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FORMULATION AND IN-VITRO EVALUATION OF FLOATING TABLETS OF TELMISARTAN

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ABSTRACT

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. Telmisartan antagonizes the effect of angiotensin II (vasoconstriction and aldosterone secretion) by blocking the angiotensin II (AT 1 receptor) in vascular smooth muscle and the adrenal gland, producing decreased BP. In the present investigation telmisartan floating tablets were prepared by using different grades of polymers such as Xanthum gum, Guar gum and Eudragit RSPO. Formulated tablets showed satisfactory results for various Post compression evaluation parameters like: tablet thickness, hardness, weight variation, floating lag time,total floating time, content uniformity and *in vitro* drug release. Formulation F8 containing Eudragit RSPO gave better in-vitro drug release and floating properties in comparison to the other formulations. The release pattern of the F8 formulation was best fitted to Korsmeyer-Peppasmodel and the release pattern from the formulation was non-Fickian diffusion or anomalous diffusion.

KEYWORDS: Telmisartan, floating drug delivery, non-Fickian diffusion.

1. INTRODUCTION

Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, low cost of therapy, patient compliance and flexibility in formulation etc.

Oral sustained drug delivery formulations show some limitations connected with the gastric emptying time. Variable and too rapid gastrointestinal transit could result in incomplete drug release from the device into the absorption window leading to diminished efficacy of the administered dose. It is evident from the recent research and patent literature that an increased interest in novel dosage forms that are retained in the stomach for a prolonged and predictable period of time exists today.

Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. One of such difficulties is the ability to confine the dosage form in the desired area of the gastrointestinal tract. To overcome this physiological problem, several drug delivery systems with prolonged gastric retention time have been investigated. Attempts are being made to develop a controlled drug delivery system that can provide therapeutically effective plasma drug concentration levels for longer durations, thereby reducing the dosing frequency and minimizing fluctuations in plasma drug concentration at steady state by delivering drug in a controlled and reproducible manner Floating drug delivery system is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. This drug delivery system not only prolongs GI residence time but does so in an area of the GI tract that could maximize drug reaching its absorption site in solution and hence ready for absorption.

Telmisartan interferes with the binding of angiotensin II to the angiotensin II AT1 receptor by binding reversibly and selectively to the receptors in vascular smooth muscle and the adrenal gland as angiotensin II is a vasoconstrictor which also stimulates the synthesis and release of aldosterone. Telmisartan does not inhibit the angiotensin converting enzyme other hormone receptors,or ion channels. Telmisartan is a partial agonist of PPARy, which is estabilished target for antidaibetic drug and also antihypertensive drug

2. MATERIALS AND METHOD

2.1 FORMULATION OF FLOATING TABLETS OF TELMISARTAN

2.1.1 MATERIALS

Telmisartan, Xanthan gum, Guar gum, Eudragit RSPO, Microcrystalline cellulose, Sodium bicarbonate, Polyvinylpyrrolidone, Magnesium stearate, Talc were used to formulate floating tablets. All the reagents were used of analytical grades.

2.1.2 Formula

Table No 1: Formulation composition of Telmisartan floating tablets

Ingredients (mg)	Formulation Code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Telmisartan	40	40	40	40	40	40	40	40	40
Xanthan gum	40	60	80	-	-	-	-	-	-
Guar gum	-	-	-	40	60	80	-	-	-
Eudragit RSPO	-	-	-	-	-	-	40	60	80
Microcrystalline cellulose	233	213	193	233	213	193	233	213	193
Sodium bicarbonate	20	20	20	20	20	20	20	20	20
PVP K30	15	15	15	15	15	15	15	15	15
Magnesium stearate	1	1	1	1	1	1	1	1	1
Talc	1	1	1	1	1	1	1	1	1
Total Weight (mg)	350	350	350	350	350	350	350	350	350

2.1.3 Preperation method of floating tablets of telmisartan

The floating tablet of telmisartan was prepared by direct compression .In this process all ingredients are weighed accurately and co sifted by passing through #40 sieve. The blending of ingredients was carried out for 15 minutes .The powder was then lubricated with magnesium state and talc for additional 3 minutes prior to compression. The powder was then compressed into tablets

3. RESULT AND DISCUSSION

3.1 PREFORMULATION STUDY

3.1.1 Characterization of drugs: In the present study, an attempt was made to formulate floating tablets of telmisartan by using xanthun gum, guar gum and eudragit as polymers and. The characterization of drug was done by the UV, FTIR Spectroscopy, and Differential Scanning Calorimetry (DSC).

