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Formulation Design for Poorly Water-Soluble Drug by Using Solid Dispersion of Telmisartan for Solubility and Dissolution Rate Enhancement

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Abstract

Formulating the drug into solid dispersion (SD) by fusion method and solvent evaporation method using different grades of PEG in comparison to plain telmisartan drug with optimised solid dispersion tablets. The Preformulation studies like FTIR and DSC studies for drug excipient compatibility stated that the drug and carrier selected for the study and are compatible for further studies. SD was prepared by using the drug Telmisartan by two methods, fusion method and solvent evaporation method, eighteen formulations were prepared and characterized in terms of various parameters. The in vitro drug for all the formulations were in the range of 82.38%-95.73% for fusion method and 91.45% to 96.81% for solvent evaporation method and tablets it ranges from 95.70% to 99.40%. The *in-vitro* release studies have shown that the cumulative drug release values were within the range of 14.23%-94.54% for fusion method, 18.57%- 95.89% for solvent evaporation method and 14.35% - 99.53% for tablets. The fast drug release about 99.53% was found in the F22 formulation by solvent evaporation method in solid dispersion tablets in the ratio of 1:2 and drug content was found to be 99.53% and disintegration time was 1.09 seconds and all parameters were found to be greater than all other formulations.

Keywords: Poor solubility; Solid dispersion; Solvent evaporation method; Fusion method

Introduction

The enhancements of oral bioavailability of poorly water-soluble drugs often show poor bioavailability because of low and erratic levels of absorption. Drugs that undergo dissolution rate limited, in gastrointestinal absorption and it shows improved dissolution and bio availability by reduction in particle size. However, drugs often lead to aggregation and agglomeration of particles, which results in poor wettability [1]. Solid dispersions of poorly water-soluble drugs with water-soluble carriers have been reduced the incidence of these problems and enhanced dissolution.

The development of solid dispersions as a practically viable method to enhance bioavailability of poorly water-soluble drugs overcame the limitations of previous approaches such as salt formation, solubilisation by co solvents, and particle size reduction. Studies revealed that drugs in solid dispersion need not necessarily exist in the micronized state [2-4]. A fraction of the drug might molecularly disperse in the matrix, thereby forming a solid dispersion. When the solid dispersion is exposed to aqueous media, the carrier dissolves and the drug releases as fine colloidal particles. Solid dispersions in water-soluble carriers have attracted considerable interest as a means of improving the dissolution rate, and hence possibly bioavailability, of a range of hydrophobic drugs.

The formulation of poorly soluble drug compound for oral delivery now presents one of the greatest challenges to formulation scientist in the pharmaceutical industry [5-6]. They can be used to increase the dissolution rate of a drug with low aqueous solubility, thereby improving its oral bio availability. Poorly water-soluble drugs present many difficulties in the development of pharmaceutical dosage forms due to their limited water solubility; slow dissolution rate and low bioavailability [4]. Solid dispersions have been widely reported as an effective method for enhancing the dissolution rate and bioavailability of poorly water-soluble drugs [7]. The dissolution rate is directly proportional to solubility of drug. The therapeutic effectiveness of any drug depends upon the bioavailability; i.e. enough drug must reach the site of action to elicit the desired pharmacological response. The bioavailability affected majorly by two factors i.e.

solubility and permeability, other factors are chemical stability, poor dissolution rate, purity. Currently only 8% of new drug candidates have both high solubility and permeability [8-10].

Materials and Methods

Telmisartan from Vasudha Pharma, Polythylene glycol from J&K chemicals, Mumbai, Sodium hydroxide from Merck chemicals, Mumbai, Microcrystalline cellulose form MYL Chem Mumbai, Magnesium stearate from S.D Fine chem. LTD Mumbai, Meglumine from Qualigens Mumbai, Crospovidone XL-10 form Merck Limited and Povidone from MYL Chem Mumbai.

Preformulation Studies

Preformulation studies

An investigation of physical and chemical properties of a drug substance alone is defined as "Pre-formulation."

Objective

It generates useful information to the formulator that is useful in developing stable and bio available dosage forms. These are

a) Organoleptic properties.

b) Solubility studies.

Organoleptic properties

Colour, Odour, taste, appearance of the drug play an important role in the identification of sample of above all properties should be recorded in descriptive terminology [11].

Solubility studies

100ml of dissolution medium with various concentration of carrier is taken in stopper flask an excess of drug was suspended in medium and equilibrated by intermittent shaking maintained at 37+0.5c, filter the solution by using what Mann filter paper, filtrate is suitably diluted. It is analyzed by UV spectroscopy [12,13].

