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Formulation, Development & Characterization of Self Nanoemulsifying Drug Delivery for Fenofibrate

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Abstract The aim of the present investigation is to preparation, Development & Characterization of Self Nanoemulsifying Drug Delivery for Fenofibrate. Accurately weighed Fenofibrate was placed in a glass vial, and required quantity of oil, surfactant, and co-surfactant were added. The mixture was mixed by gentle stirring and vortex mixing at 40ºC on a magnetic stirrer at 200rpm, until Fenofibrate was dissolved. Capmul MCM was found satisfactory as oil, Cremophor RH 40 and Transcutol-P were found best as surfactant and cosurfactant on basis of solubility data. Selection of oil, surfactant and cosurfactant. The preliminary trials were carried out using different concentration of Capmul MCM oil, Cremophor RH 40 and Transcutol-P (3:1). On the basis of results of preliminary trials for selection of lipid vehicle, the concentration of Capmul MCM oil (X1) and Concentration of Cremophor RH 40: Transcutol-P (3:1) (X2) were taken as independent variables at three levels. In vitro drug release study was carried out for the formulations, Aliquots were collected periodically (10, 15, 20, 30, 45, 60 minutes) and replaced with fresh dissolution medium. Aliquots, after filtration through 0.45µ PVDF filter paper, were analyzed by HPLC at 248nm for Fenofibrate content. The study indicated that Cremophor RH 40 (HLB: 15) and Labrasol (HLB: 12) had very good ability to emulsify Capmul MCM oil followed by Tween 80 (HLB: 15), whereas, Cremophor EL (HLB: 13) and Labrafac PG (HLB: 1) appeared to be poor emulsifier for Capmul MCM oil. Fenofibrate and Excipients were mixed in 1:1 ratio. It was analysed at 40ºC/75% RH at Initial and 1 month by IR Spectroscopy. The 3^2 factorial design was employed using concentration of Capmul MCM oil and concentration of surfactant/Cosurfactant as independent variable X1 and X2 respectively. The Globule size (GS) (Y1), Polydispersity index (PDI) (Y2), Zeta potential (Y3), drug release at 15 minutes of Fenofibrate (Y4). SNEDDS is best suited for dosage for development of poorly soluble drugs. Fenofibrate are BCS class II drugs having low solubility and high permeability.

Keywords Formulation, Development, Characterization, Self Nanoemulsifying, Drug Delivery, Fenofibrate

Introduction

Increasing number of newly discovered chemical entities have poor aqueous solubility and hence it shows low absorption. Technology Catalysts International reported in 2002 that estimates up to 35-40% of all new chemical entities exhibited poor water solubility [1]. The properties of new drug substances shifted towards higher molecular mass and increasing lipophilicity of drug and decreasing the aqueous solubility. Fenofibrate, Atorvastatin & Pitavastatin are example of such a compound suffering from lower aqueous solubility and poor bioavailability [2, 3]. Various methods to enhance the solubility and dissolution of poorly water soluble drugs have been developed and described in literature, which were at start based on modifying their physico-chemical properties. Salt formation and reduction in particle size and became often taken methods in a quest for dissolution improvement, but both methods had limitations [4, 5]. As a result, altering drug solubility or dissolution through formulation approaches has become most popular. This encouraged the development of various alternative formulation strategies including use of lipid formulations. Strategies to enhance drug bioavailability may involve altering of various key factors that determine drug dissolution, as described by Noyes-Whitney equation [6].

For drug substances which have low aqueous solubility but sufficient lipophilic properties, it will be beneficial to dose them in a predissolved state, e.g. in a lipid formulation [7- 11], thereby reducing the energy associated with a solid-liquid phase transition and overcoming the slow dissolution process after oral intake. Lipid formulations are lipidsolution, emulsion, microemulsion, and SNEDDS [12-14].

The aim of present work was to prepare stable formulations of Fenofibrate which may improve dissolution profile of drugs and ultimatelyenhance the bioavailability as compared to conventional marketed formulation.

Materials and Methods

Estimation of Fenofibrate

UV spectroscopic method was used for determination of Fenofibrate as described.

Solubility Study

Screening of excipients was done by determining the equilibrium solubility of Fenofibrate in different oils, surfactants and co-surfactants as described.

Drug-Excipient Compatibility of SNEDDS Formulations

Drug-Excipient Compatibility of SNEDDS Formulations was studied as per method described in details.

Method of Preparation of SNEDDS

Accurately weighed Fenofibrate was placed in a glass vial, and required quantity of oil, surfactant, and co-surfactant were added. The mixture was mixed by gentle stirring and vortex mixing at 40ºC on a magnetic stirrer at 200rpm, until Fenofibrate was dissolved. The mixture was stored at room temperature in closed container until further use [15].

Method of Optimization of Preliminary Parameters

Selection of oil, surfactant and co surfactant

Capmul MCM was found satisfactory as oil, Cremophor RH 40 and Transcutol-P were found best as surfactant and cosurfactant on basis of solubility data. Selection of oil, surfactant and cosurfactant [16].

Ratio of Surfactant to Co surfactant

Selection of ratio of surfactant to cosurfactant is very important in formulation development of SNEDDS. Selection was based on the results of solubility data for Fenofibrate in surfactants/co-surfactants, emulsifying ability of surfactant/co-surfactant, predicting drug solubility factors such as solubility parameter (δ), Required HLB value, Molecular weight, required chemical type of emulsifiers, solubilization capacity and Pseudo ternary phase diagram. Ratio of Cremophor RH 40: Transcutol-P was selected as in details [17].

Optimization of formulation parameters of Fenofibrate SNEDDS

The preliminary trials were carried out using different concentration of Capmul MCM oil, Cremophor RH 40 and Transcutol-P (3:1). On the basis of results of preliminary trials for selection of lipid vehicle, the concentration of Capmul MCM oil (X1) and Concentration of Cremophor RH 40: Transcutol-P (3:1) (X2) were taken as independent variables at three levels. The Globule size (GS) (Y1), Polydispersity index (PDI)

(Y2), Zeta potential (Y3), drug release at 15 minutes of Fenofibrate (Y4) and drug release at 15 minutes of was considered to play significant role in the formulation performance of SNEDDS and all the five were taken as dependent parameters in present study [18].

