WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 6.647
Volume 6, Issue 11, 659-673 Research Article ISSN 2278 – 4357

FORMULATION DEVELOPMENT AND EVALAUATION OF IMMEDIATE RELEASE TABLETS OF TELMISARTAN

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Article Received on
11 Sep. 2017,
Revised on 01 October 2017,
Accepted on 22 October 2017
DOI: 10.20959/wjpps201711-10444

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ABSTRACT

In the present research work, Telmisartan Immediate release tablets were prepared by using Super disintegrants like crosscarmellose sodium, crospovidone and sodium starch glycolate in different concentrations by direct compression method. Telmisartan Immediate release tablets prepared were evaluated for pre-compression and post-compression parameters. The pre-compression parameters evaluated are bulk density, true density, angle of repose and percentage porosity where the angle of repose of all the formulations is below 30º indicating free flowing. Post-compression parameters like hardness, weight variation, percent friability, In vitro dispersion, drug content uniformity and In-vitro drug release studies were carried out for all the formulations. Hardness of the tablet of every batch was in the range of 2.8 to 4.0 kg/cm^2.Friability of all the tablets was less than 1%. Weight variation test results of every batch showed that the weight of each tablet of the batch tested was within the range ±7.5%. All the tablets formulated using crosscarmellose sodium, crospovidone and sodium starch glycolate disintegrated within 3 minutes fulfilling the official limits of the Immediate release tablets. Drug content uniformity study results showed that the drug Telmisartan was uniformly distributed throughout the formulation of every batch. All the formulations given the result within the official limits. Formulation F2 in which Crospovidone (60mg) used, shows less disintegration time i.e. 35 seconds and highest Dissolution rate 99.9% release in 35 minutes which is considered as Best Formulation amongall.

KEYWORDS: Telmisartan, Immediate release tablets, Direct compression method, pre-compression and post-compression parameters.

1. INTRODUCTION

The term "immediate release" pharmaceutical formulation includes any formulation in which the rate of release of drug from the formulation and or the absorption of drug, is neither appreciably, nor intentionally, retarded by galenic manipulations. In the present case, immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluent or carrier, which diluent or carrier does not prolong, to an appreciable extent, the rate of drug release and/or absorption. Thus, the term excludes formulations which are adapted to provide for "modified", "controlled", "sustained", "prolonged", "extended" or "delayed" release of drug.[1-4]

In this context, the term "release" includes the provision (or presentation) of drug from the formulation to the gastrointestinal tract, to body tissues and/or into systemic circulation. For gastrointestinal tract release, the release is under pH conditions such as pH=1 to 3, especially at, or about, pH=1. In one aspect of the invention a formulation as described herein with a compound of formula (I), or an acid addition salt thereof, in crystalline form releases drug under a range of pH conditions. In another aspect of the invention a formulation as described herein with a compound of formula (I), or an acid addition salt thereof, releases drug under pH conditions such as pH=1 to 3, especially at, or about, pH=1. Thus, formulations of the invention may release at least 70% (preferably 80%) of active ingredient within 4 hours, such as within 3 hours, preferably 2 hours, more preferably within 1.5 hours, and especially within an hour (such as within 30 minutes), of administration, whether this be oral or parenteral.[5-8]

Desired criteria for immediate release drug delivery system[9-12]

In the case of solid dosage it should dissolve or disintegrate in the stomach within a short period.

1. In the case of liquid dosage form it should be compatible with taste masking.
2. Be portable without fragility concern.
3. Have a pleasing mouth feel.
4. It should not leave minimal or no residue in the mouth after oral administration.
5. Exhibit low sensivity to environmental condition as humidity and temperature.
6. Be manufactured using conventional processing and packaging equipment at low cost.
7. Rapid dissolution and absorption of drug, which may produce rapid onset of action.

Conventional techniques used in the preparation of immediate release tablets[10-14]

* Tablet molding technique.
* Direct compression technique.
* Wet granulation technique.
* Mass extrusion technique.

2. MATERIALS AND METHODS USED

2.1. MATERIALS USED

Telmisartan, Magnesium stearate, Micro crystalline cellulose, Cross carmellose sodium, Crospovidone, Sodium starch glycolate, Lactose, Talc.

2.2. METHODS USED

Preparation of Calibration Curve of Telmisartan in 0.1N HCl

Procedure: 100 mg of Telmisartan was accurately weighed and dissolved in 20ml of alcoholinto a 100ml volumetric flask and finally the volume was adjust to 100ml with 0.1N HCl (1000 µg/ml).

The standard solution of Telmisartan was subsequently diluted with 0.1N HCl to obtain a series of dilutions containing 2, 4, 6, 8, 10 µg/ml. The absorbance of the above dilutions was measured on a spectrophotometer at 296nm using 0.1 N HCl as the blank.

Preparation of Telmisartan immediate release tablets

Telmisartan immediate release tablets F_1 to F_6 Were prepared by direct compression method and the detailed composition was given in table.

