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Fast dissolving Tablet Formulation and Evaluation: Effort to Enhance Solubility of Angiotensin II Receptor Antagonist (ARB) Telmisartan Antihypertensive Drug

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ABSTRACT: An Angiotensin II receptor antagonist (ARB) Telmisartan is the Antihypertensive category drug used in the management of hypertension (HTN); it is a BCS class II medication. The low solubility of drugs place restrictions on formulation development and drug delivery. The present research work was aimed to improve the solubility of Telmisartan by solid dispersion technique, which will enhance the oral bioavailability of the drug. Solid dispersion of Telmisartan was prepared using Poloxamer 407 and Poloxamer 188 as a carrier and subsequently fast dissolving tablets using croscarmellose sodium and crospovidone as super disintegrants while mannitol as taste enhancer. During the preliminary formulation studies, it was found that the effect of croscarmellose sodium and crospovidone showed positive response on the % drug release and disintegration time of the tablet. Formulation M9 having 5% of croscarmellose sodium and 6% of crospovidone produces best effect and has 97.49 % release. This formulation had disintegration time of 31 sec. and shown better mechanical strength. Formulation M9 was compared with marketed product of Telmisartan tablets which shown 92.46 % drug release in 1 hr. From this observation it was predict that the formulated tablets of Telmisartan (M9) were improved and effective and hence can conclude that the solubility of Telmisartan increased.

Keywords: Telmisartan, solubility enhancement, solid dispersion.

INTRODUCTION

Telmisartan drug is a non-peptide ARBs intended for HTN treatment and cardiovascular risk reduction. It can be used either on its own or in conjunction with other medications like hydrochlorothiazide and amlodipine. Telmisartan is available in three different strengths tablets such as 20 mg, 40 mg, and 80 mg (Wienen *et al.,* 2000; Battershill and Scott 2006). Telmisartan is advised for treatment of mild to severe HTN. It works by relaxing blood arteries to enable easier blood flow. However, it does have some undesirable side effects, including as lightheadedness, coughing, dizziness, and pain in the sinuses. The side effects of these drugs can be overcome with some development in the formulation. If the quantity of the drug is reduced it ultimately reduces the side effects so this can be done by enhancing solubility and bioavailability of drug. So, the technique which helps to reduce the dose is taken under consideration of Telmisartan fast dissolving Tablet formulation (Sharma and Jain 2011; Ontarget Investigators, 2008).

USFDA defines Fast dissolving tablet (FDT) as 'A solid dosage form containing medicinal substance or active ingredient which disintegrates and dissolves rapidly usually within a matter of seconds when placed upon the tongue' the disintegration time ranging from several seconds to about a minute (Shravani and Rhaghavendra 2014). Antihypertensive Telmisartan FDT will illustrate various advantages of like Ease of administration to the patients, no need of water to swallow the dosage form, Rapid dissolution and absorption of the drug, which will produce quick onset of action. Pre-gastric absorption can result in improve Bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects. An increased bioavailability,

particularly in cases of insoluble and hydrophobic drugs is due to rapid disintegration and dissolution of these tablets. Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability

MATERIAL AND METHODS

Identification of drug. The sample of Telmisartan drug procured for study and was identified by melting point, Fourier transform infrared spectroscopy (FTIR) spectrum and UV spectrophotometer.

Drug Excipient compatibility studies. Drug Excipient compatibility studies was carried using FTIR, Differential scanning calorimetry (DCS), for FTIR the mixture of drug and excipients were scanned over a wave number range of 4000-400 cm^{-1}. The compatibility of drug with excipients is given in Fig. 1-3, for DSC pure drug and physical mixture of drug with excipients were subjected to DSC study (Patel *et al.*, 2012; Part *et al.*, 2013). The thermograms are given in Fig. 4 and 5. These results shown that Drug Excipient is compatibility with each other.

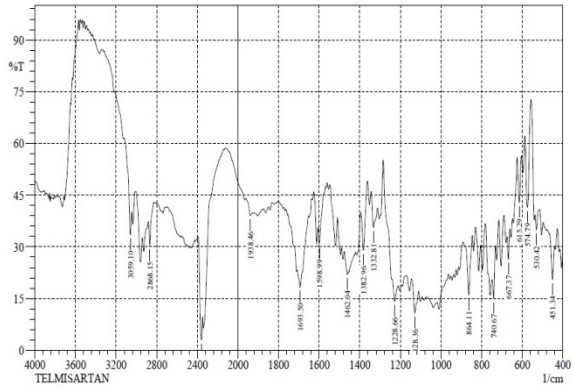

Fig. 1. IR of Telmisartan.