3.1.2 Description: Telmisartan: yellowish white to yellow powder.

3.1.3 Determination of melting point

Melting point obtained for Telmisartan is 261-266 ^{0} C. The reported melting point range for telmisartan is 266^{0}C. Hence, experimental values are in good agreement with official value.

3.1.4 UV-Visible Spectroscopic scanning- spectral analysis

Scanning of drug: The pure drug Telmisartan is scanned over a range 200-400 nm to determine its λ-max. The peak was observed at the 296 nm. Figure No.1 The obtained results conforms the identification of Telmisartan.

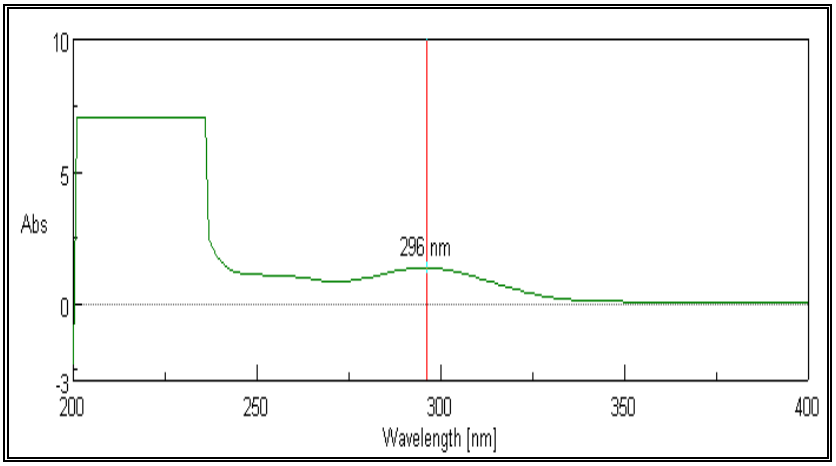

Figure No 1: Standard calibration curve of Telmisartan

Preparation of standard calibration curve of Telmisartan

The standard calibration curve of Telmisartan was obtained by plotting Absorbance V/s. Concentration. Table No.2 shows the absorbance values of Telmisartan. The standard curve is shown in Figure No. 2. The standard calibration curve shows the slope of 0.064 and correlation coefficient of 0.999. The curve was found to be linear in the concentration range of 5-30 mcg/ml (Beer's range) at 296 nm.

Table No 2: Standard calibration curve of Telmisartan

Concentration (mcg/ml)	Absorbance at 296 nm
0	0.00
2	0.132
4	0.253
6	0.384
8	0.513
10	0.643

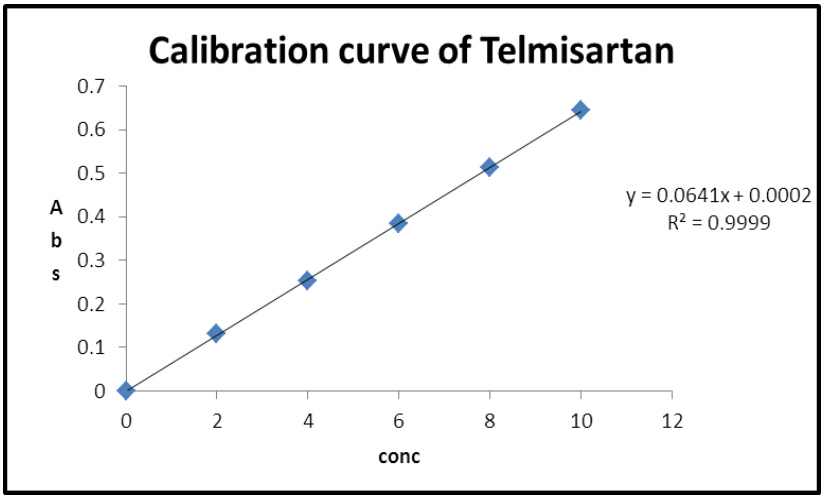

Figure No 2: Standard calibration curve of Telmisartan

3.2 EVALUATION OF TABLETS

3.2.1 Pre- Compression Parameters

1. Angle of repose (θ): Table No.3 show the results obtained for angle of repose of powder blend of Temisartan. All formulations showed the angle of repose within 30^0, which indicates a good flow property of the granules.