METHOD

- All the ingredients were passed through 60 mesh sieve separately.
- Then drug and diluents separately taking small portions of both each time and blending it thoroughly to get uniform mixture.
- The powder were compressed using 11mm size to get a tablet of 300 mg tablet weight using single punch tablet compression machine.
- A batch of 12 tablets were prepared for each batch of the designed formulation.

3. RESULTS

Table 1: composition for Telmisartan Immediate release tablets prepared by direct compression method.

Ingredients(mg)	F1	F2	F3	F4	F5	F6
Telmisartan	80	80	80	80	80	80
Crospovidone	50	60	-	-	-	-
Croscarmellosesodium	-	-	50	60	-	-
Sodium starch glycolate	-	-	-	-	50	60
Micro crystalline cellulose	90	80	90	80	90	80
Lactose	70	70	70	70	70	70
Talc	05	05	05	05	05	05
Magnesium stearate	05	05	05	05	05	05
Total	300	300	300	300	300	300

Table 2: Standard curve of Telmisartan pH 0.1N HCl at λmax 296nm.

Concentration (µg/mL)	Absorbance
0	0
2	0.127
4	0.242
6	0.342
8	0.464
10	0.576
12	0.656
14	0.779

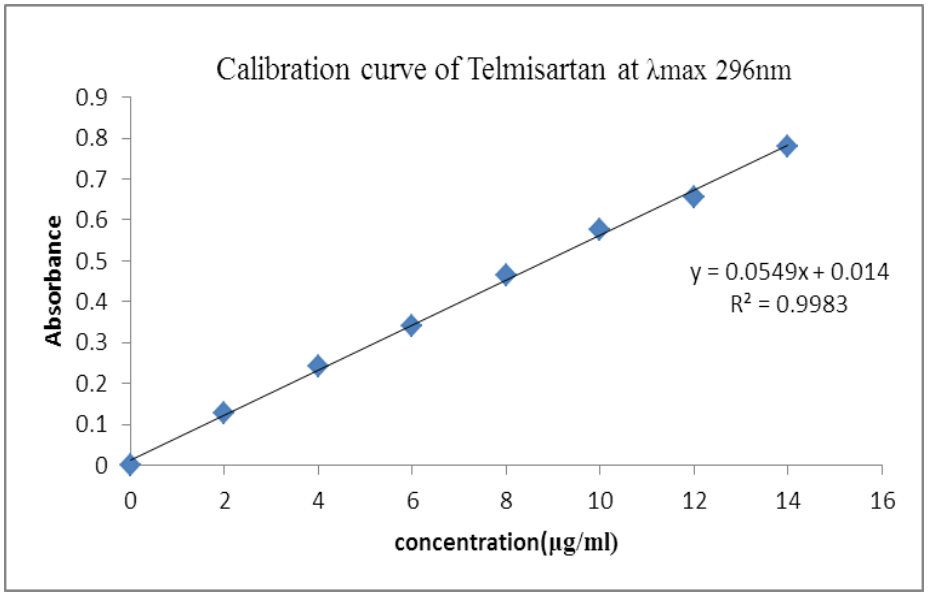

Fig No 1: standard curve of Telmisartan in pH 0.1N HCl.

Table 3: Powder Blend Parameters of Telmisartan Formulation.

Formulation code	Bulk density gm/cc	True density gm/cc	Angleofrepose (θ)=$\tan^{-1}$ h/r	%compressability index
F1	0.257	0.328	36.65	21.64
F2	0.272	0.343	35.4	20.69
F3	0.253	0.324	37.25	21.91
F4	0.267	0.338	36.81	21
F5	0.256	0.322	36	20.4
F6	0.270	0.342	36.21	21.05

Table 4: Hardness test for Telmisartan Formulations.

Formulation code	Hardness in* kg/cm^2
F1	3.22
F2	3.23
F3	3.34
F4	3.17
F5	2.9
F6	2.85

Table 5: Friability test for Telmisartan Formulations.

Formulation code	Friability (%)
F1	0.9
F2	0.5
F3	0.85
F4	0.65
F5	0.5
F6	0.63

Table 6: In vitro disintegration time for Telmisartan Formulation

Formulation code	Time in seconds
F1	40
F2	35
F3	48
F4	53
F5	70
F6	89

Table 7: Weight Variation OF Telmisartan Formulation.

