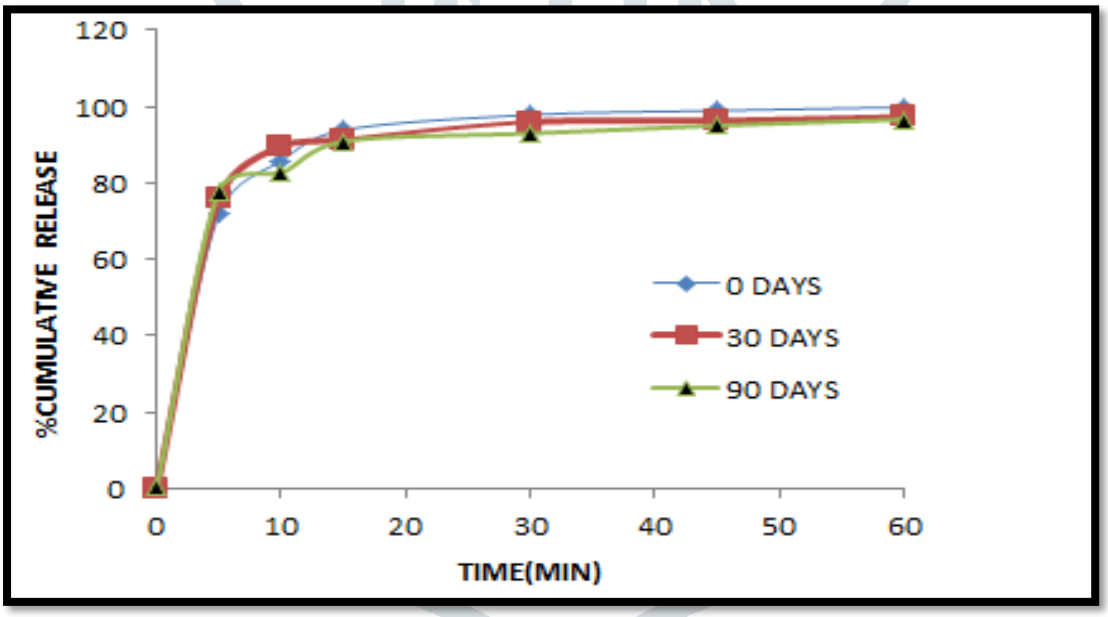

Fig.12: *In-Vitro* Dissolution Profile of Stability Studies in pH 1.2

CONCLUSION

A Solid, self-microemulsifying formulation of Lovastatin was created with Capryol PGMC acting as the oily phase, Cremophore RH40 serving as the surfactant, and Labrafil M2125 serving as the co-surfactant. According to the results of the investigation, the liquid SMEDDS that had been created was physiologically stable, had good self-emulsification efficiency, and was thermodynamically stable. Another finding of the study was that the S-SMEDDS of lovastatin made using the adsorption approach and Neusilin US2 have good flow properties and drug content. The solubilization of the drug in the lipid excipients and/or change of the drug's crystalline form to an amorphous one was confirmed by DSC and XRD data of the solid self-microemulsifying powder. The solid-SMEDDS has a better in vitro dissolution and absorption profile than pure lovastatin, which suggests that the drug's solubility, dissolution rate, and bioavailability have improved. Thus, it was determined that S-SMEDDS may be effectively created utilising an adsorption approach and Neusilin US2 as a solid carrier to increase the rate of dissolution of the lovastatin, which is poorly soluble.

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