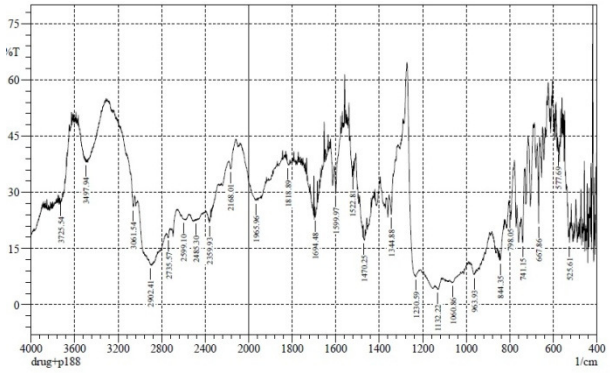

Fig. 2. IR of drug and polymer.

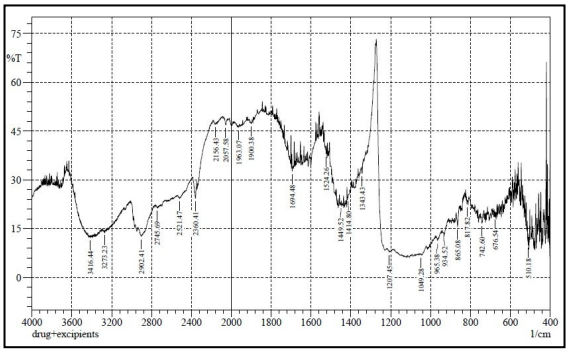

Fig. 3. FTIR spectrum of Tablet blend.

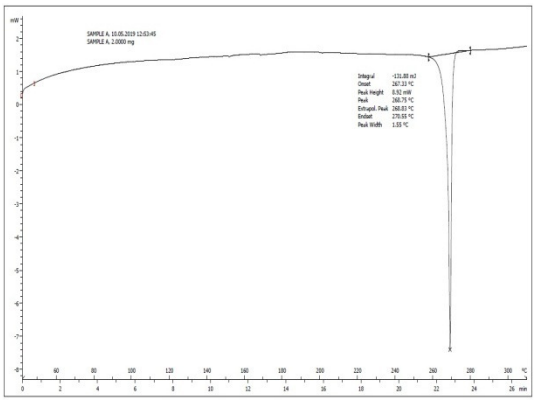

Fig. 4. DSC of Telmisartan.

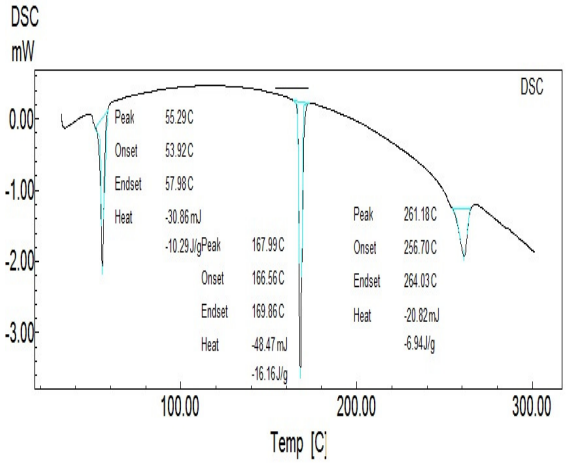

Fig. 5. DSC of Telmisartan and Excipient.

Analytical method for estimation of Telmisartan (Pandey *et al.*, 2011; Rathod *et al.,* 2012).

The validation of analytical method was done as per the ICH guidelines Q2R1. All the validation parameters *viz.* precision, linearity and range, limit of detection and limit of quantification were checked and result obtained as per Table 1, 2, and Fig. 6.

Table 1: Parameters and specifications of Analytical method.

Sr. No.	Parameters	Specifications
1.	Drug	Telmisartan
2.	Linearity range	2 µg/ml- 10 µg/ml
3.	Absorption max.	296 nm
4.	Scanning range	200-400
5.	Instrument	UV-visible spectrophotometer
6.	Sample holder	Quartz

Table 2: Observation of validation parameters.

Parameter	Observation
Absorbance maxima (λ max)	296.4 nm
Linearity range	2-10 µg/ml
Standard regression equation	Y=0.04433x + 0.00546
Correlation coefficient (r2)	0.99955
Residual Standard deviation	0.00298
Precision	Intraday 2.1268, Interday 3.5789
LOD (µg/ml)	0.642
LOD (µg/ml)	1.946

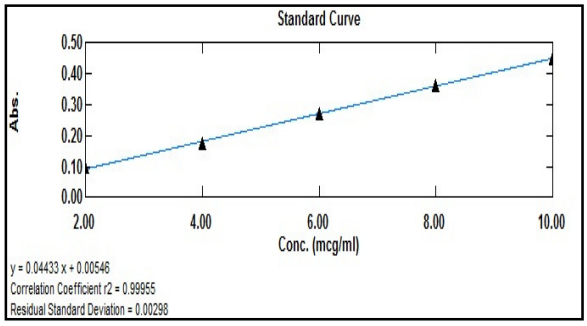

Fig. 6. Calibration curve of Telmisartan.