Formulation code	Weight Variation (mg)
F1	300.9±1.774
F2	300±1.712
F3	300.7±2.291
F4	300.2±1.446
F5	299.9±1.943
F6	300±2.026

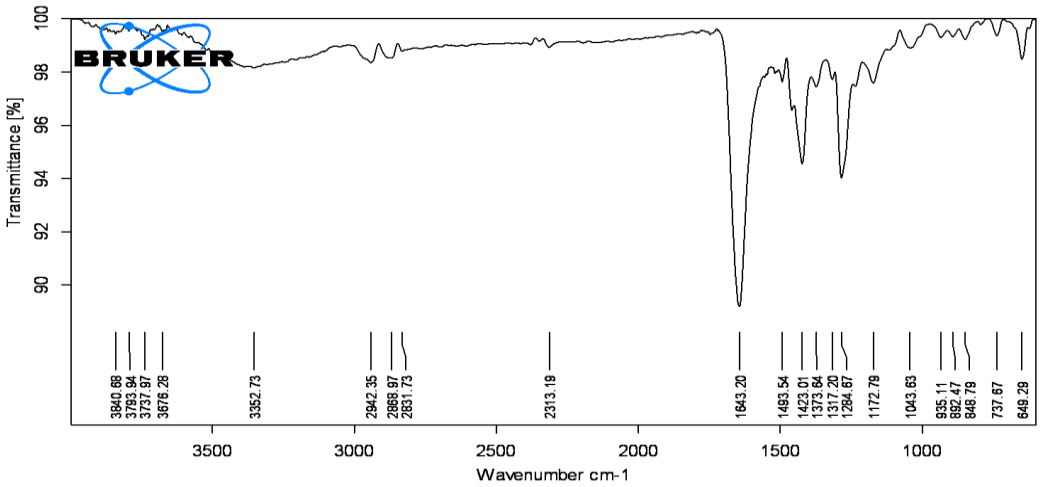

Fig no 2: IR Spectrum of Crospovidone.

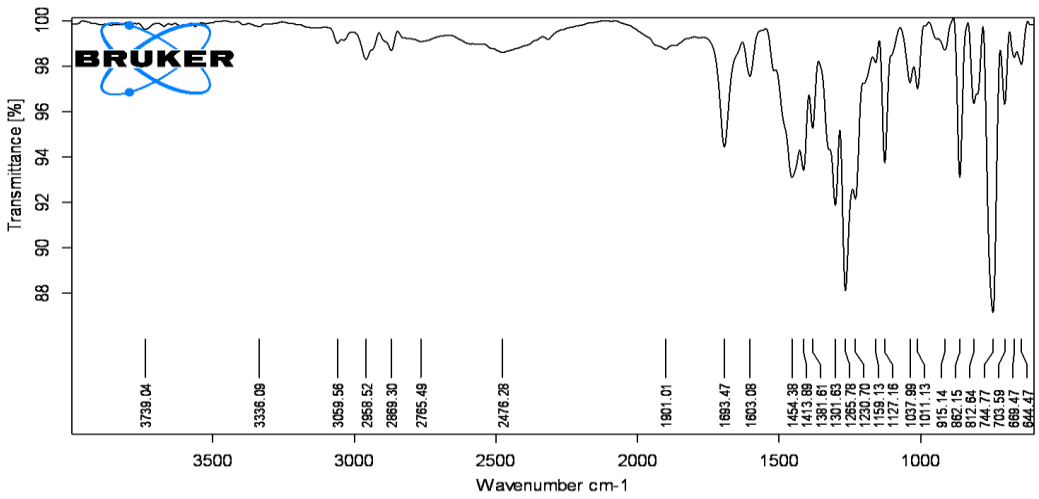

Fig no 3: IR Spectrum of Croscarmellose sodium.

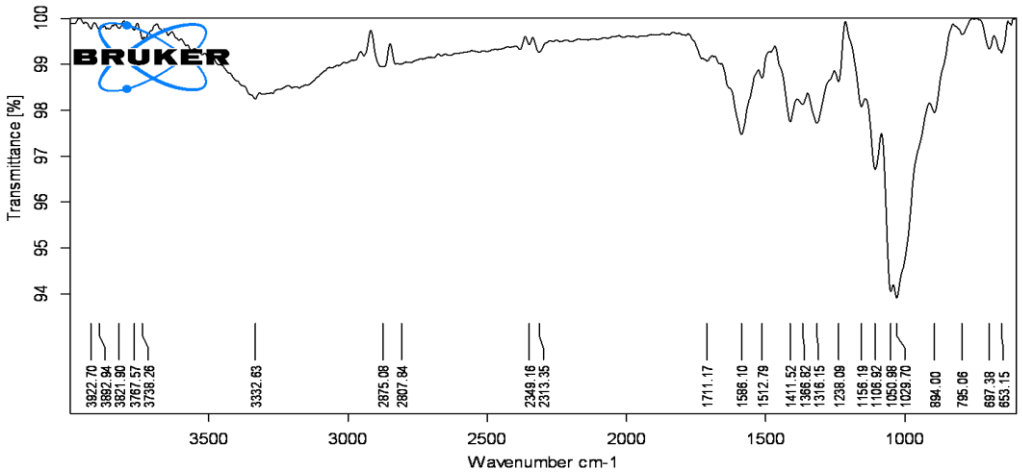

Fig no 4: IR Spectrum of Sodium starch glycolate.

