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FORMULATION DESIGN AND OPTIMIZATION OF MOUTH DISSOLVING TABLETS OF TELMISARTAN USING SOLID DISPERSION TECHNIQUE

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ABSTRACT

The purpose of this research was to formulate mouth dissolving tablet of Telmisartan for rapid action, beneficial for patients having difficulties in swallowing and in conditions where access to water is difficult. Telmisartan is an antihypertensive drug used for the treatment of hypertension. The crucial aspect in the formulation of mouth-dissolving tablets is to mask the bitter taste and to minimize the disintegration time while maintaining a good mechanical strength of the tablet. Solid dispersion was prepared to increase the solubility and dissolution rate of Telmisartan with Poloxamer188 (PXM188) by using fusion method. Drug polymer interactions were investigated using differential scanning calorimetry (DSC), x-ray diffraction (XRD) and Fourier transform infrared spectroscopy (FTIR). For the preparation of Telmisartan mouth dissolving tablets, its 1:3 solid dispersions with PXM188 was used with various synthetic superdisintegrants (Croscarmellose sodium, SSG). In an attempt to construct a statistical model for the prediction of wetting time, disintegration time and percentage friability, a 3^2 full factorial design was used to optimize the influence of the amounts of superdisintegrants. The results indicate that the optimized tablet formulation provides a DT 45 sec, WT 65 sec, cumulative percentage drug release 96.23% and acceptable friability (0.82%). Stability studies of optimized formulation revealed that formulation is stable.

KEY WORDS: Telmisartan, PXM188, solid dispersion, Fusion method, Mouth dissolving tablets, factorial design.

INTRODUCTION

Techniques that have commonly been used to improve dissolution and bioavailability of poorly water-soluble drugs, in general, include micronization, the use of surfactant, and the formation of solid dispersions.[3] Chiou and Riegelman outlined 6 types of drug-carrier interactions in solid-state dispersions: simple eutectic mixtures, solid solutions, glass solutions and glass suspensions, amorphous precipitates, and compound or complex formation. Other factors such as increased wettability, solubilization of the drug by the carrier at the diffusion layer, and the reduction or absence of aggregation and agglomeration may also contribute to increased dissolution. Telmisartan is a nonpeptide angiotensin receptor II (Type- ATI) antagonist that causes inhibition of the action of angiotensin II on vascular smooth muscle, which leads to a reduction in arterial blood pressure[4]. Telmisartan is 2-(4-{[4-methyl-6-(1-methyl-1H-1, 3-benzodiazol-2-yl)-2-propyl-1H-1, 3-benzodiazol 1yl] methyl} phenyl) benzoic acid. Studies show that Telmisartan is a partial agonist of PPAR-γ, which is an established target for diabetic persons. This suggests that Telmisartan can improve carbohydrate and lipid metabolism, as well as control insulin resistance without causing the side effects that are associated with full PPAR-γ activators. Telmisartan has a long duration of action, and has the longest half-life of any ARB (24 hours). The usually effective dose of Telmisartan is 20, 40, 80 mg once daily. In cases where the target blood pressure is not achieved, Telmisartan dose can be increased to a maximum of 80 mg once daily[5]. The bioavailability of Telmisartan is poor about 45%, which due to extensive first pass hepatic metabolism; the bioavailability can be increase by mouth dissolving formulation. So, in order to enhance oral bioavailability, solubility enhancement can be achieved via solid dispersion formation by using hydrophilic polymers. Among the carriers used in the formation of solid dispersions, poloxamer188 (PXM188) is the most commonly used[6]. The aim of the present study was to evaluate the physicochemical properties of solid dispersions of Telmisartan in PXM188. In order to characterize the prepared dispersions, differential scanning calorimetry (DSC), X-ray diffraction (XRD), and Fourier transform infrared spectroscopy (FTIR) as well as dissolution and solubility studies were performed. Moreover, a trial for the incorporation of the prepared solid dispersion in a mouth dissolving tablets was made. A 3^2 full factorial design was used to study the effect of formulation variables on the performance of these tablets[7, 8].

MATERIALS AND METHODS

Telmisartan was gift from Kwality Pharmaceutical Pvt. Ltd, PXM188, croscarmellose sodium and sodium starch glycolate were a gift from Signet Chemicals Pvt. Ltd., Mumbai. Potassium Dihydrogen Orthophosphate, diSodium Hydrogen phosphate and microcrystalline cellulose were supplied from Loba Chem Pvt. Ltd., Mumbai. Magnesium stearate was supplied from Central Drug House Pvt. Ltd., Mumbai. Other reagents and organic solvents used were of analytical grade. Buffer and its dilutions were prepared with double-distilled water.

Preparation of Solid Dispersions

Solid dispersions of Telmsartan in PXM188 containing 5 different weight ratios (1:1, 1:3, 1:5, 1:7 and 1:9) were prepared by the fusion method. Telmisartan and poloxamer188 were weighed according to different weighed ratios. Poloxamer188 was melted at 60^{O} C. Telmisartan was added to the molten polymer mixed well and cooled to room temperature to obtain a solid mass. The solidified masses was crushed and passed through 40 mesh sieve. The resulting solid dispersion was stored in desicator until further analysis[9].