Determination of melting point

Melting point of the pure drug was determined by melting point apparatus. Take a little quantity of sample in the capillary tube and placed in the apparatus and switch on the button. Observe through the viewpoint. Temperature was slowly raised and note that the temperature where the sample melts [14].

FTIR (Fourier Transform Infra-Red Spectroscopy) studies

Infrared (IR) spectroscopy studies of Telmisartan, PEG, Croscarmellose sodium, Meglumine and Microcrystalline cellulose were recorded in a FTIR spectrophotometer (Thermo-IR 200) Potassium bromide pellet method was employed, and background spectrum was collected under identical conditions. The spectrum for each sample showed the wavelength of absorbed light which is a characteristic of the chemical bonds in the sample [15-17]. Each spectrum was derived from 16 single average scans collected in the region of 4000 - 400cm-1 at a spectral resolution of 2cm-1.

Differential Scanning Calorimetry (DSC) studies

Thermal analysis of Telmisartan, PEG and physical mixture were recorded. Netzsch DSC 200PC (Netzsche, Selb, Germany), the instrument was calibrated with indium (calibration standard, >99.999%) for melting point and heat of fusion. A heating rate of 10 °C/min was employed in the range of 25-200 °C. Analysis was performed under nitrogen purge (20mL/min). The samples were weighted into standard aluminum pans and an empty pan was used as reference. The obtained DSC graphs were interpreted and compared for any presence of interactions [18-20].

Preparation of telmisartan solid dispersions by fusion method

In present work the drug and carrier were used in different ratios [1:1, 1:2 and 1:3]. The respective amount of polymer (PEG 4000, PEG 6000, PEG8000 and PEG 10000) was placed in a china dish and allowed to melt by heating up to its melting point. To the molten mass, an appropriate amount of drug module was added and stirred constantly until homogenous dispersion was obtained. The mixture was cooled rapidly by placing the dish in an ice bath for 5min to solidify. The solid mass was pulverized, sifted through sieve no. 60 and stored in desiccator for further studies [21-24]. The formulations were coded as F1, F2, F3, F4, F5, F6, F7, F8, F9, F10, F11 and F12 for drug- polymer ratios 1:1, 1:2 and 1:3 respectively (Table 1).

Table 1: Formulation of Telmisartan solid dispersions by Fusion Method.

S. No	Name of the Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Drug Module	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
2	PEG 4000	1.0	2.0	3.0									
3	PEG 6000				1.0	2.0	3.0						
4	PEG 8000							1.0	2.0	3.0			
5	PEG 10000										1.0	2.0	3.0

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Preparation of Drug module solid dispersions by solvent evaporation method

Solid dispersions of drug module with a hydrophilic carrier (PEG 6000, PEG8000) were prepared in different ratios of drug–carrier. The quantity of carriers for optimization was selected based on preliminary trial formulations. The solvent evaporation method was used for the preparation of SD in the present study. In this method, 1.0g of drug module was accurately weighed and dissolved in a minimum amount of methanol in which hydrophilic carrier was suspended [25].

The solvent was evaporated using a water bath at 450C.The obtained solid was pulverized, sieved through a sieve no. 60 and store in airtight containers. The formulations were coded as F13, F14, F15, F16, F17 and F18 for drug- polymer ratios 1:1, 1:2 and 1:3 respectively [26] (Table 2 & 3).

Table 2: Formulation of Telmisartan solid dispersions by Solvent Evaporation method.

S. No	Name of the Ingredients	F13	F14	F15	F16	F17	F18
1	Drug Module	1	1	1	1	1	1
2	Mannitol	1	1	1	1	1	1
3	PEG 6000	1	2	3			
4	PEG 8000				1	2	3
5	Methanol	20	20	20	20	20	20

Table 3: Formulation of Telmisartan tablets.

S. No	Formulation	F19	F20	F21	F22	F23
1	Pure drug(mg)	40.00	-	-	-	-
2	Telmisartan SDs by F8	-	40.00	-	-	-
3	Telmisartan SDs by F11	-	-	40.00	-	-
4	Telmisartan SDs by F14	-	-	-	40.00	-
5	Telmisartan SDs by F17	-	-	-	-	40.00
6	Microcrystalline Cellulose PH 101	350.00	350.00	350.00	350.00	350.00
7	Croscarmellose sodium	50.00	50.00	50.00	50.00	50.00
8	Sodium hydroxide	6.80	6.80	6.80	6.80	6.80
9	Meglumine	28.00	28.00	28.00	28.00	28.00
10	Povidone K-30	5.00	5.00	5.00	5.00	5.00
11	Microcrystalline Cellulose PH 102	40.20	40.20	40.20	40.20	40.20
12	Magnesium Stearate	5.00	5.00	5.00	5.00	5.00

