Formulation, Development and Evalution of Telmisartan Immediate Release of Tablet

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Abstract - The primary aim of this study was to develop and evaluate Telmisartan immediate-release tablets for effective hypertension management. Telmisartan, an angiotensin II receptor blocker, is commonly prescribed for hypertension, but its formulation into an immediate-release tablet requires optimization to ensure optimal bioavailability and therapeutic efficacy. Telmisartan immediate release tablets were formulated using various excipients and processing techniques. The formulation process included blending Telmisartan with different fillers, binders, and disintegrants to achieve the desired tablet characteristics. The tablets were then subjected to a range of evaluations including physical characteristics (hardness, friability, and weight variation), in vitro dissolution studies, testing. The dissolution profiles were compared with a commercially available reference product to assess the bioequivalence. The developed tablets demonstrated satisfactory physical properties, with appropriate hardness, low friability, and consistent weight variation. In vitro dissolution studies showed that the formulated tablets had a dissolution profile comparable to that of the reference product, meeting the required pharmacopoeial standards. The study successfully developed Telmisartan immediate-release tablets with desirable physical characteristics and a dissolution profile that supports their efficacy in managing hypertension. The formulation meets the required standards for pharmaceutical quality and has potential for clinical use, offering available alternative to existing products. Telmisartan, immediate release tablets, formulation development, in vitro dissolution, pharmaceutical evaluation.

Keywords: Telmisartan, immediate-release tablets, formulation development, in vitro dissolution, pharmaceutical evaluation.

1.INTRODUTION

The Oral route is one of the most sought-after routes for the systemic effect due to its ease of ingestion, simple, safest, convenient, non-invasive, versatility and most importantly, patient compliance. Solid oral delivery systems are cheaply manufactured because they don't require sterile conditions. Although, increased focus and interest generated in the area of controlled release and targeted drug delivery system in recent years, tablet dosage forms that are intended to be swallowed whole, disintegrate, and release their medicaments fast and furiously in the gastrointestinal tract. An ideal dosage regimen of drug therapy is the one, which immediately nab the desired therapeutic concentration of drug in plasma (or at the site of action) and maintains it constantly for the entire duration treatment. Of late, the scientists have focused their attention on the formulation immediately released tablet. The effort of developing a rapidly disintegrating tablet is accomplished by using suitable diluent s and super disintegrants.

1.1 CRITERIA FOR IMMEDIATE RELEASE DRUG DELIVERY SYSTEM

- Immediate release dosage form should in the case of solid dosage it should dissolve or disintegrate in the stomach within a short period.
- In the case of liquid dosage form it should be compatible with taste masking.
- Be portable without fragility concern.
- Have a pleasing mouth feel.
- It should not leave minimal or no residue in the mouth after oral administration.
- Exhibit low sensitivity to environmental condition as humidity and temperature.
- Be manufactured using conventional processing and packaging equipment at low cost.
- Rapid dissolution and absorption of drug, which may produce rapid onset of action.

2. MATERIALS& METHODS

Materials:

S.NO	Chemicals	Source
1	Telmisartan	Cipla Pvt. Ltd., Goa.
2	Sodium starch glycolate	Colorcon Asia Pvt. Ltd., Goa.
3	Polyplasdone xl	Colorcon Asia Pvt. Ltd., Goa
4	AC-DI-SOL:	Colorcon Asia Pvt. Ltd., Goa
5	Magnesium stearate	S.D. Fine Chem. Ltd.,Mumbai
6	Talc	S.D. Fine Chem. Ltd.,Mumbai
7	Mannitol	S.D. Fine Chem. Ltd.,Mumbai
8	Lactose	S.D. Fine Chem. Ltd.,Mumbai

Methodology:

2.1 Buffer Preparation:
Preparation of 0.2M Potassium dihydrogen orthophosphate solution: Accurately weighed 27.218 gm of monobasic potassium dihydrogen orthophosphate was dissolved in1000mL of distilled water and mixed.

Preparation of 0.2M sodium hydroxide solution:
Accurately weighed 8 gm sodium hydroxide pellets were dissolved 1000ml of distilled water and mixed.

