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MICROWAVE INDUCED SOLUBILITY ENHANCEMENT OF POORLY WATER SOLUBLE DRUG SIMVASTATIN USING POLOXAMER 188 BY MICROWAVE IRRADIATION METHOD

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Keywords:

Solid dispersion, Microwave method, Simvastatin, Poloxamer 188, Poorly water-soluble drug

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ABSTRACT: To increase the solubility of poorly water-soluble drug simvastatin using hydrophilic carrier poloxamer 188 using solid dispersion techniques by microwave irradiation method. The microwave irradiation technique was used to prepare solid dispersions in minimum time interval in different drug carrier ratios, *i.e.* 1:2, 1:5, 1:8 and was subjected to microwave for different times, *i.e.* 3 min, 5 min, and 7 min. Solid dispersions were characterized for drug content, percentage yield, saturation solubility studies, and *in-vitro* dissolution studies. A 3^2 full factorial design was selected to study the influence of the individual and combined effect of independent variables drug carrier ratio (X_1) and microwave time (X_2) on the dependent variables percent dissolution efficiency (% DE) at 60 min and percent yield. In this design, two factors were evaluated, each at three levels, and experimental trials is performed at all nine possible combinations. The optimized batch obtained using design expert was having drug carrier ratio of 1:5.75 and microwave time of 5.68 min.

INTRODUCTION: Solid dispersion is one of the most successful strategies to improve the drug release of poorly soluble drugs. Solid dispersions can be defined as "molecular mixtures of poorly water-soluble drugs in hydrophilic carriers which present a drug release profile that is driven by the polymer properties". The application of solid dispersion as a method for bioavailability enhancement of poorly soluble drugs was laid by Sekiguchi and Obi in 1961. They noted that the formulation of eutectic mixtures improves the rate of drug release and consequently the bioavailability of poorly water-soluble drugs [1, 2, 3].

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The term solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. The matrix can be either crystalline or amorphous. The drug can be dispersed molecularly, in amorphous particles or in crystalline particles [4]. It involves dispersion of one or more active ingredients in an inert carrier or matrix at solid state.

Melting (fusion) method, solvent evaporation method, or melting evaporation methods can be employed for the preparation of the solid dispersions. In the microwave method, ability of the materials to absorb microwave energy and convert it into heat is known as microwave heating. Microwave heating of materials mainly occurs due to dipolar and ionic mechanisms. Different from the conventional heating method, the microwave technique provides fast and uniform heating of a

material [5]. This technology is generally applicable to syntheses in medicinal and combinatorial chemistry, and compared to conventional methods offers enhanced speed, reproducibility and scalability [6].

Simvastatin is a very useful potent drug used to treat hyperlipidemia. It reduces LDL-cholesterol as well as plasma triglycerides and apolypoprotein B. Simvastatin belongs to BCS class II drug and so it faces problems of low solubility (30µg/ml) in water and low bioavailability (5%) due to first-pass effect. As a result it becomes mandatory to formulate it in such a fashion to improve the release rate of drugs, to improve the oral bioavailability of drug, and to achieve good patient compliance [7, 8]. The aim is to increase the solubility of poorly water-soluble drugs, simvastatin using hydrophilic carrier, poloxamer 188 by formulating solid dispersion using microwave method [9]. Poloxamer 188 is selected as carrier because of its low melting point (57-58 °C) and oral safety.

MATERIALS AND METHODS:

Material: Simvastatin was used as a model drug and it was gifted by Ranbaxy Pvt. Ltd, Gurgaon, India, Poloxamer 188 (Balaji Pharmaceuticals, Pvt. Ltd., Gujarat, India) was selected as a dispersion base. All other chemicals used were of analytical grade. Other chemicals used were of analytical grade and supplied by the pharmacy department, ASBASJSM College of Pharmacy, Bela

Preparation of Solid Dispersion of Simvastatin by Microwave Irradiation Method: [10] Solid dispersions using Simvastatin (SIM) with Poloxamer188 (PXM) were prepared using the microwave-induced fusion method in different drug carrier ratios 1:2, 1:5 and 1:8 followed by gentle mixing using glass mortar and pestle. A fixed amount of this mixture (2 g) was subjected to microwave for different times 3 min, 5 min and 7 min on a microwave instrument (Godrej GMG-22B). Only one beaker at a time was placed inside the microwave. The samples were exposed in the microwave for a predetermined time interval. The beaker was then placed at room temperature for solidification. Solid dispersions were collected and stored in the desiccator for 24 h, and then the product was pulverized, and powders were then passed through an 80 # sieve.

Preparation of Solid Dispersion by Conventional Fusion Method: In this, the solid dispersion was prepared by conventional heating method. The poloxamer 188 was heated to a molten mass at 55°C - 60°C in a china dish over the water bath, and to this a weighed amount of simvastatin (10 mg) was added with continuous stirring until dissolved. The china dish was then placed at room temperature for solidification. The solidified mass was then collected and stored in a desiccator for 24 h and then pulverized using a porcelain mortar and pestle. The pulverized powders were passed through an 80# sieve.

TABLE 1: RATIO AND MICROWAVE TIME FOR SOLID DISPERSIONS

Formulation code	Drug: carrier ratio	Microwave time (min)
SIM 1	1.2	3
SIM 2	1.2	5
SIM 3	1.2	7
SIM 4	1.5	3
SIM 5	1.5	5
SIM 6	1.5	7
SIM 7	1.8	3
SIM 8	1.8	5
SIM 9	1.8	7

Characterization of Solid Dispersions:

Drug Content: Drug content of the simvastatin 10 mg and solid dispersions equivalent to 10 mg of simvastatin were dissolved in a suitable quantity of methanol, filtered, suitably diluted, and drug content was determined at 238 nm by UV spectrophotometer against methanol as blank. Each sample was analyzed in triplicate.