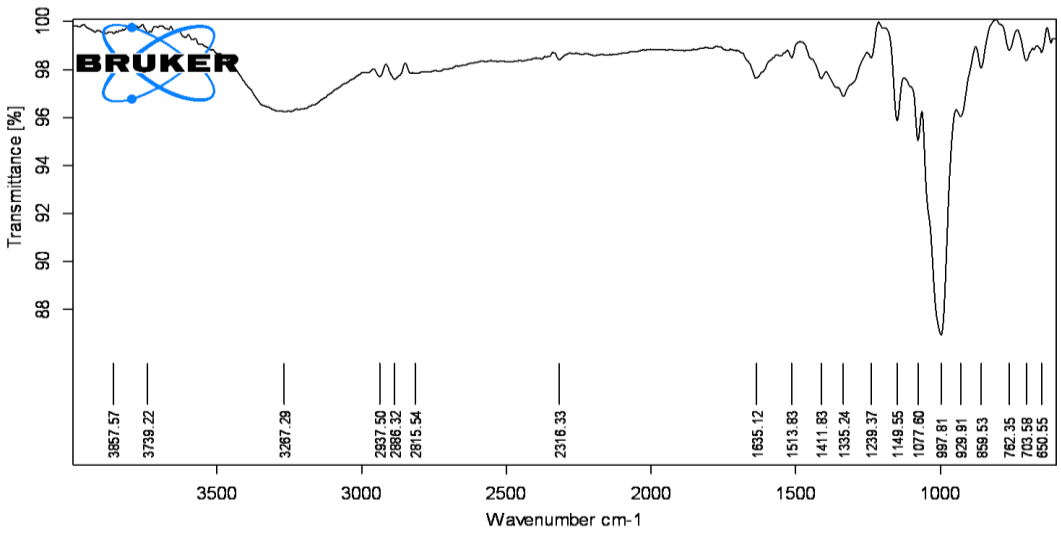

Fig no 5: IR Spectrum of pure drug.

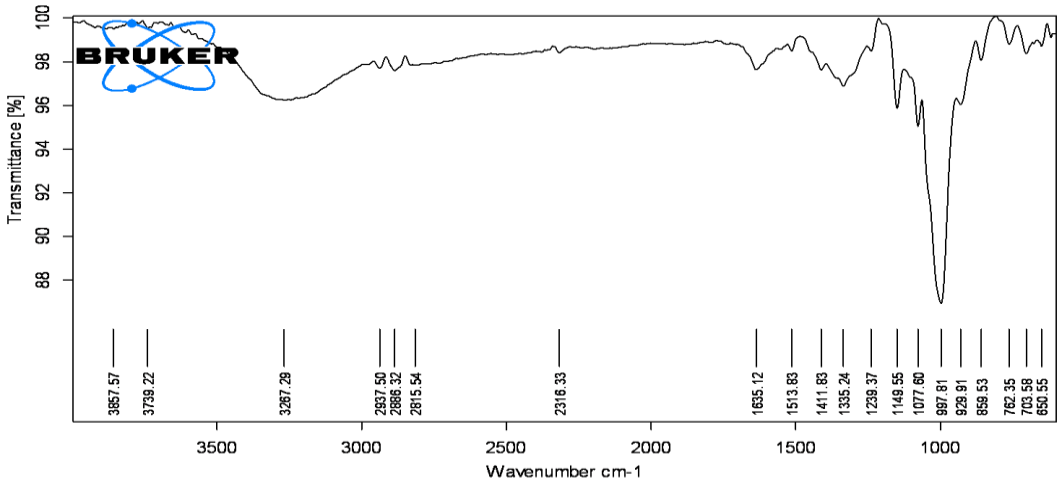

Fig no 6: IR Spectrum of optimized formulation.

Table 8: Drug content of Telmisartan Formulation.

Sr. no.	Formulation code	Absorbance	Concentration in mcg/ml	Average content
1	F1	1.202	19.9	99.5
2	F2	1.205	20	100.0
3	F3	1.173	19.4	97.0
4	F4	1.162	19.2	96.0
5	F5	1.209	20.06	99.3
6	F6	1.205	20	99.0

Table 9: In-vitro Drug Release of Telmisartan Immediate release Tablet F1.

Time in minutes	Absorbance	Concentration in mg	% drug release
5	0.150	5.4	27.0
10	0.221	7.95	39.78
15	0.272	9.79	48.95
20	0.335	12.02	60.12
25	0.405	14.58	72.90
30	0.455	16.38	81.9
35	0.510	18.36	91.8
40	0.525	18.9	94.5
45	0.539	19.40	97.02

