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Formulation and Evaluation of Solid Self Emulsifying Drug Delivery System of Ezetimibe

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ABSTRACT

Ezetimibe is the selective cholesterol absorption inhibitor. It is indicated for the treatment of primary hypercholesterolemia. The current investigation was aimed to formulate Solid self-emulsifying drug delivery system (S-SEDDS) for Ezetimibe to enhance solubility and dissolution rate which will leads to minimize the variability in absorption and it may enhance oral bioavailability of the poorly soluble drug, ezetimibe. Various modified oils, surfactant, co-surfactant mixtures were screened for their suitability in the formulation of SEDDS and composition of Solid self-emulsifying drug delivery system (S-SEDDS) was optimized. The optimized formulation was added on to an adsorbent, Aerosil 200. The drug release from these optimized formulations was studied and found to be better compared to conventional dosage form. Our studies indicate that Solid-SEDDS can be effectively formulated by adsorption technique. Solid-SEDDS were characterized by X-ray diffraction pattern, DSC, SEM and dissolution profile. It was supported by SEM studies, which did not show evidence of precipitation of the drug on the surface of the carrier. Dissolution studies revealed remarkable increase in dissolution of the drug as compared to marketed product.

Key words: Ezetimibe, Solid-self emulsifying drug delivery system (S-SEDDS), Solid adsorption technique, Aerosil 200, Dissolution studies.

INTRODUCTION

Ezetimibe is a first member of new class (BCS class II) of cholesterol absorption inhibitors indicated for use as a mono therapy or in combination with statins for the treatment of primary hypercholesterolemia. It prevents the transport of dietary and biliary cholesterol across the intestinal wall without affecting the absorption of fat soluble vitamin, triglycerides and bile acids [1].

Approximately 40% of new drugs have poor water solubility and the oral delivery of such drugs is frequently associated with low bioavailability, high intra- and inter-subject variability, and a lack of dose proportionality. To overcome these problems, various formulation strategies are exploited including the use of surfactants, lipids, permeation enhancers, micronization, salt formation, cyclodextrins complex, liposome formation, nanoparticles and solid dispersion [2]. Recently, much attention has been paid to lipid-based formulations with particular emphasis on self-emulsifying drug delivery system to improve the oral bioavailability of lipophilic drugs. SEDDS is an isotropic mixture composed of oil, surfactant, co-surfactant and drug. It can readily disperse in aqueous environment of GIT and upon mild agitation followed by dilution in aqueous media, such as GI fluids, these systems can form fine oil-in-water (O/W) emulsions or nano emulsions or self micro-emulsifying drug delivery system (SMEDDS).

Solid self-emulsifying powder of ezetimibe using various modified oils, surfactants, co-surfactants and solidifiers mixture has been prepared. The solid self-emulsifying powder of ezetimibe filled into hard gelatin capsules showed increase in the dissolution rate as compared to plain drug filled capsule signifying its potential in improved delivery of lipophilic drugs.

Many research works are reported on SEDDS of Ezetimibe but not much work has been reported yet on Solid SEDDS of Ezetimibe. Hence, aim of present investigation was to develop Solid SEDDS for Ezetimibe with oleic acid as oil, Labrasol as surfactant and Transcutol-P as co-surfactant and convert it in to a powder by using adsorbent like Aerosil 200.

MATERIALS AND METHODS

Materials:

Ezetimibe was gifted by Lupin Ltd. (Pune, India). Transcutol P (TP), was gifted by Subhash Chemicals, Pune. Colloidal silicon dioxide (Aerosil 200) was kindly provided as a gift sample from Aurobindo Pharmaceutical Pvt. Ltd., Mumbai. Oleic acid was purchased from National Chemicals, Baroda.

Methods:

Solubility Study

The solubility of Ezetimibe in various oils, surfactants and co-surfactants was determined as follows –

5ml of each selected component was added to test tube containing an excess of ezetimibe. After capping tubes, the mixtures were shaken at 25°C for 72 hrs to achieve solubility equilibrium. Then each tube was centrifuged at 4000 rpm/min for 10 min and supernatant was passed through a membrane filter (0.45µm) to remove undissolved drug [3]. Solubility of ezetimibe was determined by analyzing the filtrate with UV-Visible Spectrophotometer (V 630, Jasco) after appropriate dilution with methanol at 232 nm.

Construction of Pseudo Ternary Phase Diagram

To evaluate the effect of drug on the robustness/stability of the SEDDS, phase diagrams were constructed in the absence and presence of drug. On the basis of solubility data, Oleic acid was selected as oil, Labrasol as surfactant, Transcutol-P as co-surfactant. Pseudo ternary phase diagram of oil, surfactant/co-surfactant (S_{mix}), water were developed using water titration method. Surfactant and co-surfactant were mixed in different volume ratios (1:1, 1:2, 1:3, 1:4, 4:1, 3:1). Oil and surfactant/ co-surfactant mixture (S_{mix}) were mixed thoroughly in different volume ratios (1:9, 2:8, 3:7, 4:6, 5:5, 6:4, :3, 8:2 and 9:1 w/w) and titrated with water by drop wise addition under gentle agitation until the required clarity and flow ability was achieved. Phase diagram was constructed to determine the boundaries of self-emulsion region. The physical state of SEDDS was marked on a pseudo-ternary phase diagram with one axis representing aqueous phase, second representing oil phase and third representing a mixture of surfactant and co-surfactant (S_{mix}) at different volume ratios.

Preparation of Liquid SEDDS

Based on the solubility study it was found that ezetimibe has maximum solubility in Oleic acid (oil), Labrasol (surfactant) and Transcutol-P (co-surfactant). Ezetimibe was dispersed into the mixture of oil, surfactant, and co-surfactant. Then the components were mixed by gentle stirring for 30 mins. After the drug was completely dissolved then mixture was stored at room temperature until used [4]. The formulations are represented in **Table 1**.