2. Bulk density and tapped density: Both loose bulk density (LBD) and tapped bulk density results are shown in Table No.3. The values obtained lies within the acceptable range and not large differences found between loose bulk density and tapped bulk density. This result helps in calculating the % compressibility of the powder.

3. Percentage compressibility: This percent compressibility of powder mix was determined by Carr's compressibility index. Table No.3 shows the results obtained for percentage compressibility. All formulations are showing good compressibility.

4. Hausner's Ratio: This is an indirect index of ease of powder flow. Table No.3 shows the results obtained for Hausner's Ratio**.** All formulations are showing good Hausner's Ratio.

Table No.3: Pre-Compression parameters of powder blend

Sr. No.	Angle of repose (θ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's index %	Hausner's Ratio
F1	28.12±0.32	0.532±0.03	0.619±0.34	16.48±1.46	1.22±0.05
F2	29.28±0.32	0.527±0.03	0.622±0.38	15.45±1.46	1.18±0.02
F3	28.31±1.73	0.535±0.02	0.624±0.38	14.44±1.26	1.19±0.008
F4	27.50±0.65	0.554±0.02	0.643±0.31	1493±0.98	1.17±0.003
F5	29.27±0.56	0.527±0.03	0.655±0.29	15.13±0.81	1.18±0.002
F6	28.22±0.95	0.541±0.07	0.624±0.38	15.04±0.74	1.18±0.02
F7	29.29±0.66	0.538±0.07	0.632±0.36	14.93±0.78	1.17±0.03
F8	29.28±0.32	0.5391±0.08	0.645±0.37	14.05±0.71	1.16±0.07
F9	28.22±0.32	0.537±0.07	0.644±0.36	14.88±0.75	1.17±0.03

3.2.2 Post-compression parameters

All the tablet formulations were subjected for evaluation according to various official specifications and other parameters. Shape, thickness, hardness, friability, weight variation, drug content, *in vitro* dissolution studies, model fitting of release profile were carried out.

1. Shape and colour of tablets: Randomly picked tablets from each formulation batch examined under lens for shape and in presence of light for colour. All tablets of all the batches showed Oval in shape and white, yellow in colour.

2. Uniformity of thickness: The thickness of the tablets was measured by using vernier calliper by picking the tablets randomly. The mean values are shown in Table.No 4. The values are almost uniform in all formulations.

3. Hardness test: Table No.4 shows results obtained for of all the formulation of hardness. Hardness test was performed by Monsanto hardness tester. Hardness was found to be within 4.0kg/cm^2 to 4.1 kg/cm^2. The lower standard deviation values indicated that the hardness of all the formulations were almost uniform in specific method and possess good mechanical strength with sufficient hardness.

4. Friability test: The study results are tabulated in Table No.4 was found well within the approved range (<1%) in all the formulations. Formulation F1 to F9 possesses good mechanical strength.

5. Weight variation test: The percentage weight variation for all the formulation is tabulated in Table No.4 All the tablets passed weight variation test as the % weight variation was within the pharmacopoeias limits of not more than 10%. It was found to be from 348-350 mg. The weight of all the tablets was found to be uniform.

6. % Drug content uniformity: The content uniformity was performed for all the formulations and results are shown in Table No. 4. Three trials from each formulation were analyzed spectrophotometrically. The mean value and standard deviation of all the formulations were calculated. The drug content of the tablets was found between 95-99% . The results indicated that in all the formulations the drug content was uniform. The cumulative percentage drug released by each tablet in the in vitro release studies were based on the mean content of the drug present in the respective tablet.

Table No.4: Post-Compression parameters of Tablets.

Sr. No.	Weight variation(mg)	Hardness (kg/cm^2)	Thickness (cm)	Friability (%)	Drug Content (%)
F1	348±0.478	4.1±0.75	5.1±0.15	0.162	96.1
F2	348.75±0.478	4.0±0.77	4.55±0.01	0.171	97.22
F3	350±0.49	4.2±0.76	5.0±0.01	0.131	98.8
F4	349±0.50	4.0±0.7	5.03±0.15	0.133	98.84
F5	349±0.50	4.2±0.75	5.1±0.15	0.229	96.76
F6	348±0.50	4.1±0.75	4.83±0.57	0.146	97.1
F7	348.75±0.50	4.0±0.77	5.1±0.01	0.191	95.82
F8	349±0.50	4.1±0.77	5.0±0.01	0.215	99.70
F9	350±0.50	4.±0.7	5.0±0.01	0.211	99.33

7. Buoyancy / Floating Studies: The time between introduction of dosage form and its buoyancy on the simulated gastric fluid and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT).