Phase Solubility Study

Solubility studies were performed according to the method described by Higuchi and Connors[10]. Excess amount drug and solid dispersion (equivalent to 20 mg drug) was added to 100 ml volumetric flask containing 25 ml distilled water. The system was agitated on a rotary shaker for 24 h at 100 rpm maintained at room temperature and filtered. The filtrate was suitably diluted and analyzed on a Spectrophotometer at 297 nm.

Dissolution Studies

Dissolution experiments were performed in triplicate in phosphate buffer pH 6.8 at 37^{O} C using dissolution apparatus II (paddle method) at a rotation speed of 75 rpm. Powdered samples of each preparation equivalent to 20 mg of Telmisartan were added to the dissolution medium. At appropriate time intervals, 5 ml of the mixture was withdrawn. The initial volume was maintained by adding 5 ml of fresh dissolution medium. The removed samples were assayed for Telmisartan content at 297 nm. The dissolution profiles were examined as follows: the percentage of the drug dissolved after 30 min (PD30), and the dissolution efficiency (DE %) parameter after 30 min. The dissolution efficiency can be defined as the area under the dissolution curve up to a certain time. It is measured using the trapezoidal

method and is expressed as a percentage of the area of the rectangle divided by the area of 100% dissolution in the same time.

Drug Content

Solid dispersions equivalent to 20 mg of Telmisartan were weighed accurately and dissolved in suitable quantity of phosphate buffer (pH 6.8). The drug content was analyzed at 297 nm by UV spectrophotometer (Shimadzu 1700). Each sample was analyzed in triplicate.

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectra of pure drug, Poloxamer188 and solid dispersion were recorded on samples prepared in KBr (2 mg sample in 200 mg KBr). The scanning range was 400 to 4000 cm^{-1} using FTIR Spectrophotometer.

Differential Scanning Calorimetry (DSC)

The DSC thermograms were recorded on a DSC (model 50, Shimadzu). Samples of 2 mg weight were heated in hermetically sealed aluminum pans over a temperature range of 30˚C to 300˚C at a constant rate of 10˚C/min under nitrogen purge (40 ml/min).

X-ray Diffraction (XRD)

XRD patterns were obtained using a CuKα monochromated radiation. Diffractograms were run at a scanning speed of 8˚/min over a 2θ range of 0˚ to 80˚.

Preparation of Mouth Dissolving Tablets

Different Telmisartan mouth dissolving tablets were prepared according to the proportions given in Table 1. The raw materials were passed through a screen (40 mesh) prior to mixing. Powdered 1:3 solid dispersion, containing amount equivalent to 20 mg Telmisartan, was mixed with the other excipients and compressed on a single-punch tablet machine equipped with convex-faced 8-mm punches. The tablet weight was adjusted to 200 mg.

Experimental Design of Telmisartan Mouth Dissolving Tablets

A 3^2 full factorial design was used in order to investigate the joint influence of 2 formulation variables. In this design, 3 factors are evaluated, each at 2 levels, and experimental trials are performed at all 9 possible combinations[8, 9]. The amounts of croscarmellose sodium (X_1) and SSG (X_2) were selected as dependent variables. The wetting time, disintegration time and percentage friability were selected as dependent variables. In addition, contour plots and response surface plots were used to graphically represent the effect of the dependent

variables. Statistical model incorporating interactive and polynomial terms is used to evaluate the response[11]. $Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}(X_1)^2 + b_{22}(X_2)^2$ (1) Where, Y is the dependent variable, b_0 is the arithmetic mean response of the nine runs, and b_1 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. 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 MDT1 to MDT9 is shown in Table 2.

Table1: Percentages of different ingredients used in preparation of Telmisartan mouth dissolving tablets

Ingredients	F1	F2	F3	F4	F5	F6
Solid dispersion (1:3)	80	80	80	80	80	80
Croscarmellose sodium	5	10	15	-	-	-
SSG	-	-	-	5	10	15
Avicel pH 101	105	100	95	105	100	95
Aspartame	5	5	5	5	5	5
Talc	3	3	3	3	3	3
Mg. Stearate	2	2	2	2	2	2

Table 2: Composition of factorial design batches

Batch code	Variable levels in coded form		D.T.	W.T.	Friability
	X1	X2	Y1 (Sec)	Y2 (Sec)	Y3 (%)
MDT1	-1	-1	68	100	0.55
MDT2	0	-1	52	76	0.65
MDT3	+1	-1	41	52	0.96
MDT4	-1	0	60	65	0.60
MDT5	0	0	48	56	0.98
MDT6	+1	0	37	49	0.91
MDT7	-1	+1	35	44	0.82
MDT8	0	+1	24	36	0.92
MDT9	+1	+1	19	28	0.98
	Actual Values				
Coded Value	X1	X2			
-1	2.5	2.5			
0	5	5			
+1	7.5	7.5			