Percentage Yield: Percentage yield was determined by the following formula according to the recoverable final weight of solid dispersions and the total weight of drug and carrier used.

$$\% \text{ Yield} = [a / (b + c)] \times 100 \quad \ldots..(1)$$

Where a = weight of the solid dispersion sifted through sieve no 80, b = weight of drug taken for solid dispersion preparation, c = weight of polymer taken for solid dispersion preparation.

Determination of Solubility: The solubility studies of solid dispersions were carried out in phosphate buffer pH 6.8. The solid dispersions equivalent to 10 mg of the drug were added in 10 ml phosphate buffer pH 6.8 of each screw-capped

vials and the vials were placed in a water bath shaker at 28 ºC room temperature for 24 h until the equilibrium was attained. The saturated solution then filtered through Whatman filter paper, suitably diluted, and was analyzed by UV spectrophotometer at 238.5 nm.

Experimental Design Selection: A 3^2 full factorial design was selected to study the influence of the individual and combined effect of independent variables drug carrier ratio (X_1) and microwave time (X_2) on the dependent variables percent dissolution efficiency at 60 min (% DE60) and percent yield. In this design, two factors were evaluated, each at three levels, and experimental trials is performed at all nine possible combinations.

The statistical model using interactive and polynomial terms is used to calculate the response.

$$Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}(X_1)^2 + b_{22}(X_2)^2 \quad .....(2)$$

Where, Y is the dependent variable, b_0 is the arithmetic mean response of the nine runs, and bi is the estimated coefficient for the factor X_1 The main effects (X_1 and X_2) represent the average result of changing one factor at a time from its low to high value[11]. The interaction terms (X_1X_2) show how the response changes when two factors are simultaneously changed. The polynomial terms [$(X_1)^2$ and $(X_2)^2$] are included to investigate nonlinearity. The composition of the factorial design batches SIM 1 - SIM 9 is represented in **Table 2**.

TABLE 2: COMPOSITION OF FACTORIAL DESIGN BATCHES

Batch code	Variables levels in coded		% DE_{60} ± SD	% Yield ± SD
	X_1	X_2		
SIM 1	-1	-1	33.85 ± 0.24	71.3 ± 0.35
SIM 2	-1	0	35.98 ± 0.19	77.86 ± 0.80
SIM 3	-1	+1	43.22 ± 0.39	82.1 ± 1.15
SIM 4	0	-1	53.80 ± 0.43	88.11± 0.11
SIM 5	0	0	69.11 ± 0.32	91.44 ± 0.50
SIM 6	0	+1	70.91 ± 0.58	90.5 ± 0.50
SIM 7	+1	-1	50.1 ± 1.45	79.09 ± 0.01
SIM 8	+1	0	60.97 ± 1.16	82.03 ± 0.94
SIM 9	+1	+1	66.34 ± 0.32	80.33 ± 0.57
	Actual Values			
Coded terms	X_1	X_2		
-1	1:2	3		
0	1:5	5		
+1	1:8	7		

X_1 = drug to polymer ratio; X_2 = microwave time; % DE_{60} = dissolution efficiency at 60 min
Data are expressed as mean ± S.D. (n=3)

***In-vitro* Dissolution Studies:** *In-vitro* dissolution of simvastatin was carried in USP apparatus II (paddle type). Solid dispersions equivalent to 10 mg of simvastatin was spread over the surface of the dissolution medium (900 ml of phosphate buffer at pH 6.8) maintained at a temperature of 37 ± 0.5 ºC stirring at 100 rpm. The samples (5ml) were withdrawn at predetermined time intervals 5, 10, 15, 20, 30, 45 and 60 min filtered and analyzed using a UV-spectrophotometer at 238.5 nm. Each test was performed in triplicate [12].

Percent dissolution efficiency (% DE) was also computed to compare the relative performance of various carriers in solid dispersion formulations. The magnitude of % DE at 60 min (% DE 60 min) for each formulation was computed as the percent ratio of area under the dissolution curve up to the time, t, to that of the area of the rectangle described by 100% dissolution at the same time:

Percent Dissolution efficiency (% DE) = $((\int_0^t y \times dt) / (y100 \times t) \times 100$ .....(3)

Angle of Repose: To get an idea about flowability properties of the solid dispersions, the angle of repose for optimized formula of experimental design was determined. If the angle exceeds 50°, the material will not flow satisfactorily, whereas materials having values near the minimum flow easily and well. The rougher and more irregular the surface of the particles, the higher is the angle of repose. The angle of repose was measured by

passing solid dispersions through a sintered glass funnel of internal diameter 27 mm on the horizontal surface. The height (h) of the heap formed was measured with a cathetometer, and the radius (r) of the cone base was also determined. The angle of repose was calculated from:

$$\Theta = \tan^{-1} (h / r)$$

Differential Scanning Calorimetry (DSC): Thermal analyses were performed using differential scanning calorimeter (DSC-6-Perkin-Elmer). In this about 2 mg of simvastatin, poloxamer 188 or physical mixture were placed in a sealed aluminum pan and heated at a scanning rate of 10°C/min from 30 °C to 300 °C under a nitrogen flow of 20ml/min. An empty aluminum pan was used as reference.