Evaluation of Solid Dispersion

Prepared solid dispersions were evaluated for the following parameters:

a) Percentage yield

b) Drug content

c) *In vitro* dissolution studies

Percentage yield

Percentage yield was calculated to know about efficiency of any method and thus its help in selection of appropriate method of production. The final weights of the prepared solid dispersions were taken, and percentage yield was calculated by using the given formula [26,27].

$$\%yield = \frac{Practical\ yield}{Theoretical\ yeild}\ x\ 100$$

Drug content

Equivalent weight of prepared solid dispersions containing 100mg drug were taken and transferred into 100ml Standard flask Then take 1ml from above solution and diluted up to 100ml simulated salivary fluid pH 6.8 and repeat the same again by take 1ml from above solution and diluted up to 100ml simulated salivary fluid pH 6.8. The resulting solutions were filtered through a 0.45µ membrane filter and diluted accordingly. The absorbance of the solutions was measured at 296 nm. Percentage of drug content was calculated by using the given formula [28].

$$\%\ Drug\ content = \frac{Observed\ value}{Actual\ value}\ x\ 100$$

In vitro dissolution studies

In vitro dissolution studies of pure telmisartan and solid dispersions were conducted with the USP type II apparatus (paddle type). The dissolution studies were performed using 900ml simulated salivary fluid of pH 6.8 as dissolution medium at 37±0.5°C with 50rpm speed. Samples of each preparation equivalent to 10 mg of drug were added into the dissolution medium. The sample of 5ml aliquots were withdrawn periodically (15, 30, 45 and 60min) and filtered through 0.45µ membrane filter. The withdrawn sample was replaced every time with same quantity of fresh dissolution medium. The

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filtered solutions were diluted suitably, and the samples were analyzed for their drug content by using UV spectrophotometer at wavelength of 269nm. Percentage of drug dissolved at various time intervals was calculated by plotting time on X- axis against percent cumulative drug release on Y-axis [29-31].

Pre compression characterization of blend

The capecitabine and metoclopramide blend were evaluated for

a) Angle of repose

b) Bulk density

c) Tapped density

d) Carr's index

e) Hausner's ratio

Angle of repose

The flow property of blend was determined by the angle of repose values. The maximum angle that can be attained between the surface of the pile of the powder and the horizontal plain is defined as "angle of repose" [32].

Angle of repose was determined by fixed funnel method.

Angle of repose =Tan-1(h /r)

h =Height of pile

r =Radius of pile

7.6. Bulk density

It is defined as the ratio of given mass of powder and its bulk volume. Bulk density values having less than 1.2g/cm^3 indicates good packing and greater than 1.5g/cm^3 indicates poor packing [33].

$$Bulk\ density = \frac{weight\ of\ powder}{volume\ of\ packing}$$

Tapped density

$$Tapped\ density = \frac{mass\ of\ powder}{final\ tipping\ volume\ of\ packing}$$

Hauser's ration

It indicates the flow property of blend; it is defined as the ratio of tapped density and bulk density. It was related to antiparticle friction. Values less than 1.25 indicates good flow property [34].

$$Hausner's\ ratio = \frac{Tapped\ density}{Bulk\ density}$$

Compressibility

It was obtained from bulk and tapped densities. Less compressibility indicates more flowing property of powder. The CI value less than 10 indicates excellent flow property.

Formula: $$\%Compressibility = \frac{Tapped\ density - Bulk\ density}{Bulk\ density} \text{x} 100$$

Preparation of tablets

The tablets were prepared by direct compression technique. Powder was compressed by using 12 stationary rotary compression machines with below mentioned tooling [35].

Tooling

Upper Punch: 12.70mm, Circular shaped, standard concave with plain surface.

Lower punch: 12.70mm, Circular shaped, standard concave with plain surface.

Die: 12.70mm

Evaluation of tablets

After the preparation of tablets were evaluated for post compression parameters.

a) Weight variation

b) Thickness

c) Hardness

d) Friability

e) Drug content

f) Disintegration time

g) *In-vitro* drug release

Evaluation studies are important in the design of tablets and to monitor product quality. There are various standards have been set regarding the quality of pharmaceutical tablets [36,37].

Weight variation test

These tests are based on the comparison of the individual tablets with upper and lower percentage limits of observed sample average(x-mean). USP provides limits for average weight of tablets. When tablets contain more than 150mg these limits are applicable.

$$\%Weight\ variation\ \text{x} = \frac{WA - W1}{WA} \text{x} 100$$

Where

WA= Average weight of tablet in mg.

WI= Individual weight of tablet in mg.

Thickness

Thickness was determined using Vernier callipers. It is expressed in millimeter. It was mostly related to the tablet hardness. Can be uses as initial control parameter [38].