Optimization of SNEDDS formulation using overlay plot by Design Expert software

The desirability function approach is a technique for the simultaneous determination of optimum settings of input variables that can determine optimum performance levels forone or more responses.

Measurement of evaluation parameters of Fenofibrate SNEDDS Formulations

(i) Measurement of Globule Size, Polydispersity Index (PDI) and Zeta Potential

Globule size, Polydispersity index (PDI) and zeta potential of SNEDDS were determinedusing Zetasizer Nano ZS (Malvern Instruments, UK), which follows principle of LASER light diffraction. SNEDDS was added (after suitable dilution) to the sample cell and put into the sample holder unit and the measurements were carried out with the help of software of same instrument.

(ii) In-Vitro Drug Release Study

In vitro drug release study was carried out for the formulations, Aliquots were collected periodically (10, 15, 20, 30, 45, 60 minutes) and replaced with fresh dissolution medium. Aliquots, after filtration through 0.45µ PVDF filter paper, were analyzed by HPLC at 248nm for Fenofibrate content [19].

Stability Study of Fenofibrate SNEDDS

Chemical and physical stability of Fenofibrate SNEDDS was assessed at 40 ± 2°C/75 ± 5% RH and 25 ± 3°C/60 ± 5% (room temperature) as per ICH guidelines [6, 7]. Stability study of SNEDDS formulation was carried out.

Comparison of in vitro drug release between Optimized SNEDDS formulation, pure drug powder and marketed product

In vitro drug release study was performed as method optimized SNEEDS formulations, marketed product and active drug substance to compare the in vitro drug release profile [20].

Dissolution Efficiency

The dissolution efficiency of the batches was calculated by the method mentioned by Khan. It is defined as the area under the dissolution curve up to a certain time, t, expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time.

Results and Discussion

Optimization of preliminary parameters

Screening of SNEDDS formulation involves formulation composition should be simple, safe, non-toxic and compatible. It should possess good solubility and large efficient self- nanoemulsification region which should be found in pseudo-ternary phase diagram, and have efficient droplet size after forming nanoemulsion [21]. Vehicles should have goodsolubilizing capacity of drug substance, which is essential for composing SNEDDS.

Capmul MCM oil (Glyceryl Caprylate/Caprate) was found satisfactory as oil. Fenofibrate had excellent solubility in Labrasol, Cremophor RH 40 (Polyoxyl 40 hydrogenated Castor oil) and Transcutol-P as compare to other surfactant and co- surfactant. Capmul MCM Oil (Glyceryl Caprylate/Caprate) as oil, Labrasol, Cremophor RH 40 (Polyoxyl 40 hydrogenated Castor oil) as surfactant and Transcutol-P as co- surfactant were selected for optimal SNEDDS formulation for improved drug loading capabilities.

Evaluation of surfactant and co-surfactant for its emulsifying ability

The study indicated that Cremophor RH 40 (HLB: 15) and Labrasol (HLB: 12) had very good ability to emulsify Capmul MCM oil followed by Tween 80 (HLB: 15), whereas, Cremophor EL (HLB: 13) and Labrafac

PG (HLB: 1) appeared to be poor emulsifier for Capmul MCM oil. This observation was in line with the investigation reported by Malcolmson and Warisnoicharoen who concluded that micro emulsification is also influenced by the structure and chain length of the surfactant.

They provides a flexible film around the droplet that can readily collapse and also provides a curvature at the interfacial region for the desired different types of nanoemulsion like o/w type, w/o type and/or bicontinuous type, depending upon the lipophilicity of the surfactant.

The turbidimetric method was used to judge emulsification efficacy of the co-surfactant to improve the nanoemulsification ability and also to select best co-surfactant. All the co-surfactants increased the spontaneity of the nanoemulsion formation as it leads to greater penetration of the surfactant monomers, thereby further decreasing the interfacial tension. Interestingly, PEG-400 and propylene glycol as cosurfactants appeared to be equivalent in improving nano emulsification ability of Cremophor RH 40 and Labrasol. In case of lipophilic co-surfactants such as Transcutol-P, good correlation was observed between the structure i.e. the chain length of co-surfactant and the transmittance values of resulting dispersions. This observation was also in line with investigation reported by Malcolmson and Warisnoicharoen.

Selection of variable was based on the results of solubility data for Fenofibrate in oils and surfactants/co-surfactants, emulsifying ability of surfactant/co- surfactant, predicting drug solubility factors such as solubility parameter (δ), Required HLB value, Molecular weight, required chemical type of emulsifiers, solubilization capacity, dielectric constant (ε), dipole moment (μ), excipient fatty acid chain length, surface tension, viscosity etc. Cremophor RH 40 and Transcutol-P were found best as surfactant and cosurfactant on basis of solubility data.

Drug-Excipient Compatibility of SNEDDS Formulations

Drug-Excipient compatibility study was done to check presence or absence of drug excipients interaction [64]. Fenofibrate and Excipients were mixed in 1:1 ratio. It was analysed at 40ºC/75% RH at Initial and 1 month by IR Spectroscopy.