Fourier Transform Infrared Spectroscopy (FT-IR): The Fourier Transform Infra-Red (FT- IR) analysis of the drug and polymer were carried out for qualitative compound identification using Perkin Elmer 1600. The pellets were prepared on KBr – press. The spectra were scanned over wavenumber range of 4000 cm^{-1} – 400 cm^{-1}. Since FT-IR is related to covalent bonds, the spectra can provide detailed information about the structure of molecular compounds. FT-IR is helpful to confirm the identity of the drug and to detect the interaction of the drug with excipients.

Powder X-Ray Diffraction Analysis (XRD): The PXRD spectra of samples were recorded using a high-power powder X-ray diffractometer (Ru-200B, India) with Cu as target filter having a voltage/current of 40 KV/40 mA at a scan speed of 4°/min. The samples were analyzed at a 2θ angle range of 2–45°. Step time was 0.5 sec, and the acquisition time was 1 h.

Scanning Electron Microscopy (SEM): The surface characteristics of the mixtures were studied by scanning electron microscopy. The samples of pure drug, PXM and optimized formulation were coated with gold-palladium and then observed with an electron microscope at ambient temperature 10 ºC / min from 30 to 2 ºC.

RESULTS:

Drug Content: The drug content of nine formulations was found to be in the range of 90.91-98.13%. The data of drug content is represented in **Table 3**.

TABLE 3: DRUG CONTENT OF NINE SOLID DISPERSIONS

Formulation Code	Drug Content ±S.D
SIM 1	94 ± 0.87
SIM 2	91.79 ± 2.49
SIM 3	95.48 ± 0.31
SIM 4	95.09 ± 3.84
SIM 5	97.46 ± 0.54
SIM 6	98.13 ± 1.26
SIM 7	91.27 ± 0.62
SIM 8	90.91 ± 0.79
SIM 9	92.04 ± 2.74

Data are expressed as mean ± S.D. (n=3)

Percentage Yield: Percentage yield of all nine formulations was found to be in the range 71.3-91.44%. The data of percentage yield is tabulated in **Table 4**.

TABLE 4: PERCENTAGE YIELD OF NINE SOLID DISPERSIONS

Formulation Code	Percentage Yield ± S.D
SIM 1	71.3 ± 1.01
SIM 2	77.86 ± 0.80
SIM 3	82.1 ± 0.10
SIM 4	88.11 ± 1.32
SIM 5	91.44 ± 0.50
SIM 6	90.5 ± 0.50
SIM 7	79.09 ± 1.00
SIM 8	82.03 ± 0.94
SIM 9	80.33 ± 0.57

Data are expressed as mean ± SD (n=3)

Solubility Studies: The saturation solubility studies data of pure drug and all the solid dispersions in phosphate buffer pH 6.8 at 37 ºC ± 2 ºC are shown in **Table 5**.

TABLE 5: SOLUBILITY ENHANCEMENT DATA OF PURE DRUG AND NINE SOLID DISPERSIONS

Formulation code	Solubility (µg/ml) ± SD
Pure drug	20.22 ± 0.55
SIM 1	26.98 ± 0.63
SIM 2	36.58 ± 0.88
SIM 3	43.26 ± 0.61
SIM 4	58.13 ± 1.71
SIM 5	76.06 ± 1.14
SIM 6	97.38 ± 0.57
SIM 7	46.5 ± 0.44
SIM 8	85.18 ± 0.35
SIM 9	91.06 ± 0.83

Data are expressed as mean ± SD (n = 3)

Results of Factorial Design: Preliminary experiments for the preparation of solid dispersions indicated that factors X_1 and X_2 are effective variables on the *in-vitro* dissolution and yield percent so were used for further systematic studies.

The % DE_{60} of pure drug and all nine formulations was found to be in the range of 33.85- 70.91% respectively, as tabulated in **Table 6**. The statistical evaluation of dependent variables was performed by using Design-Expert version 8.0.7.1 software. The data clearly indicate that X_1 and X_2 strongly influence the % DE_{60} and yield percent

TABLE 6: DISSOLUTION EFFICIENCY OF PURE DRUG AND NINE SOLID DISPERSIONS

Formulation code	Dissolution efficiency (%DE_{60})
Pure drug	30.16 ± 30.16
SIM 1	33.85 ± 0.24
SIM 2	35.98 ± 0.19
SIM 3	43.22 ± 0.39
SIM 4	53.80 ± 0.43
SIM 5	69.11 ± 0.31
SIM 6	70.91 ± 0.58
SIM 7	50.1 ± 0.65
SIM 8	60.97 ± 1.16
SIM 9	66.34 ± 0.33

The regression analysis results (p-value) of the variables on percentage dissolution efficiency (% DE) at 60 min and percent yield of solid dispersion are shown in **Table 7**. The ANOVA results of solid dispersion are shown in **Table 8**. According to p-value, full model or reduced model can be selected, so in the present study, full model having both significant and non-significant p values was used in obtaining dependent variables because the fitness of full model to the system is better than reduced model. The coefficients for the equations representing the quantitative effect of the independent variables on percentage dissolution efficiency at 60 min and percent yield of solid dispersion are shown in **Table 7**.

The equations for each polymer can be generated by putting values of coefficients in equation 2 given as under in terms of coded factors. Coefficients with one factor indicate the effect of that particular factor, while the coefficients with more than one factor and those with second-order terms represent the interaction between those factors and the quadratic nature of the phenomena, respectively. Positive sign of the term indicates a positive (additive) effect, while the negative sign indicates a negative (antagonistic) effect of the factor on the response. It can be concluded from the equations that X_1 (drug: polymer ratio) shows the larger positive effect than term X_2 (microwave time) on percentage dissolution efficiency at 60 min and yield percent. The quadratic terms of X_1 and X_2 also had effect on percentage dissolution efficiency at 60 min and yield percent.