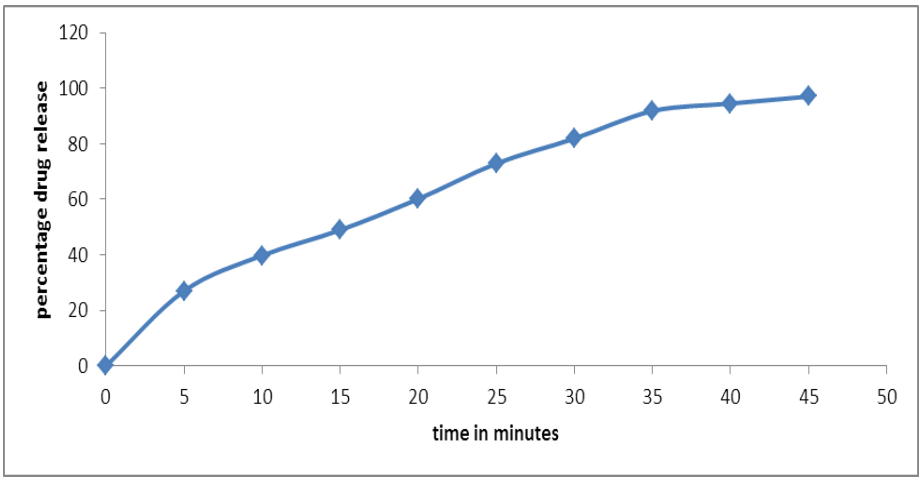

Fig no 7: In vitro Drug release of Telmisartan Immediate release tablets F1.

TABLE 10: In vitro Drug Release of Telmisartan Immediate release Tablet F2

Time in minutes	Absorbance	Concentration in mg	% Drug release
5	0.144	5.184	25.92
10	0.289	10.404	52.02
15	0.310	11.235	59.15
20	0.345	12.144	63.05
25	0.415	14.904	74.52
30	0.518	18.648	93.24
35	0.555	19.98	99.9

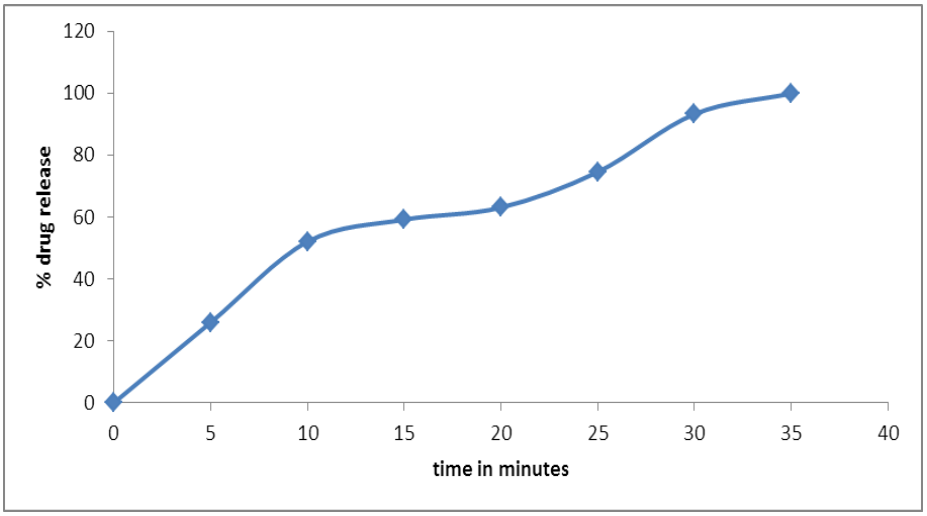

Fig no 8: In vitro Drug release of telmisartan Immediate release tablets F2.

Table 11: In vitro Drug Release of Telmisartan Immediate release Tablet F3.

Time in minutes	Absorbance	Concentration in mg	% Drug release
5	0.080	2.88	14.4
10	0.160	5.76	28.8
15	0.222	7.92	39.6
20	0.268	9.648	48.24
25	0.340	12.24	61.2
30	0.400	14.40	72
35	0.460	16.56	82.8
40	0.520	18.72	93.6
45	0.539	19.404	97.02

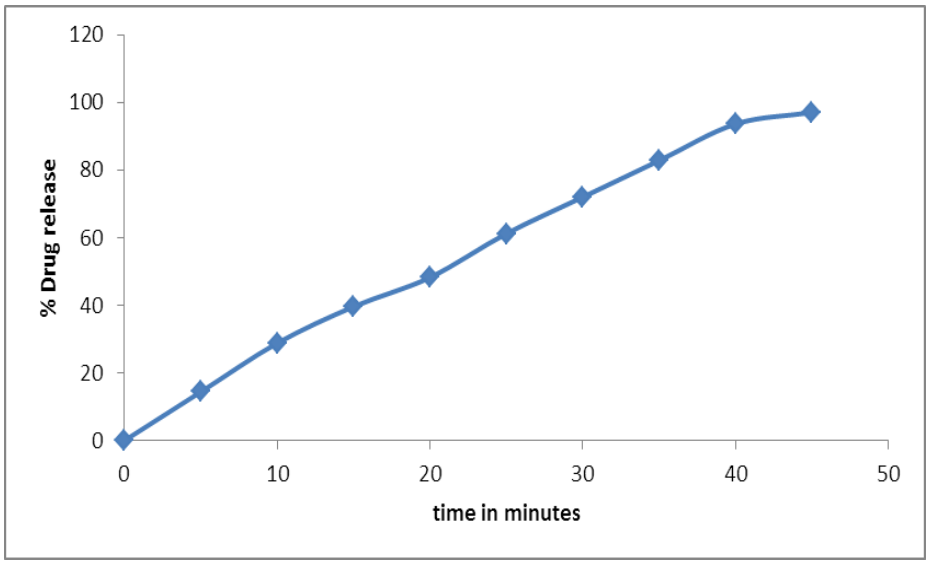

Fig no 9: In vitro Drug release of telmisartan Immediate release tablets F3.