Table 1: Formula for Liquid SEDDS

Sr. No.	Drug (mg)	Oil (ml)	Surfactant (ml)	Co-surfactant (ml)
F1	10	2	4	4
F2	10	2	3.33	6.66
F3	10	2	2	6
F4	10	2	1.6	6.4
F5	10	2	6.4	1.6
F6	10	2	6	2

Preparation of Solid SEDDS

Aerosil 200 (2 gm) was dissolved in 100 ml methanol by magnetic stirring. This solution was filtered by Whatmann filter paper to remove undissolved particles. The liquid SEDDS (5 ml) was then added in this solution with constant stirring for 20 min. Allow it to solidify at room temperature. Solid SEDDS equivalent to 10mg of ezetimibe were weighed and filled in hard gelatin capsule. The capsules were capped and stored in moisture proof container until used [5].

CHARACTERIZATION AND EVALUATION

A. Dispersibility Test

The self-emulsion efficiency of formulations was assessed using a standard USP type II dissolution apparatus. One ml of each formulation was added to 900ml of distilled water at 37 ± 0.5°C. A standard stainless steel dissolution

paddle rotating at 50 rpm provided gentle agitation [6]. The *in vitro* performance of the formulations was visually assessed using the following grading system. The grades of dispersibility are represented in **Table 2**.

Table 2: Grading system for SEDDS

Grade	Dispersibility& Appearance	Time for Self Emulsification
A	Rapid forming emulsion which is clear or slightly bluish in appearance	Within 1 min
B	Rapid forming, slight less clear emulsion which has a bluish white appearance	Within 1 min
C	Rapid forming, slight less clear emulsion which has a bluish white appearance	Within 2 min
D	Dull, grayish white emulsion with a slight oily appearance that is slow to emulsify.	More than 2 min
E	Dull, grayish white emulsion with a slight oily appearance that is slow to emulsify	More than 3 min

B. Thermodynamic Stability studies

The physical stability of lipid based formulations are essential to its performance, which can be inauspiciously affected by precipitation of the drug in the excipient matrix. In addition, the formulation having poor physical stability can affect the formulation performance and it also leads to phase separation of the excipients and hence Heating Cooling cycle, Centrifugation, Freeze thaw test studies were conducted.

1. Heating Cooling Cycle

Six cycles were carried out between the temperature 40°C and 45°C. In between this temperature, formulation was stored and storage at each temperature was not less than 48 Hrs. Those formulations which were stable at these temperatures were subjected to centrifugation test.

2. Centrifugation

The selected formulations which passed the above test were centrifuged at 3500 rpm for 30 min. Those formulations that did not show any phase separations were taken for freeze thaw test.

3. Freeze Thaw Cycle

Three freeze thaw cycles were carried out between -21°C and +25°C with storage at each temp for not less than 48 Hrs was done for these formulations.

C. Drug Content

The drug content in the drug loaded self-emulsion was determined in triplicate using a UV- Spectrophotometric method. The weighed samples were dissolved in methanol and filtered using whatman filter paper, then volume was made up to 10 ml. 1ml of this solution was successfully diluted 10 fold with methanol, which is then again diluted 10 fold. The content was estimated spectrophotometrically (V–630, Jasco) at 232 nm. The drug content was extrapolated from the standard curve.

D. Turbidity Measurement

Turbidometric evaluation is made to observe the growth of emulsification. 0.5ml of self-emulsion system is added to 150ml methanol under continuous stirring (50 rpm) on magnetic plate and increase in turbidity is measured using a turbidity meter.

E. Viscosity Determination

The viscosity of the formulations was evaluated by a Brookfield viscometer at 25°C using a spindle 61, 62 and 63 at 50 rpm. Experiments were performed in triplicate for each sample and results were presented as average ± standard deviation [7].

F. Refractive Index and % Transmittance

Refractive index and % transmittance proved the transparency of formulation. The refractive index was measured by using Abbe's refractometer, by placing a drop of emulsion in prism box. The % transmittance of the system was measured at 232 nm using UV-Visible spectrophotometer keeping distilled water as a blank.

G. Infrared Spectroscopy

The potassium bromide (KBr) discs with ezetimibe were prepared using electrically operated KBr Press Model HP-15. About 2 mg of drug was triturated with about 10 mg of dry KBr and then pressed into the pellet by a pneumatic press. An IR spectrum of the prepared disc of ezetimibe was measured by Jasco FTIR-5300 spectrophotometer with scanning range 4000-500 cm^{-1}. The spectrum was compared with that of reported literature.

H. Differential Scanning Calorimetery (DSC) Analysis

DSC study of powdered sample of Ezetimibe API and mixture of excipients with drug enables us to know the compatibility of drug with other material. DSC analyses the sample and data were recorded using DSC instrument. The thermal traces were obtained by heating the sample from 0-300°C at heating rate of 10°C/min. The thermograms, transition temp. range, the onset of peak transition and maximum peak of transition were recorded.

I. Zeta Potential

Zeta potential is used to identify the charge on droplets. 10mg of solid formulation was dissolved in 10 ml of methanol. Zeta potential was determined by Brookhaven instrument and was monitored at 25°C at a scattering angle 90°.

J. Scanning Electron Microscopy (SEM)

The shape and surface characteristics of the prepared solid formulation were evaluated by means of SEM.

K. X-ray Diffraction

X-ray diffraction study was carried out for studying diffraction patterns in drug before and after formulation. X-ray diffraction study was done by using XRD instrument.

L. In-Vitro Dissolution Testing

The dissolution of Solid SEDDS was done in 900ml of 0.45% SLS 0.05M acetate buffer pH 4.5, at 37± 0.5°C using USP dissolution tester, type II apparatus with rotating speed of 75rpm. Aliquots from dissolution medium were withdrawn at regular time intervals of 5, 10, 15, 20, 30, 40, 45, 50 and 60 min., then filtered and adequately analyzed for drug content using UV- spectrophotometric method.