TABLE 7: RESULT OF REGRESSION ANALYSIS

Response	Coefficients estimates						R^2
	b_0	b_1	b_2	b_{12}	b_{11}	b_{22}	
%DE_{60}	66.15	10.73	7.12	1.72	-16.20	-2.32	0.9776
p-value		0.0046	0.0147	0.3902	0.0068	0.4097	
% yield	91.26	1.70	2.40	-2.39	-11.23	-1.87	0.9855
p-value		0.0474	0.0193	0.0334	0.0011	0.1304	

TABLE 8: THE RESULTS OF ANALYSIS OF VARIANCE

Response		Coefficients estimates				R^2
		df	SS	MS	F	
%DE	Regression	5	1541.73	308.5	26.24	0.9776
	Error	3	35.26	11.75		
%Yield	Regression	5	334.17	66.83	40.83	0.9855
	Error	3	4.91	1.64		

Fig. 1 and **Fig. 2** show the contour plots and response surface plots for percentage dissolution efficiency at 60 min and yield percent respectively. The contour lines indicated that the higher the polymer and longer microwave time, the more significant is the dissolution enhancement. However, for yield percent, a decrease at higher polymer ratio was observed, which may be attributed to difficulty of sieving when higher polymer ratio was used.

The optimized formula suggested by the factorial design from design expert was:

- Drug: Polymer ratio $X_1 = 0.25$
- Microwave Time $X_2 = 0.48$

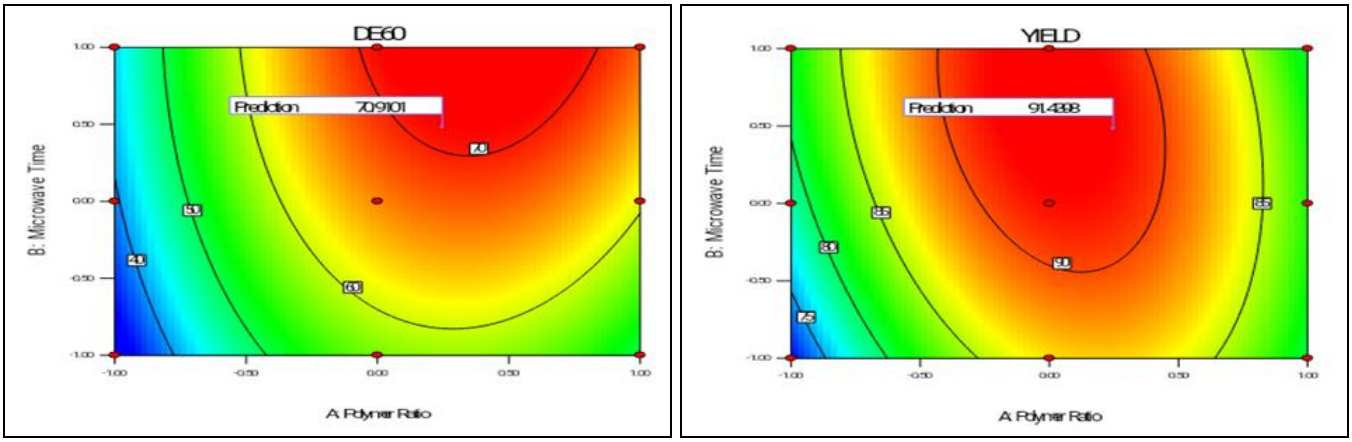

FIG. 1: CONTOUR PLOT OF SHOWING A) PERCENTAGE DISSOLUTION EFFICIENCY AT 60 min; B) PERCENTAGE YIELD

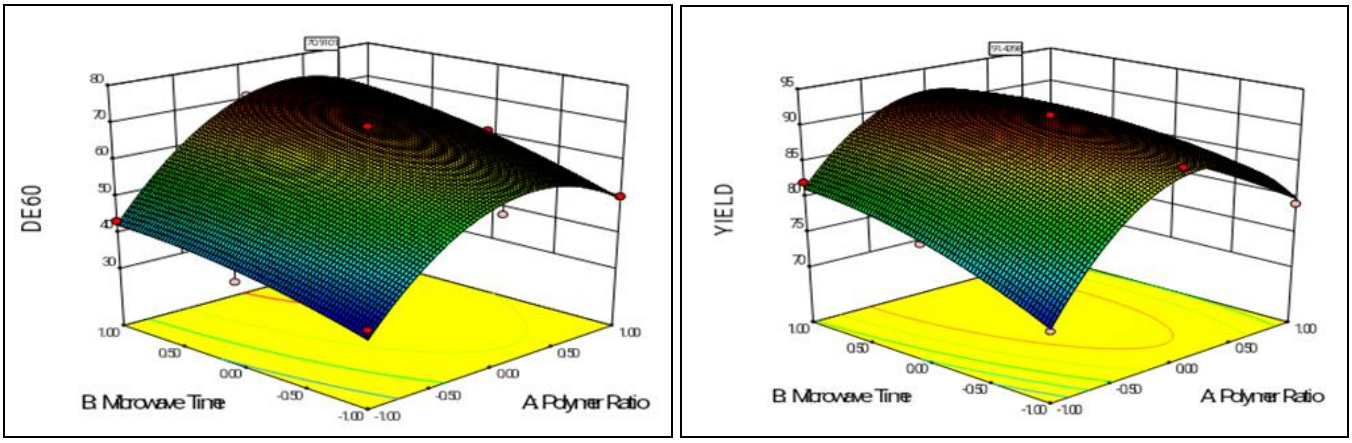

FIG. 2: RESPONSE SURFACE PLOTS SHOWING A) PERCENTAGE DISSOLUTION EFFICIENCY AT 60 min; B) PERCENTAGE YIELD

Characterization of Optimized Batch:

***In-vitro* Dissolution Studies:** The dissolution profiles of pure drug, conventional batch (1:0.25 drug to polymer ratio) and optimized batch (1:0.25) is shown in **Table 9**. It is clearly evident from **Fig. 3**, the percent drug released from an optimized batch (71.77%) is more than that of pure drug (30.90%) and conventional batch (43.14%).

