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Formulation and Evaluation of SEDDS containing lipid lowering Drug

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ABSTRACT:

The present study was done to formulate the self emulsifying drug delivery system of Lovastatin, a lipophilic drug for improvement in in-vitro dissolution and thereby oral bioavailability. Final optimized formulation consisted of oil (), surfactant (Cremophore El) and co-surfactant (Capmul MCM) and solid carrier (Neusilin US2) for adsorption. At first, calibration curve of lovastatin was generated, and then based on saturation solubility studies in different vehicles; oil, surfactant and co-surfactant were screened. Pseudo ternary phase diagrams were used to get micro emulsion region, based on which liquid self emulsifying drug delivery systems of lovastatin were formulated. They were characterized by macroscopic evaluation by visual assessment, self-emulsification time, % Transmittance, globule size, zeta potential, and thermodynamic stability study. In vitro drug dissolution of optimized liquid self emulsifying formulation showed that % release of lovastatin found 99.03±0.31within 30 min which was comparable to marketed tablet of lovastatin 72.91±0.5. The globule size found was 16.1 nm from the optimized Liquid self emulsifying formulation. Optimized liquid self emulsifying formulation was successfully solidified using carrier Neusilin US2 by adsorption technique. Solid SEDDS was characterized by flow property, particle size, zeta potential measurement, % Transmittance, % drug content and in-vitro dissolution test and found that there was not much difference in dissolution behavior of solid and liquid SEDDS. Even it passed stability studies. So it was concluded that lovastatin solid self emulsifying drug delivery system was successfully developed to improve its rate and extent of dissolution.

KEYWORDS: Lovastatin, BCS class II drug, Self emulsifying drug delivery system, dissolution

INTRODUCTION:

Lovastatin is a crystalline and non-hygroscopic powder. Its IUPAC name is (1S,3R,7S,8S,8aR)-8-{2-[(2R,4R)-4-hydroxy-6-oxooxan-2-yl]ethyl}-3,7-dimethyl-1,2,3,7,8,8a-hexahydronaphthalen-1-yl (2S)-2-methylbutanoate. Its melting point is 174.5 °C. [1][2]

Lovastatin is HMG co-A reductase (3-hydroxy-3-methyl-glutaryl coenzyme A) enzyme competitive inhibitor. Lovastatin is metabolized via hydrolysis by cytochrome-3A system to β-dihydroxy acid (metabolite, structure similarity with HMG co-A), compete with hepatic enzyme HMG co-A reductase. Reduction in enzyme activity leads to inhibition of mevalonate (cholesterol synthesis precursor) in the liver, here main step of cholesterol synthesis is arrested and even LDL cholesterol catabolism is increased via hepatic LDL receptors induction. It is a lipid lowering and hypolipidemic drug and is widely used in treatment hypercholesterolemia orally.[3]

According to Biopharmaceutical Classification system, Lovastatin belongs to Class II drug list having low solubility and high permeability. Its bioavailability is approximately <5%. Its log P value is 4.26, means highly lipophilic drug.[1]it is insoluble in water, so it is poorly absorbed from GIT and absorption is dissolution rate limited. It shows high variability in pharmacological effects. Therefore, it's a need to improve its solubility and

rate of dissolution of lovastatin for improvement in oral bioavailability. So attempt to increase the solubility by lipid based approach to be made.[4,5]

Lipid based formulation, especially self emulsifying system was chosen to exhibited major role in overcoming the problems related to oral delivery of lipophilic compounds. Self emulsifying systems are isotropic mixtures of drug, oil, surfactant and co-surfactant, which forms O/W micro emulsion in contact with aqueous gastric medium with a very low globule size ranges in nm. They give additional advantages like production ease, physical and thermodynamic stability and improvement in solubility and its bioavailability. Facilitation of para-cellular and trans cellular absorption, protection of drug from hepatic first pass metabolism and reduction of cytochrome p450 metabolism are some different mechanism for this system. Liquid self-emulsifying systems have disadvantages like chemical instability, leakage from hard gelatin capsule, precipitation of drug; these drawbacks can be overcome by converting the liquid system to solid by adsorption onto solid carrier without disturbing its self-emulsification performances.

Here, the main objective of work was to (1) formulate and characterize the liquid self emulsifying formulation of poorly soluble lovastatin to improve its solubility and (2) the solidification of optimized liquid self emulsifying system of lovastatin by adsorption onto carrier without affecting its self emulsification performance and release rate.