RESULTS AND DISCUSSION

Solubility Study

The oils included for solubility screening in the present studies represent oils from natural sources and also semisynthetic oils. Solubility of ezetimibe was determined in different oils to find the oil showing highest solubility of ezetimibe. Amongst these oils screened, oleic acid shows highest solubility followed by peanut oils shows higher solubility for ezetimibe in comparison to the others. Hence oleic acid was chosen as oil phase for preparation of SEDDS**.** The results of solubility of ezetimibe in various oils are as shown in **Fig.1.** Solubility in all excipients is relevant for drug loading and transparency of formulations. Hence surfactants and co-surfactants were also screened. Surfactants like Labrasol showed the maximum solubility of Ezetimibe, followed by Tween-80. Co-surfactant like Transcutol-P and PEG also showed very good solubility for ezetimibe and hence these were chosen as different surfactants and co-surfactants combinations for the preparation of SEDDS. Excipients showing maximum solubility were used for the phase behavior study as more drug loading possible with this selection. The solubility of ezetimibe in various surfactants and co-surfactants is presented in **Fig. 2** and **3**. So, selection of oleic acid as oil, Labrasol as surfactant and Transcutol-P as co-surfactant is done for further study.

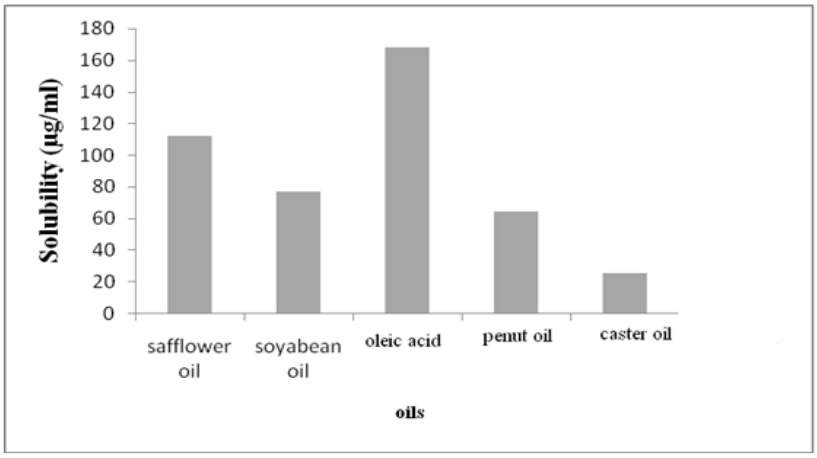


Fig. 1: Solubility study of Ezetimibe in various oils

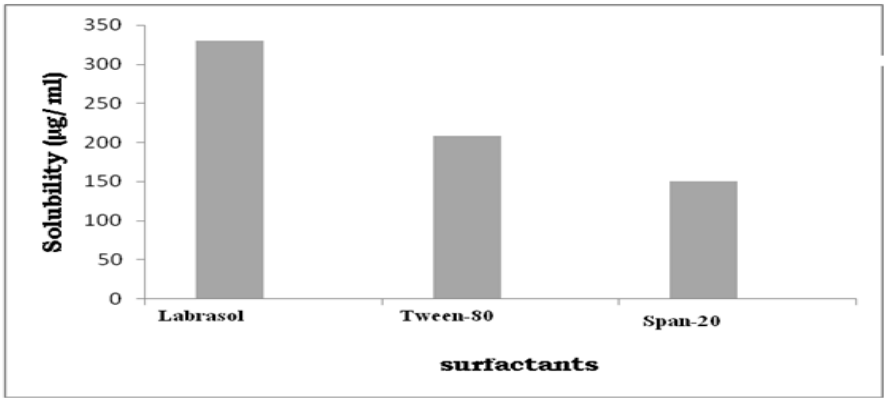


Fig. 2: Solubility studies of ezetimibe in various surfactants

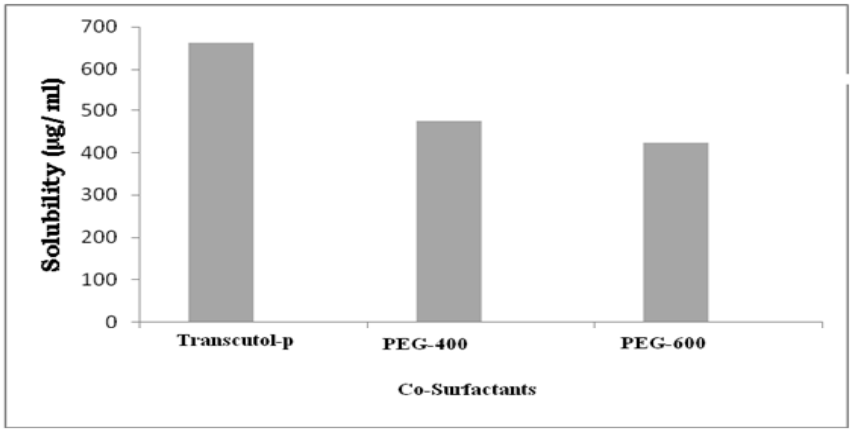
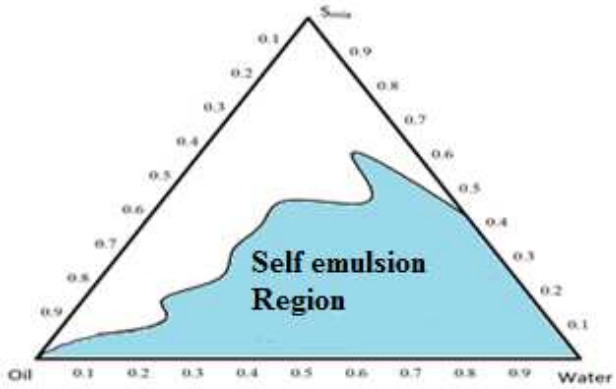