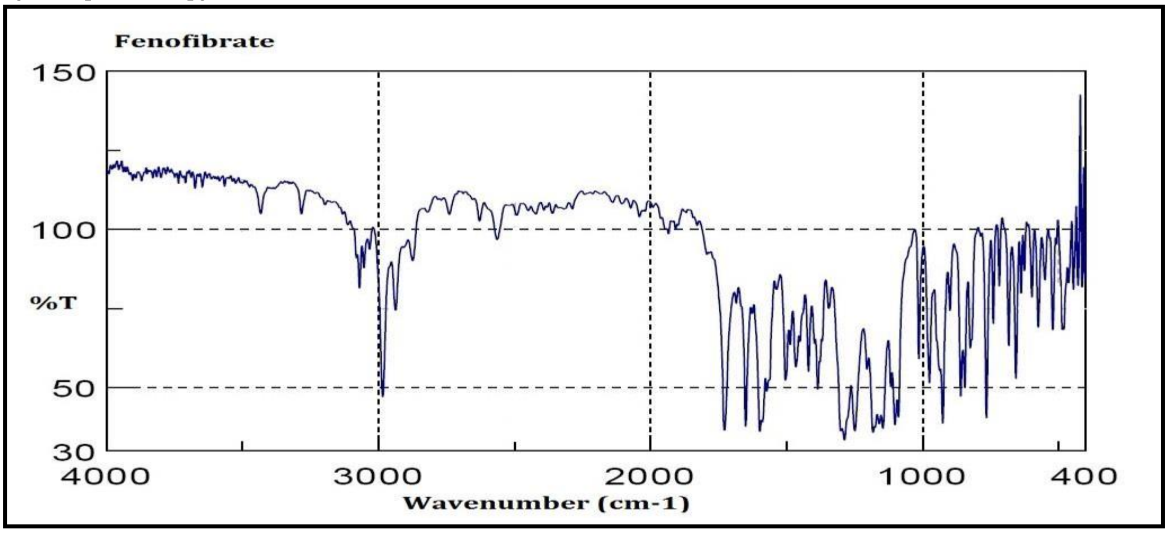

Figure 1: IR Spectrum of Fenofibrate

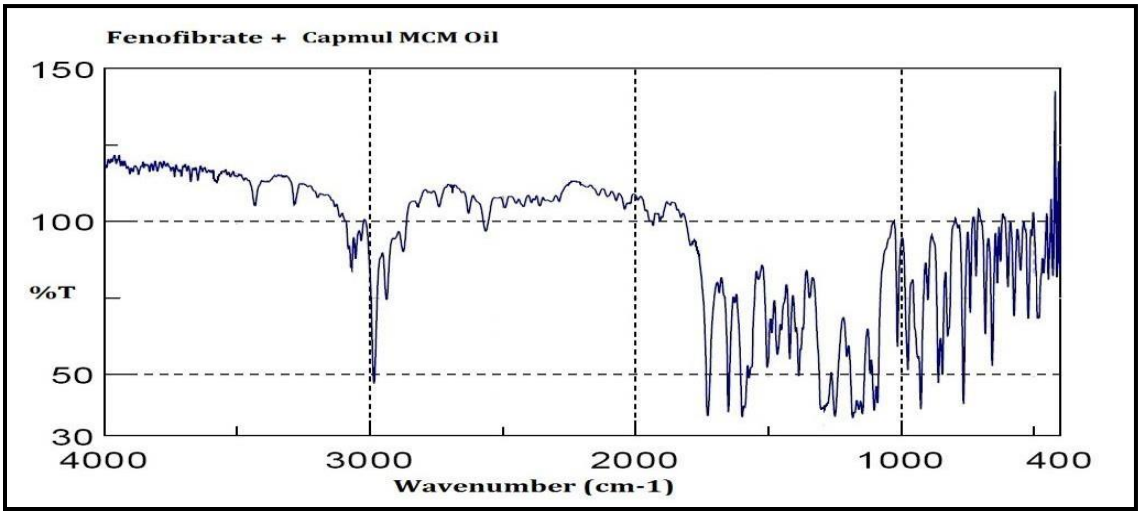

Figure 2: IR Spectrum of Fenofibrate + Capmul MCM oil

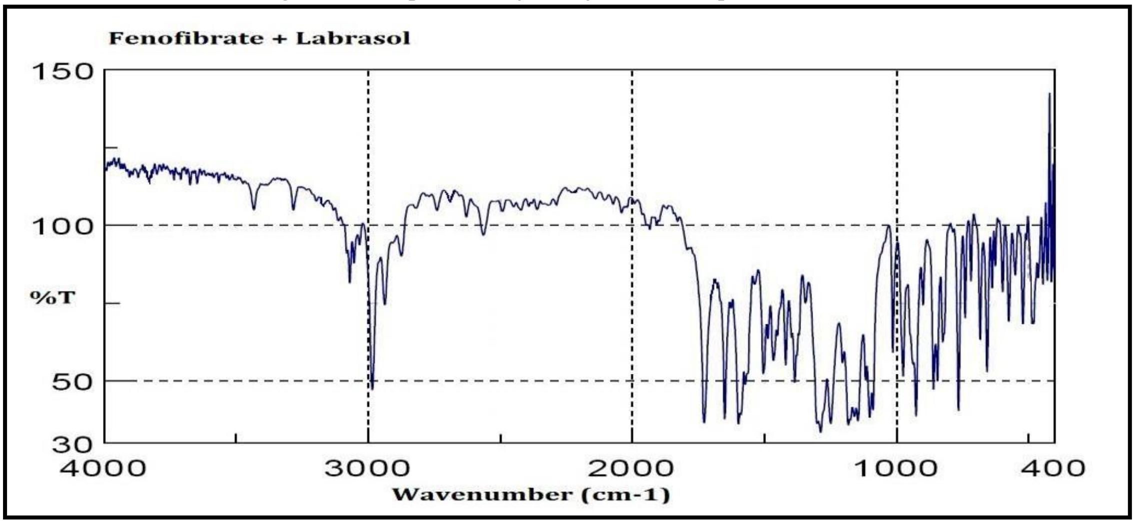

Figure 3: IR Spectrum of Fenofibrate + Labrasol