Table 12: In vitro Drug Release of Telmisartan Immediate release Tablet F4.

Time in minutes	Absorbance	Concentration in mg	% Drug release
5	0.91	3.276	16.56
10	0.190	6.84	34.2
15	0.262	9.432	47.16
20	0.321	11.55	57.78
25	0.420	15.12	75.60
30	0.469	16.884	84.42
35	0.531	19.11	95.58
40	0.549	19.76	98.82
45	0.549	19.76	98.82

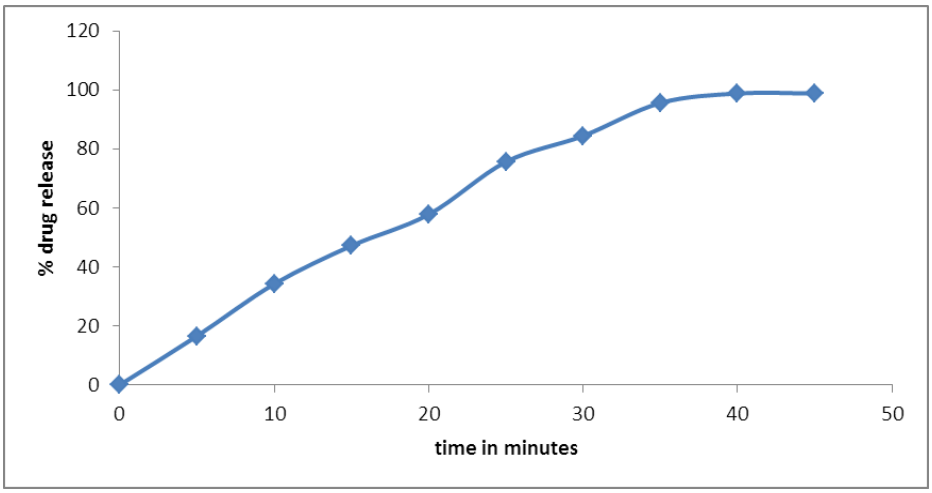

Fig no 10: In vitro Drug release of telmisartan Immediate release tablets F4.

Table 13: In vitro Drug Release of Telmisartan Immediate release Tablet F5.

Time in minutes	Absorbance	Concentration in mg	% Drug release
5	0.112	4.032	20.66
10	0.231	8.316	41.58
15	0.321	11.550	57.78
20	0.400	14.40	72.0
25	0.460	16.56	82.80
30	0.482	17.35	86.76
35	0.500	18.00	90.00
40	0.520	18.72	93.60
45	0.530	19.08	95.40

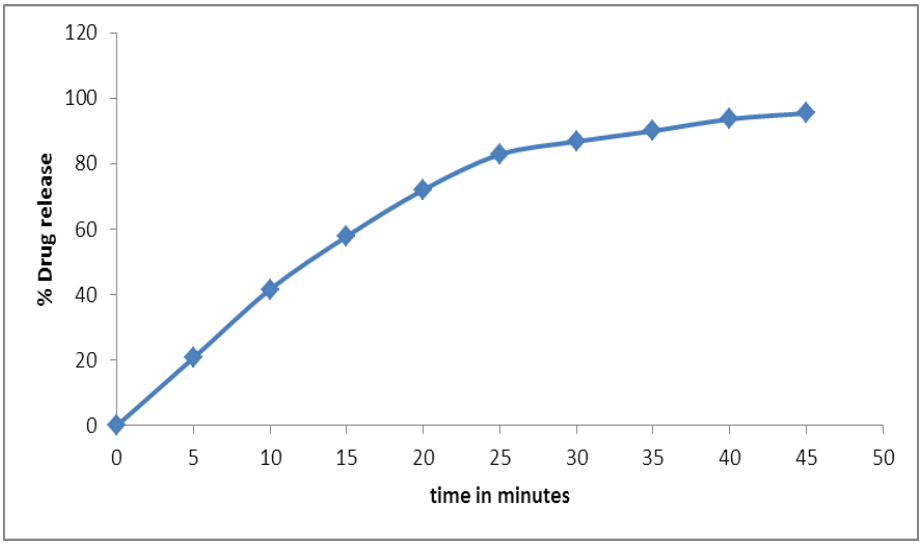

Fig no 11: In vitro Drug release of telmisartan Immediate release tablets F5.

Table 14: In vitro Drug Release of Telmisartan Immediate release Tablet F6.