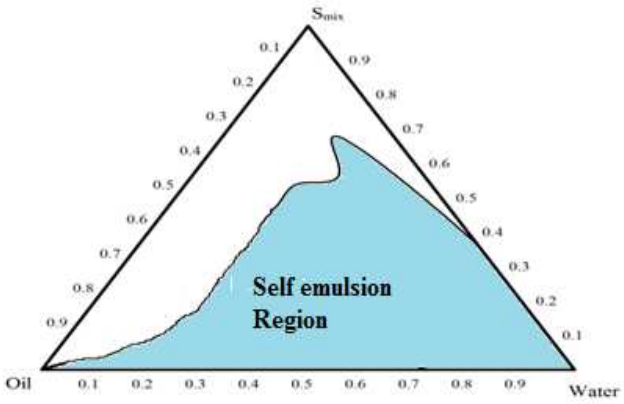
Fig. 3: Solubility studies of ezetimibe in various Co-surfactants

Study on Phase Behavior using Water Titration Method

The construction of pseudo ternary phase diagram considered to be important to determine the spontaneity of SEDDS to form the emulsion within the GI conditions. Ternary phase behaviour investigations help to choose the proper concentration of excipients i.e., oil proportion and optimum Smix ratio in the formulation to produce emulsions with good stability [8]. Also one of the most important characteristics of SEDDS is the change that occurs when the system is diluted (since it will be diluted by body fluids after administration), which may cause drug precipitation due to the loss of solvent capacity [9]. Therefore, the phase behavior of each SEDDS needs to be carefully studied using the phase diagram as a guide. The oil oleic acid was examined for phase behavioral studies with Labrasol as surfactant, with Transcutol-P as co-surfactant based system showing self-emulsion at various S_{mix} ratios but in the optimization step, selection of formulation with good stability, water loading capacity and able to deliver drug dose in less dose formulation is selected. Pseudo-ternary phase diagram of SEDDS system for phase behavior study was shown in **Fig. 4**. From the trail, it has shown that the emulsifying effect was good if ratio of S_{mix} was 1:1.



a) S_{mix}**(S/CoS ratio)**=1:1



b) S_{mix}(S/CoS ratio)=1:2

Fig. 4: Pseudo-ternary phase diagrams of SEDDS system containing oleic acid as oil, Labrasol as surfactant, Transcutol-P as co-surfactant. Ratio (% v/v) of surfactant to co-surfactant in a) 1:1, (b) 1:2

Evaluation of Liquid SEDDS and Solid SEDDS:

Dispersibility Test

The dispersibility test was carried out in methanol and results were shown as follows-

Table 3: Dispersibility test

Sr.No.	Dispersion	Grade
F1	Clear	A
F2	Clear	A
F3	Translucent	B
F4	Translucent	B
F5	Translucent	B
F6	Dull	C

Thermodynamic Stability Studies

On the basis of thermodynamic stability studies it was found that formulation F1 and F2 were stable at different temp. and speed condition.

Table 4: Thermodynamic Stability Studies

Formulation	Heating-Cooling Cycle	Centrifugation	Freeze-Thaw Cycle
F1	√	√	√
F2	√	√	√
F3	√	√	×
F4	×	√	×
F5	×	√	√
F6	×	×	×

Drug Content

Drug content of self-emulsion containing ezetimibe was determined by UV-Visible Spectrophotometer at 232nm using methanol.

Table 5: Drug Content of SEDDS containing ezetimibe

Formulation	% Drug Content ± SD*
F1	90±0.013
F2	90±0.024
F3	87±0.02
F4	80±0.08
F5	74±0.052
F6	68±0.06

**SD= Standard deviation (n=3)*

Turbidity Measurement

Appearance of six formulations (F1-F6) was tested against white and black background and turbidity was checked. The test was carried out as described in the United state Pharmacopoeia [10]. Turbidity values have been reported

that are used in SEDDS characterization. In turbidity measurement, amount of scattered light is measured. The results found that formulation F1 and F2 had least turbidity whereas F6 had maximum turbidity.

Table 6: Turbidity Measurement

Formulation	Turbidity (NTU)
F1	06
F2	09
F3	27
F4	35
F5	54
F6	78

Viscosity Determination

The viscosity of self-emulsion system can be monitored by standard rheological techniques. It depends on oil and surfactants used. The optimized formulation F1 has minimum viscosity 0.8872 Cp. The results of viscosity are as shown in **Table 7**. Formulation F1 is very clear, transparent and low viscous liquid.

Table 7: Viscosity Determination

Formulation	Viscosity (Cp)
F1	0.8872±0.57
F2	0.8875±0.57
F3	0.8874±0.23
F4	0.8877±0.57
F5	0.9574±0.5
F6	1.121±0.14

Refractive Index and % Transmittance:

Refractive Index

The Refractive index of formulations was indicated in **Table 8**. These values were found to be comparable with that of water, indicating good transparency.

Table 8: R.I. measurement

Formulation	Refractive Index
F1	1.334 ± 0.005
F2	1.361 ± 0.003
F3	1.352 ± 0.002
F4	1.344 ± 0.004
F5	1.343 ± 0.006
F6	1.428 ± 0.004
Water	1.333

Percent Transmittance

Percentage Transmittance for various formulations is shown in **Table 9**. Percentage transmittance of formulation F1 and F2 was found to be more than 99% which indicates that these were transparent self-emulsion compared to other formulations.