MATERIALS AND METHODS:

Lovastatin was gifted by Sun pharmaceuticals Ltd, Baroda, India. Polyglycolized glycerides vehicles like Labrafil M2125CS, Labrafac CC, Labrasol, Lauroglycol 90, Capryol 340 were gifted from Gattefosse, France. Captex 100, Captex 200, Captex 355**,** Capmul MCM, Peceol, Acconon MC 82 were gifted by ABITEC Co., USA. Cremophore EL was a generous gift sample from Astron research centre, Ahmedabad. Cremophore RH 40 was gifted by BASF Co., Germany. Olive oil, Soyabean oil, Sunflower oil, Peanut oil, Cottonseed oil, Sesame oil were provided by Bright lab, Hyderabad. Oleic acid, Tween 80, Tween 20, span 20, span 80, Propylene glycol, PEG 400 were purchased from S.D. fine chemicals, Mumbai. Acrysol K-140 was gifted by Corel Pharma, Ahmedabad. Neusilin US2 was generous gift from Jay Radhe sales, Ahmedabad. Hard gelatin capsules were provided by Zydus research centre, Ahmedabad. Other chemicals were of analytical grade. All solvents used in the study were also of analytical grade. Fresh distilled water was used in the study.

METHODOLOGY

- **UV SPECTROMETRY ANALYSIS OF LOVASTATIN:[6,7]**

Calibration curve of lovastatin in methanol: 100 mg of Lovvastatin was accurately weighed taken in 100 ml volumetric flask and dissolved in 100 ml of methanol to get stock solution of 1000 µg/ml (1 mg/ml).From this, pipetted out 10 ml (1mg /ml) was further diluted with same solvent to obtain 100 µg/ml solution. The aliquot was scanned in the wavelength range of 200 to 400 nm on UV spectrophotometer to determine the wavelength of maximum absorbance, which was found at 238 nm. Working standard solutions having concentration of 2-20µg/ml were prepared by diluting 100 µg/ml with methanol. The absorbance of each working standard solution was measured at absorption maxima in UV spectrophotometer using methanol as a blank. Absorbances were plotted against concentration using Microsoft Excel. Beer's law was obeyed in the range of 2-20 µg/ml. same calibration curve tobe plotted in pH 7.0 phosphate buffer also.

- **SATURATED SOLUBILITY STUDIES:[8]**

Saturation solubility study of Lovastatin in various vehicles like oils, surfactants and co-surfactants were done in triplicates. Excess amount of lovastatin (drug) was added into 2 ml of each selected individual vehicle contained in stoppered vials separately and after sealing, the mixture was heated at 40 °C in a water-bath to facilitate the solubilization using a vortex mixer. Then the mixtures in vials were then shaken using shaker at 37°C±1°C for 48 hour then allowed them to reach equilibrium. The equilibrated samples in each vial were centrifuged (5000 rpm) for 5-10 min to separate the undissolved drug and the supernatants of oil were taken out and filtered through a membrane filter (0.45µm,13mm, Whatman, India) and after appropriate dilution with methanol, the absorbance was measured against respective blank by UV spectroscopy at 238 nm λmax. The concentration of lovastatin was calculated by the UV Spectrophotometer using calibration curve.

Vehicles to be used were Olive oil, Tween 80,Propylene glycol, Soyabean oil, Cremophore ELP,PEG 400, Sunflower oil, Cremophore RH 40, Capmul MCM, Peanut oil, Labrafil M2125CS, Lauroglycol 90, Cottonseed oil, Labrasol, Capryol 340, Sesame oil, Span 20, Peceol, Oleic

acid, Tween 20, Acconon MC 82, Captex 100, Span 80, Captex 200, Acrysol K-140, Captex355, Labrafac CC.

PSEUDO TERNARY PHASE DIAGRAM:[9,10,11]

Based on the data observations of solubility studies, excipients of SMEDDS like oil, surfactant and co surfactant having highest solubility of Lovastatin were selected. The phase diagrams of oil, surfactant: co-surfactant and water were constructed using water titration method. Here seven ratios of surfactant: co-surfactant (Smix) (1:1, 1:2, 1:3, 1:4, 2:1, 3:1, 4:1 W/W) were mixed together. Each ratio of Smix blended with oil in a proportion of 9:1, 8:2, 7:1, 6:4, 5:5, 4:6, 3:7, 2:8 and 1:9 with constant stirring by magnetic stirring. Each blend of mixture was titrated with distilled water in increment of 0.5% (W/W) with proper stirring to form clear transparent micro emulsion. The point which indicates the clear and isotropic mixtures were considered to be within the micro emulsion region. Optimization of the concentration of vehicles (oil, surfactant and co-surfactant) was based on maximum uptake of water by formed micro emulsion. Chemix software was used to optimize the concentration of vehicles. Drug loading capacity was checked on self-micro emulsifying domain of ternary phase diagram.