Formulation F1 to F3 (Xanthun gum) showed floating lag time of 77 to 99 seconds. The formulation F4 to F6 (Guar gum) showed good floating time of about 55 to 70 seconds with total floating time of about 6-10 hours. While the formulation of F7 to F9 (eudragit) showed good floating time of about 42 to 57 sec and total floating time of about < 12 hours. This may be due to amount of polymer so total floating time got increased.

Table. No. 5: Floating profile for Telmisartan tablets.

Formulation Code	Floating lag time (sec)	Total floating time (hours)
F1	99	6
F2	86	4
F3	72	6
F4	60	6
F5	55	10
F6	70	8
F7	57	10
F8	42	<12
F9	49	<10

Fig.No.3: Floating tablet of Telmisartan

3. 3 *In vitro* dissolution studies: *In vitro* release studies were carried out using tablet dissolution test apparatus USP.

Dissolution Apparatus

Table No. 6: various parameters for Dissolution test.

PARAMETERS	CONDITIONS
Dissolution Apparatus	USP- Type II (Paddle)
Medium	0.1 N HCL
Volume	900ml
Speed	50 rpm
Temperature	$37^0C \pm 0.5^0C$
Sample volume withdrawn	5ml
Time points	0,5,1,2,3,4,6,8,10,12
Analytical method	Ultraviolet Visible Spectrosopy
λ max	248nm

The release rate of floating tablets of Telmisartan was determined using USP Dissolution Testing Apparatus II (Paddle type). The dissolution test was performed using 900 ml of 0.1N HCl, at 37 ± 0.5°C and speed of 50 rpm. Aliquot (5 ml) of the solution was collected from the dissolution apparatus hourly for 12 hours and were replaced with fresh dissolution medium. The aliquots were filtered through whatmann filter paper no. 41. Absorbance of these solutions was recorded at 248nm (Telmisartan) in photometric mode for single drug. Aliquots were withdrawn at one hour interval from a zone midway between the surface of dissolution medium and the top of rotating paddle not less than 1 cm apart from the vessel wall. Drug content in dissolution sample was determined by software (PCP disso v3) version.

Table No. 7: % drug release of F1 to F5 formulations

Time(hr)	F1	F2	F3	F4	F5
0	0	0	0	0	0
0.5	17.517	18.324	22.027	23.956	28.461
1	19.738	22.027	29.876	35.542	36.945
2	25.707	29.876	39.784	47.161	45.969
3	39.312	40.28	49.008	56.408	55.414
4	45.293	49.008	52.411	65.471	62.244
6	54.671	58.709	63.677	71.535	68.587
8	59.854	63.667	68.326	74.576	74.756
10	63.092	71.613	74.316	78.861	83.365
12	73.632	78.511	81.213	83.942	86.763

Table No. 8: % drug release of F6 to F9 formulations

Time(hr)	F6	F7	F8	F9
0	0	0	0	0
0.5	31.428	38.034	38.066	35.612
1	42.162	48.271	47.271	44.751
2	52.411	56.667	56.094	54.598

3	62.399	65.53	65.53	64.528
4	69.233	73.596	73.596	69.921
6	77.138	80.944	80.944	76.867
8	84.908	88.725	85.562	79.841
10	87.709	94.197	92.89	85.351
12	92.426	96.896	99.078	95.444