Table 9: Percent Transmittance

Formulation	% Transmittance
F1	99.12 ± 0.021
F2	99.21 ± 0.016
F3	98.58 ± 0.009
F4	98.73 ± 0.011
F5	98.23 ± 0.013
F6	48.23 ± 0.01

IR Spectroscopy Analysis

FT-IR analysis of optimized formulation and the drug was performed for investigating any drug-excipient interactions by using KBr disc method along with scanning range of 4000-500 cm^{-1} and resolution 1 cm^{-1}. The IR spectrum of drug sample was matched with standard IR spectra of ezetimibe. The FTIR spectra of ezetimibe showed peaks at 3411.84-3235.30 cm^{-1} (O-H, Alcohol/Phenol), 3085.75-3015.34 cm^{-1} (C-H, Aromatic), 1684.28 cm^{-1} (N-C=O Amide), and 1097.31 cm^{-1} (C-F bending). These peaks can be considered as characteristic peaks of ezetimibe and were not affected and prominently observed in IR spectra of ezetimibe along with oil, surfactant and co-

surfactant. So it was concluded that drug and excipients are compatible with each other. The data for FT-IR analysis of ezetimibe pure drug and its optimized Formulation F1 is shown in **Table 10** and **11** respectively.

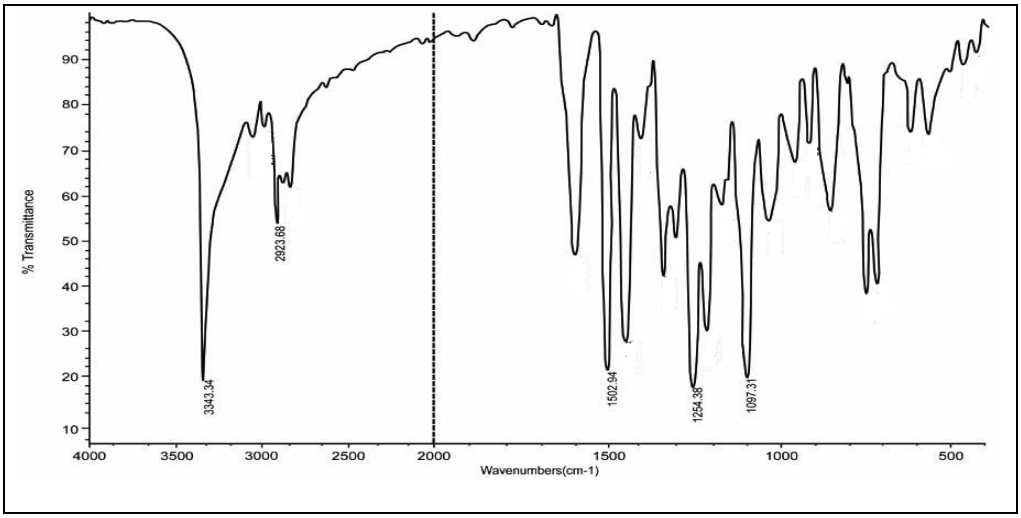


Fig. 5: FTIR spectra of Pure Ezetimibe pure drug

Table 10: Functional groups of Ezetimibe pure drug

Functional group	Observed value	Reported value
O-H_{Ar} stretch	3315.63	3600-3400
O-H_{Ali} stretch	3343.34	3600-3400
C=O_{Amide}	1684.28	1700
C=C_{Ar}	1588.33	1600
C-N	1271.09	1400
C-F	1097.31	1100

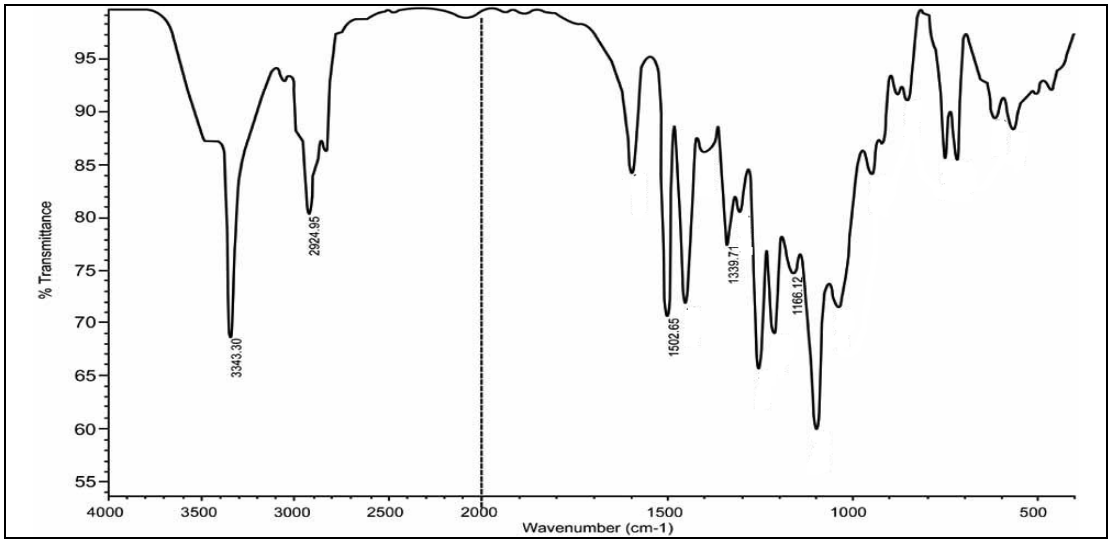


Fig. 6: FTIR spectra of Ezetimibe optimized Formulation F1

Table 11: Functional groups of Ezetimibe optimized Formulation F1

Functional group	Observed value	Reported value
O-H_{Ar} stretch	3343.30	3600-3400
O-H_{Ali} stretch	3231.40	3600-3400
C=O_{Amide}	1734.01	1700
C=C_{Ar}	1578.25	1600
C-N	1278.81	1400
C-F	1055.06	1100

DSC Analysis

DSC is very useful in investigation of thermal properties of SEDDS providing both qualitative and quantitative information about the physical state of drug inside SEDDS [11]. The DSC thermogram of drug and formulation F1 are shown in **Fig. 7**and **8**. The DSC thermogram of ezetimibe shows a sharp endothermic peak at 165.22°C indicated melting point as per reported in literature. Excipients showed broad endotherms over the temperature range studied. No representative peaks for drug were observed for SEDDS indicating the transformation of crystalline structure of ezetimibe as it may be present in amorphous or molecularly dissolved state in self-emulsifying powder. It is also observed that DSC thermograms of some of the excipients were overlapping with that of plain ezetimibe thermogram.