Solubility studies (Patel *et al.,* 2012). Telmisartan has low aqueous solubility. The solubility was determined in distilled water, pH 6.8 phosphate buffer and 0.1 N hydrochloric acid, Excess amounts of the drug was added to 10 ml of each solvent in rubber stoppered vials and shaken for 24 hours in an orbital shaker. Sampling was done after 24 hrs. Quantitative solubility was determined by UV- spectrophotometer at 296 nm. Solubility studies are depict in Table 3.

Table 3: Saturated Solubility study of drug.

Solubility medium	Duration (hr.)	Solubility (mg/ml)
Distilled Water	24 hr	0.0063
pH 6.8 phosphate buffer (IP)	24 hr	0.0040
0.1 N HCl	24 hr	0.9080

Preparation of solid dispersions and evaluation of solid dispersions (Najmuddin *et al.,* 2010; Sridhar *et al.*, 2013). Solid dispersions of Telmisartan were prepared by using Poloxamer 407 and Poloxamer 188 in a ratio 1:1, 1:2, 1:3 of each as a carrier by melt or fusion method and solvent evaporation method table no. 04 and it was evaluated for flow properties like Angle of repose, Bulk density, tapped density, Carr's index, Hausner's ratio and Drug content uniformity, result obtained are as per Table 5 (Sharma *et al*., 2012; Vasanthan and Narayanasamy 2016).

Table 4: Composition of various solid dispersions of Telmisartan.

Method	Formulation Code	Composition	Ratio (Drug + carrier)
Fusion (melting) method	PA1	TEL + Poloxamer 407	1:1
	PA2	TEL + Poloxamer 407	1:2
	PA3	TEL + Poloxamer 407	1:3
Solvent Evaporation method	PC1	TEL + Poloxamer 407	1:1
	PC2	TEL + Poloxamer 407	1:2
	PC3	TEL + Poloxamer 407	1:3
Fusion (melting) method	PB1	TEL + Poloxamer 188	1:1
	PB2	TEL + Poloxamer 188	1:2
	PB3	TEL + Poloxamer 188	1:3

In-vitro dissolution of solid dispersion (Jain *et al.*, 2012). Dissolution studies on solid dispersions were performed in a calibrated eight stage dissolution test apparatus equipped with baskets employing 900 ml of 0.1 N HCl as a medium. Samples were withdrawn at 0, 2, 4, 6, 8, 10, 15, 20 and 25 minutes and result obtained are as per Tables 6 and shown in Fig. 7.

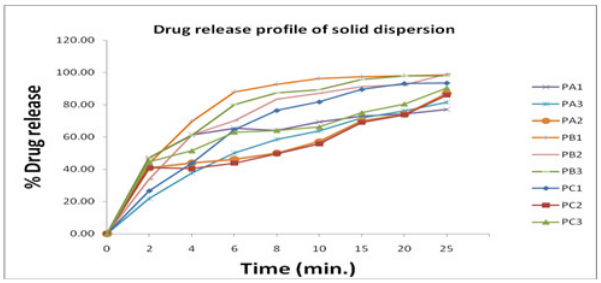

Fig. 7. Release of Telmisartan from solid dispersion.

Table 5: Evaluation of flow properties of Telmisartan solid dispersions.

Formulation code	Angle ofRepose	Bulk Density (g/cm3)	Tappeddensity (g/cm3)	Carr's index (%)	Hausner ratio	Drug content(mg)
PA1	22.34±0.26	0.46 ±0.005	0.50 ±0.01	7.94 ±1.37	1.09 ±0.016	39.99 ±0.047
PA2	21.63±0.78	0.47±0.005	0.52 ±0.01	9.52 ±1.59	1.11 ±0.019	39.78 ±0.029
PA3	23.12±0.49	0.43±0.001	0.46 ±0.01	7.04 ±1.7	1.08 ±0.020	39.81 ±0.010
PC1	22.15±0.75	0.46±0.01	0.51 ±0.004	9.52 ±2.38	1.11 ±0.029	40.01 ±0.101
PC2	24.11±0.84	0.48±0.002	0.52 ±0.003	9.14 ±0.93	1.10 ±0.011	39.63 ±0.112
PC3	21.23±0.64	0.43±0.002	0.47 ±0.005	9.16 ±0.63	1.10 ±0.008	39.89 ±0.042
PB1	20.28±0.18	0.36±0.003	0.40 ±0.005	9.88 ±1.07	1.11 ±0.013	39.78 ±0.066
PB2	21.39±0.68	0.40±0.003	0.44 ±0.002	7.76 ±0.79	1.08 ±0.009	39.70 ±0.021
PB3	20.53±0.49	0.38± 0.002	0.42 ±0.003	10.03 ±1.12	1.11 ±0.014	40.13 ±0.061

All values are mean ± SD (n=3)

Table 6: Release of Telmisartan from solid dispersions.