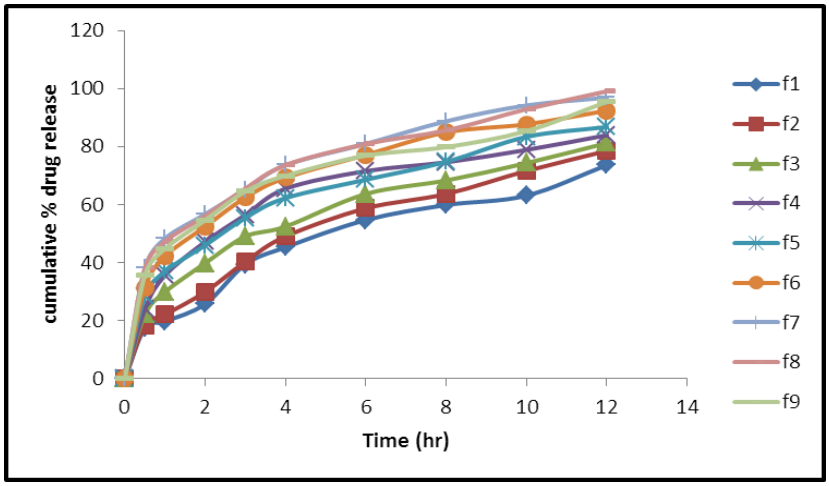

Fig No. 4: % drug release graphical presentation of all formulations

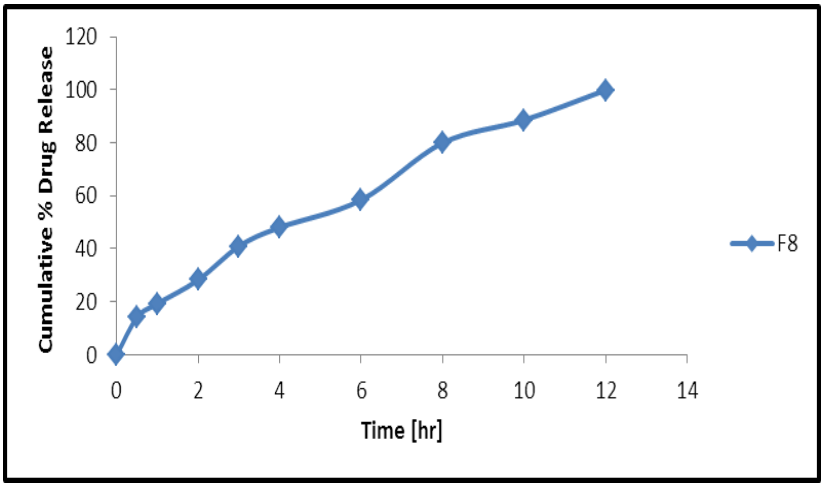

Fig No. 5: % drug release graphical presentation of optimized formulation (F8)

Release kinetics and mechanism

To know the release mechanism and kinetics of Telmisartan optimized formulation (F8) were attempted to fit into mathematical models and n, r^2 values for zero order, first order, matrix Korsmeyer Peppas and Hixon- Crowel models were represented in Table No.9. The criteria to choose the best fit model the correlation coefficient values were used along with the k values.

Table No. 9: In-vitro Drug Release kinetics of F8 Formulation of telmisartan

	R	K
Zero order T-test	0.9721 11.726	9.2963 (Passes)
1st order T-test	0.8984 5.787	-0.2846 (Passes)
Matrix T-test	0.9771 12.990	26.4156 (Passes)
Peppas T-test	0.9962 32.275	18.2904 (Passes)
Hix.Crow. T-test	0.9787 15.660	-0.0577 (Passes)

The data obtained from the dissolution studies for optimized formulation (f8) was fitted in different models. The r^2 values for different models were estimated. The r2 values of Korsemeyer-Peppas were found to be highest 0.9962 .It shows that best fit model for the formulation is Korsemeyer-Peppas model. Slope (N) value in Peppas equation was found to be 1.03 which is between 0.5 to 1 it suggests that the release of floating tablet of Telmisartan follows, Non- Fickian transport mechanism.

Table No.10: The r^2, N values of optimized formulation (F8)

Formulation code	Zero order	First order	Hixon-Crowell	Korsemeyer-Peppas	
	r2	R^2	r2	r2	N
F8	0.9721	0.8984	0.9387	0.9962	1.03

Korsmeyer-Peppas model: To find out the mechanism of drug release, first60% drug release data were fitted in Korsmeyer Peppas model.

$Mt / M\infty = Ktn$

Where $Mt / M\infty$ is a fraction of drug released at time t,k is the release rate constant and n is the release exponent. The n value is used to characterize different release for cylindrical shaped matrices.

In this model, the value of *n* characterizes the release mechanism of drug.

For the case of 0.5 =n corresponds to a Fickian diffusion mechanism, 0.5 < n <1 to non-Fickian transport, n = 1 to Case II (relaxational) transport, and n > 1 to super case II transport. A plot between log drug release up to 60% against log of time will be linear obeys peppas equation and the slope of this plot represents n value. Nature of release of the drug from

designed tablets was inferred based on correlation coefficient obtained from plots of kinetic media.