Hardness

It is defined as the force required to breaking a tablet diametrically. It was determined using the Monsanto hardness tester. It is measured in kg/cm^2. 4kg/cm^2 is usually considered as minimum satisfactory value to tablets. Tablet requires a certain

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amount of hardness to withstanding of mechanical shocks during manufacturing, packing and shipping [39].

Friability

Friability was measured by using Roche friabilator. It is closely related to tablet hardness. It is used in determination of the ability of the tablet to with stand abrasion in packing, hand lining and shipping. Tablets that loss less than 10% of its weight was generally considered as accepted formulation.

%friability was calculated by the following formula

$$\%Friability = \frac{Initial\ weight - Finalweight}{Initial\ weight} x100$$

The friability value should be less than 1.0%.

Drug content

The drug content was calculated by using following formula.

$$Drug\ content = \frac{Testabsorbence}{standard\ absorbence} x100$$

Disintegration time

It was determined by using disintegration test apparatus using water as immersion fluid. One tablet was placed in each tube of all 6 tubes. Then it was subjected to disintegration at 28-32 cycles/minute. The time taken for complete disintegration was measured in seconds [40].

In-vitro dissolution studies

Drug release studies were carried out by using USP dissolution test apparatus type II. 900ml dissolution medium (pH 6.8 phosphate buffer) is taken in each bucket. Maintain temperature 37+0.5C. Paddle was rotated at 75rpm for 30 minutes. 1ml of samples was withdrawn at predetermined time intervals of 5, 10, 15, 20, 25 and 30 minutes respectively. Replacing the same amount of dissolution medium by replacing with equal quantity of drug free pH 6.8 phosphate buffer. It was diluted and filtered through membrane filter. Absorbance of sample was analyzed by UV spectrophotometer at 296nm [41-42].

Results and Discussion

UV-VIS spectrum

10µg/ml solution of Telmisartan was prepared in 0.1N HCl, Phosphate buffer pH 6.8, Phosphate buffer pH 7.4 and Distilled water. UV-VIS scan was taken between the wavelengths 200-400nm using UV-VIS spectrophotometer (Shimadzu, UV-1700) (Table 4 & 5).

Table 4: Physical properties of Telmisartan.

Description	Results
Colour	White to slightly yellowish solid
Odour	Odour less
Appearance	Powder
Melting point	261-263 °C
Solubility	Methanol

Table 5: Melting point of the drug and the physical mixture.

S. No	Composition	Melting Point (oC)
1	Pure drug	262.24
2	Physical mixture	264.71

Infrared (IR) spectro scopy studies of telmisartan PEG, Croscarmellose sodium Meglumine and micro crystalline cellulose were recorded in a FTIR spectro photometer (themo-IR200) potassium bromide pellet method was employed and background spectrum was collected under identical conditions the spectrum for each sample showed the wavelength of absorbed light which is a characteristic of the chemical bonds the sample each spectrum was derived from 16 single average collected in the region of 4000-400cm-1 at a spectral resolution of 2cm^{-1} (Figure 1-5).

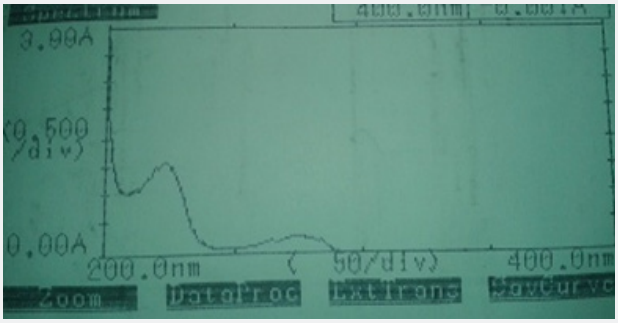

Figure 1: UV-VIS spectrum of Telmisartan in phosphate buffer pH 7.4.

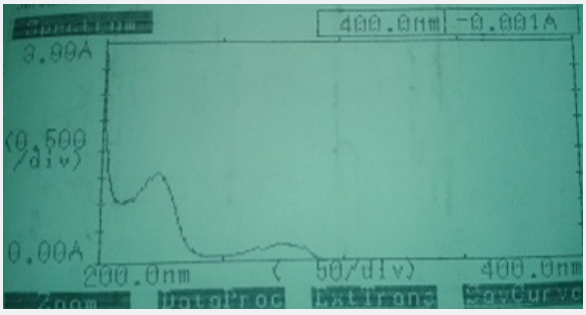

Figure 2: UV-VIS spectrum of Telmisartan in phosphate buffer pH 6.8.