Time (min.)	Cumulative % of Telmisartan released								
	PA1	**PA2**	**PA3**	**PC1**	**PC2**	**PC3**	**PB1**	**PB2**	**PB3**
0	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
2	47.10±0.06	40.82±0.29	21.95±0.35	26.72±0.52	41.01±0.37	44.56±0.45	43.72±0.61	33.89±0.85	47.27±0.64
4	61.42±0.20	43.88±0.34	37.67±0.61	43.84±3.94	40.38±0.38	51.50±0.68	69.81±0.51	61.34±0.88	61.24±0.54
6	65.39±0.18	46.20±1.71	50.23±0.51	64.69±0.59	43.85±0.49	63.01±0.68	88.13±0.57	70.14±0.60	80.18±0.66
8	64.17±0.19	50.13±0.68	58.43±0.61	76.53±0.60	49.61±0.50	64.15±0.69	92.83±0.43	83.53±0.59	87.47±0.78
10	69.39±0.42	57.18±0.69	63.82±0.68	81.85±0.33	55.75±0.59	66.29±0.58	96.48±0.36	86.97±0.66	89.56±0.62
15	72.96±0.07	70.07±0.77	71.91±0.65	89.58±0.66	69.12±0.41	75.10±0.63	97.67±0.39	91.24±0.53	95.79±0.57
20	74.27±0.09	74.10±0.19	76.26±0.61	93.27±0.50	73.74±0.38	80.50±0.59	98.18±0.43	92.17±0.69	98.07±0.48
25	77.10±0.24	87.05±0.38	81.49±0.45	93.57±0.46	85.93±0.40	90.44±0.59	98.97±0.43	98.86±0.33	97.98±0.43

All values are mean ± SD (n=3)

Preparation of tablets with solid dispersions (Srinarong, 2009, Vemula and Reddy 2015). Among the solid dispersions prepared and as per dissolution studies performed, the (PB1) optimized dispersions were selected for further preparation as tablets. They were prepared by direct compression process.

The compositions of various tablet formulations were as per Table 7 and the tablets were further evaluated for weight uniformity, hardness, friability, wetting time, water absorption ratio, drug content and in vtiro dissolution and result are as per Table 8 and 9.

In the present study, superdisintegrants used were croscarmellose sodium (CCS), crospovidone (CP) in formulation and as per the results obtained, it was found that superdisintegrant CCS (8 mg) and CP (10 mg) in combination gave the good result rather than when used alone. The F9 batch combination was selected and Design Expert was applied.

Table 7: Composition of various telmisartan preliminary batches.

Ingredient (mg)/Tablet	Formulation code								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Telmisartan dispersion (eq. to 40 mg telmisartan)	80	80	80	80	80	80	80	80	80
Croscarmellose sodium (CCS)	4	6	8	0	0	0	4	6	8
Crospovidone (CP)	0	0	0	6	8	10	6	8	10
Mannitol	40	40	40	40	40	40	40	40	40
Microcrystalline cellulose (MCC)	72	70	68	70	68	66	66	62	58
Talc	4	4	4	4	4	4	4	4	4
Total Weight	200	200	200	200	200	200	200	200	200

Table 8: Physical parameter of Telmisartan preliminary batches.

Evaluation Parameter	Formulation Code								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Wt. Variation	201±3.06	202±1.15	198±2.31	200±3.21	198±2.52	201±2.65	201±3.79	201±3.00	199±3.06
Hardness(kg/cm^2)	2.9±0.10	2.9±0.10	2.9±0.17	2.9±0.20	2.9±0.25	3.1±0.06	3.1±0.06	3.1±0.10	3.1±0.06
Thickness (mm)	3.3±0.15	3.3±0.20	3.3±0.10	3.3±0.17	3.3±0.10	3.4±0.25	3.4±0.21	3.4±0.15	3.4±0.20
Friability (%)	0.37	0.43	0.43	0.54	0.49	0.55	0.54	0.48	0.55
In vitro DT (sec)	79±1	76±2	71±1	67±2	59±2	54±3	52±2	48±4	43±3
Drug Content (%)	99.98 ±0.11	99.46 ±0.07	99.53 ±0.15	100.1 ±0.28	99.07 ±0.28	99.5 ±0.24	99.48 ±0.61	99.1 ± 0.99	100.3 ± 0.16
Water Absorption Ratio(%)	75.47±3.96	67.45±2.63	74.60±5.9	78.53±43	77.35± 5.92	74.10 ±4.51	69.96 ±3.58	72.68±4.91	74.84±6.06
Wetting time(sec)	69 ± 1	64 ± 1	58 ± 2	55 ± 2	51 ± 2	42 ± 3	40 ± 1	41 ± 1	34 ± 2

All values are mean ± SD (n=3); In-vitro dissolution of tablets of preliminary batches

Table 9: Dissolution profile of Telmisartan preliminary batches.