Where X_1 indicates croscarmellose sodium and X_2 indicates SSG

Evaluation of the Prepared Tablets

The tablet geometry was determined by a means of a micrometer (Mityato, Japan), while the tablet breaking strength (hardness) and the tablet friability were determined using Pfizer hardness tester and Roche fribilator, respectively. The disintegration and wetting times were measured according to the method described. Briefly, the disintegration time was measured using a modified disintegration method. For this purpose, a cylindrical vessel was used in which 10-meshscreen was placed in such way that only 2 ml of disintegrating or dissolution medium would be placed below the sieve. To determine disintegration time, 6 ml of phosphate buffer (pH 6.8), was placed inside the vessel in such way that 2 ml of the media was below the sieve and 4 ml above the sieve. Tablet was placed on the sieve and the whole assembly was then placed on a shaker. The time at which all the particles pass through the sieve was taken as a disintegration time of the tablet. On the other hand, the wetting time was measured as follows: A piece of tissue paper (12 cm x 10.75 cm) folded twice was placed in a small petri dish (ID = 65 cm) containing 10 ml of phosphate buffer (pH 6.8). A tablet was put on the paper, and the time for the complete wetting was measured. Three trials for each batch were performed and the standard deviation was also determined.

RESULTS AND DISCUSSION

Solubility Measurement

Solubility data of pure drug and solid dispersion in phosphate buffer (pH 6.8) at 37±2^{O} C were shown in table 3 respectively and graph is represented in fig. 1.

Dissolution Studies

The dissolution profile of pure drug and solid dispersions were carried out in phosphate buffer (pH 6.8). Dissolution release values are shown in table 4. From the data, it is event that the onset of dissolution of pure drug was very low. The dissolution release from pure drug was only 28.16% in 30 min. Therefore, this release suggested a strong need to enhance the dissolution of pure drug. The presence of poloxamer188 increases the dissolution of pure drug from the solid dispersion, which increases the dissolution rate as shown in fig 2. This is clear from the dissolution studies that the solid dispersion (1:3) of Telmisartan: Poloxamer188 gives fastest dissolution of drug as compared to other formulations. The release profile showed 2 different phases of drug release. An initial rapid phase followed by a slower one. These results could be attributed to the general phenomenon of particle size reduction during the dissolution process medium by Poloxamer188. Solid dispersion technique has improved the dissolution rate of Telmisartan to greater extent. The presence of

PXM188 increases the dissolution rate of Telmisartan up to a drug to polymer ratio of 1: 3. The DE_{30} value (i.e. dissolution efficiency value for 30 min) for SD2 (1: 3) was 70.52%, whereas DE_{30} value for SD5 (1:9) was 65.09%. This might be due to the formation of viscous boundary layer around the drug particles, leading to a decrease in the dissolution rate, as seen in table 4.

Table 3: Solubility data of pure drug and solid dispersions in phosphate buffer (pH 6.8) at 37±2 ^{o}C

Formulation number	Solubility(µg/ml)
Pure	27.86±0.001
SD1	147.54±0.006
SD2	286.60±0.006
SD3	172.65±0.008
SD4	184.23±0.003
SD5	195.34±0.002