TABLE 9: MEAN PERCENT DRUG RELEASED OF PURE DRUG, CONVENTIONAL BATCH AND OPTIMIZED BATCH

Time (min)	Cumulative percentage drug released ± Standard deviation		
	Pure drug	Conventional batch	Optimized batch
5	23.85 ± 1.16	27.47 ± 0.36	52.19 ± 0.71
10	25.84 ± 0.99	29.43 ± 0.57	53.00 ± 1.37
15	26.51 ± 1.04	30.83 ± 0.78	58.91 ± 1.01
20	28.46 ± 0.50	35.61 ± 0.79	66.05 ± 2.17
30	30.17 ± 0.55	37.10 ± 0.43	66.99 ± 2.86
45	30.55 ± 0.14	39.49 ± 0.61	69.35 ± 0.97
60	30.90 ± 0.79	43.14 ± 0.72	71.77 ± 1.53

Data are expressed as mean ± SD (n=3)

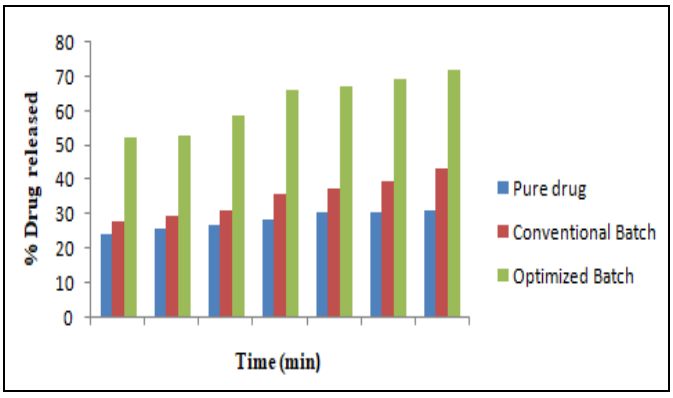

FIG. 3: CUMULATIVE PERCENTAGE DRUG RELEASED PROFILE OF PURE DRUG, CONVENTIONAL BATCH, AND OPTIMIZED BATCH

Angle of Repose: The angle of repose for the optimized formulation was found to be mean 22.37± 0.94 which indicated acceptable flow.

Differential Scanning Calorimetry (DSC): DSC curve of Simvastatin (SIM), Poloxamer 188 (PXM) and the optimized formula of solid dispersion are shown below in **Fig. 4**, **Fig. 5** and **Fig. 6**.

The SIM, PXM 188, and optimized formula of solid dispersion show endothermic peak at 138.51 °C, 59.35 °C, and 58.08 °C, respectively. The endothermic peak corresponding to melting point of SIM is absent in the DSC thermogram of optimized formula of solid dispersion. It might be due the presence of the amorphous form of SIM in the solid dispersion.