Cumulative % of Telmisartan release	Formulation Code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0 min	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
5 min	39.29±0.59	38.86±0.63	48.59±0.83	49.32±1.13	51.83±0.63	51.54±1.04	45.25±0.87	48.05±0.57	52.77 ±1.01
10 min	49.69±0.83	58.03±0.57	60.68±0.91	51.56±1.06	54.99±0.75	59.57±0.86	60.27±0.81	63.20±0.61	64.79±0.84
15 min	70.69±0.94	71.39±0.59	79.59±0.80	69.96±1.09	63.60±1.00	67.91±0.98	63.48±0.90	70.70±0.77	83.29±1.17
20 min	71.64±0.65	79.29±0.46	81.02±0.96	76.15±1.22	70.12±1.05	82.80±1.04	69.29±0.71	82.77±0.83	86.21±1.03
25 min	72.07±0.47	80.24±0.81	81.55±0.94	78.12±0.96	76.83±0.84	89.24±1.01	71.79±1.04	83.91±0.74	91.31±1.09
30 min	72.66±0.63	80.90±0.67	82.16±0.96	79.39±1.05	82.57±0.77	89.99±0.85	83.74±0.99	89.32±0.82	91.65±0.57

All values are mean ± SD (n=3)

Optimization of FDT by 3^2 Factorial Design (Nandare *et al.,* 2011). To know the actual amount of 2 superdisintegrant for the desirable property of fast dissolving tablets a 32 randomized full factorial design was used. The amount of CCS (X1) and the amount of crospovidone (X2) was selected as independent variables. The % drug release and disintegration time were selected as dependent variables. The actual formulation design of FDT of telmisartan according to full factorial design (3^2) layout is shown in the Table 10. The tablets were prepared and Evaluation of tablets of factorial design batches were done for physical parameters such as weight uniformity, hardness, friability and drug content as shown in Table 10.

Wetting time (Jadhav *et al.,* 2011). A piece of tissue paper folded double was placed in clean and dry petri plates containing 10 ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds.

Water absorption ratio. A piece of tissue paper folded twice was placed in a small petri dish (5.5 cm diameter) containing about 10 ml of water. A tablet was put on the tissue paper and allowed to wet completely. The wetted tablet was then reweighed. Water absorption ratio, R was
determined using following equation,

$R = 100 \times (Wa-Wb)/Wb$

Where, Wa = weight of the tablet after water absorption and Wb = weight of tablet before water absorption.

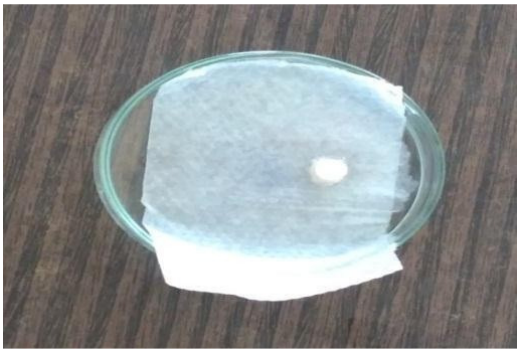

Fig. 8. Wetting time of FDT.

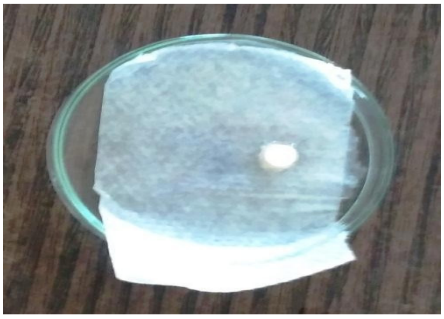

Fig. 9. Water absorption ratio of FDT.

Table 10: Composition of Telmisartan 3^2 Factorial Design Batches.

Ingredient (mg)/ Tablet	Formulation code								
	M1	M2	M3	M4	M5	M6	M7	M8	M9
Tel. dispersion (eq. to 40 mg drug)	80	80	80	80	80	80	80	80	80
(CCS)	6	8	10	6	8	10	6	8	10
(CP)	8	8	8	10	10	10	12	12	12
Mannitol	40	40	40	40	40	40	40	40	40
(MCC)	62	60	58	60	58	56	58	56	54
Talc	4	4	4	4	4	4	4	4	4
Total Weight	200	200	200	200	200	200	200	200	200

***In vitro* dissolution studies factorial batches.** The drug release from tablet was conducted in triplicate. The dissolution profiles are depicted in Table 9 for preliminary batches and Table 12 for factorial batches. The dissolution profiles are shown in Fig. 10 for preliminary batches and Fig. 11 for factorial batches.

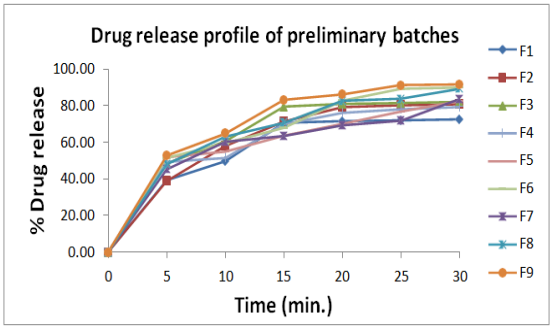

Fig. 10. Dissolution profile of Preliminary batches.