- **FORMULATIONS OF LIQUID SELF-EMULSIFYING DELIVERY SYSTEM:[11]**

A series of self emulsifying formulations of lovastatin were being prepared using oil (Captex 355), surfactant (Cremophore EL) and co-surfactant (Capmul MCM). Lovastatin amount in all formulations were kept constant (i.e. 20 mg per unit dose). Here, in a glass vial, accurately weighed lovastatin, oil, surfactant and co-surfactant were mixed be vortex mixing for some time till it dissolves properly and stored till further use.

- **CHARACTERIZATION OF LIQUID SEDS OF LOVASTATIN:**

1. Macroscopic evaluation by visual assessment

Small amount of SMEDDS diluted with distilled water (100 ml) and stirred with glass rod. Macroscopic assessment like self-emulsification efficiency, appearance like color, transparency, phase separation and precipitation of lovastatin was carried out visually immediately after dilution. Any change in color & transparency or phase separation during normal storage condition (37±2°C) was checked in micro emulsion formulation.

All SMEDDS were diluted by distilled water, 0.1N HCl (1.2 pH) and pH 7.0 phosphate buffer and micro emulsions were checked for precipitation or phase separation after 24 hours. Precipitation was checked after 24 hr to categorize the formulation like clear (transparent or transparent with bluish tint), nonclear (turbid), stable (no precipitation after 24 hr) or unstable (if sign of precipitates within 24 h)[8]

2. Dispersibility test and Determination of self emulsification time

The emulsification time of SMEDDS was determined According to USP dissolution apparatus. Formulation was added drop wise to 500ml water at 37 °C and agitated by dissolution paddle rotating at 50 rpm. Emulsification time was assessed visually and appearance of dispersion was also being checked and compared from table 1 for grading system. [12]

Table: 1 Visual assessments of efficiency of self-micro emulsification

Grade	Dispersibility & Appearance	Time of SME
I.	Rapid forming micro emulsion which is clear or slightly bluish in appearance	< 1 min
II.	Rapid forming, slightly less clear emulsion which has a bluish white appearance	< 2 min
III.	Bright white emulsion (similar to milk)	< 3 min
IV.	Dull, grayish white emulsion with slightly oily appearance that is slow to emulsify	> 3 min
V.	Exhibit poor or minimal emulsification with large oil droplets present on the surface	> 3 min

3. %Transmittance test

Stability of optimized micro emulsion of SMEDDS with respect to dilution was checked by measuring % Transmittance. One mL of SMEDDS was diluted to 100 mL with distilled water and observed at 650 nm using UV spectrophotometer and for each sample three replicates were performed[13]

4. Droplet/Globule size measurement

Globule Size analysis of micro emulsion of SMEDDS carried out by dynamic light scattering with Malvern Zetasizer. SMEDDS were dispersed in 100 ml distilled water, at 37 ± 0.5˚C and emulsions were prepared by gentle agitation using a magnetic stirrer. Samples were placed in square glass cuvettes & droplet size analysis was carried out.[14]

5. Zeta potential measurement

Zeta potential for micro emulsion was determined using Malvern Zetasizer. SMEDDS were dispersed in distilled water, at 37 ± 0.5˚C and emulsions were prepared by gentle agitation using a magnetic stirrer. Samples were placed in clear disposable zeta cells & results were recorded. Before putting the fresh sample, cuvettes were washed with the methanol & rinsed using the sample to be measured before each experiment.[15]

6. Refractive index measurement

Refractive index of Drug loaded SMEDDS and SMEDDS without drugs was measured using Abbes refractometer.