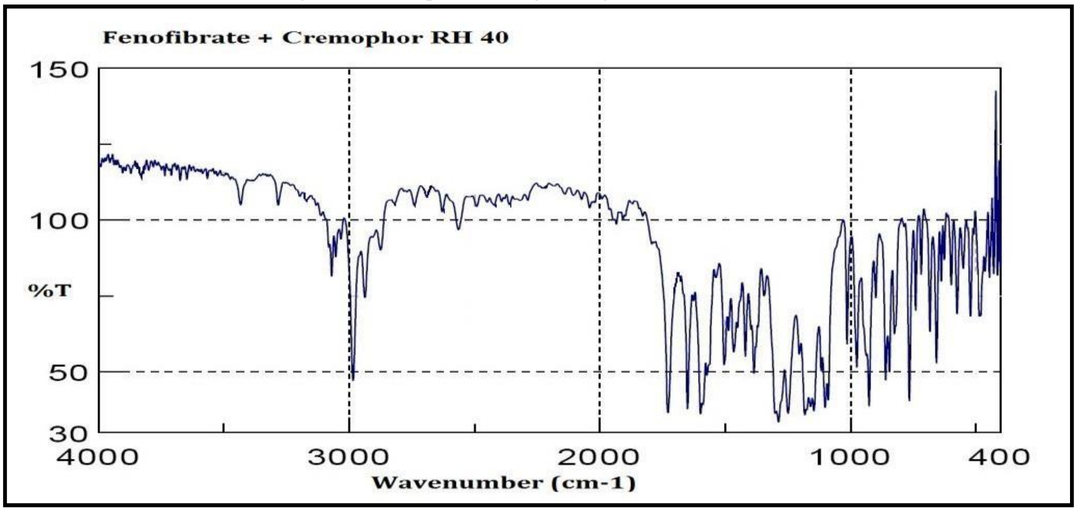

Figure 4: IR Spectrum of Fenofibrate + Cremophor RH 40

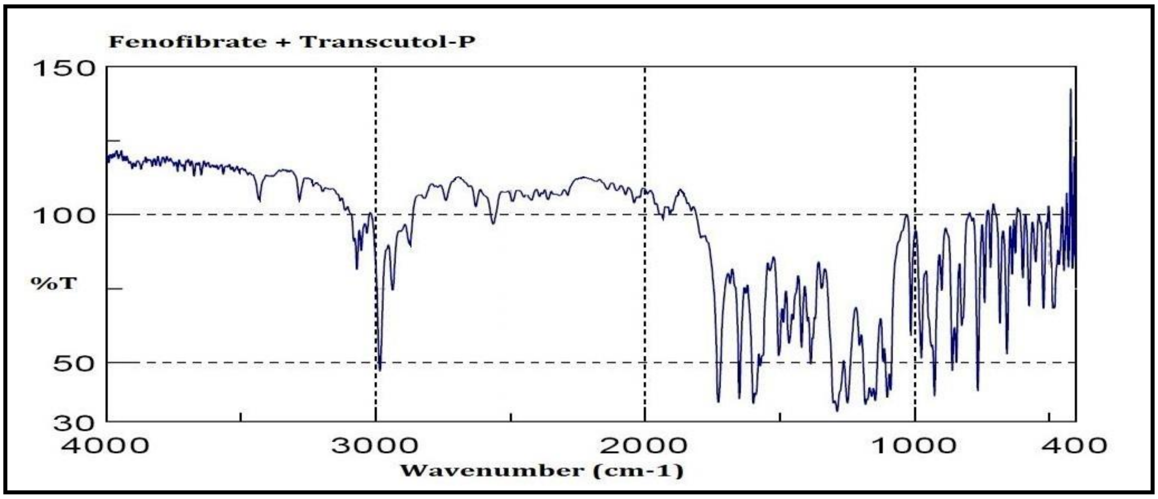

Figure 5: IR Spectrum of Fenofibrate + Transcutol-P

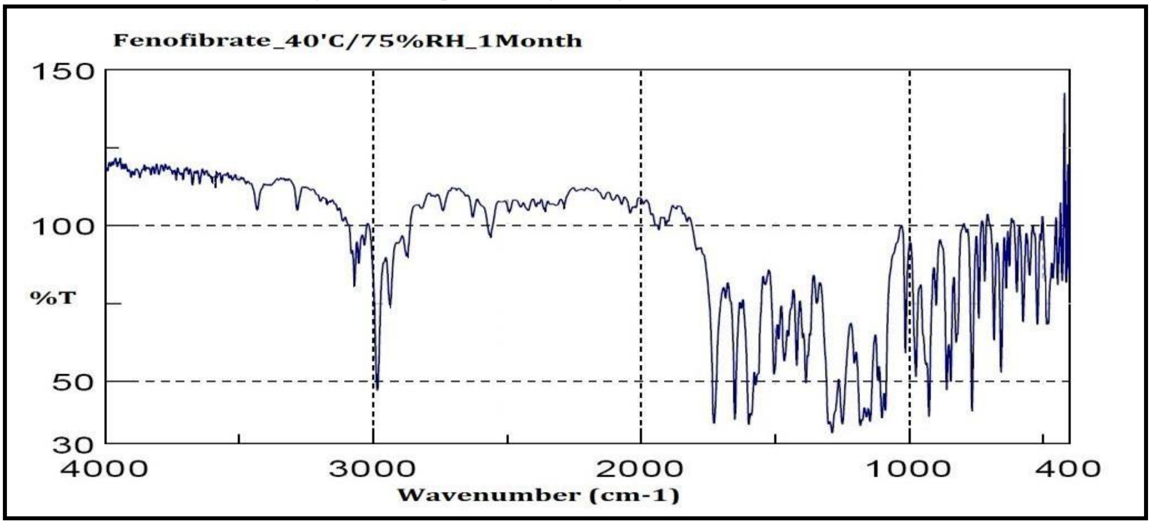

Figure 6: IR Spectrum of Fenofibrate (40°C/75%RH for 1 month)