3.4 DRUG EXCIPIENT COMPETIBILITY STUDY.

3.4 .1 Infrared spectroscopy: The peaks present in IR spectra of of telmisartan formulation are clearly seen in the IR spectra of API telmisartan with minor shifts. It indicates that there was no interaction between the drug and polymer.

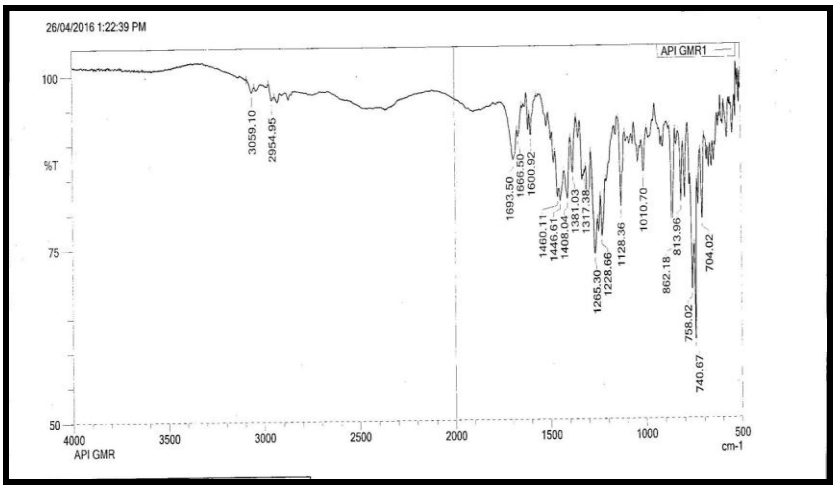

Fig.No.6 FTIR spectra of API Telmisartan

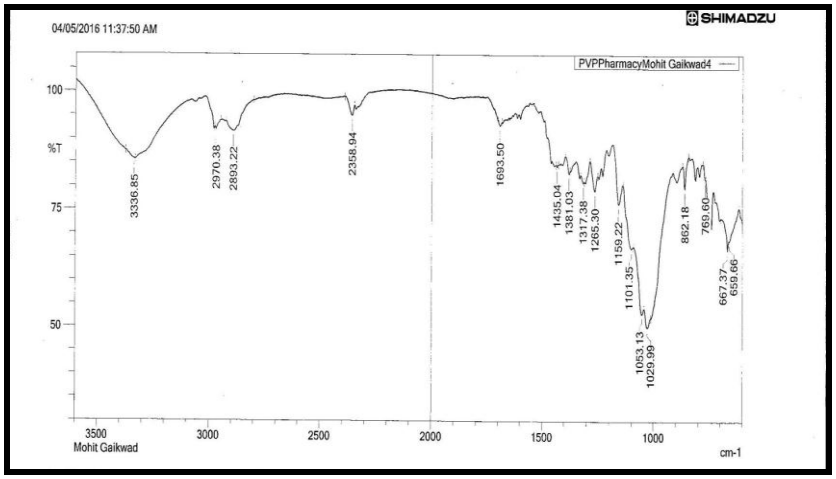

Fig.No.7 FTIR spectra of optimized batch F8

3.4.2 Differential scanning calorimetry

Differential Scanning Calorimetry (DSC) is a thermo analytical technique used for analyzing thermal transitions involving thermal energy with a great sensitivity.

The DSC thermo gram shows there was no sharp change in melting point of drug. Thus there was no significant interaction between the drug, and polymer fig no.8 and 9.