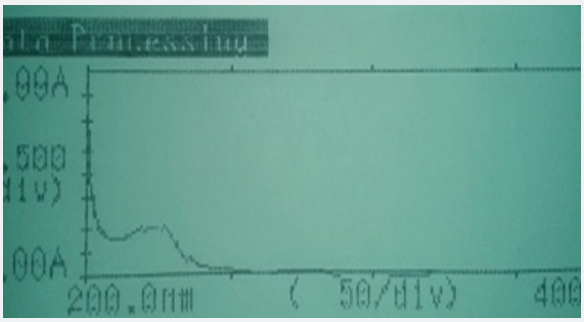

Figure 3: UV-VIS spectrum of Telmisartan in 0.1 N HCl. 100mg /ml solution of telmisartan was prepared in 0.1N HCl, Phosphate buffer pH 6.8& 7.4 and distilled water. UV –VIS spectra meter (shimadzu. UV-1700).

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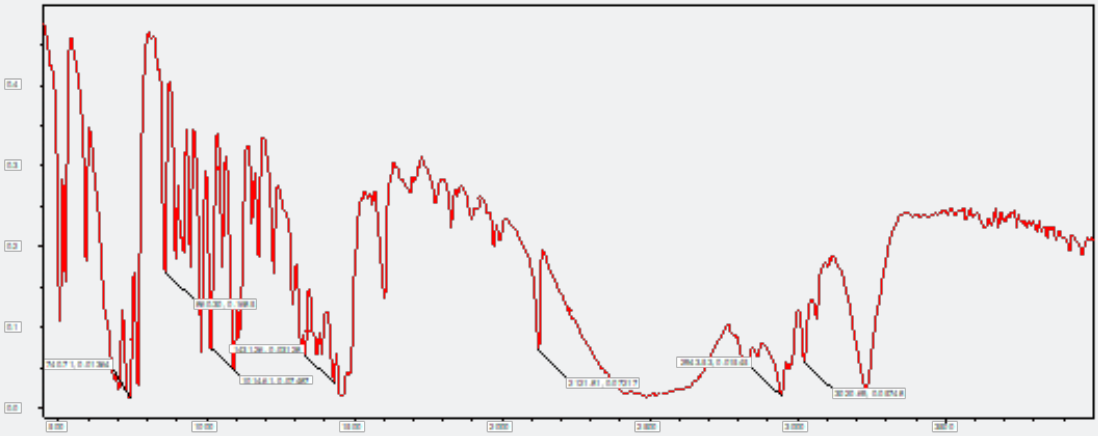

Figure 4: FT-IR of Telmisartan.

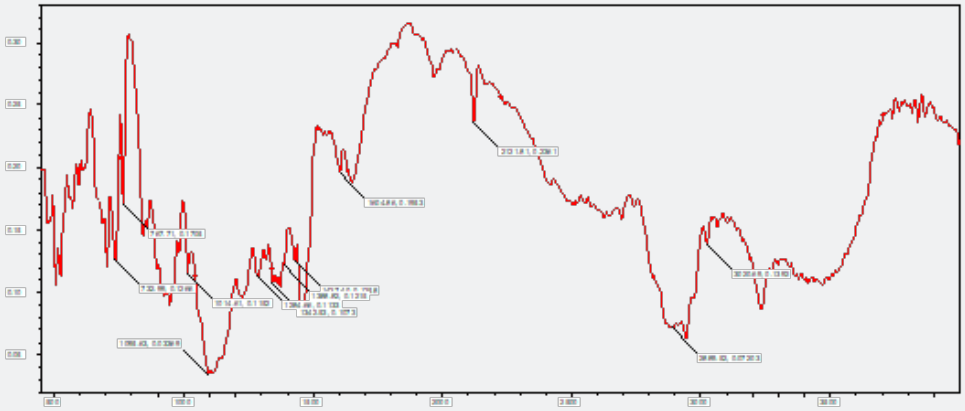

Figure 5: FT-IR of optimized formula by fusion method.

FT-IR Studies did not show any significant interactions between the drugs and their respective excipients. From the compatibility studies PEG, Croscarmellose sodium, Meglumine, Povidone and microcrystalline cellulose are compatible with Telmisartan and its optimized formula for solid dispersion and for tablets states there is no significant interactions between the excipients (Figure 6 & 7).