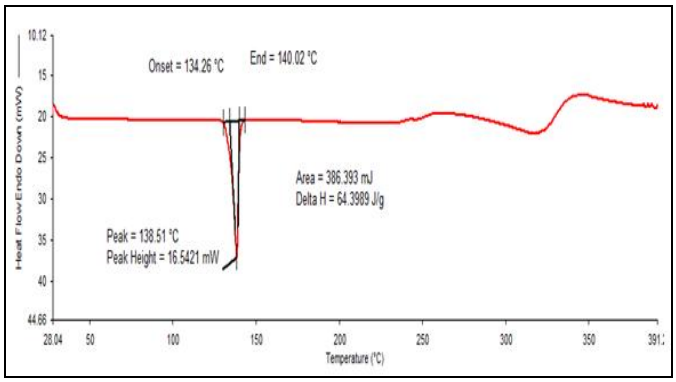

FIG. 4: DSC THERMOGRAM OF PURE DRUG

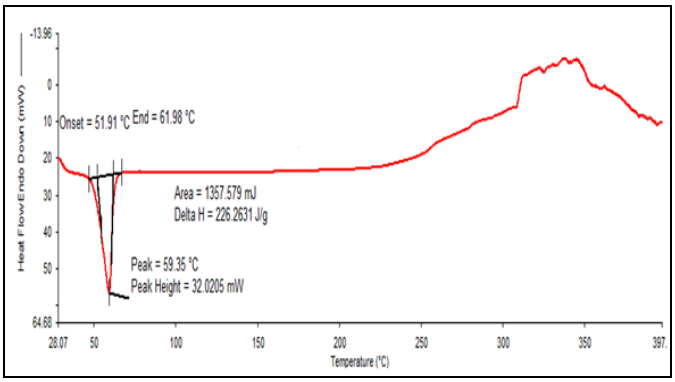

FIG. 5: DSC THERMOGRAM OF PXM 188

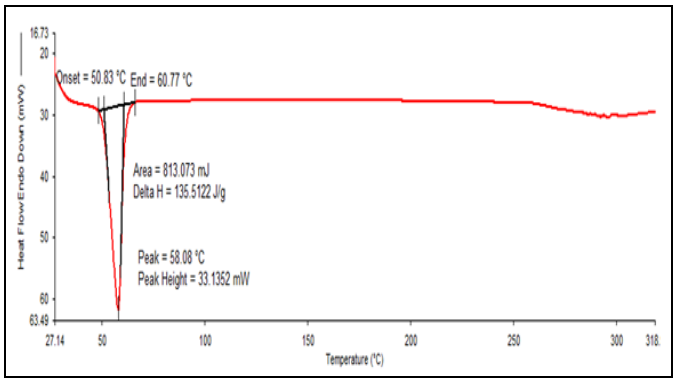

FIG. 6: DSC THERMOGRAM OF OPTIMIZED BATCH

Fourier Transform Infrared Spectroscopy: Fig. 7, **Fig. 8** and **Fig. 9** show the spectrum of simvastatin, poloxamer 188, and optimized batch. The spectrum of pure simvastatin shows a peak at 3551cm^{-1} indicates the presence of O-H stretching vibrations, peaks at 3011cm^{-1}, 2955cm$^{-1,}$ and 2872 cm^{-1} indicates the presence of C-H stretching vibrations of alkane group. Peak present at 1698 cm^{-1} indicates the presence of stretching carbonyl group. A peak at 1468 cm^{-1} and 1390 cm^{-1} and indicates the presence of C-H bending vibration of alkane. 1268 cm^{-1} indicates the presence of C-O-C stretch. Poloxamer 188 shows a characteristic peak at 3377cm^{-1} due to O-H stretching, at 2862 cm^{-1} due to the presence of C-H stretching, at 1282 cm^{-1} and 1246 cm^{-1} due to the C-O stretching, peaks at 2164 cm^{-1} shows the presence of C=C alkyne stretching. The spectra peaks of drug are almost unchanged in the optimized formula of solid dispersion, which indicates that the overall symmetry of molecule is not significantly affected. The decrease and shifting of peaks of OH stretch and C-H stretching may be due to intermolecular hydrogen bonding.