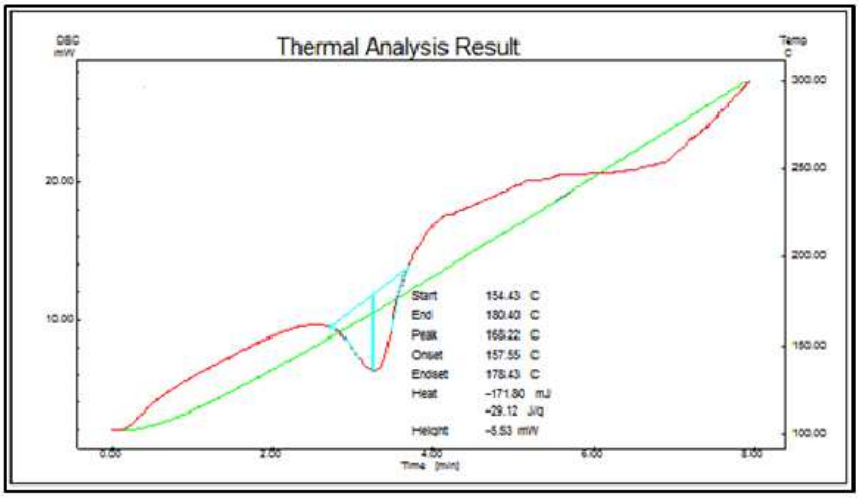


Fig 7: DSC Thermogram of Ezetimibe Pure Drug

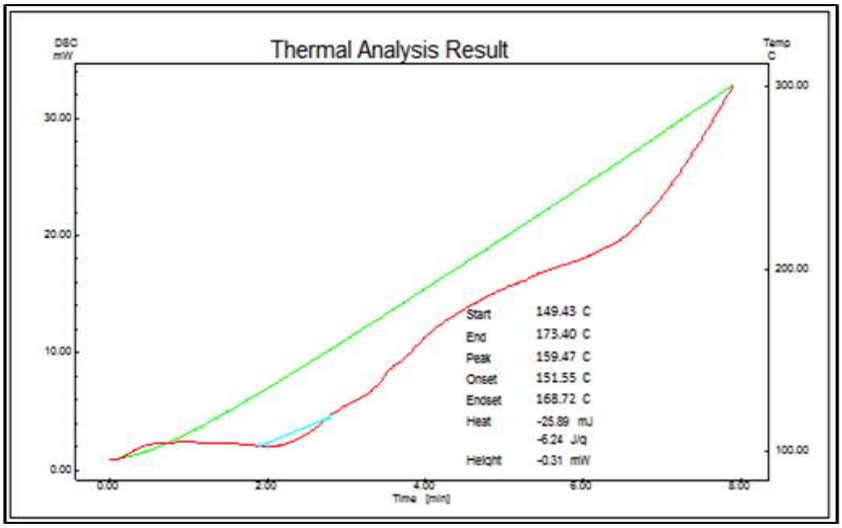


Fig 8: DSC Thermogram of optimized formulation F1

Zeta Potential

The magnitude of zeta potential gives an indication of the potential stability of colloidal system. If all particles have a large – ve or + ve zeta potential they will repel each other and there is dispersion stability. If particles have low zeta potential values then there is no force to prevent particles coming together and there is dispersion instability. A dividing line between stable and unstable aqueous dispersion is generally taken at either +30 or -30 mV. Particles with zeta potential more positive than +30 mV are normally considered stable. The zeta potential of optimized formulation F1 was monitored by Zetasizer. Zeta potential of optimized formulation was found to be -52.68. The particles did not exhibit any flocculation and the formulation was found to be stable. The result is represented in **Fig. 9**.

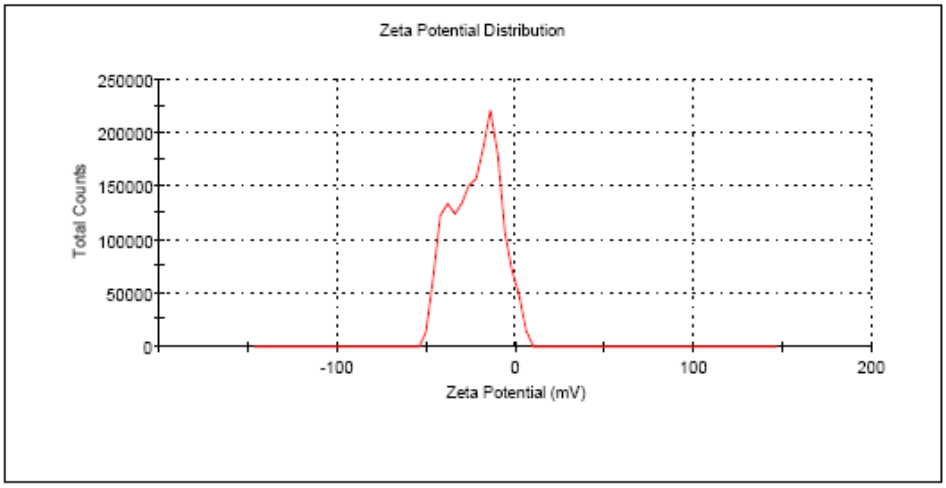


Fig 9: Zeta Potential Distribution

Scanning Electron Microscopy

The formulation F1 was analyzed by SEM for studying particle shape and surface structure. The particles were in high abundance, medium sized, non uniform size and surface of the particles was found to be rough which may be due to Aerosil 200 to avoid agglomeration.