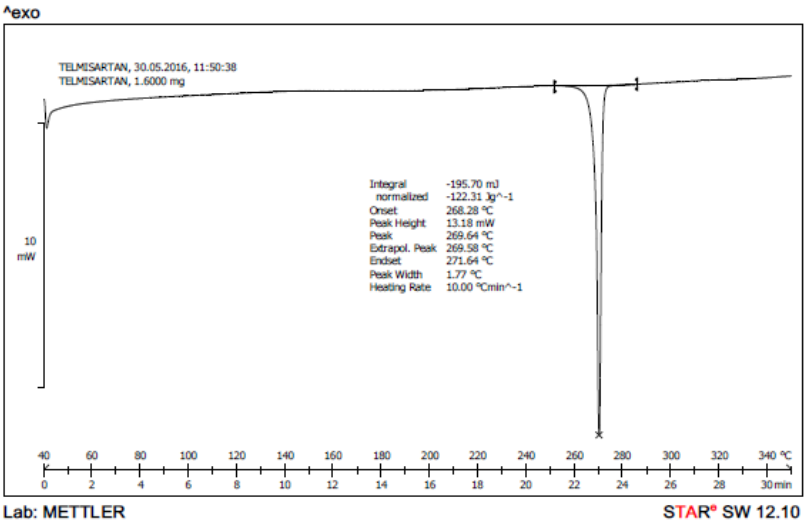

Fig. No. 8 DCS of pure drug Telmisartan

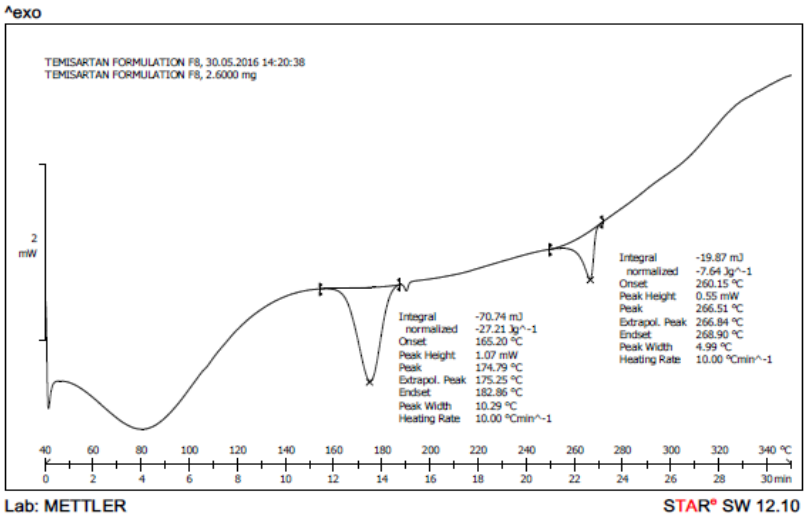

Fig. No.9: DCS of optimized batch f8

4. CONCLUSION

On the basis of DSC it was observed that the drugs Telmisartan were compatible with the used excipients. Eudragit RSPO, in concentration of 60% was optimized as sustained release polymer for Telmisartan. The tablets were evaluated for pre compression parameters and post compression parameters and good results were obtained. Formulation F8 was selected as the best on the basis of *In-vitro* drug dissolution study and release kinetics .From *in vitro* dissolution studies conducted for 12 hrs, formulations F8 indicated consistent floating characteristics as well as sustained release properties. The release kinetics study shows drug Telmisartan passes from First-Order, Zero-Order and Peppas Models respectively. The optimized formulation F8 showed maximum % drug release of 99.07% which is highest of all

formulations and it passes from korsemeyer Peppas model showing r^2 value of about 0.999, N value about 1.03 showing Non-fickian transport. A Floating tablet of Telmisartan can be prepared. The optimized formulation F8 showed good floating lag time of about 42-57 seconds, and remained buoyant for more than 12 hours showing good total floating time (floating log time). It can be finally concluded that formulating Floating Tablet of Telmisartan considered for a good Antihypertensive activity.

5. AKNOWLEDGMENTS

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6. REFERENCES

1. Amit Kumar Nayak , Ruma Maji, Biswarup Das, Gastroretentive drug delivery systems: a review, 3.
2. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery system. Expert Opin Drug Deliv, 2006; 3(2): 217- 33.
3. Arora S, Javed Ali, Ahuja A, Khar K, Sanjula Babota,Floating drug delivery system: A Review. AAPS Pharmscitech. 2006; 06(03): E372 - E390.
4. Shirwaikar AA, Kumar SMR, Jacob S, Rashi W, Ravi K. Recent Developments in floating drug delivery system for gastric retention of drugs. Indian Drugs. Sept 2006; 43(9).
5. Chawla G, Gupta P, Koradia V, Bansal A, Gastroretention. A means to address regional variability in intestinal drug absorption. Pharmaceutical technology, July 2003.
6. Davis SS, Stockwell AF, Taylor MJ, et al. The effect of density on the gastric emptying of single and multiple unit dosage forms. Pharma Res. 1986; 3: 208-213. DOI: 10.1023/A: 10163 34629169.
7. Nikita Dixit, Floating Drug Delivery System: an overview, Journal of Current Pharmaceutical Research, 2011; 7(1): 6-20.
8. Desai S. A Novel Floating Controlled Release Drug Delivery System Based on a Dried Gel Matrix Network [master's thesis]. [thesis]. Jamaica, NY: St John's University; 1984.
9. Abhishek Chandel, Kapil Chauhan, Bharat Parashar, Hitesh Kumar, Sonia Arora Floating drug delivery systems: A better approach, International Current Pharmaceutical Journal 2012; 1(5): 110-118.