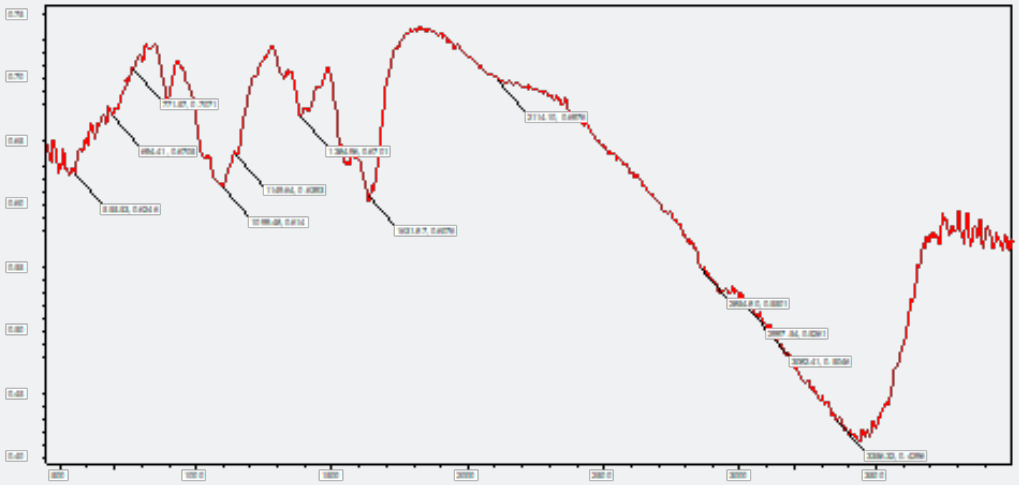

Figure 6: FT-IR spectrum of optimized formula by solvent evaporatin method.

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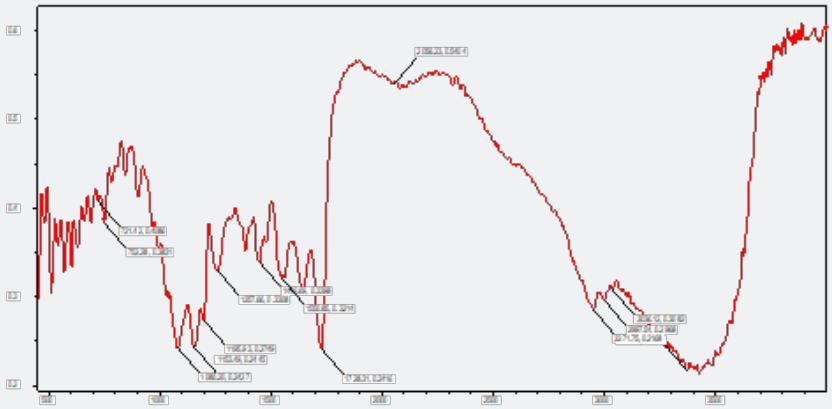

Figure 7: FT-IR spectrum of optimized formulation of Tablet.

Interpretation of Drug –Excipient Compatibility Studies

The Preformulation studies for compatibility by FTIR concluded the drug and carrier selected for the study were compatible and can be used for the further studies. The *in-vitro* drug content for all the formulations were in the range of 82.38% - 95.73% for fusion method and 91.45% - 96.81% for solvent evaporation method and for tablets it ranges from 95.70%- 99.40% (Table 6-12) (Figure 8 & 9).

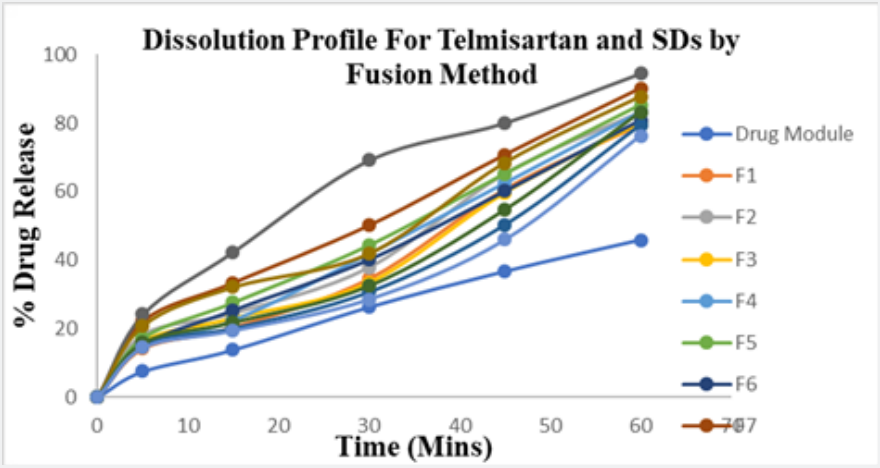

Figure 8: *In-vitro* drug release of Telmisartan SDs by Fusion method.