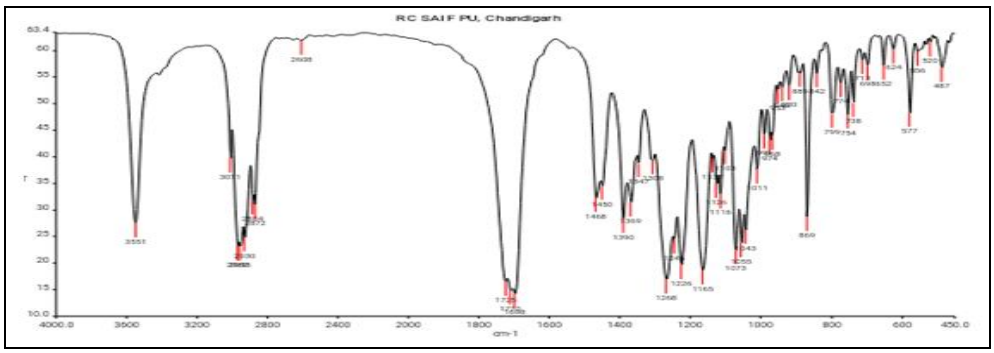

FIG. 7: FT-IR SPECTRUM OF PURE DRUG

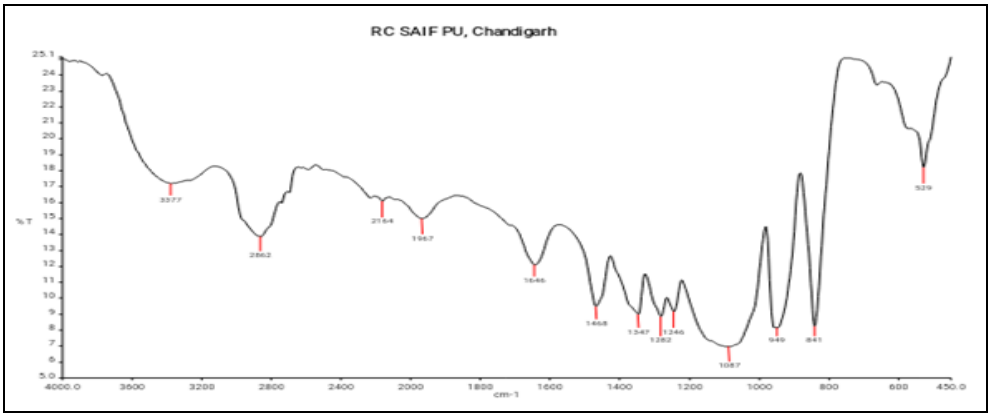

FIG. 8: FT- IR SPECTRUM OF POLOXAMER 188

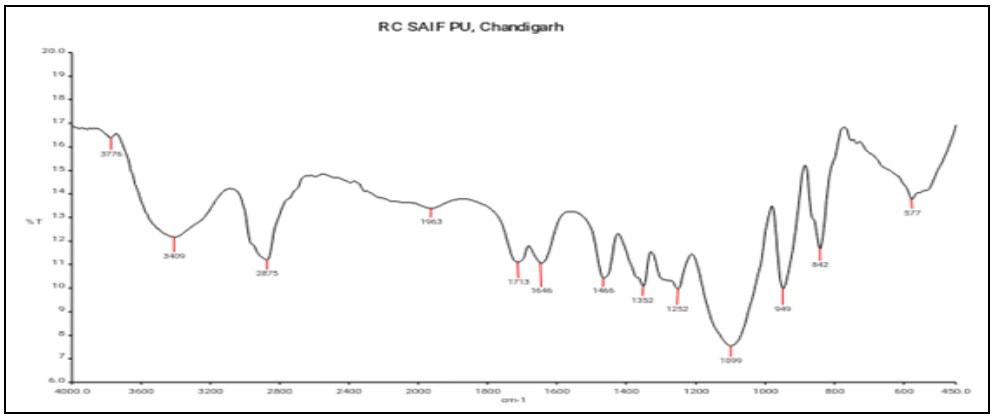

FIG. 9: FT- IR SPECTRUM OF OPTIMIZED BATCH

Powder X-ray diffraction analysis (XRD): The diffraction pattern of the pure drug as shown in **Fig. 10** exhibit characteristic high-intensity diffraction peaks at a diffraction angle (2θ) of 9.44, 9.68, 15.07, 15.91, 17.35, 17.54, 17.88, 18.04, 18.91, 19.03, 19.07 and 19.50 which indicate that the drug is present in the crystalline form are shown in **Fig. 10**, that is also confirmed by DSC results as shown in **Fig. 4**. X-ray diffraction pattern of PXM 188 shows sharp peaks at a diffraction angle (2θ) of 19.39, 21.33, 22.24, 23.45, 23.68, and 36.36 of which the strong reflection of peaks was observed at 19.39, 23.45 and 23 in **Fig. 11**.

The diffraction pattern of pure drug showed characteristic high-intensity diffraction peaks at a diffraction angle(2θ) of 9.44, 9.68, 15.07, 15.91, 17.35, 17.54, 17.88, 18.04, 18.91, 19.03, 19.07 and 19.50 which indicate that the drug is present in the crystalline form that is also confirmed by DSC results. It shows strong reflections of peaks at angles and they do get reduced to a minimum level in the XRD of optimized batch after the formation of solid dispersion by microwave method, which proves that the drug has changed its state from crystalline to amorphous shown in **Fig. 12**.