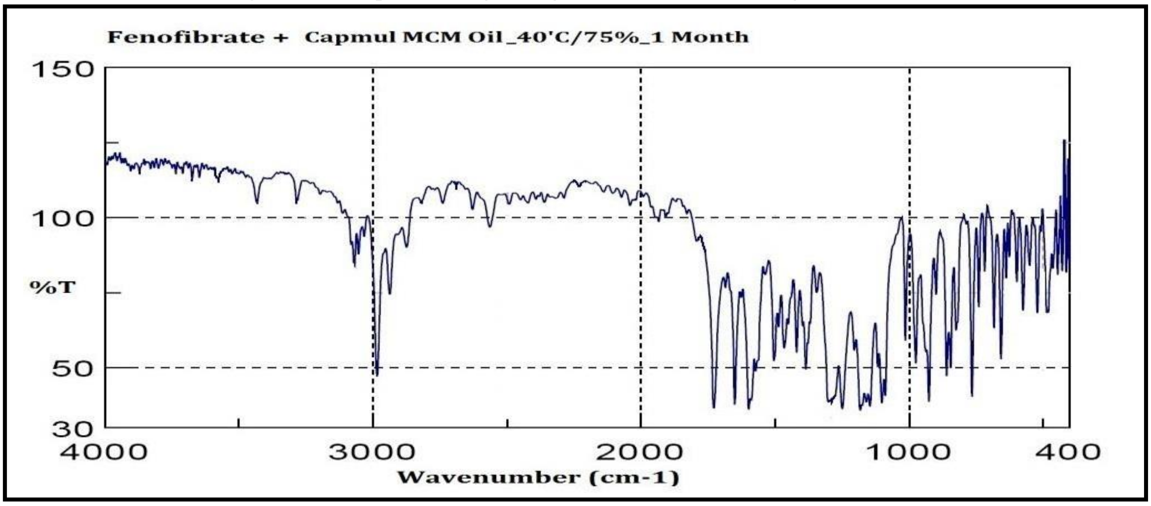

Figure 7: IR Spectrum of Fenofibrate + Capmul MCM oil (40°C/75%RH for 1 month)

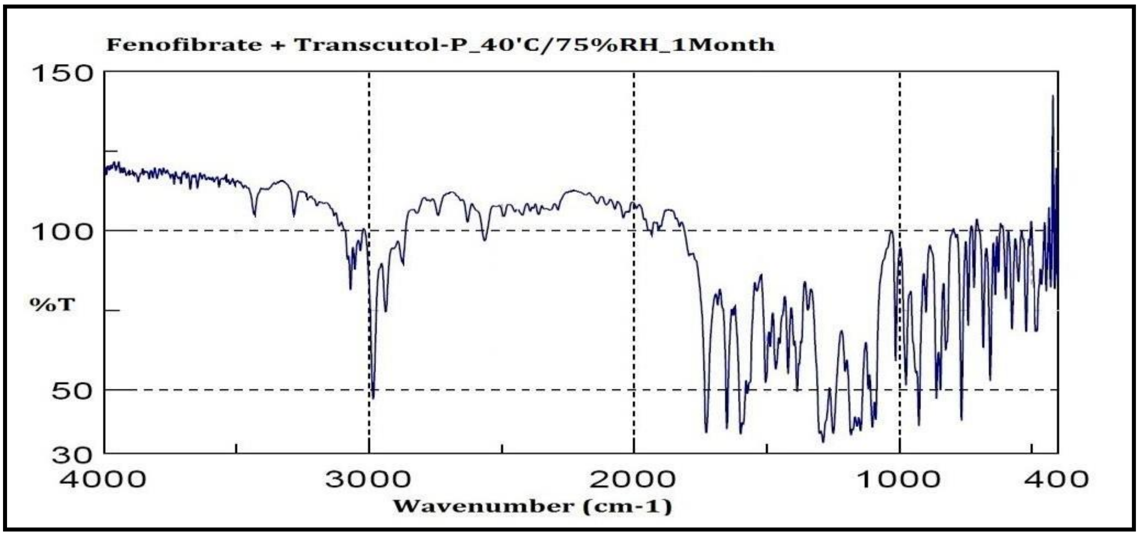

Figure 8: IR Spectrum of Fenofibrate + Transcutol-P (40°C/75%RH for 1 month)

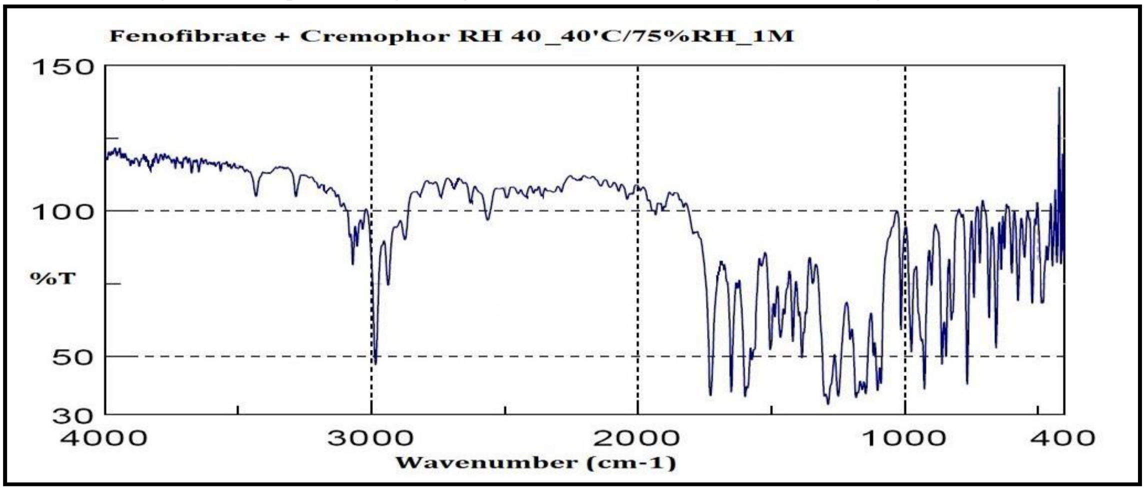

Figure 9: IR Spectrum of Fenofibrate + Cremophor RH 40 (40°C/75%RH for 1 month)

Optimization of SNEDDS of Fenofibrate using factorial design

The concentration of Capmul MCM oil and concentration of surfactant/Cosurfactant play important role in stable formulation of Self Nanoemulsifying drug delivery system (SNEDDS); hence concentration of Capmul MCM oil (0.5mL) and concentration of Cremophor RH 40: Transcutol-P (3:1) (1.5mL) were selected as independent variables in factorial design on the basis of the results of preliminary trials. The 3^2 factorial design was employed using concentration of Capmul MCM oil and concentration of surfactant/Cosurfactant as independent variable X1 and X2 respectively. The Globule size (GS) (Y1), Polydispersity index (PDI) (Y2), Zeta potential (Y3), drug release at 15 minutes of Fenofibrate (Y4).