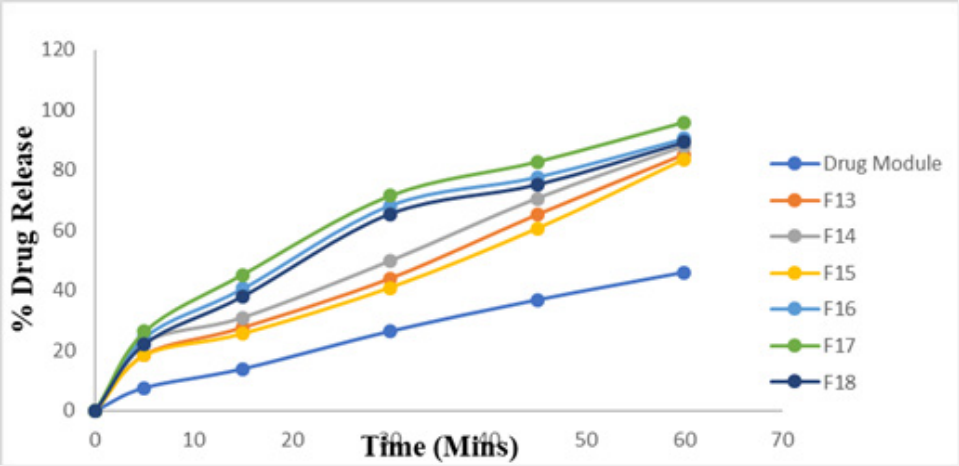

Figure 9: *In-vitro* drug release of Telmisartan SDs by Solvent evaporation method.

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Table 6: Interpretation of Drug –Excipient Compatibility Studies.

S.No	Chemical Constituents	Bond	Wavelength	Mode
1	Telmisartan(drug)	N-H	740	ROCKING
		C-H	860	ROCKING
		C-H	1931	BENDING
				PLANE
2	formulation for fusion method	C-H	767	ROCKING
		C=N	2121	STRETCH
		C=O	1604	STRETCH
3	formulation for solvent evaporation method	C-H	694	ROCKING
		C-C	1099	STRETCH
		C=N	1631	STRETCH
4	formulation for tablets	O-H	1257	BENDING
		C=O	1728	STRTCH
		C=N	1446	STRTCH

Table 7: Estimation of % Practical yield of Telmisartan Solid Dispersions by Fusion method.

S. No	Formulation Codes	% Practical Yield
1	F1	87.21
2	F2	90.29
3	F3	88.05
4	F4	89.11
5	F5	88.56
6	F6	88.43
7	F7	93.24
8	F8	94.68
9	F9	93.75
10	F10	91.26
11	F11	92.56
12	F12	92.09

Table 8: Estimation of % Practical yield of Telmisartan Solid Dispersions by Solvent evaporation method.

S. No	Formulation Codes	% Practical Yield
1	F13	93.46
2	F14	92.88
3	F15	93.26
4	F16	95.22
5	F17	96.01
6	F18	94.53

Table 9: Estimation of drug content of Telmisartan SDs by Fusion Method.

S. No	Formulation Codes	Drug Content
1	F1	85.51
2	F2	86.59
3	F3	83.16
4	F4	90.55
5	F5	92.86
6	F6	88.47
7	F7	94.62
8	F8	95.73
9	F9	93.41
10	F10	84.67
11	F11	85.53
12	F12	82.38

Table 10: Estimation of drug content of Telmisartan SDs by Solvent evaporation method.

S. No	Formulation Codes	Drug Content
1	F13	92.66
2	F14	94.28
3	F15	91.45
4	F16	96.43
5	F17	96.81
6	F18	93.13

Table 11: *In-vitro* drug release of Telmisartan SDs by Fusion method.

Time (min)	Telmisartan	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	00	00	00	00	00	00	00	00	00	00	00	00	00
5	7.54	14.23	18.29	16.35	14.86	17.23	15.14	22.18	24.16	20.84	15.66	15.89	14.51
15	13.82	20.47	24.58	23.14	22.45	27.62	25.43	33.43	42.45	32.11	20.15	21.86	19.48
30	26.28	34.62	37.92	33.48	41.85	44.30	40.15	50.16	69.18	41.88	30.72	32.47	28.60
45	36.71	60.79	65.24	59.7	62.49	65.18	60.13	70.76	80.11	68.4	50.32	54.69	45.95
60	45.88	79.58	83.26	80.14	83.26	85.22	80.83	90.16	94.53	87.67	79.46	83.16	76.35

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Table 12: *In-vitro* drug release of Telmisartan SDs by Solvent evaporation method.