Preparation of pH6.8 Phosphate buffer:
Accurately measured 250ml of 0.2M potassium. Dihydrogen orthophosphate and 112.5 ml 0.2M NaOH was taken into the 1000ml volumetric flask. Volume was made up to 1000ml with distilled water.

2.2 Pre formulation Studies:

Pre formulation involves the application of biopharmaceutical principles to the physicochemical parameters of drug substance are characterized with the goal of designing optimum drug delivery system.

2.3 Analytical method development for Telmisartan:
a) Determination of absorption maxima. A spectrum of the working standards was obtained by scanning from 200-400nm against the reagent blank to fix absorption maxima. The λ max was found to be 296 nm. Hence all further investigation was carried out at the same wavelength.

b) Preparation of Standard graph in pH 6.8 phosphate buffer 100 mg of Telmisartan was dissolved in 100 mL of pH 6.8 phosphate buffer to give a concentration in 1mg/Ml (1000µg/mL) 1 ml was taken and diluted to 100 ml with pH 6.8 phosphate buffer to give a concentration of 0.01 mg/ml (10µg/ml). From this stock solution aliquots of 0.5 ml, 1 ml, 1.5 ml, 2 ml, 2.5 ml, were pipette out in 10 ml volumetric flask and volume was made up to the mark with pH 6.8 phosphate buffer to produce concentration of 5,10, 15, 20 and 25µg/ml respectively. The absorbance of each concentration was measured at respective (λmax) i.e., 296 nm.

2.4 Formulation Development:
A) Drug and different concentrations for super Disintegrates and required ingredients were accurately weighed and passed through a 40-mesh screen to get uniform size particles and mixed in a glass mortar for 15 minutes.

B) The obtained blend was lubricated with Magnesium stearate and glidant (Talc) was added and mixing was continued for further 5 minutes.

C) The resultant mixture was directly compressed into tablets by using puch of rotary tablet compression machine. Compression force was kept constant for all formulations.

INGREDIENTS (MG)	FORMULATIONS								
	T1	T2	T3	T4	T5	T6	T7	T8	T9
Telmisartan	20	20	20	20	20	20	20	20	20
Sodium starch glycolate	20	40	60	-	-	-	-	-	-
Polyplasdone XL10	-	-	-	20	40	60	-	-	-
Ac- Di- Sol	-	-	-	-	-	-	20	40	60
Talc	5	5	5	5	5	5	5	5	5
Mg.stearate	4	4	4	4	4	4	4	4	4
Mannitol	15	15	15	15	15	15	15	15	15
Lactose	136	116	96	136	116	96	136	116	96
Total weight (mg)	200	200	200	200	200	200	200	200	200

Table 1: Formulation of Immediate Release tablets
Total weight of tablets = 200mg

2.5 Evaluation parameters:
Pre compression parameters:
Measurement of Micromeritic Properties of Powders
1. Angle of repose
The angle of repose of API powder is determined by the funnel method. The accurately weight powder blend are taken in the funnel. The height of the funnel is adjusted in way that, the tip of the funnel just touched the apex of the powder blend. The powder blend is allowed to flow through the funnel freely on the surface. The diameter of the powder cone is measured and angle of repose is calculated using the following equation.
$\tan \theta = h/r$ ……..(1)
where, h and r are the height and redius of the powder cone.

Flow Property	Angle of Repose (^{0})
Excellent	25-30
Good	31-35
Fair- aid not needed	36-40
Passable-may hang up	41-45
Poor-must agitate, Vibrate	46-55
Very Poor	56-65
Very, very Poor	>66

Table 2 : Flow Properties and Corresponding Angle of Repose Referencing style

Bulk density
The powder sample under test is screened through sieve No.18 and the sample equivalent to 25 gm is weighed and filled in a 100 ml graduated cylinder and the power is leveled and the unsettled volume, Vo is noted. The bulk density is calculated in g/cm3 by the formula.
Bulk density = M/V0 …… (2)
M= Powder mass
V 0= apparent unstirred volume

1. Tapped density
The powder sample under test is screened through sieve No.18 and the weight of the sample equivalent to 25 gm filled in 100 ml granulated cylinder. The mechanical tapping of cylinder is carried out using tapped density tester at a nominal rate for 500 times initially and the tapped volume V0 is noted. Tappings are proceeded further for an additional tapping 750 times and tapped volume, Vb is noted. The difference between two tapping volume is less than 2%, Vb is considered as a tapped volume Vf . the tapped density is calculated in g/cm3 by the formula.
Tapped density=M/Vf ……..(3)
M= weight of sample power taken
V f= Tapped volume