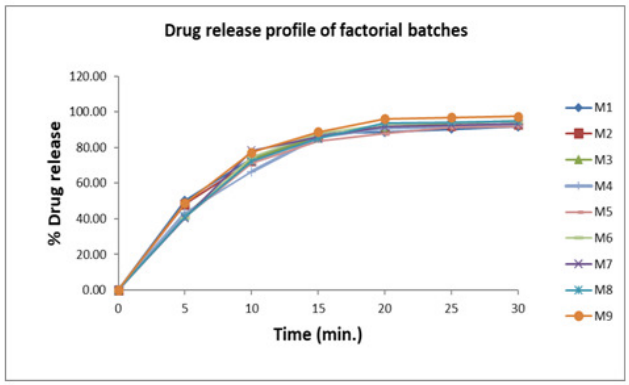

Fig. 11. Dissolution profile of factorial batches.

Analysis of data by design expert software (Dave *et al.*, 2017). The 32 full factorial design was applied to study the effect of independent variables on dependent variables. The amount of croscarmellose sodium (X1) and crospovidone (X2) were selected as independent variables. % drug release and In vitro disintegration time (DT) was selected as dependent variables. The response data was analyzed by using Stat ease Design Expert 11.1.2.0 software. The software gives statistical analysis of data. The summary of statistical design and summary of response are reported in Table 13 and 14.

Table 11: Evaluation Parameters of Telmisartan FDT.

Evaluation Parameter	Formulation code								
	M1	M2	M3	M4	M5	M6	M7	M8	M9
Appearance	White colored, 6 mm round flat faced	White colored, 6 mm round flat faced	White colored, 6 mm round flat faced	White colored, 6 mm round flat faced	White colored, 6 mm round flat faced	White colored, 6 mm round flat faced	White colored, 6 mm round flat faced	White colored, 6 mm round flat faced	White colored, 6 mm round flat faced
Wt. Variation	199 ± 2.08	198 ± 1.53	200 ± 2.65	202 ± 3.21	199 ± 3.06	203 ± 2.08	203 ± 2.00	199 ± 1.53	198 ± 2.52
Hardness(kg/cm^2)	3.0 ± 0.10	3.2 ± 0.25	3.1 ± 0.15	3.0 ± 0.25	2.9 ± 0.15	3.1 ± 0.36	2.8 ± 0.17	2.8 ± 0.12	2.9 ± 0.26
Thickness (mm)	3.7 ± 0.2	3.5 ± 0.3	3.6 ± 0.3	3.5 ± 0.3	3.3 ± 0.2	3.6 ± 0.2	3.3 ± 0.1	3.2 ± 0.2	3.6 ± 0.4
Friability (%)	0.67	0.49	0.86	0.78	0.48	0.49	0.42	0.67	0.36
In vitro DT (sec)	55 ± 2	52 ± 3	50 ± 1	44 ± 2	46 ± 1	47 ± 2	45 ± 1	37 ± 3	31 ± 4
Drug Content (%)	100.10 ± 1.39	98.46 ± 0.92	99.97 ±1.26	98.58± 1.26	96.82±0.90	97.87 ± 2.97	99.16 ±1.15	98.92 ±0.85	101.01 ±0.53
Water Absorption Ratio (%)	74.50 ± 1.42	71.00 ± 1.87	75.84 ±2.93	82.00 ± 2.27	78.51 ± 1.51	70.07 ±2.38	66.99 ±1.73	71.41 ±1.98	75.29 ±1.91
Wetting time (sec)	49 ± 1	42 ± 3	40 ± 2	37 ± 1	39 ± 1	40 ± 1	36 ± 2	30 ± 1	26 ± 1

Table 12: Dissolution profile of Telmisartan factorial design batches

Cumulative % of Telmisartan release	Formulation Code								
	M1	M2	M3	M4	M5	M6	M7	M8	M9
0 min	0.00 ± 0.00	0.00±0.00	0.00± 0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
5 min	50.39 ±1.13	48.08 ± 1.10	42.08 ± 3.44	43.35 ± 1.58	41.00 ± 0.77	40.40 ± 1.01	40.43 ± 1.06	41.00 ± 0.96	48.75 ± 0.76
10 min	73.74 ± 1.20	72.41 ± 0.82	73.34 ± 1.04	66.32 ± 1.54	71.31 ± 0.84	74.78 ± 0.88	78.28 ± 0.77	72.26 ± 1.03	77.23 ± 1.05
15 min	87.72 ± 0.90	86.42 ± 0.97	86.45 ± 0.88	85.77 ± 0.41	83.66 ± 1.05	87.94 ± 0.70	85.87 ± 0.92	85.03 ± 0.91	88.76 ± 0.96
20 min	88.49 ± 0.96	91.53 ± 0.70	91.47 ± 1.06	90.83 ± 0.76	87.70 ± 0.53	92.92 ± 1.07	91.62 ± 0.83	93.71 ± 0.82	96.13 ± 0.74
25 min	90.30 ± 0.79	92.40 ± 0.66	93.65 ± 0.85	91.72 ± 0.78	91.21 ± 0.69	93.97 ± 1.11	92.54 ± 0.61	94.17 ± 0.49	96.79 ± 0.65
30 min	91.64 ± 0.55	93.01 ± 0.61	94.75 ± 0.69	92.70 ± 0.68	91.88 ± 0.66	94.65 ± 1.22	93.17 ± 0.59	94.91 ± 0.43	97.49 ± 0.61

Table 13: Summary of statistical design.