Time in minutes	Absorbance	Concentration in mg	% Drug release
5	0.121	4.356	21.78
10	0.233	8.388	41.94
15	0.333	11.988	59.94
20	0.409	14.724	73.62
25	0.462	16.632	83.16
30	0.491	17.676	88.38
35	0.511	18.396	91.98
40	0.529	19.044	95.22
45	0.535	19.26	96.3

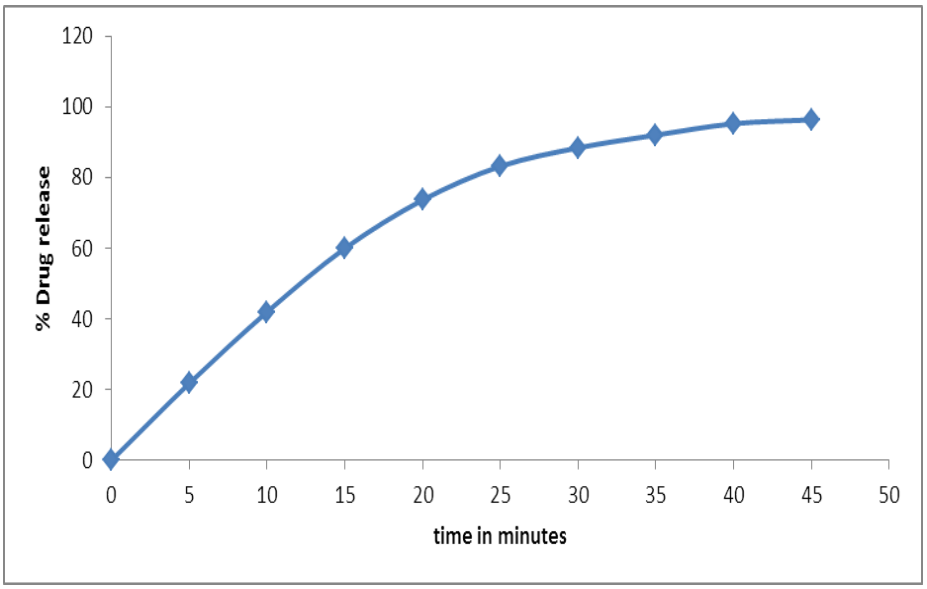

Fig no 12: In vitro Drug release of telmisartan Immediate release tablets F6.

Table 14: Comparative dissolution profiles for all formulations in 0.1N HCl as Dissolution media.

TIME IN MINUTES	% DRUG RELEASE F1	% DRUG RELEASE F2	%DRUG RELEASE F3	% DRUG RELEASE F4	% DRUG RELEASE F5	% DRUG RELEASE F6
5	27.0	25.92	14.4	16.56	20.66	21.78
10	39.78	52.02	28.8	34.2	41.58	41.94
15	48.95	59.15	39.6	47.16	57.78	59.94
20	60.12	63.05	48.24	57.78	72.0	73.62
25	72.90	74.52	61.2	75.60	82.80	83.16
30	81.9	93.24	72	84.42	86.76	88.38
35	91.8	99.9	82.8	95.58	90.00	91.98
40	94.5	99.9	93.6	98.82	93.60	95.22
45	97.02	99.9	97.02	98.82	95.40	96.3

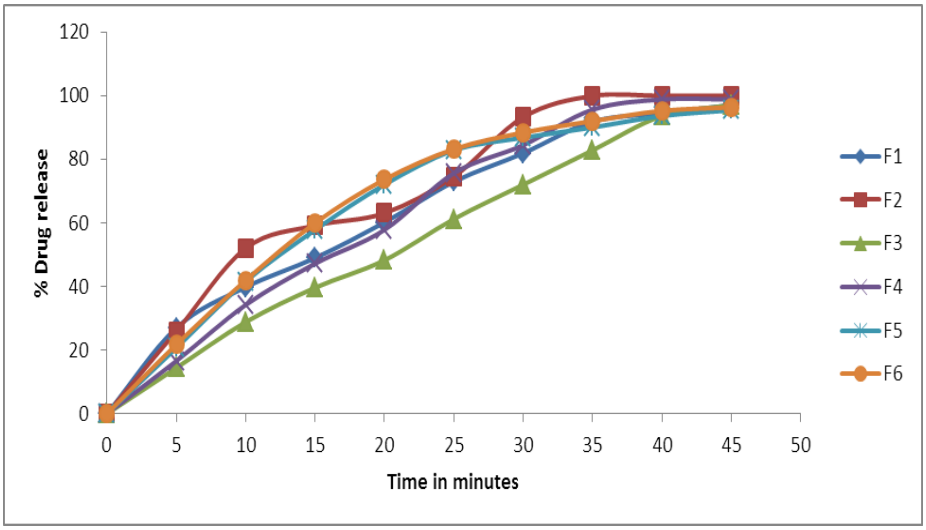

Fig. No.13: comparative dissolution profiles for all the formulations.