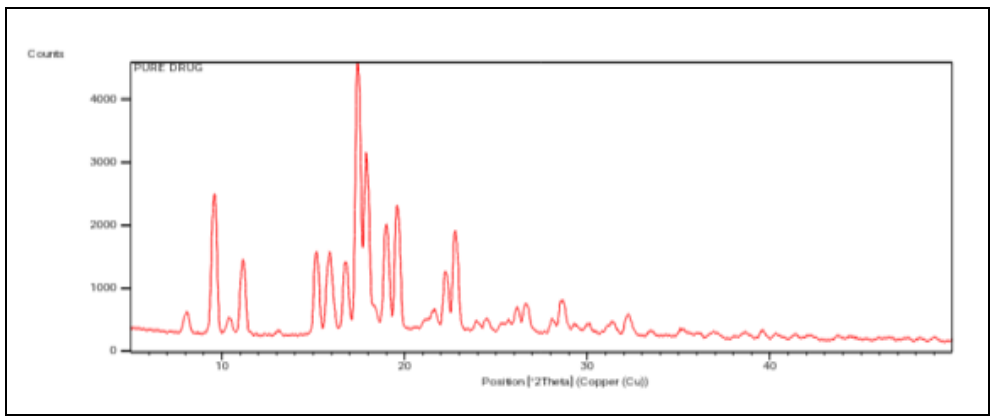

FIG. 10: PXRD SPECTRUM OF PURE DRUG

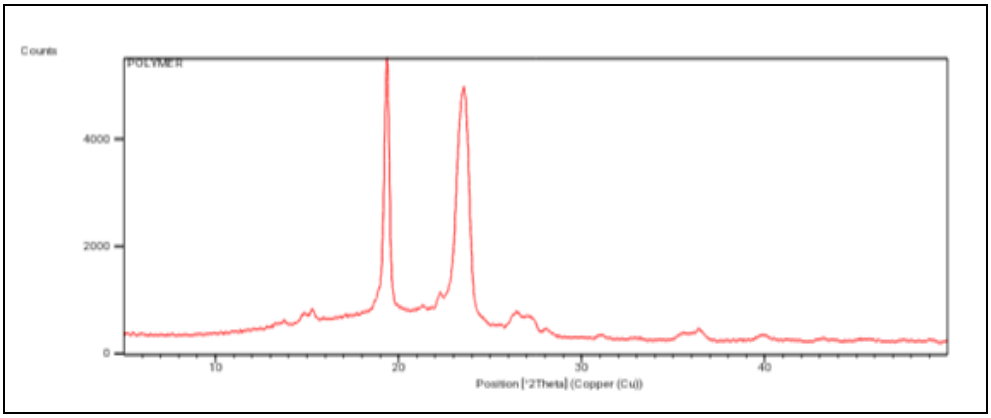

FIG. 11: SPECTRUM OF POLOXAMER 188

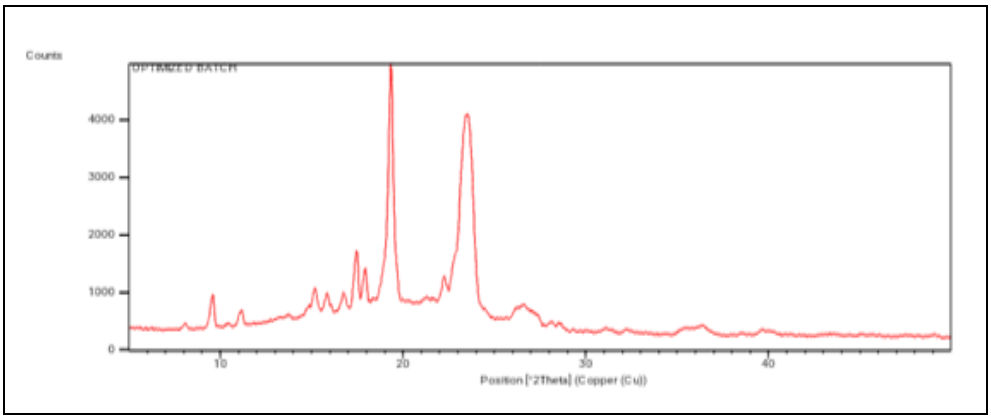

FIG. 12: SPECTRUM OF OPTIMIZED BATCH

Scanning Electron Microscopy (SEM): The SEM images for simvastatin, poloxamer188, and optimized solid dispersion are shown in **Fig. 13**, **Fig. 14** and **Fig. 15**. The drug powder consisted of irregular rod-like crystals whereas an image of optimized solid dispersion of drug does not show any irregular crystals. This shows that the drug no more in crystalline form and complete amorphization of drug in optimized solid dispersion.

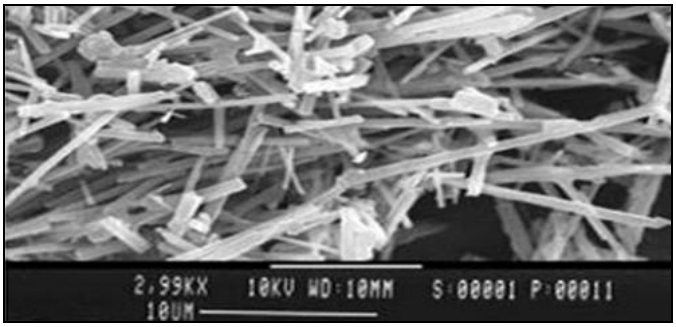

FIG. 13: SEM OF SIMVASTATIN

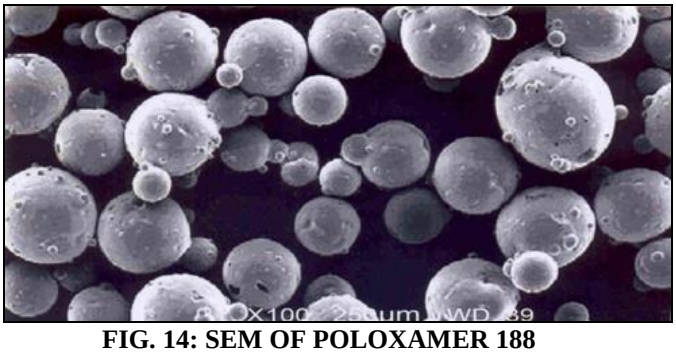

FIG. 14: SEM OF POLOXAMER 188

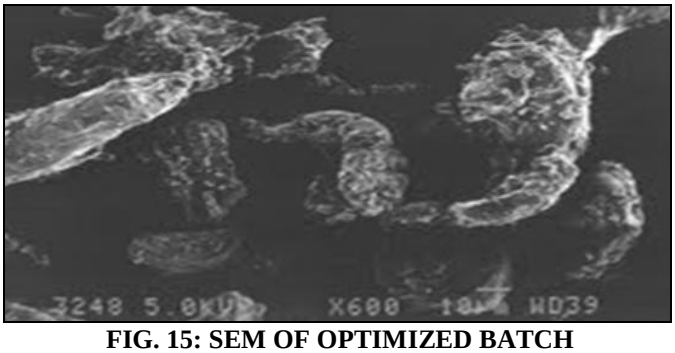

FIG. 15: SEM OF OPTIMIZED BATCH

DISCUSSION: The effect of the incorporation of super disintegrants in solid dispersion tablets on the dissolution behavior was investigated. The superdisintegrants were incorporated at a concentration of 1% to 4% w/w. This optimized formula was used to prepare tablets utilizing Avicel pH 101, croscarmellose, magnesium stearate, talc. The concentration of croscarmellose sodium was varied from 1-4%.

The T4 formulation containing 4% croscarmellose showed best dissolution efficiency. It was compared with the marked tablet of simvastatin and T4 was found to be having better dissolution efficiency at 60 min (%DE60). The percent dissolution release of T4 formulation was found to be 81.04% and that of marketed tablet of simvastatin was found to be 43.65%.

CONCLUSION: The aim of this project was to investigate the influence of the type of carrier and other excipients incorporated the solid dispersions on dissolution behavior of solid dispersion tablets, and to study their physical stability. The solid dispersions investigated in this project were prepared by a novel microwave method.

The present study was undertaken to enhance the dissolution rate of simvastatin (SIM), a practical water-insoluble drug having low oral bioavailability (5%) by preparation of its solid dispersion with poloxamer 188 (PXM) as a carrier. Solid dispersions using SIM with PXM were prepared using the microwave-induced fusion method in different drug carrier ratios *i.e.* 1:2, 1:5, 1:8 and were subjected to microwave for different times i.e. 3 min, 5 min and 7 min on a microwave instrument. The optimized batch obtained using design expert was having drug carrier ratio of 1:5.75 and microwave time of 5.68 min. The study has demonstrated remarkable enhancement of the dissolution rate of optimized solid dispersion prepared by microwave method in comparison with pure SIM and solid dispersion prepared by conventional fusion method.

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AUTHOR CONTRIBUTIONS: All authors have equally contributed in the research work.

CONFLICTS OF INTEREST: Nil

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