7. Viscosity determination

The Rheological properties of the micro emulsion were being evaluated. SMEDDS (0.5 g) was diluted 10 times with distilled water with continuous stirring on magnetic stirrer and the viscosity of SMEDDS and resultant micro emulsion were being determined using Brookfield viscometer (DVIII+ Rheometer) at room temperature.[16]

8. Thermodynamic stability study

Thermodynamic stability studies like centrifugation test, heating cooling cycle and freeze thaw cycle were carried out on selected SMEDDS to check physical stability of same.

a. Heating cooling cycle

SMEDDS were exposed to six cycles between 4 ºC and 40 ºC with storage at same temperature for at least 48 hrs. Formulation which showed turbidity at the end of test was discarded and stable formulations were subjected to centrifugation test

b. Centrifugation stress test

Formulations were exposed to centrifugation at 3500 rpm for 30 mins. Formulation showing phase separation was discarded and remaining were being tested for freeze thaw cycle.

c. Freeze thaw cycle

Formulations were passed to 3 cycles at -21°C and +25°C.Formulation which were stable in this test were considered for next characterization.

9. In-vitro dissolution study

The quantitative in vitro test of was performed in 900ml pH 7.0 phosphate buffer, at 37 ± 0.5°C using USP method (dissolution apparatus type I, at 100 rpm). Lovastatin SMEDDS filled in hard gelatin capsule was placed in basket during the release period and release profile were compared with conventional marketed tablet. 10ml of sample solution was withdrawn at predetermined 5, 10, 15, 20, 30, 45 min time intervals, samples were filtered through a 0.45 µm membrane filter, dilute suitably & analyzed spectrophotometrically at λmax 238 nm using calibration curve. Equal amount of fresh dissolution medium was replaced immediately after withdrawal of the test sample to maintain the volume. In vitro dissolution was carried out three times & mean value was tabulated. Percentage drug dissolved at different time intervals was calculated using calibration curve.[17,18]

10. Solidification of liquid SEDDS of optimized liquid lovastatin :

Solid SMEDDS of Lovastatin was prepared using adsorption technique using Neusilin US2 and aerosil 200 carrier by mixing in a mortar and pestle till uniform distribution of blend and after sieving, it was dried and stored till evaluation tests. [19]

11. CHARACTERIZATION OF LOVASTATIN SOLID SEDDS:

1. Micromeritics properties like Angle of repose, Bulk density and tapped density, Compressibility Index (% C.I.) and Hausner ratio (H.R.) were tabulated.

2. Drug content [20]

Drug content was estimated by extracting Lovastatin from Solid SMEDDS in methanol and analyzed spectrophotometrically at 238 nm.

3. Droplet/Globule size measurement

Solid SMEDDS of lovastatin were diluted to 100 ml with distilled water at room temperature under magnetic stirrer. The droplet size measurements of the resultant micro emulsions were done like liquid SMEDDS formulations.

4. Zeta potential measurement

Diluted solid SMEDDS of lovastatin were undergone to zeta potential measurements as like liquid SMEDDS formulations.

5. %Transmittance

Stability of micro emulsion of solid SMEDDS with respect to dilution was checked by measuring % Transmittance. Solid Lovastatin SMEDDS were accurately weighed and diluted with distilled water to 100 ml. After mixing, resultant emulsion was kept for rest for and emulsion was observed for % transmittance. Each sample were performed triplicates were performed.

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Statistical analysis was being used for in-vitro dissolution comparison of liquid-solid SMEDDS and solid SMEDDS-marketed tablet by Model independent mathematical method of similarity (f2) values and ANOVA test.

7. Solid state characterization

The lovastatin Solid SMEDDS optimization was done on the basis of globule size and zeta potential results, % drug content, % Transmittance and *in-vitro* dissolution study and optimized formulation was undergone for solid state characterization like Differential scanning calorimetry (DSC), scanning electron microscopy (SEM), powder x-ray diffraction (PXRD) ,FT-IR study.

- **Differential scanning calorimetry (DSC)**

Thermograms of Lovastatin and optimized Solid SMEDDS were obtained using differential scanning calorimeter to check the thermal behaviour of optimized formulation.

- **Scanning electron microscopy (SEM)**

Morphological analysis of optimized lovastatin Solid SMEDDS can be done using Scanning electron microscope and scanning electron micrographs were recorded and analysed.

- **Powder X- ray diffraction (PXRD)**

The physical state and changes in crystallinity of drug Lovastatin and its optimized solid SMEDDS were characterized by powder X-ray powder scattering (XRD) measurements using X ray diffractometer.