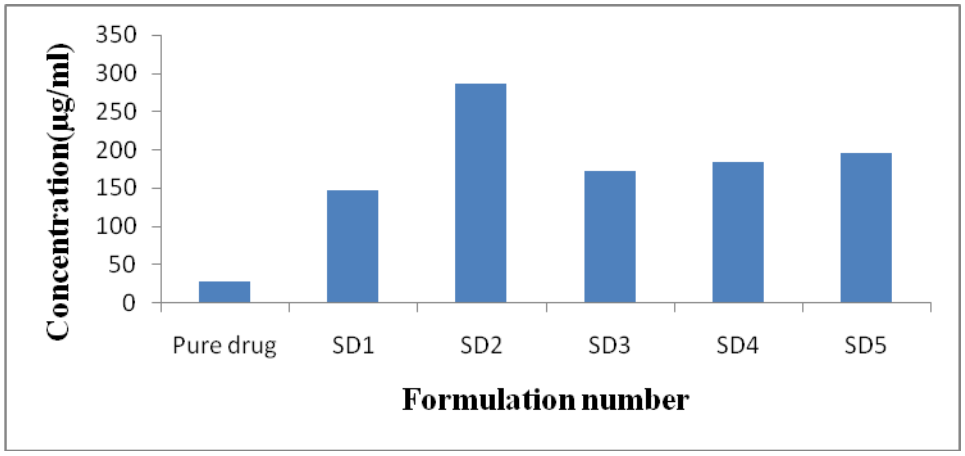

Fig. 1: Solubility plot of pure drug and solid dispersion at 37± 2^{o}C

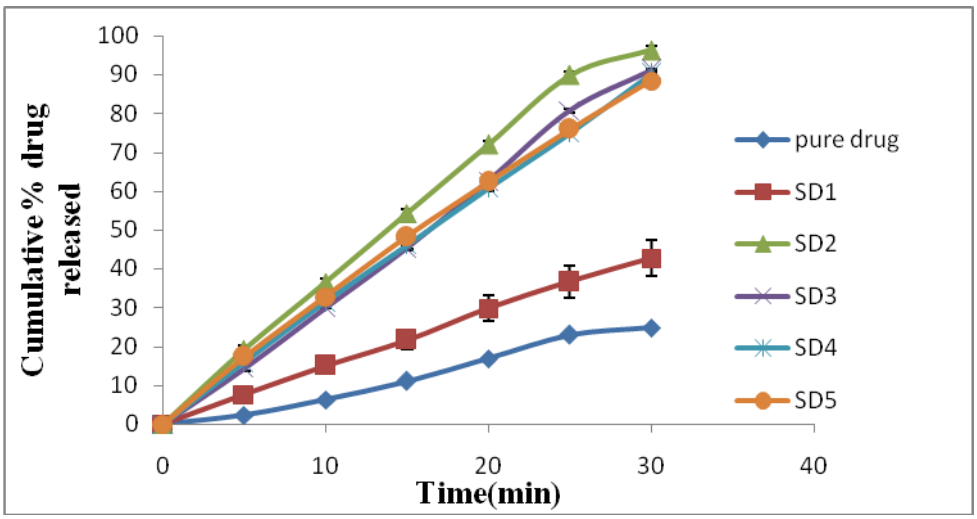

Fig. 2: Percent release of pure drug and from solid dispersion

Table 4: Dissolution Parameters of pure drug and different Solid Dispersions

Time (min)	Pure drug	SD1	SD2	SD3	SD4	SD5
PD30	24.82±0.29	42.75±0.19	96.23±0.39	91.24±0.19	90.22±0.19	88.55±0.19
DE%	21.70	32.32	70.52	68.50	66.24	56.09

Fourier Transform Infrared Spectroscopy

The FTIR studies were performed to check the possible interaction of the drug with the polymer. IR spectra of pure Telmisartan, Poloxamer and their formulations are shown in fig. 3 shows the FTIR of Telmisartan, poloxamer188, physical mixtue and their SD prepared by fusion method. The spectrum of pure Telmisartan depict the characteristic peaks at 3058.74 cm^{-1} (aromatic C-H stretch), 2958.92 cm^{-1} (aliphatic C-H stretch), 1696.72 cm^{-1} (COOH acid), 1599.53 cm^{-1} (aromatic C=C bend and stretch), 1461.11 cm^{-1} (C-H bend), 1383cm^{-1} (OH bending and C=O stretching of COOH acid), 742.30 cm^{-1} 756.85 cm^{-1} (ring vibration due to 1,2 disubstituted benzene), respectively.

The presence or absence s of characteristic peaks associated with specific structural group of the drug molecules was noted. The chemical interaction has been reflected by changes in the characteristic peaks of TEL, depending on the degree of interaction. The FT-IR spectra showed shift in peaks and also absence of peaks of Poloxamer188 and TEL indicating chemical interaction between poloxamer188 and TEL during fusion. The FTIR spectra showed the absence of the characteristic peak of TEL at 3058 cm^{-1} (aromatic C-H stretch) and shifting of 2958.92 cm^{-1} (aliphatic C-H stretch), 1461.11 cm^{-1} (C-H bend), 1383.43 cm^{-1} (OH bending and C=O stretching of – COOH acid). . There were no extra peaks observed in the IR spectrum of solid dispersion. This established that the drug Telmisartan and poloxamer188 used in the study showed no interaction and indicated that they were compatible with each other.

DSC analysis

The DSC runs for Telmisartan, Poloxamer188 and solid dispersion (prepaerd by fusion method) are shown in fig. 4. The DSC curve of pure TEL and PXM188 exhibited single endothermic peaks at 268.46^{O}C (TEL) and 59.35^{O}C (PXM188) which corresponded to their intrensic melting points. The characteristic peaks of PXM188 were invariably identified in the DSC curves of SD, suggesting that the PXM188 was present in the same physical state after making the SD powder by the fusion method. No charateristic melting peak of TEL was identified in the DSC curves obtained from these PXM188 based SD formulation. This might

be due to the higher polymer concentration and uniform distribution of drug in the crust of polymer, resulting in complete miscibility of molten drug in polymer. Absence of peak for the drug indicates that the drug is distributed homogenously in an amorphous state within in the solid dispersions without any interaction.

XRD Analysis

XRD pattern of pure Telmisartan, poloxamer188 and solid dispersion are shown in fig. 5. The XRD pattern of Poloxamer188 had two characteristic peaks of high intensity at 19.0^{O} and 23.0^{O}. In the X-ray diffractrogram of Telmisartan, sharp peaks at diffraction angle (2θ) were 6.0^{O}, 14.0^{O}, 18.0^{O}, 23.0^{O}, 25.0^{O} indicate the presence of highly crystalline in nature and the main peak at 6.0^{O} was particularly more distinctive. It is known that the lack of a distinctive peak of a drug in SD systems demonstrates that a high concentration of the drug is dissolved in the solid state.