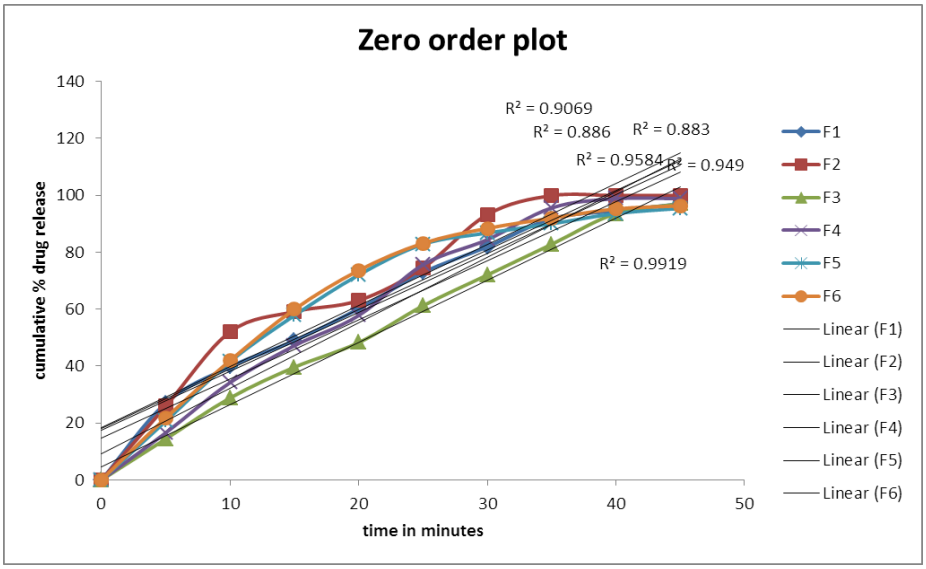

Fig. No.14: Zero order plot for the formulations F1-F6.

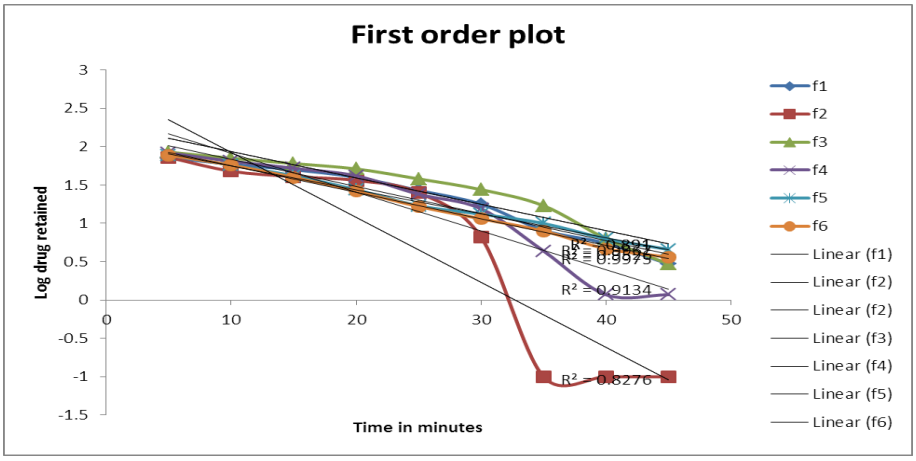

Fig. No.15: First order plot for the formulations F1-F6.

Table 15: R^2 values for zero order and first order plots for the formulations F1-F6.

Formulation code	Zero order(R^2)	First order(R^2)
F1	0.949	0.952
F2	0.906	0.827
F3	0.991	0.891
F4	0.958	0.913
F5	0.886	0.996
F6	0.883	0.997

4. SUMMARY AND CONCLUSION

4.1. SUMMARY

In some cases of Hypertension Quick onset of action is desired, the immediate release tablet plays a vital role. Immediate release tablets have many number of advantages over the conventional tablets like rapid disintegration, faster dissolution, ease of administration and quick onset of action etc.In the present research work, Telmisartan Immediate release tablets were prepared by using Super disintegrants like crosscarmellose sodium, crospovidone and sodium starch glycolate in different concentrations by direct compression method. Telmisartan Immediate release tablets prepared were evaluated for pre-compression and post-compression parameters. The pre-compression parameters evaluated are bulk density, true density, angle of repose and percentage porosity where the angle of repose of all the formulations is below 30º indicating free flowing. Post-compression parameters like hardness, weight variation, percent friability, In vitro dispersion, drug content uniformity and In-vitro drug release studies were carried out for all the formulations. Hardness of the tablet of every batch was in the range of 2.8 to 4.0 kg/cm^2. Friability of all the tablets was less than 1%.Weight variation test results of every batch showed that the weight of each tablet of the

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4.2. CONCLUSION

Formulation F2 in which Crospovidone (60mg) used, shows less disintegration time i.e. 35 seconds and highest Dissolution rate 99.9% release in 35 minutes which is considered as Best Formulation amongall.

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