10. Roy Chowdhury,Verma Poojaet.al, Floating drug delivery system – A new era in novel drug deliery system,Review Article Santanu Roy Chowdhury, IJPRBS, 2012; (1): 91-107, ISSN: 2277-8713.
11. Praveen Nasa, Sheefali Mahant, Deepika Sharma, Floating systems: A Novel approach towards Gastroretentive drug delivery system. International Journal of Pharmacy and Pharmaceutical Sciences, 2010; 2(3): ISSN- 0975-1491.
12. Rani SB, Hari VBN, Reddy BA, Punitha S, Devi P, Rajamanickam V. The Recent Developments on Gastric Floating Drug Delivery Systems. An overview International J. Pharm Tech Research 2010 Jan-March; 2(1): 524-34.
13. Kaza R, Usharani E, Nagaraju R, Haribabu R, Reddy PVS. Design and Evaluation of Sustained release Floating tablets for the treatment of Gastric Ulcers. J. Pharm. Sci & Res 2009; 1: 81-7.
14. Ali J, Arora S, Ahuja A, Babbar AK, Sharma RK and Khar RK. Formulation and Development of Floating Capsules of Celecoxib In-Vitro and In-Vivo Evaluation. AAPS 2007; 8(4): 119.
15. Mathur P, Saroha K, Syan N, Verma S, Nanda S, Valecha V. An overview on recent advancements and developments in Gastroretentive buoyant drug delivery system. Pelagia Research Library Der Pharmacia Sinica 2011.
16. Gupta SN, Aggarwal N. A gastro-retentive floating delivery system for 5-Fluorouracil. Asian J. Pharmaceutical Sciences 2007; 2(4): 143-9.
17. Narasaiah VL, Saravanan G et al., Formulation, characterisation and in-vitro evaluation of Sumatriptan Succinate floating tablets. JITPS 2010; 1.
18. Chaturvedi K, Umadevi S, Vaghani S. Floating Matrix Dosage Form for Propranolol Hydrochloride Based on Gas Formation Technique, Development and In Vitro Evaluation. Sci Pharm 2010; 78: 927–39.
19. Sharma S, Sharma A, Jha KK. The Study of Captopril Floating matrix tablets using different Polymers as release retarding agent. The Pharm Research 2009.
20. Kumar S, Pandey M, Saraf SA. Formulation and in-vitro Evaluation of Novel Sustained Release Gastroretentive Floating Matrix Tablets of Acyclovir. J. Pharmacy Research 2009 April; 2.
21. Kiran RS, Shekar BC, Babu BN. Preparation and Evaluation of Floating Tablets by Non aqueous wet granulation method of Famotidine. International J. Pharmaceutical Sciences 2011 Jan-Apr; 3: 939.

22. Khan T, Nazem S, Shaik S, Shaik A. Design and in-vitro Evaluation of floating anti-hypertensive drug tablets based on gas formation. International J. Pharma and Bio Sciences 2011-Apr-Jun; 2.
23. Verma S, Narang N. Development and in-vitro evaluation of Floating Matrix Tablets of Retroviral drug. International J. Pharmacy and Pharmaceutical Sciences 2011; 3.
24. International journal of current trends in peutical sciences and research, IJCTPR, (2): 669-679.
25. International journal of pharma research and review, IJPR, 9-18.
26. International journal of pharma science and research, ISSN, (vol 7).
27. www.wikipedia.co.in
28. P Subhash Chandra Bose, P Srikanth Reddy, Valluru Ravi, D Sarita, T M Pramod Kumar; formulatin and evaluation of sustained release floating tablets of diltiazemHcl using xanthan gum, RJPBCS, 2011; 2(2).
29. Aulton ME, Wells TI, Pharmaceutics: The Science of Dosage Form Design, London, England: Churchill Livingstone; 1988.