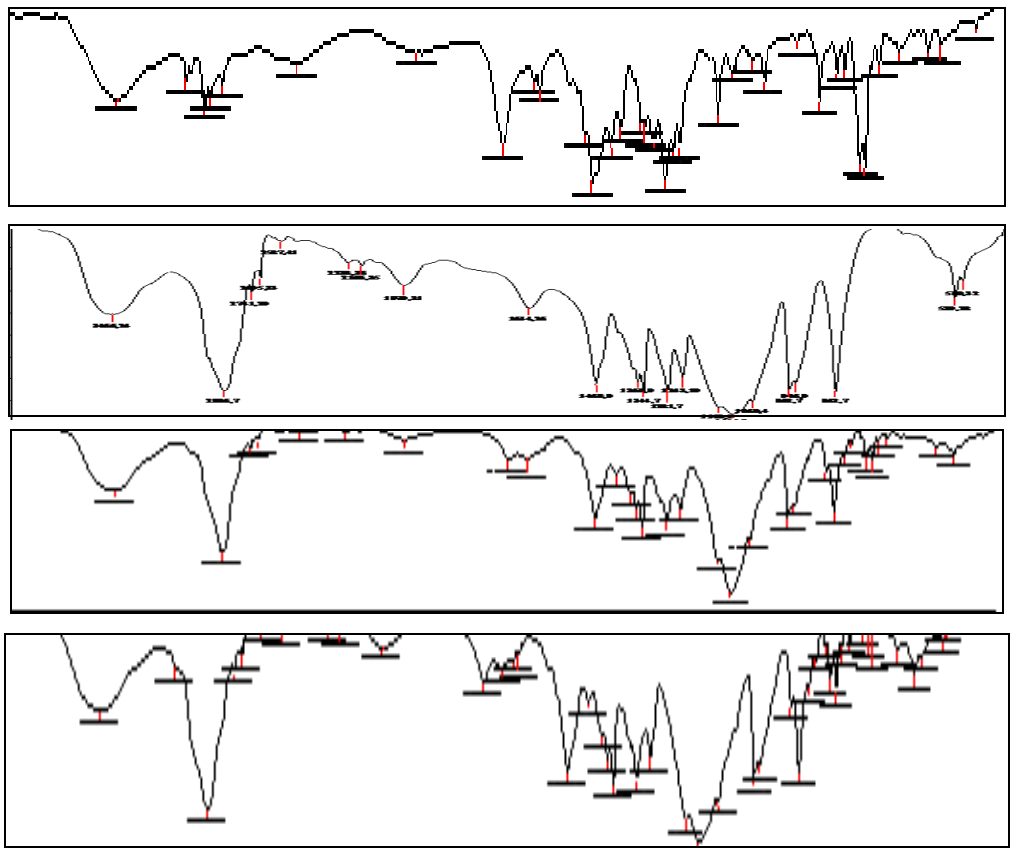

Fig. 3: FTIR spectra of(a) Telmisartan(b) PXM188 (c) 1:3 physical mixture of Telmisartan/PXM188 (d) 1:3 solid dispersion of Telmisartan/PXM188.

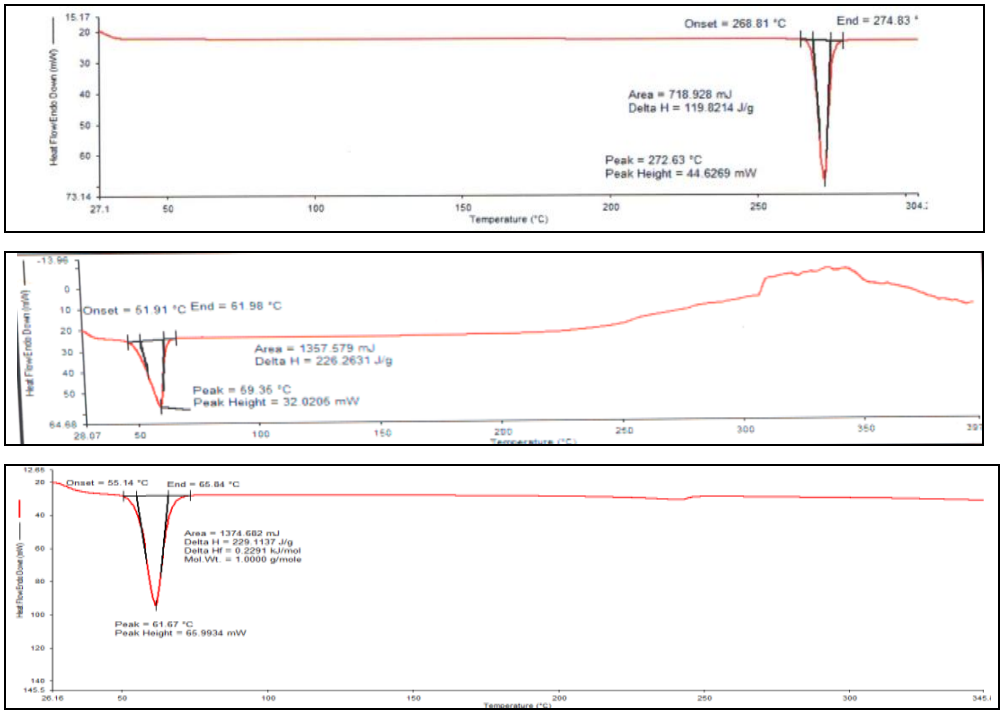

Fig. 4: (a) DSC of Telmisartan (b) PXM188 (c) 1:3 solid dispersion of Telmisartan / PXM188