Factor	Name	Units	Type	Min.	Max.	Coded Low	Coded High	Mean	Std. Dev
A	CCS	mg	Numeric	6.00	10.00	-1 ↔6.00	+1 ↔10.00	8.00	1.73
B	CP	mg	Numeric	8.00	12.00	-1 ↔8.00	+1 ↔12.00	10.00	1.73

Table 14 : Summary of responses.

Response	Name	Units	Obs.	Analysis	Min.	Max.	Mean	Std Dev.
R1	Percentage Drug Release	%	9	Polynomial	91.64	97.49	93.80	1.84
R2	Disintegration Time	sec	9	Polynomial	31	55	45.22	7.41

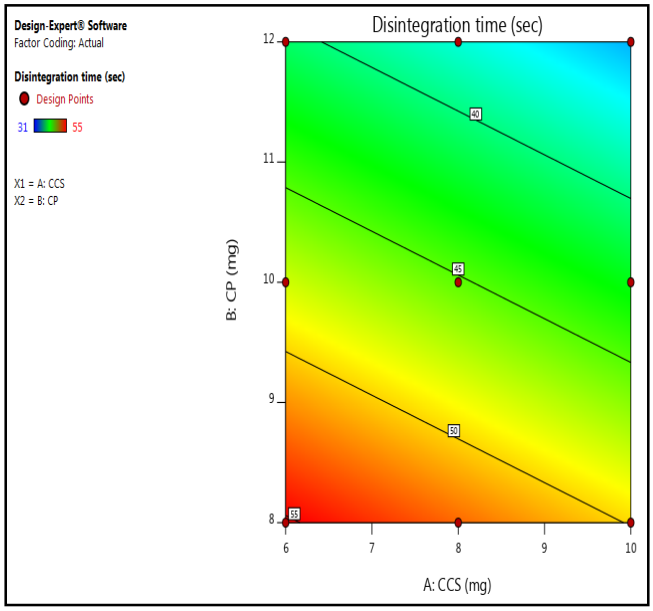

Fig. 12. Response surface contour plot of in vitro disintegration time.

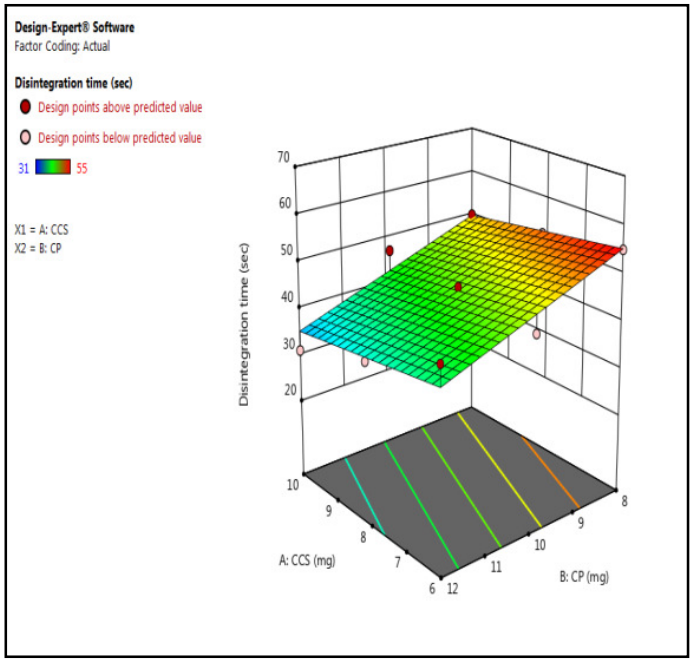

Fig. 13. Response surface 3D plot of in vitro disintegration time.

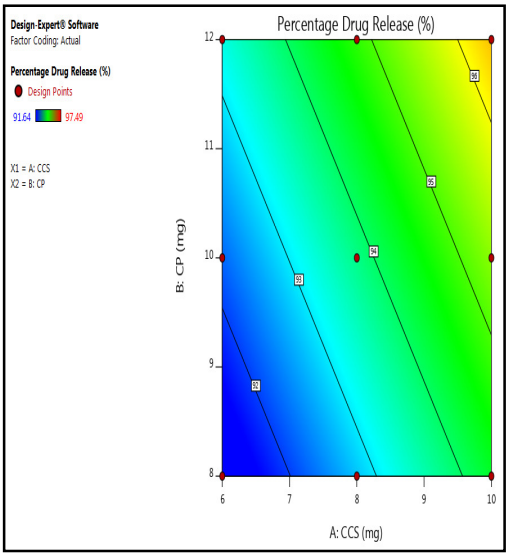

Fig. 14. Response surface contour plot of in vitro % drug release.