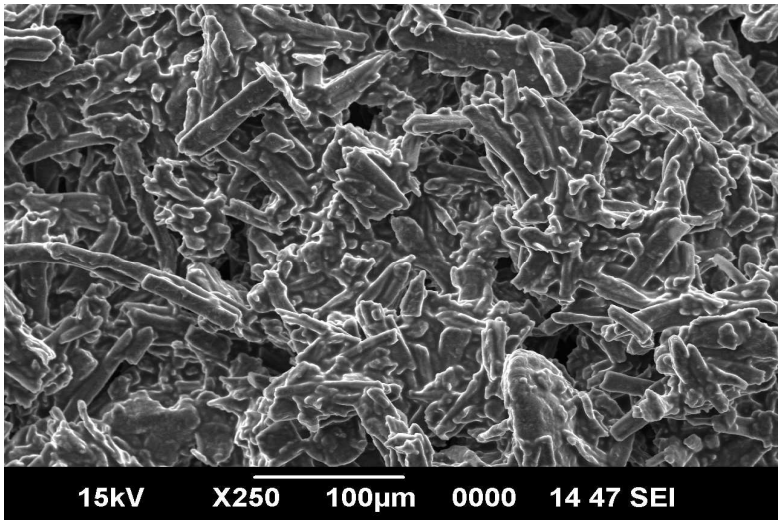


Fig 10: Scanning electron micrograph of formulation F1

XRD Analysis

The X-ray diffraction spectra were recorded for pure ezetimibe and formulation F1. The X-ray diffractogram of ezetimibe has sharp peaks at different diffraction angles (2θ) of 13.92°, 15.32°, 18.66°, 18.20°, 19.29°, 20.42°, 20.87°, 21.54°, 22.65°, 23.22°, 24.49° and 26.37° are present which show a typical crystalline pattern. These sharp diffraction peaks were still detectable in formulation F1 shows peaks but with low intensity. The XRD data for ezetimibe and formulation F1 was shown in **Fig. 11** and **12**.

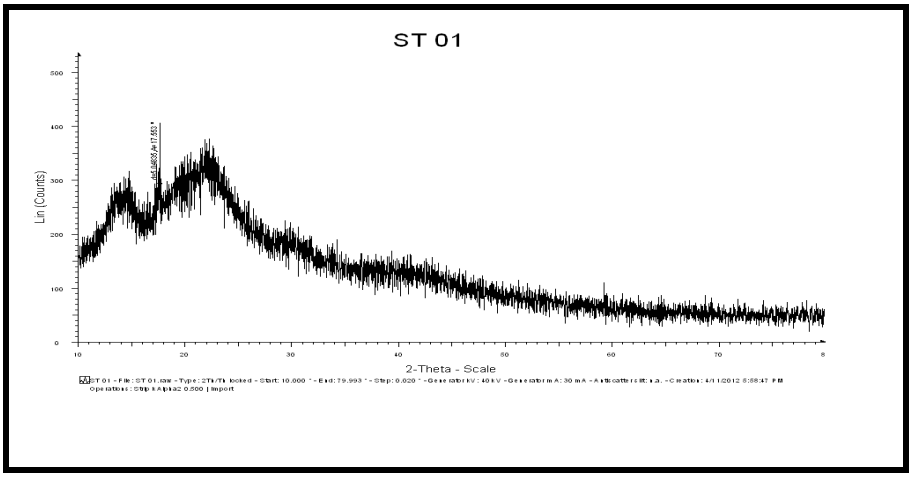


Fig 11: XRD spectra of Ezetimibe pure drug

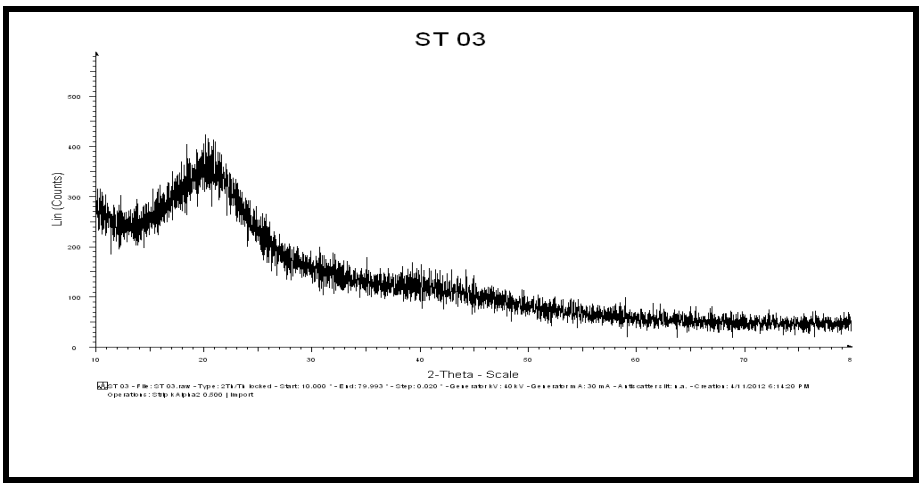


Fig 12: XRD spectra of Formulation F1

In-Vitro Dissolution Studies

In-vitro dissolution studies were carried out for all formulations F1 to F6 and compared with marketed formulation using type-II dissolution apparatus (Basket type) as per USP. The formulation F1 showed highest release rate among all the SEDDS formulations i.e. 93.11% as shown in **Fig. 13**. The results of this study are shown in **Table 12**.Thus, formulation F1 was taken as the optimized SEDDS formulation.

Comparison with marketed product

The prepared optimized batch F1 of SEDDS was compared with marketed product (Ezetimibe 10 mg USP) with respect to drug release [12]. The % drug dissolution data is shown in **Table 13**. This study revealed that solid self-emulsion powders dissolution study release a drug in medium faster when compared to marketed formulation. It was also found that total % drug release was much higher for the solid self-emulsion system than marketed formulation. The comparative data of dissolution profile of optimized batch (F1) with marketed product was shown in **Fig. 14**.