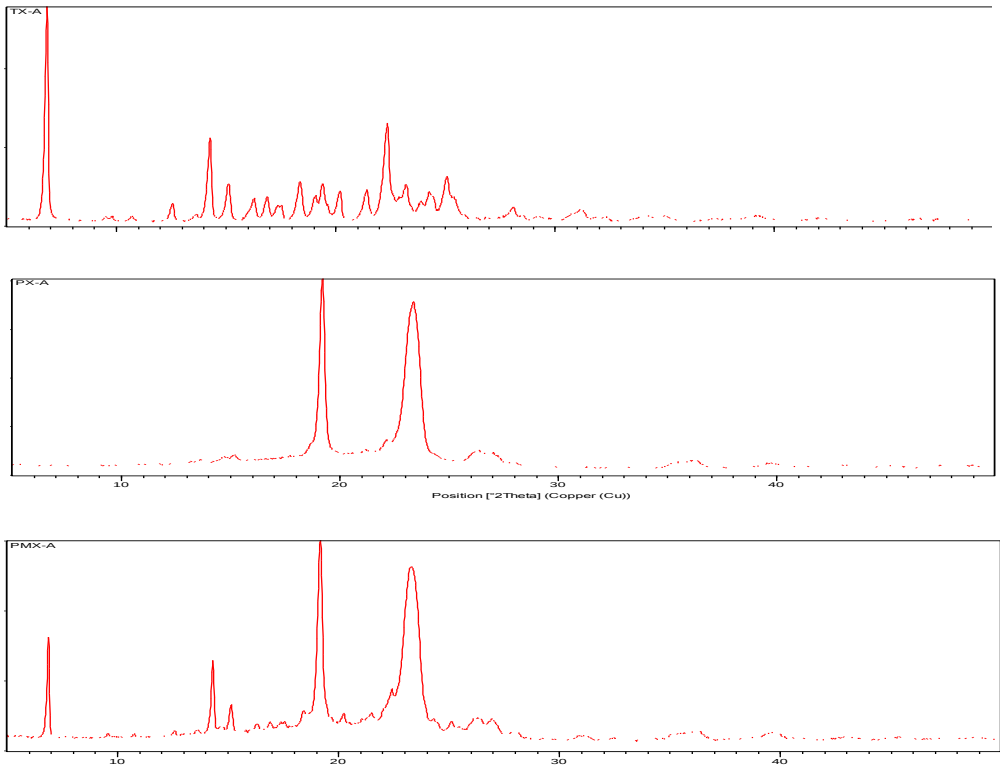

Fig. 5: XRD pattern of (a) Telmisartan (b) PXM188(c) 1:3 solid dispersion of Telmisartan/ PXM188

Evaluation of Telmisartan Mouth Dissolving Tablets

In order to select the best superdisintegrants, preliminary trials were conducted as shown in Table 3. All the prepared tablets are characterized by a uniform thickness, diameter, and weight. Based on the disintegration and dissolution results in Table 3, the investigated superdisintegrants can be ranked according to their ability to swell in water as croscarmellose sodium › SSG stated that wicking and capillary action are postulated to be major factors in the ability of these superdisintegrants to function. As a result, the superdisintegrants croscarmellose sodium and SSG exhibited faster disintegration and dissolution release. Hence, they were selected for further studies.

Table 5: Evaluation of Telmisartan Mouth DissolvingTablets Pre-compression parameter

Formulation codes	Bulk density(g/cc)	Tapped density(g/cc)	Hausner's ratio	Compressibility index (%)	Angle of repose(°)
F1	0.658±0.001	0.762±0.005	1.158±0.007	13.648±0.537	34.04±1.004
F2	0.532±0.002	0.623±0.003	1.171±0.001	14.607±0.075	32.59±0.907
F3	0.618±0.002	0.723±0.003	1.170±0.011	14.523±0.817	30.39±0.501
F4	0.553±0.004	0.652±0.003	1.179±0.016	15.184±1.270	28.33±0.608
F5	0.672±0.002	0.768±0.003	1.143±0.011	12.500±0.857	27.52±1.031
F6	0.522±0.002	0.642±0.003	1.230±0.013	18.692±0.993	25.77±0.996

Post-compression parameters

Formulation	Average Weight(mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)
F1	195.5±1.54	3.118±0.089	3.216±0.086	0.74
F2	198.3±1.76	3.216±0.086	3.334±0.094	0.61
F3	199.2±1.98	3.230±0.083	3.467±0.095	0.57
F4	197.7±2.12	3.153±0.187	3.083±0.069	0.86
F5	198.5±1.98	3.220±0.091	3.200±0.058	0.62
F6	198.2±2.07	3.218±0.090	3.300±0.100	0.57