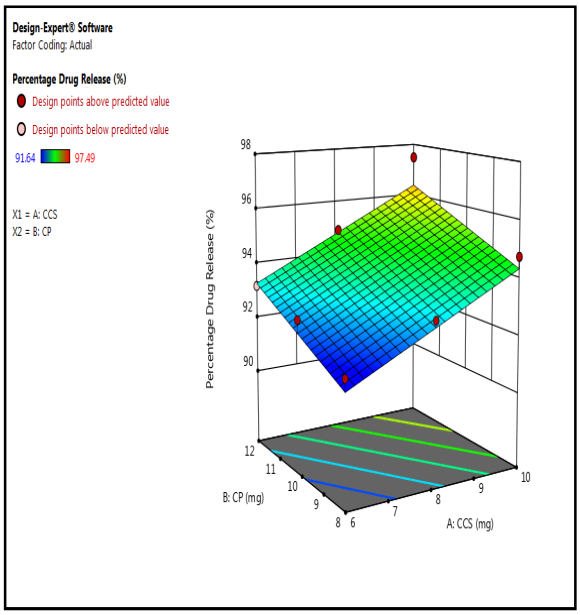

Fig. 15. Response surface 3D plot of in vitro % drug release.

ANOVA Study. Evaluation and interpretation of research finding are almost important and the p-value serves a valuable purpose in these findings. Following tables 15 and 16 show ANOVA for the dependent variables % drug release and disintegration time at R1 and R2; respectively. The coefficient of X1 and X2 were found to be significant at $p < 0.05$, hence confirm the significant effect of both the variables on the selected responses.

The increase in the concentration of croscarmellose sodium and crospovidone resulted in decrease in disintegration time and increase in % drug release of Telmisartan. Overall both the variables caused significant change in responses. ANOVA was done using Stat-ease Design Expert 11.1.2.0 software

Table 15: Analysis of variance for % drug release.

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	21.01	2	10.50	10.42	0.0112	significant
A-CCS	14.66	1	14.66	14.55	0.0088	
B-CP	6.34	1	6.34	6.30	0.0460	
Residual	6.05	6	1.01			
Cor Total	27.06	8				

Table 16: Analysis of variance for disintegration time.

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	365.33	2	182.67	14.77	0.0048	significant
A-CCS	42.67	1	42.67	3.45	0.1127	
B-CP	322.67	1	322.67	26.08	0.0022	
Residual	74.22	6	12.37			
Cor Total	439.56	8				

Comparison with conventional marketed product. The promising formulation was compared with marketed product (XYZ 40 mg Tablet) formulation. A comparative study of in-vitro drug release was made with marketed product of Telmisartan which shows 92.46 % drug release in one hour as shown in Fig. 16.

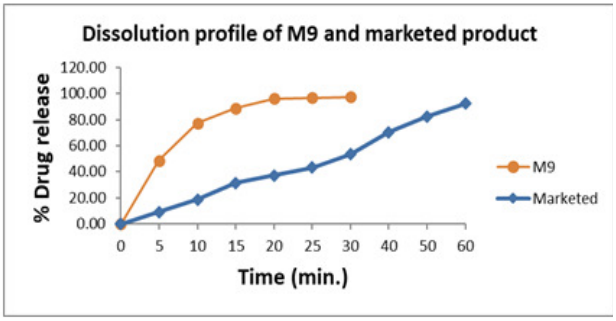

Fig. 16. Dissolution profile of optimized (M9) and marketed product.

CONCLUSIONS

The study was aimed to improve the solubility of poorly soluble antihypertensive drugs using Solid dispersion technique. It was observed that for preparation of solid dispersion, fusion method was selected with drug: Poloxamer 188 in 1:1 proportion and using this solid dispersion fast dissolving tablet with superdisintegrants croscarmellose sodium and crospovidone were formulated.

Design expert software, version 11.1.2.0 was used to generate statistical model. It was found that the tablet showed minimum disintegration time (31 sec) and maximum (97.49 %) drug release at 5% of croscarmellose sodium and 6% of crospovidone *viz.,* batch M9.

The final optimized formulation (M9) was compared with marketed product of Telmisartan tablets which shows 92.46 % drug release in 1 hr. From this observation it was concluded that the formulated tablets of Telmisartan (M9) were better as shown better dissolution.

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Conflict of Interest. None.

FUTURE SCOPE

Fast dissolving tablet formulation is better alternative to the conventional dosage form and future perspectives are to study and perform like XRD, SEM studies, Stability studies as per ICH guidelines, *In vivo* study leading to IVIVC.

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