Table 1: Factors and levels of independent variables in 3^2 factorial design for formulation of Fenofibrate SNEDDS

Independent variables	Level		
	Low (-1)	**Medium (0)**	**High (+1)**
Capmul MCM oil concentration (X1), (mL)	0.4	0.5	0.6
Cremophor RH 40: Transcutol-P (3:1) concentration (X2), (mL)	1.2	1.5	1.8

Batch	X_1	X_2	Globule size (nm) (Y_1)	PDI(Y_2)	Zeta potential (mV) (Y_3)	Drug release at 15 min for Fenofibrate (Y_4)
T1	-1	-1	357.3	0.42	-15.14	91.4
T2	0	-1	64.5	0.28	-16.46	93.5
T3	1	-1	55.7	0.22	-17.15	93.3
T4	-1	0	332.3	0.42	-15.62	93.6
T5	0	0	20.5	0.18	-27.94	96.8
T6	1	0	44.7	0.23	-17.67	94.9
T7	-1	1	307.9	0.46	-15.99	93.3
T8	0	1	26.3	0.15	-24.21	94.7
T9	1	1	29.7	0.19	-21.14	95.7

(a) Polydispersity index (PDI) (Y_2)

A full model equation of polydispersity index (YPDI) was written as Equation.

The results of coefficients estimated by multiple regression for polydispersity index (PDI) was presented in Table

Table 2: Coefficients estimated by multiple linear regression for polydispersity index (PDI) (Y_2)

Factors	Coefficients	Calculated t values	p-values
Intercept	0.217	8.228	0.0375**
X1	-0.106	-7.331	0.0524**
X2	-0.020	-1.383	0.2656
$X1^2$	0.098	3.939	0.0914*
$X2^2$	0.007	0.306	0.7951
X1X2	-0.007	-0.395	0.7905

**very significant ($p<0.01$), *significant ($p<0.05$)

The polydispersity index for batch T1 to T9 ranges from 0.189 to 0.428. The coefficient of X1 was -0.1060 and X2 was -0.0200, which indicated that large negative value of X1 was predominantly reducing the polydispersity index of SNEDDS. The regression coefficient of $X1^2$ was 0.0987 and $X2^2$ was 0.0077, which indicated their positive influence on polydispersity index. When the coefficients of the two independent variables were compared, the value for the variable X1(b1= -0.1060) was found to be maximum and hence the variable X1 was considered to be a major contributing variable for PDI.

(b) Zeta potential (ZP) (Y_3)

A full model equation of zeta potential (YFZP) was written as Equation. The zeta potential for batch T1 to T9 ranges from -27.96 to -15.12. The coefficient of X1 was -1.5133 and X2 was -2.1200, which indicated that large negative value of X2 was predominantly reducing the zeta potential of SNEDDS. The regression coefficient of $X1^2$ was 5.7800 and $X2^2$ was 2.0800, which indicated their positive influence on zeta potential. When the coefficients of the two independent variables in Equation 6.9 were compared, the value for the variable X2(b2= -2.1200) was found to be maximum and hence the variable X2 was considered to be a major contributing variable for zeta potential.

(c) Drug release at 15 minutes for Fenofibrate (DRF) (Y_4)

A full model equation of drug release at 15 minutes for Fenofibrate (YFDRF) was written.

The results of coefficients estimated by multiple regression for drug release at 15 minutes for Fenofibrate (DRF) was present in Table.

Table 3: Coefficients estimated by multiple linear regression for drug release at 15 minutes for Fenofibrate (DRF) (Y_4)

Factors	Coefficients	Calculated t values	p-values
Intercept	95.855	141.224	0.00000**
X1	0.516	1.389	0.2587
X2	0.700	1.882	0.1562
$X1^2$	-1.483	-2.303	0.1046
$X2^2$	-1.233	-1.915	0.1513
X1X2	0.050	0.109	0.9194

**very significant ($p<0.01$), *significant ($p<0.05$)

The drug release at 15 minutes for Fenofibrate (DRF) for batch T1 to T9 ranges from 91.8 to 96.7. The coefficient of X1 was 0.5167 and X2 was 0.7000, which indicated that large positive value of X2 was predominantly increasing the drug release at 15 minutes for Fenofibrate (DRF) of SNEDDS. The regression coefficient of $X1^2$ was -1.4833 and $X2^2$ was -1.2333, which indicated their positive influence on drug release at 15 minutes for Fenofibrate (DRF). When the coefficients of the two independent variables were compared, the value for the variable X2 (b2= 0.7000) was found to be maximum and hence the variable X2 was considered to be a major contributing variable for drug release at 15 minutes for Fenofibrate (DRF).

Drug release at 15 minutes for Fenofibrate (DRF)

Contour plot for drug release at 15 minutes for Fenofibrate (DRF) at prefixed values of 92.55, 93.55, 94.55, and 95.55. The contour plot was found to be non- linear. Hence, the relationship between independent variables for drug release at 15 minutes for Fenofibrate (DRF) could be non-linear because drug release at 15 minutes for Fenofibrate (DRF) may not be directly proportional to variable X1 & X2.

Response surface plot obtained as a function of concentration of Capmul MCM oil and concentration of Cremophor RH 40: Transcutol-P (3:1) for drug release at 15 minutes for Fenofibrate (DRF). An increase in drug release with increase in the concentration of Capmul MCM oil and concentration of Cremophor RH 40: Transcutol-P (3:1) was observed.