4. Compressibility Index
The Compressibility Index of the power blend is determined by Carr's compressibility index to know

the flow character of a powder. The formula for Carr's Index is an below:

Carr's Index (%)=[(TD-BD)/TD]x100 ……..(4)

5. Hauser's ratio

The Hauser's ratio is a number that is correlated to the flowability of a powder or granular material. The ratio of tapped density to bulk density of the powders is called the Hauser's ratio. It is calculated by the following equation.

H=ρT / ρB ……(5)

Where ρT= tapped density, ρB = bulk density

Compressibility Index (%)	Flow Character	Hausner Ratio
≤ 10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16 20	Fair	1.19 1.25
21-25	Passable	1 26-1 34
26-31	Poor	1.35-1.45
32-37	Very Poor	1.46-1.59
-> 38	Very, very Poor	-> 1.60

Table 3 : Scale of Flowability

Post compression parameters:

a) Thickness

The thickness of tablets was determined by using Digital micrometer. Ten individual tablets from each batch were used and the results averaged.

b) Weight variation

Twenty tablets randomly selected from each batch and individually weighed. The average weight and standard deviation three batches were calculated. It passes the test weight variation test if not more than two of the individual tablets weights deviate from the average

weight by more than the allowed percentage deviation and more deviate by more than twice the percentage shown. It was calculated on an electronic weighing balance.

c) Friability

The friability values of the tablets were determined using a Rochetype friabilator. Accurately weighed six tablets were placed in Roche friabilator and rotated at 25rpm for 4 min. Percentage friability was calculated using the following equation.

Friability = ([w0-w] / w0) x 100

d) Assay

The content of drug was carried out by five randomly selected tablets of each formulation. The five tablets were grinded in mortar to get powder; this powder was dissolved in pH 6.8 phosphate buffer by sonication for 30 min and filtered through filter paper. The drug content was analyzed spectrophotometrically at 296nm using UV spectrophotometer. Each measurement was carried out in triplicate and the average drug content was calculated.

e) Disintegration test

Six tablets were taken randomly from each batch and placed in USP disintegration apparatus baskets. Apparatus was run for 10 minutes and the basket was lift from the fluid, observe whether all of the tablets have disintegrated.

f) Dissolution test of Telmisartan tablets

Drug release from Telmisartan tablets was determined by using dissolution test United States Pharmacopoeia (USP) 24 type II (paddle). The parameters used for performing the dissolution were pH 6.8 Phosphate Buffer as the dissolution medium of quantity

900ml. the whole study is being carried out at a temperature of 37°C and at speed of 50 rpm.5 ml aliquots of dissolution media were withdrawn each time at suitable time intervals (5, 10, 15, 20, 25 and 30 minutes) and replaced with fresh medium. After withdrawing, samples were filtered and analyzed after appropriate dilution by UV Spectrophotometer. The concentration was calculated using standard calibration curve.

Drug-Excipients compatibility studies: Drug Excipients compatibility studies were carried out by mixing the drug with various excipients in different proportions.

RESULTS AND DISCUSSION

Determination of λ max:

The prepared stock solution was scanned between 200-400 nm to determine the absorption maxima. It was found to be 296nm.

Calibration curve of Telmisartan

the standard curve of Telmisartan was obtained and good correlation was obtained with value of 0.999 the medium selected was pH 6.8 phosphate buffer.