Time	Telmisartan	F13	F14	F15	F16	F17	F18
0	00	00	00	00	00	00	00
5	7.54	18.57	22.49	18.29	24.31	26.23	22.15
15	13.82	27.60	30.88	25.53	40.57	45.21	37.98
30	26.28	43.95	49.72	40.82	68.22	71.4	65.43
45	36.71	65.21	70.54	60.48	77.69	82.70	75.16
60	45.88	85.26	87.88	83.49	90.51	95.89	89.23

Pre-Compression Parameters

All formulation blends were evaluated to Pre compression parameters such as angle of repose, bulk density tapped density, compressibility index, Hausner's ratio. Angle of repose values of all formulations blend was found in the range of 23.14 to 25.67 it indicates free flowing of powder blend. The Carr s index values were found in between 12.23 to 15.60 indicates them having good compressibility. Hausner's ratio was present in the range of 1.11 to 1.25 that indicates good flow of powder blend. All Pre compression parameters were present within the limits whereas for F19 all the parameters were not found to be satisfactory (Table 13).

Table 13: Pre compression parameters.

Formulation Code	Bulk Density (mg/mL)	Tapped Density (mg/mL)	Compressibility Index (%)	Hausner's Ratio	Angle of Repose
F19	0.52	0.69	13.12	1.09	27.31
F20	0.44	0.58	14.71	1.25	25.23
F21	0.41	0.48	15.11	1.17	24.83
F22	0.45	0.52	15.6	1.15	25.67
F23	0.45	0.5	12.23	1.11	23.14

Post Compression Parameters

The post compression parameters were measured for tablet. Weight variation was in the range of 522.8 to 528.4mg for 525.00mg. Hardness of all formulation was found to be in the range of 4.3 to 4.9kg/cm2. Friability values were found to be 0.32 to 0.61. Drug content were found to in the range of 95.70 to 99.50. Thickness of IR layer was found between 5.52 to 5.57mm. Disintegration time for all formulation was found to be below 2 minutes except F19 (Table 14 & 15) (Figure 10).

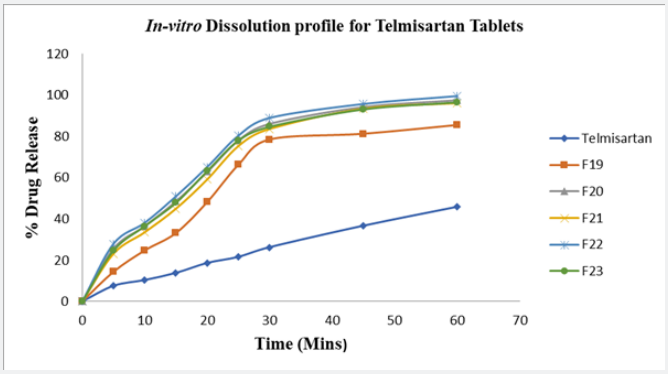

Figure 10: *In-vitro* drug release of Telmisartan Tablets.

Table 14: Evaluation parameters for tablets.

Formulation Code	Thickness (mm)	Hardness (kg/cm2)	Friability (%)	Weight Variation	Drug Content	Disintegration(sec)
F19	5.52	4.3	0.61	Pass	95.7	5 minute 59 seconds
F20	5.54	4.5	0.32	Pass	98.5	1 minute 18 seconds
F21	5.57	4.7	0.34	Pass	97.8	1 minute 22 seconds
F22	5.53	4.7	0.36	Pass	99.4	1 minute 09 seconds
F23	5.54	4.9	0.35	pass	97.4	1 minute 28 seconds

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Table 15: *In-vitro* drug release of Telmisartan tablets.

Time	Telmisartan	F19	F20	F21	F22	F23
0	00	00	00	00	00	00
5	7.54	14.35	25.68	23.16	27.95	24.68
10	10.35	24.69	36.54	33.54	38.11	36.47
15	13.82	33.13	48.61	44.97	50.92	47.85
20	18.64	48.16	62.84	59.16	65.17	63.24
25	21.57	66.27	78.19	75.38	80.38	78.11
30	26.28	78.49	86.22	83.65	88.95	84.72
45	36.71	81.24	94.38	93.46	95.71	93.18
60	45.88	85.48	97.66	96.13	99.53	96.57

The *in-vitro* release studies have shown that the % drug release values were within the range of 14.23% - 94.53% for fusion method, 18.57% - 95.89% for solvent evaporation method and 14.35% - 99.53% for tablets.

Conclusion

The present study was carried out to develop telmisartan immediate release tablets by direct compression method Telmisartan SDs in two methods namely fusion followed by solvent evaporation method respectively which tends to improve the solubility of telmisartan. Formulation characteristics were found to be satisfactory in all formulations shows acceptable internal specification for weight variation, thickness, hardness, friability, drug content, disintegration time and in vitro drug release. The fast drug release about 99.53% was found in the F22 formulation by solvent evaporation method SDs tablets in the ration of 1:2, drug content was found to be 99.53% and disintegration time was 1 minute 09 seconds and all parameters were found to be greater than all other formulations.

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