Dissolution Data

Formulation	Disintegration time (sec)	Wetting time (sec)	Drug content (%)
F1	55±0.47	75±1.25	99.11±0.33
F2	48±1.25	62±1.24	99.12±0.43
F3	35±1.24	52±0.82	99.90±0.77
F4	86±0.82	95±0.81	99.32±0.52
F5	65±1.24	84±0.95	99.10±0.88
F6	52±1.52	64±1.21	99.21±0.57

Time (min)	F1	F2	F3	F4	F5	F6
0	0±0	0±0	0±0	0±0	0±0	0±0
5	30.32±0.19	44.11±0.49	48.32±0.39	28.69±0.50	33.41±0.98	40.27±0.78
10	41.97±0.39	51.34±0.59	52.67±0.69	35.92±0.49	42.33±0.70	57.53±0.58
15	57.60±0.49	65.94±0.68	68.39±0.59	51.63±0.68	59.59±0.78	65.79±0.49
20	69.03±0.49	78.03±0.29	78.99±0.49	64.02±0.78	75.67±0.49	78.47±0.37
25	75.59±0.58	88.72±0.34	90.42±0.78	76.63±0.83	80.02±0.59	85.03±0.57
30	83.85±0.37	92.33±0.79	94.03±0.53	80.46±0.47	88.22±0.48	91.38±0.35

Result of Factorial Design

Preliminary experiments for preparation of solid dispersion indicated that factors X_1 (croscarmellose sodium), X_2 (SSG) are effective variables on the disintegration time, wetting time and percentage friability so were used for further systemic studies.

The statistical evaluation of dependent variables was performed by using design expert version 8.0.7.1.Software. The regression analysis results (p value) of the variables on disintegration time, wetting time and percentage friability of tablets are shown in table 6. The ANOVA result of tablets is shown in table 7. According to p value, full model or reduced model can be selected[10] , 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 significance level of coefficient was found to be $P > 0.05$, hence they were omitted from the full models. On the other hand, the coefficient of significant at $P < 0.05$, hence they were retained in the reduced models[11]. The outcomes for response parameter, i.e., DT, WT and % friability, were subjected to regression analysis and statistical models were found to be significant. The high values of correlation coefficient for DT, WT and % friability indicate a good fit. The coefficients for the equation representing the quantitative effect of the dependent variables on DT, WT and % friability of tablets are shown in table 6. The equations for each polymer can be generated by putting values of coefficients in Eq. 1 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 positive (additive) effect, while negative sign indicates negative (antagonistic) effect of the factor on the response. The quadratic terms of X_1 and X_2 also had effect on DT, WT and % friability.

Fig. 6 and 7 show the counter plots and response surface plots for DT, WT and % friability, respectively. The disintegration time, wetting time and % friability for the 9 patches (MDT1

to MDT9) showed a wide variation from 19-68 sec, 28-100 sec and 0.55-0.98% respectively (Table 2). The data clearly indicate that the disintegration time, wetting time and % friability values strongly depend on the selected dependent variables. The polynomial equations can be used to draw conclusions after considering the magnitude of coefficient and the mathematical sign it carries (positive or negative). It was observed that DT, WT and % friability were dependent on the factors. There was linear decrease in the disintegration time, wetting time and % friability with increase in concentration of both superdisintegrants (croscarmellose, SSG).

Table 6: Summary of results of regression analysis

Response	Coefficients estimates					
	b_0	b_1	b_2	b_{12}	b_{11}	b_{22}
D.T.	47.00	-11.00	-13.83	2.75	2.00	-8.50
p value		0.0001	0.0001	0.0123	0.0684	0.0013
W.T.	56.44	-13.33	-20.00	8.00	0.33	-0.67
p value		0.0088	0.0027	0.0580	0.9353	0.8713
%Friability	0.91	0.12	0.093	-0.062	-0.066	-0.097
p value		0.0390	0.0716	0.2316	0.9173	0.2004

Table 7: The result of analysis of variance

Response		df	Sum of Square	Mean of Square	F	R^2
DT	Model	5	2056.92	411.38	400.26	0.9985
	Residual	3	3.08	1.03		
WT	Model	5	3723.78	744.76	26.04	0.9775
	Residual	3	85.78	28.59		
% friability	Model	5	0.17	0.035	4.96	0.8920
	Residual	3	0.021	0.069		