- **FT-IR studies**

FTIR studies were performed to check interaction of drug and excipients in the optimized solid SMEDDS formulation.

12. STABILITY STUDY

Stability study was conducted as per ICH guidelines for final selected solid SMEDDS formulation. Hard Gelatin Capsule filled with final selected solid SMEDDS of lovastatin were stored in air-tight screw capped containers protected from light and maintained under real time (25 ± 2 ^{0}C / 60 ± 5% RH) for 6 months and accelerated conditions (40 ± 2 ^{0}C, 75 ± 5% RH) for 3 months. Samples were taken at 0, 1, 2 , 3 and 6 month for long term and at 0 ,1 ,2 and 3 month for accelerated conditions and evaluated for appearance, self-emulsifying properties, drug content and in-vitro drug release.

RESULT AND DISCUSSION:

UV SPECTROMETRY ANALYSIS

From the scanning of Lovastatin from 200-400 nm in UV spectra, Maximum absorption (λmax) of Lovastatin found tobe 238 nm.

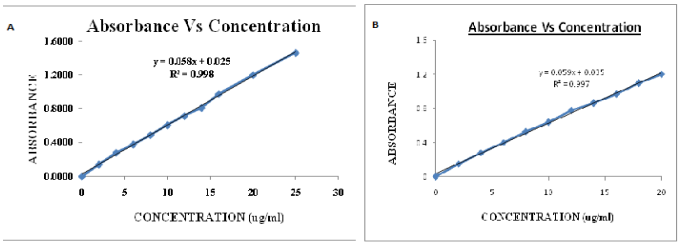

Figure 1 Standard calibration curve of Lovastatin in (A) methanol & (B) pH 7.0 phosphate buffer

From the figure 1 (a) and (b), Graphs of absorption Vs concentration for pure Lovastatin were found to be linear in concentration range 2-20 µg/ml at 238 nm. So pure Lovastatin obeys Beer-Lambert's law in the range 2-20 µg/ml in both medium.

- **SATURATED SOLUBILITY STUDIES:**

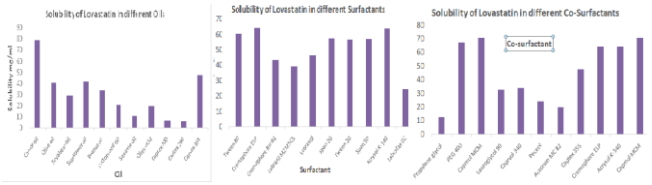

Figure 2 Saturation solubility of Lovastatin in oils, surfactants and co-surfactants

Figure 2 shows solubility of lovastatin in oils, surfactants and co-surfactants. As per maximum solubility data of Lovastatin in different oils, surfactants and co-surfactants; Captex 355 as oil, Cremophore El as surfactant and Capmul MCM as co-surfactant were selected for ternary phase diagram.

- **PSEUDO TERNARY PHASE DIAGRAM:**

From the Lovastatin ternary phase diagrams shown in figure 3, the highest microemulsion zone was found in S mix =s/c = 4:1 with 50 mg lovastatin loading in comparison to other phase diagrams. So that was selected for preparation of Lovastatin liquid SMEDDS.

- **FORMULATIONS OF LIQUID SELF-EMULSIFYING DELIVERY SYSTEM:**

From the ternary phase diagram study, boundary formulations were being selected for the formulation (table 2) and characterization study.

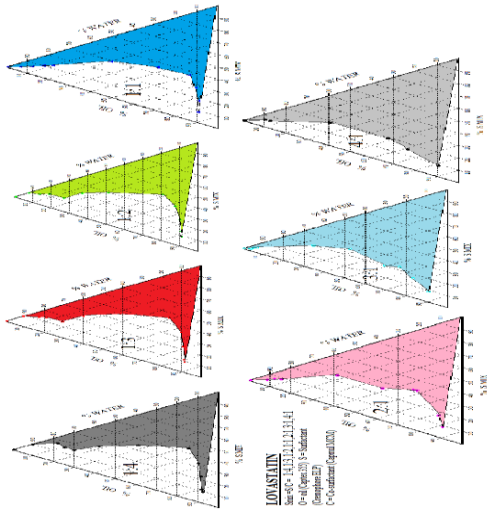

Figure 3 Pseudo ternary phase diagrams of lovastatin with O= Captex 355, S= Cremophore El , C= Capmul MCM at different S mix=S/C = 1:4,1:3,1:2,1:1,2:1,3:1,4:1