Table 12: Comparative drug release profile of formulations F1 to F6

Time (min)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	24.45±0.31	33.20±0.21	34.03±0.12	41.54±0.14	39.66±0.11	15.25±0.15
10	36.51±0.27	41.65±0.16	41.90±0.23	52.10±0.25	53.20±0.13	21.25±0.17
20	46.67±0.12	43.53±0.22	50.52±0.15	53.21±0.29	53.51±0.18	29.29±0.19
30	49.44±0.35	45.09±0.31	56.69±0.18	54.31±0.17	56.88±0.23	34.48±0.25
40	75.79±0.18	49.66±0.35	59.07±0.27	58.43±0.19	58.62±0.27	42.38±0.32
45	84.95±0.16	76.24±0.24	76.05±0.32	65.60±0.27	63.42±0.16	51.38±0.28
50	87.96±0.26	84.19±0.14	83.81±0.25	70.17±0.34	71.26±0.22	58.87±0.21
60	93.11±0.15	91.68±0.26	87.76±0.17	70.73±0.24	71.52±0.14	62.49±0.16

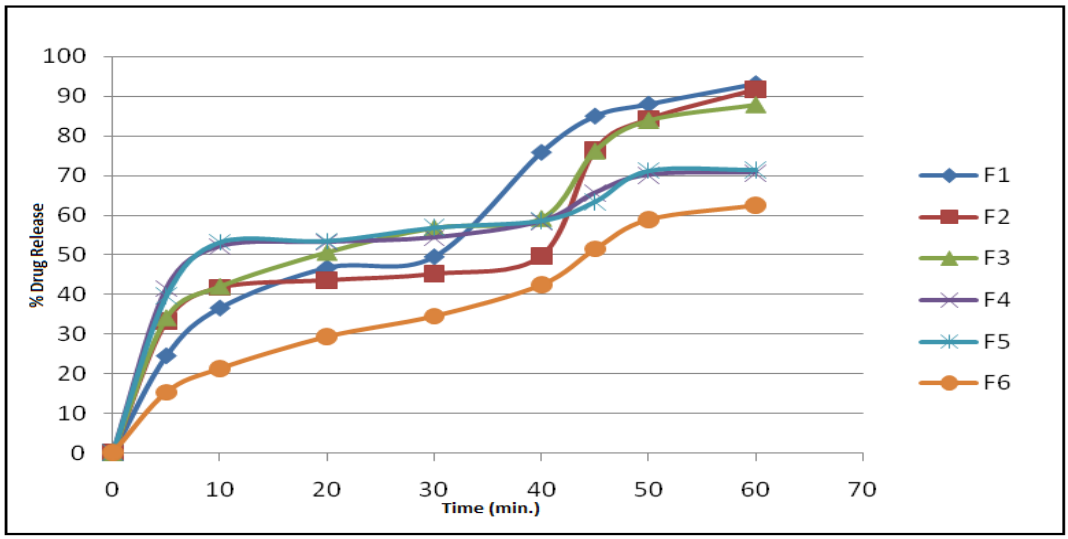


Fig 13: In vitro drug release profile of Ezetimibe formulations (F1 to F6)

Table 13: Comparative dissolution study of optimized formulation F1 with marketed product

Time (Mins)	% Drug release*	
	F1	Marketed product
0	0	0
5	24.458±0.24	10.372±0.52
10	36.519±0.32	17.385±0.37
20	46.676±0.65	24.381±0.45
30	49.444±0.38	30.489±0.61
40	75.796±0.86	38.389±0.87
45	84.957±0.91	44.513±1.21
50	87.963±1.05	51.526±0.95
60	93.114±0.78	60.528±0.83

**Values are mean ±SD; standard deviation (n=3)*

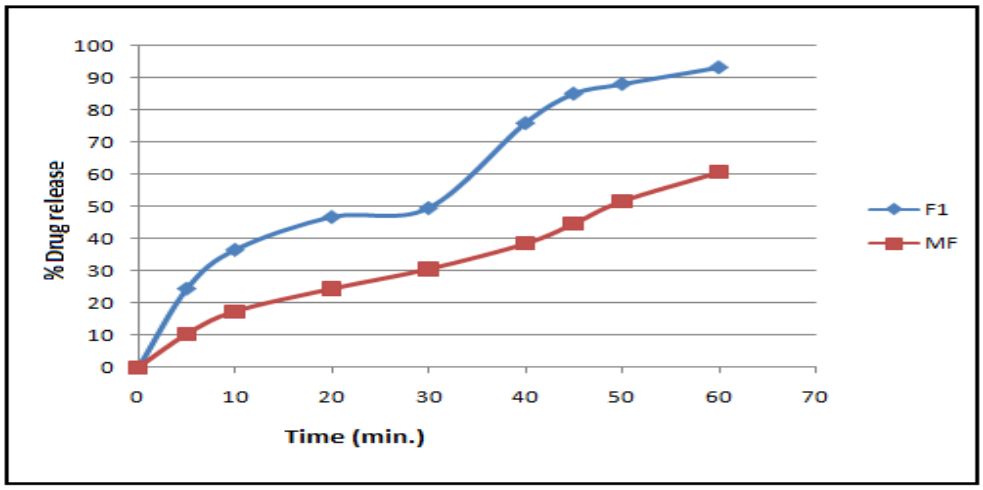


Fig 14: Dissolution profile of optimized batch (F1) with marketed product

CONCLUSION

In this study, the solid SEDDS containing a poorly water soluble drug ezetimibe was formulated for oral administration. Optimization studies were carried out using various components such as oil, surfactant and co-surfactant. These studies were further investigated by conducting solubility studies and constructing pseudo ternary phase diagram. The formulation F1 was found to be the optimized formulation on the basis of results of pseudo ternary phase diagram, *in vitro* drug release, zeta potential and other parameters. Solid SEDDS of ezetimibe were also prepared using Aerosil 200 by adsorption technique. These formulations showed good flow properties and drug content. From this study it was concluded that solid SEDDS of ezetimibe was efficiently formulated which enhances

solubility and dissolution rate so that it can be used as possible alternative to traditional oral formulation of ezetimibe.

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