Concentration (µg/ml)	Absorbance
0	0
5	0.112
10	0.215
15	0.322
20	0.433
25	0.538

Table 4: Standard graph values of Telmisartan at 296 nm in pH 6.8 phosphate buffer

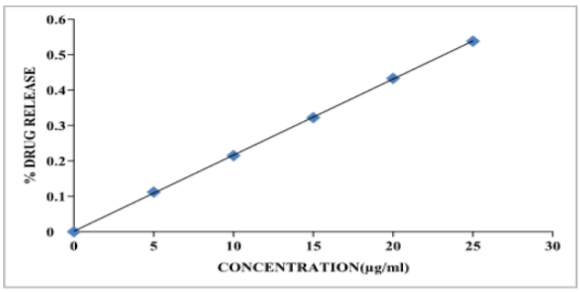

Fig 1: Standard curve of Telmisartan

Evaluation:

Characterization of precompression blend:

The precompression blend of Telmisartan was characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio. Angle of repose was less than 29.9˚, Carr's index values were less than 27.75 for the precompression blend of all the batches indicating good to fair flowability and compressibility. Hausner's ratio was less than 1.43 for all batches indicating good flow properties.

Physical properties:

Table 5 : Physical properties of precompression blend

Formulation code	Angleofrepose (Θ)	Bulk density (gm/cm 3)	Tapped Density (gm/cm 3)	Carr's index (%)	Hausner's ratio
T1	25.8 0	25.8 0	25.8 0	25.8 0	25.8 0
T2	27.5 0	27.5 0	27.5 0	27.5 0	27.5 0
T3	29.5 0	29.5 0	29.5 0	29.5 0	29.5 0
T4	29.7 0	29.7 0	29.7 0	29.7 0	29.7 0
T5	29.9 0	29.9 0	29.9 0	29.9 0	29.9 0
T6	26.8 0	26.8 0	26.8 0	26.8 0	26.8 0
T7	27.3 0	27.3 0	27.3 0	27.3 0	27.3 0
T8	28.4 0	28.4 0	28.4 0	28.4 0	28.4 0
T9	29.6 0	29.6 0	29.6 0	29.6 0	29.6 0

All the values represent n=3

Evaluation of tablets:

Physical evaluation of Telmisartan Immediate release tablets:

The results of the weight variation, Hardness, Thickness, Friability, and Drug content of tablets are given in table 8.3. All the tablets of different batches complied with the official requirement of weight variation as their weight variation passes the limit. The hardness of the tablets ranged from 3.15 – 3.95 kg/cm 2 and the friability values were < than 0.69 % indicating that the tablets were compact and hard. The thickness of the tablets ranged from 3.11 – 3.98. All the formulations satisfied the content of the drug as they contained 96.12-99.35 % of Telmisartan and good uniformity in drug content was observed. Thus all physical attributes of the prepared tablets were found to be practically within control limits.

Table 8.3: Evaluation of Telmisartan Immediate release tablets

Formulation code	Weight variation (mg)	Thickness (mm)	Hardness (Kg/cm²)	Friability (%)	Content uniformity (%)	*In Vitro* Disintegration time (seconds)
T1	199.92	3.96	3.68	0.23	96.34	61
T2	200.01	3.62	3.95	0.41	98.15	53
T3	199.34	3.85	3.27	0.40	99.56	35
T4	200.12	3.71	3.15	0.51	99.34	69
T5	198.67	3.11	3.78	0.49	98.25	57
T6	197.32	3.98	3.89	0.32	97.69	50
T7	200.01	3.76	3.52			
T8	200.25	3.69	3.17			
T9	196.81	3.57	3.28			

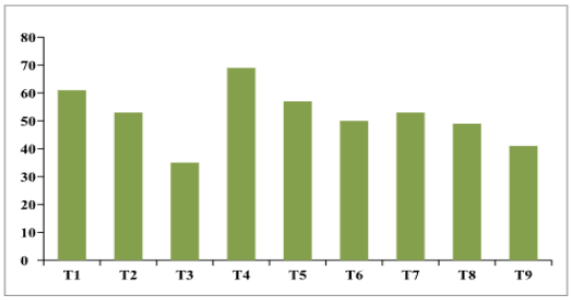

Figure 2: In vitro dissolution time graph

In vitro Dissolution: The drug release rate from tablets was studied using the USP type II dissolution test apparatus. The dissolution medium was 900 ml of pH 6.8 phosphate buffer at 50 rpm at a temperature of 37±0.5 ˚C. Samples of 5 ml were collected at different time intervals up to 30min and has analyzed after appropriate dilution by using UV spectrophotometer at 296nm.