Table: 2 Formulations of liquid SMEDDS of lovastatin

Sr no.	Formulation code	Oil %	% Smix	Ratio of sur/co-sur = S mix
1	L1	25	75	4:1
2	L2	30	70	4:1
3	L3	35	65	4:1
Oil (Captex 355), surfactant (Cremophore El) and co-surfactant (Capmul MCM)				
Lovastatin amount in unit dose = 20 mg				

CHARACTERIZATION OF LIQUID SEDDS OF LOVASTATIN:

Table 3 shows characterization of liquid SMEDDS like visual assessment, dispersion, self-emulsification time, % Transmittance, particle size, zetapotential, refractive index, viscosity, thermodynamic study etc.

Table 3: Characterization of liquid SMEDDS of lovastatin

Parameter/ Formulation	L1	L2	L3
Visual assessment	Clear and uniform emulsion without precipitation;Robust to dilution without pH effect	Clear and uniform emulsion without precipitation;Robust to dilution without pH effect	Less clear emulsion; Robust to dilution without pH effect
Dispersion	Grade II slightly bluish micro emulsion	Grade I microemulsion	Grade III bluish white emulsion
Self-emulsification time	within 1.05 min	Spontaneous within 20 seconds	2 min
% Transmittance	89.73±0.07	99.52±0.005	76.45±0.014
Particle size (nm)	22.68	16.1	43.74
Polydispersity index	0.296	0.164	0.423
Zeta potential (mv)	-4.41	-22.02	Not found
Refractive index	1.438 ± 0.07	1.419 ± 0.03	1.477 ±0.1
Viscosity (cps)	183	198	221
Thermodynamic stability study	Passed	Passed	Passed

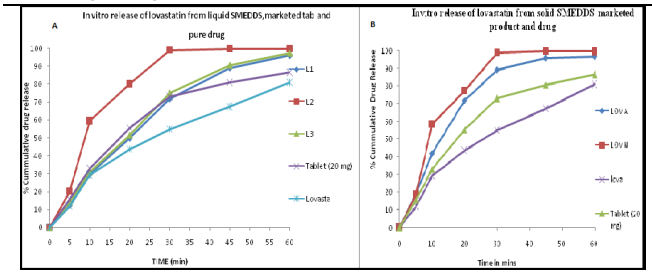

Figure 4: Dissolution profiles of lovastatin from (A) liquid SMEDDS, marketed tablet and pure drug (B) Solid SMEDDS, marketed tablet and pure drug

Figure 4 (A) shows dissolution profile of lovastatin from liquid SMEDDS L1, L2, L3. From all characterization studies, liquid SMEDDS L2 found tobe best than L1 and L3; as L2 showed % Transmittance near to 100 and low globule size distribution and poly dispersibility index and high value of zeta potential. Refractive index of L2 was near to water and viscosity of it was pourable in capsules. From In vitro dissolution, rate and extent of lovastatin release from L2 found tobe significantly higher than L1, L3, marketed formulation and pure drug. So, L2 can be optimized for solidification of liquid SMEDDS.

- **SOLIDIFICATION OF LIQUID SEDDS OF OPTIMIZED LIQUID LOVASTATIN**

Solid SMEDDS of lovastatin (LOV A and LOV N) were successfully prepared by adsorbing carriers aerosil 200 and Neusilin US2 with high loading capacity (1:0.7 and 1:0.5 = L2: Adsorbent) respectively.

- **CHARACTERIZATION OF LOVASTATIN SOLID SMEDDS:**

Table 4: Characterization of solid SMEDDS of lovastatin

Parameter/ Formulation	LOV A	LOV N
% drug content	96.84±0.062	98.867±0.058
Angle of repose Ɵ	21.037±0.03	16.38±0.05
Bulk density (g/ml)	0.9±0.02	0.89±0.05
Tapped density (g/ml)	1.21±0.05	1.04±0.04
C.I. (%)	25.62±0.06	14.42±0.03
HR	1.34±0.04	1.17±0.02
% Transmittance	95.8 ± 0.22	100.2± 0.14
Globule size (nm)	22.9	19.4
Polydispersity index	0.146	0.212
Zeta potential	-8.1	-17.5
Emulsification ability	Good	Good

Table 4 shows characterization of solid SMEDDS like micromeritics properties, % Transmittance, % drug content, particle size, zetapotential and emulsification etc. Figure 4(b) shows dissolution profiles of solid SMEDDS (LOV N and LOV A), marketed tablet and pure drug.