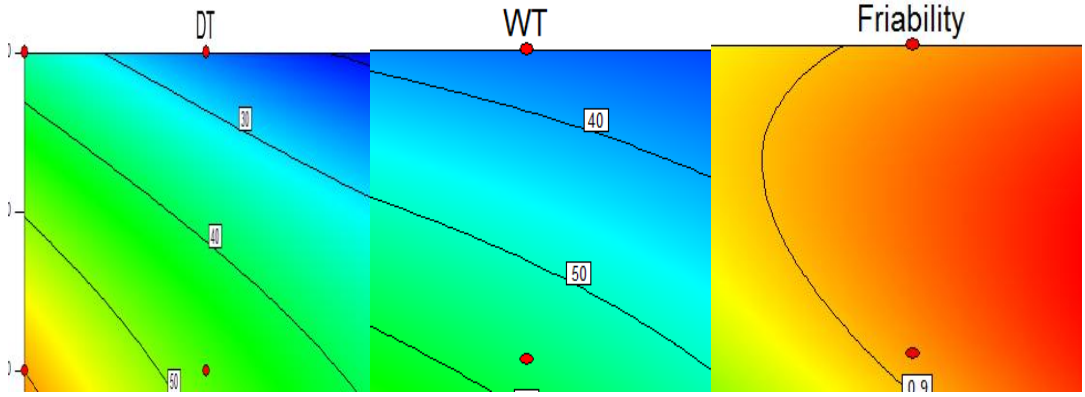

Fig.6: Counter plot for disintegration time, wetting time and % friability

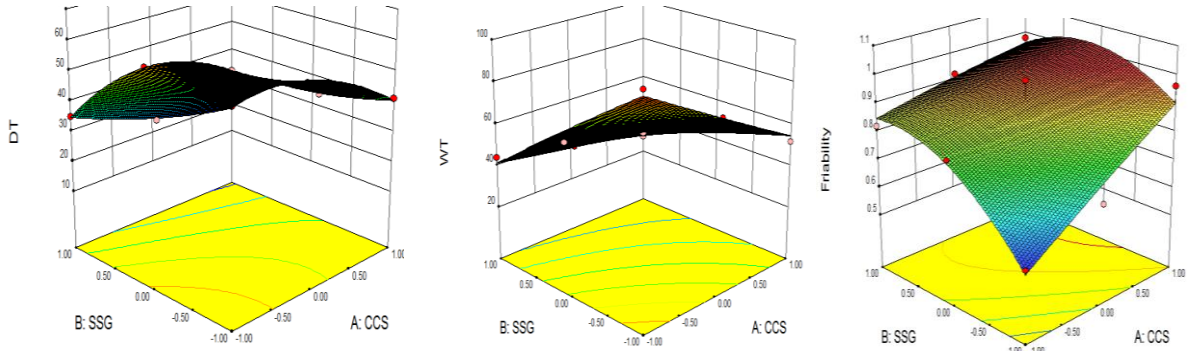

Fig.7: Response surface plot for disintegration time, wetting time and % friability

The desirability of the optimized batch was found to be 0.903 which was very close to the 1, that means the targeted value of disintegration time, wetting time and % friability which we selected for the optimized batch were closely achieved.

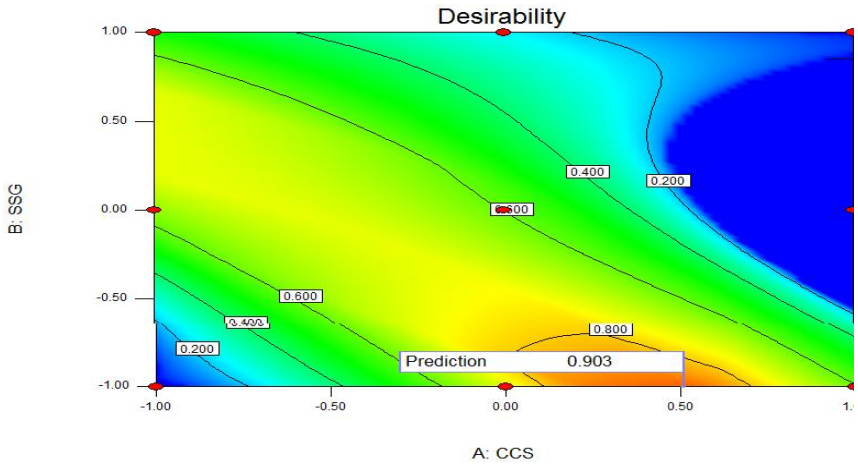

Fig.8: Desirability plots of telmisartan mouth dissolving tablets

The optimized formula suggested by the factorial design was croscarmellose sodium of 6.25% (12.5 mg) and SSG of 2.5% (5 mg). Hence, this formula was prepared and characterized further.

Table 8: Optimized formulation of mouth dissolving tablets of Telmisartan

Ingredients	Quantity per tablet (mg)
Solid dispersion(1:3)	80.00
CCS	12.5
SSG	5.00
Avicel PH101	92.5
Aspartame	5.00
Talc	3.00
Magnesium Stearate	2.00

Table 9: Evaluation parameter of optimized batch

Parameters	Optimized Formulation
Avg. weight (mg)	198.3±0.99
Thickness (mm)	3.20±0.38
Hardness (kg/sq.cm)	3.33±0.094
Drug content (%)	99.74±0.68
% CDR at 30 min	96.23±0.30

DT (Sec) 45±0.34, WT (Sec) 65±0.86, Friability (%) 0.81±0.35

CONCLUSION

The results of 3^2 full factorial design revealed that the amount of croscarmellose sodium and sodium starch glycolate significantly affect the dependent variables such as disintegration time, wetting time and percentage friability. Thus it is concluded that by adopting the systematic formulation approaches, an optimum point can be reached in the shortest time with minimum effort.

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