Optimization of SNEDDS Formulation

Optimized formulation was selected by arbitrarily fixing the criteria of 20.7 – 357nm of the Globule size (GS), 0.189 – 0.428 Polydispersity index (PDI), -30mV to -21mV Zeta potential (ZP), more than 95% drug released at 15 minutes for Fenofibrate. These constrains were shown in Table for the SNEDDS formulation. The recommended concentrations of the independent variables were calculated by the Design Expert software using overlay plot with desirability approach. The results gave one optimized solution with theoretical target profile characteristics which were shown in Table.

Table 4: Constrains for SNEDDS Formulation

Name	Goal	Lower limit	Upper limit	Importance
Conc. of Capmul MCM oil	is in range	-1	1	+++
Conc. of Cremophor RH 40:Transcutol-P (3:1)	is in range	-1	1	+++
Globule Size (nm)	minimize	20.7	357	+++
Polydispersity index	maximize	0.189	0.428	+++
Zeta potential (mV)	is target = -27	-30	-21	+++
Drug Release at 15 minutes for Fenofibrate	is in range	95	96.7	+++
Drug Release at 15 minutes for Atorvastatin calcium	is in range	95	97.4	+++

Evaluation parameters of Fenofibrate SNEDDS of factorial design batches

(a) Refractive Index and Turbidimetric Evaluation

The results of refractive index and % transmittance of batches T1 to T9 were shown in Table. The refractive index and percent transmittance data proved that transparencyof system.

Table 5: Refractive Index and %Transmittance of various SNEDDS formulations

Batches	Refractive Index Water (250 ml)	% Transmittance Water (250 ml)
T1	1.37	91.32
T2	1.35	97.45
T3	1.35	97.88
T4	1.36	92.72
T5	1.33	100.11
T6	1.34	98.15
T7	1.36	93.58
T8	1.33	99.39
T9	1.34	98.93

(b) Measurement of Globule Size, Polydispersity Index, and Zeta Potential

Globule size distribution following self nanoemulsification is a critical factor to evaluate self-nanoemulsion system. The smaller droplets have larger interfacial surface area will be provided for drug. Globule size analysis, Polydispersity Index and Zeta Potential data were shown in Table.

Table 6: Droplet size analysis, Polydispersity Index, and Zeta Potential data of SNEDDS formulation

Batches	Globule Size (nm)	Polydispersity Index	Zeta Potential (mV)
T1	357.0	0.428	-15.14
T2	64.1	0.283	-16.46
T3	55.8	0.221	-17.18
T4	332.0	0.427	-15.65
T5	20.7	0.189	-27.94
T6	44.0	0.233	-17.68
T7	307.0	0.426	-15.97
T8	26.6	0.195	-24.29
T9	29.2	0.191	-21.14

(c) Drug Content

Drug content of SNEDDS formulation can be found by methanolic extract of SNEDDS was analyzed by HPLC at 248nm for Fenofibrate respectively. Drug content of various formulation shown in Table.

Table 7: Drug content in various SNEDDS formulations (Fenofibrate)

Batches	% Drug Content			Average	Standard Deviation
	I	II	III		
T1	99.1	98.3	99.3	98.9	0.53
T2	98.3	98.6	98.9	98.6	0.30
T3	99.4	100.2	99.1	99.6	0.57
T4	99.8	99.1	100.4	99.8	0.65
T5	100.2	101.1	100.5	100.6	0.46
T6	99.2	100.4	99.5	99.7	0.62
T7	101.4	99.8	100.6	100.6	0.80
T8	99.6	100.7	99.9	100.1	0.57
T9	100.3	99.1	100.9	100.1	0.92

(d) Effect of Dilution and Aqueous Phase Composition on SNEDDS

Data was shown for various SNEDDS formulation at 25 ± 2°C for 24 hour.

(e) Measurement of Viscosity and pH of SNEDDS

Viscosity of SNEDDS was measured by using Brookfield viscometer at 25°C temperature. Spindle S-61 was selected for measurement of viscosity of various SNEDDS formulations. Viscosity measurement was done at 30 rpm before and after dilution with water. pH of SNEDDS formulations were measured by using pH meter at room temperature. pH of SNEDDS formulations were also measured before and after dilution with distil water.

Table 8: Viscosity and pH of various SNEDDS formulations

Batches	Viscosity (CP)		pH	
	Dilution		Dilution	
	Before	After	Before	After
T1	97.8	1.04	7.73	6.42
T2	114.9	1.01	7.68	6.46
T3	105.6	1.08	7.65	6.53
T4	106.0	1.04	7.18	6.50
T5	109.4	1.02	7.71	6.49
T6	107.3	1.03	7.52	6.48
T7	104.5	1.05	7.53	6.49
T8	117.0	1.02	7.48	6.51
T9	115.0	1.05	7.56	6.50

(f) In Vitro drug release Study

It could be suggested that the SNEDDS formulation resulted in spontaneous formation of a nanoemulsion with a small droplet size, which permitted a faster rate of drug release into the aqueous phase, much faster than that of plain fenofibrate drug powder and marketed drug formulation.