Table 6: In vitro data for disintegration formulation T1

TIME (Minutes)	*IN VITRO* DRUG RELEASE								
	T1	T2	T3	T4	T5	T6	T7	T8	T9
0	0	0	0	0	0	0	0	0	0
5	55.75	60.20	63.96	52.42	58.71	61.58	57.99	64.14	67.73
10	62.18	73.71	77.14	60.95	62.96	65.74	60.57	72.61	79.92
15	70.62	76.17	80.27	67.15	70.35	74.93	65.52	76.39	82.70
20	86.10	89.92	90.58	76.50	78.82	86.46	71.78	82.27	87.21
25	87.73	90.80	92.16	81.89	85.96	90.33	76.44	87.98	91.64
30	93.14	95.42	99.10	86.32	91.28	94.92	89.12	92.71	95.83

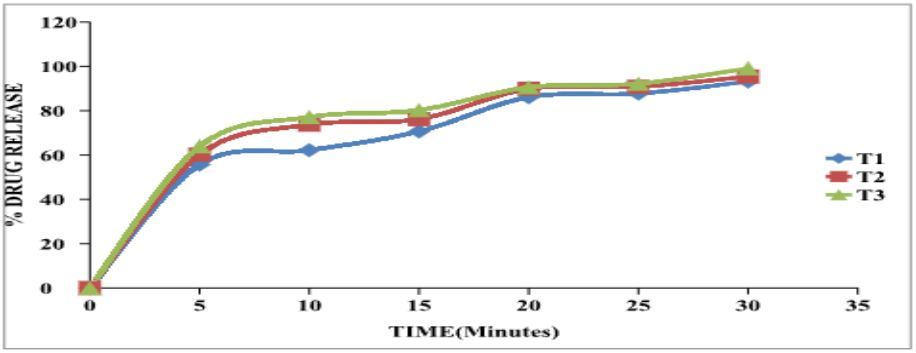

Fig 8.3: *In vitro* dissolution data for formulation T1-T3

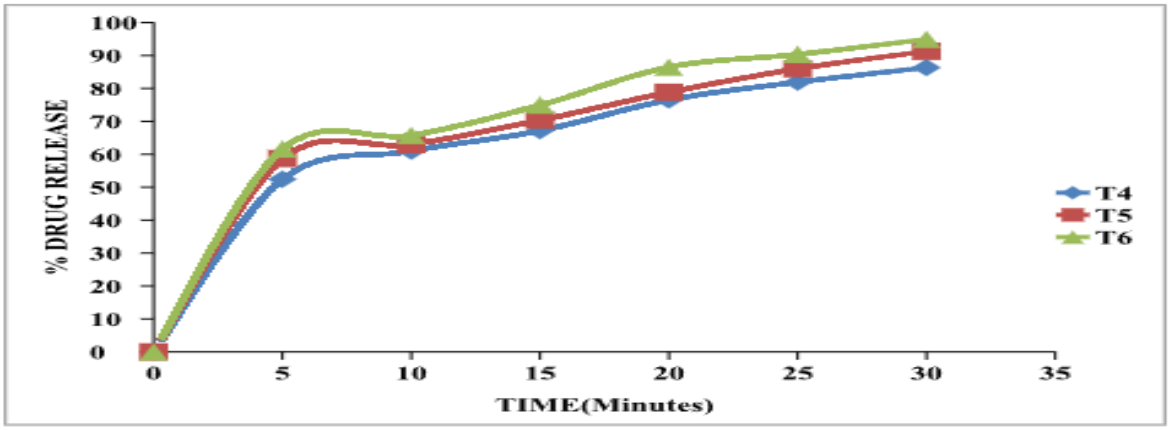

Fig 8.4: *In vitro* dissolution data for formulations T4-T6

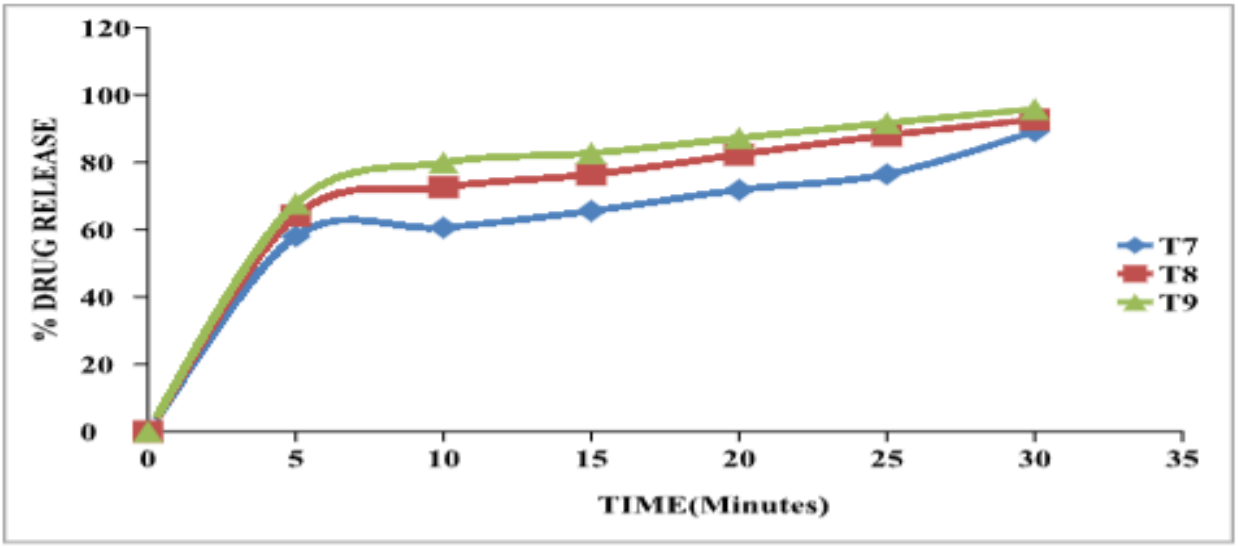

Figure 8.5: *In vitro* dissolution data for formulations T7-T9

From the table it was evident that the formulation prepared with Sodium starch glycolate were showed good drug release i.e., T3 formulation (99.10 %) in higher concentration of blend i.e 60 mg. Formulations prepared with Polyplasdone XL10 showed good drug release i.e., 94.92 % (T6 formulation) in 60 mg concentration. When increase in the concentration of PolyplasdoneXL10 drug able to retarded. Formulations prepared with Ac- Di- Sol showed maximum drug release i.e., 95.83 % (T9 formulation) at 30 min in 60mg of blend. Among all formulations T3 considered as optimised formulation which showed maximum drug release at 30 min i.e., 99.10 %. Finally concluded that T3 formulation contains Sodium starch glycolate was optimized formulation.

Drug-Excipient compatibility studies by FTIR studies:

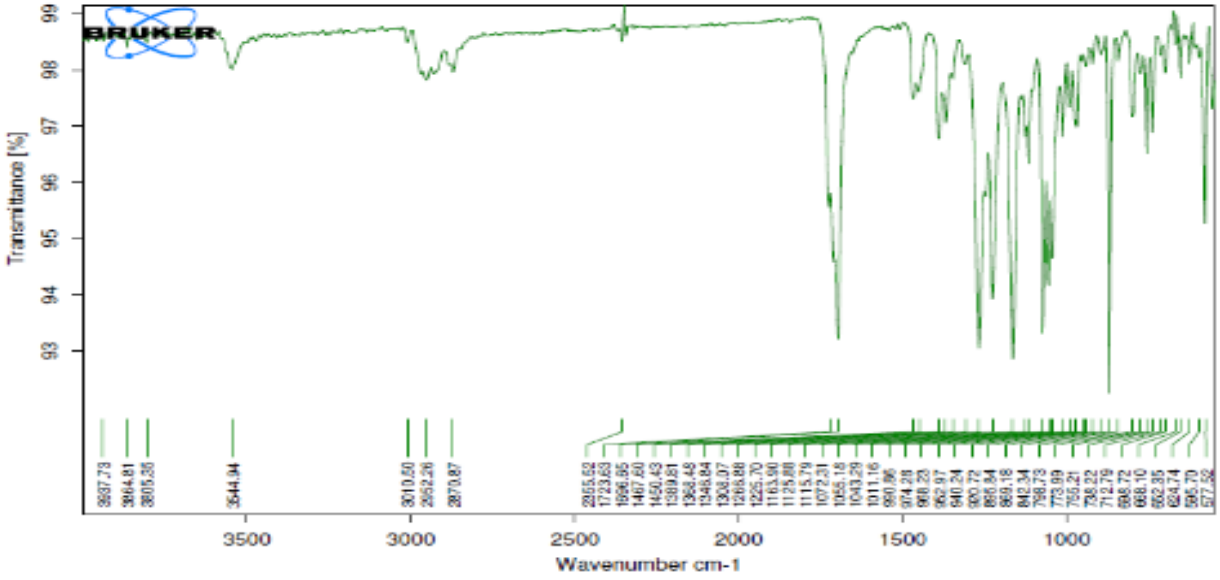

Fig 8.6: FTIR spectra of pure drug

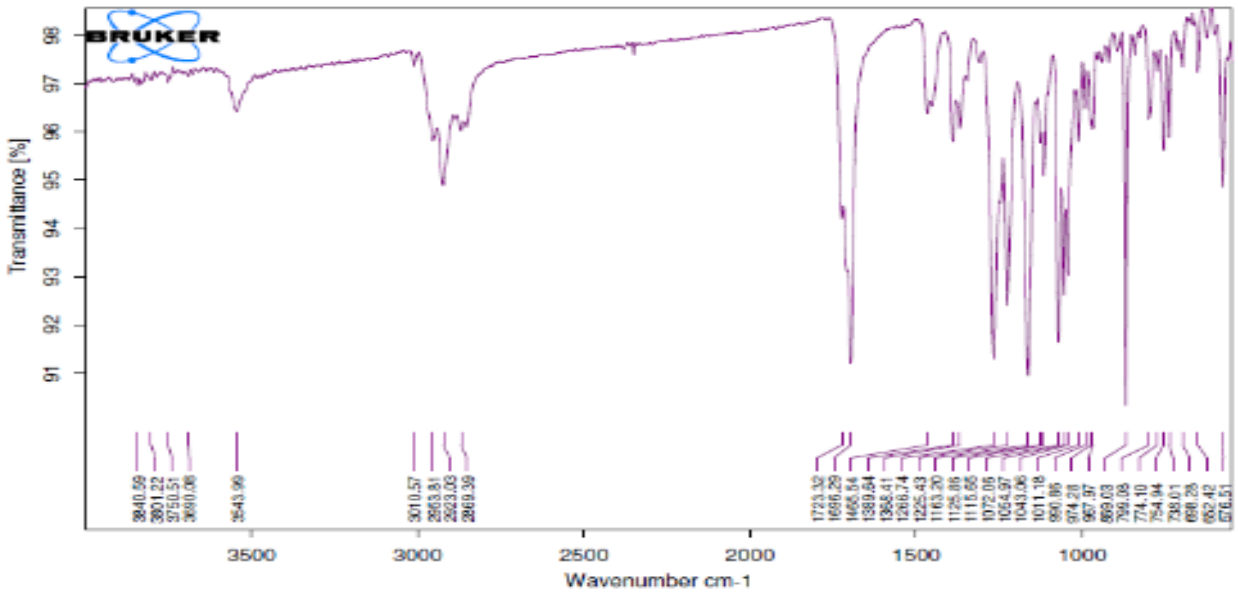

Fig 8.7: FTIR spectra of optimized formulation

Telmisartan was mixed with various proportions of excipients showed no colour change at the end of two months, providing no drug –excipient interactions.

CONCLUSION

The formulation development and evaluation of Telmisartan immediate-release tablets have successfully met the desired objectives, demonstrating that the optimized formulation can effectively deliver the drug with the necessary therapeutic efficacy. Through a series of rigorous tests and evaluations, the formulation was confirmed to possess desirable characteristics, including adequate drug release profiles, suitable tablet hardness, and acceptable dissolution rates. The immediate-release tablets of Telmisartan developed in this study meet the required quality standards, showing robust performance in In vitro tests. The formulation was found to be stable under various conditions, and the drug release profile aligns well with the pharmacokinetic requirements for effective hypertension management.

The successful development of this formulation underscores the effectiveness of the chosen excipients and manufacturing processes. It also suggests that the immediate-release tablets can offer a reliable and efficient treatment option for patients, ensuring optimal therapeutic outcomes.

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