From the characterization studies, LOV N shown tobe excellent solid SMEDDS compared to LOV A; as LOV N showed excellent flow property compared to LOV A. LOV N showed % Transmittance near to 100 and low globule size distribution and poly dispersibility index and high value of zeta potential. Invitro dissolution profile of LOV N and L2 had no significant difference (supported by similarity value *f2=90 and one way ANOVA*) and Invitro dissolution profile of LOV A and L2 were significantly different (supported by similarity value *f2=54 and one way ANOVA*). From In vitro dissolution, rate and extent of lovastatin release from LOV N found tobe significantly higher than LOV A, marketed formulation and pure drug. So, LOV N can be optimized and taken for solid state characterization to check drug and excipient compatibility in the formulation.

Solid state characterization

Figure 5, 6, 7 shows SEM, XRD and FTIR graphs respectively for both lovastatin pure drug and optimized solid SMEDDS LOV N.

DSC of LOV N, sharp endothermic peak of crystalline lovastatin was not obtained at 172°C, which showed dissolution of lovastatin in formulation and no drug-excipient interaction. DSC was supported by SEM, in which clear adsorption of L2 on carrier Neusilin US2 was seen. In XRD of LOV N, characteristic peaks of lovastatin were reduced. In FTIR of LOV N, characteristic peaks were retained showed no incompatibility between drug and excipients.

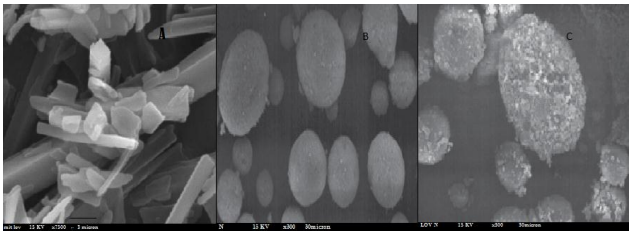

Figure 5 SEM of (A) Lovastatin drug; (B) Neusilin US2; (C) Solid SMEDDS LOV N

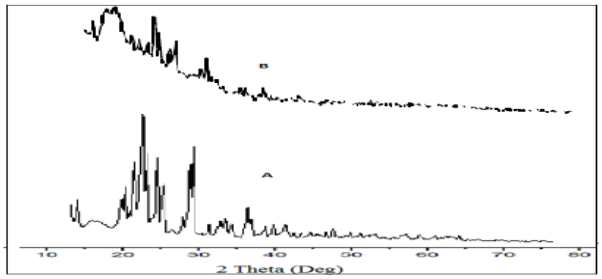

Figure 6 X-ray diffractogram of (A) Lovastatin drug and (B) solid SMEDDS LOV N

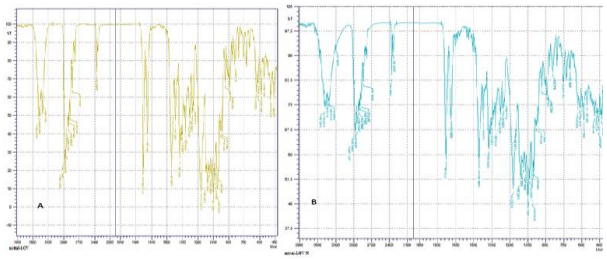

Figure 7 FTIR spectra of (A) Lovastatin drug and (B) Formulation LOV N

So, from all the characterization tests, LOV N found tobe optimized formulation and was undergone to stability study as per ICH guideline.

STABILITY STUDY

In the stability study, physical parameters like homogeneity, phase separation and self emulsifying performance and % drug content, invitro dissolution were observed and no significant change was observed up to 3 months (accelerated conditions) and up to 6 months (real time conditions) compared to o days in any of parameters for LOV N, meaned it showed physical and chemical stability in both conditions. So, LOV N passed stability studies test as per ICH guidelines.

CONCLUSION:

Solid SMEDDS of lovastatin found to be a better and novel approach for improvement in problems associated with oral delivery of lovastatin. Lovastatin SMEDDS formulation was being proved as better than marketed formulation in regard to in vitro dissolution profile and Neusilin US2 proved as better carrier as adsorbent of liquid by adsorption method. Thus SMEDDS proved as a

good commercial alternative to existing marketed formulation.

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