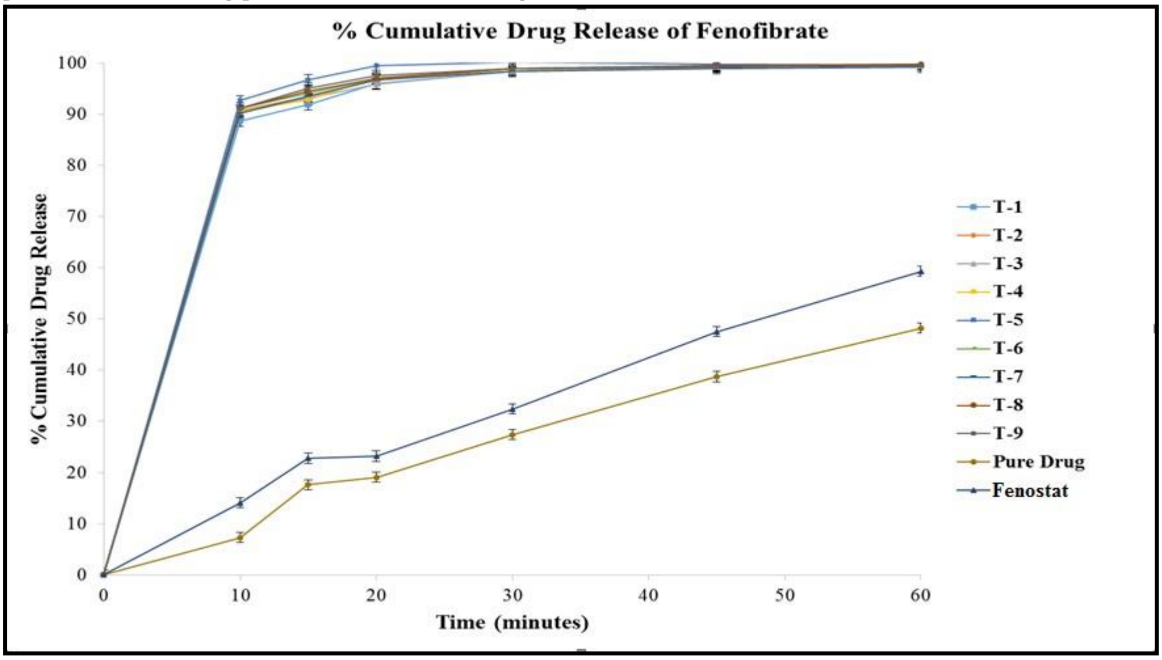

Figure 10: Comparison of drug release profile of various SNEDDS formulation with pure drug and marketed formulation (Fenofibrate)

(g) In Vitro Diffusion Study

To understand characteristics of drug release from SNEDDS, an in vitro release study was carried out. When SNEDDS encountered aqueous media, drug existed in system in different forms including a free molecular form, or mixed in micelles or in nanoemulsion droplets.

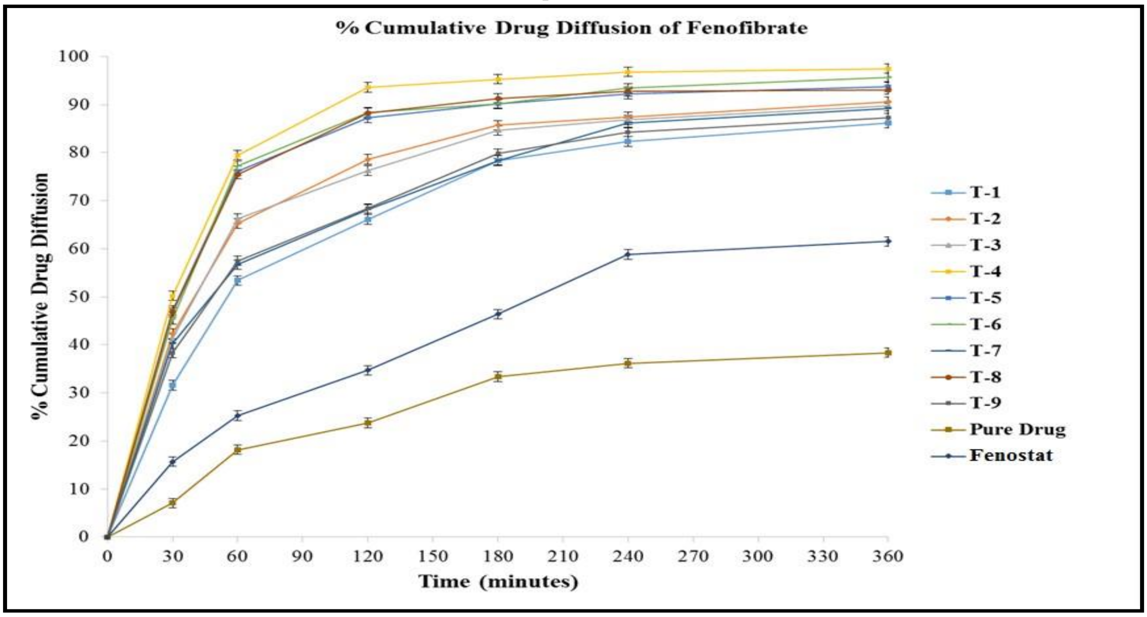

Figure 11: Comparison of diffusion profile of various SNEDDS formulation with pure drug and marketed formulation (Fenofibrate)

Stability study of Fenofibrate SNEDDS optimized batch (OP1)

Stability chamber was used for accelerated condition. The change in globule size, zeta potential, drug content and drug release at 15 minutes for Fenofibrate were carried out periodically to determine the stability of drug in the formulation at various storage conditions.

Results of Globule size and Zeta potential at storage conditions

Globule size and Zeta potential of optimized batch (OP1) were measured by Zetasizer atperiodic intervals. Globule size and Zeta potential were measured after 1, 3 and 6 months. The results wererecorded in Table.

Table 9: Globule size of optimized batch at storage conditions

Storage Conditions	Average of Globule Size (nm)			
	Initial	**1 Month**	**3 Month**	**6 Month**
Room Temperature	78.3	79.2	82.1	82.5
Accelerated Conditions	78.3	79.8	83.3	83.9

Table 10: Zeta Potential of optimized batch at storage conditions

Storage Conditions	Zeta Potential (mV)			
	Initial	**1 Month**	**3 Month**	**6 Month**
Room Temperature	-23.13	-22.38	-22.24	-21.79
Accelerated Conditions	-23.13	-22.45	-22.92	-21.47

Conclusion

SNEDDS is best suited for dosage for development of poorly soluble drugs. Fenofibrate are BCS class II drugs having low solubility and high permeability. The present study was aimed to explore stable SNEDDS formulation development using 3^2 factorial design for dissolution improvement compared to marketed formulation of Fenofibrate.

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