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Preparation and evaluation of press coated floating pulsatile drug delivery system of telmisartan

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ABSTRACT

The aim of present investigation was to develop press coated tablets for Floating pulsatile drug delivery of Telmisartan used for is a medication used for high blood pressure, heart failure, and diabetic kidney disease. The drug delivery system was designed to deliver the drug such a time when it could be needful of patient conditions. The press coated tablets containing Telmisartan in the inner core were formulated by direct compression method with an outer coating of different amount of Chitosan. The release profile of press coated tablet exhibited a lag time. The optimized batch F9 gave good drug release of 99.58 %

Keywords: Telmisartan, Sodium Alginate, HPMC K100M and Chitosan and press coated method

INTRODUCTION

In recent years, a major goal for the drug delivery research is turned towards the development of efficacious drug delivery systems with already existing active ingredients in case of new drug discovery. Many of pharmaceutical therapeutic agents are mostly effective when made available at constant rates or near to absorption sites. Much effort has been going on to develop sophisticated drug delivery systems such as osmotic devices for oral application. Oral drug delivery system is more favored on popular controlled drug delivery system in pharmaceutical research and development (R & D) business due to increase in awareness of medical and pharmaceutical community about the importance of safe and effective use of drug. This system aims to maintain plasma drug concentration within the therapeutic window for long period of time[1].

Traditionally, it is becoming increasingly more evident with the specific time that patients have to take their medication may be even more significant than was recognized in the past. The tradition of prescribing medication at evenly spaced time intervals throughout the day, in an attempt to maintain constant drug levels throughout a 24-hr period, may be changing as researcher's report that some medications may work better if their administration is coordinated with day-night patterns and biological rhythms. In the human body systems such as cardiovascular, pulmonary, hepatic and renal systems show variation in their function throughout a typical day. They are naturally followed by the internal body clocks and are controlled by the sleep wake cycle. This system focused on controlled or sustained release of drug of which has such advantages of nearly constant level of drug at site of administration, minimizing peak - valley fluctuation of drug concentration in body and avoidance of adverse effect because R eduction in dose, dosage frequency and patient efficacy and compliance by this delivery system also expected[1].

A release pattern of drug is not suitable in certain disease condition. At that time, release profile of a delivery system characterized by lag time. In other words, the drug should not release during its initial period of administration, followed by a rapid and complete release (pulse release) of drug that is called pulsatile drug delivery system. This system aims to deliver a drug via the oral route at a rate different

than constant i.e., zero order release. The lag time is the time interval between the dosage forms is placed into the aqueous environment and drug get to release from its dosage form after rupturing or eroding outer layer. The lag time between 0.5 hr to 4 hr is desire for upper region of gastrointestinal tract and more than 4 hr for lower portion of small intestine[2].

"Chronopharmaceutics" consist of two words chronobiology and pharmaceutics. Chronobiology is the study of biological rhythms and their mechanisms. Mainly mechanical rhythms in our body are:

- Circadian - this word comes from Latin word "circa" means about and "dies" means day and oscillation completed in 24 hr
- Ultradian - oscillation of shorter duration (more than one cycle per 24 hr)
- Infradian - oscillations that are longer than 24 hr (less than one cycle per day)[7]

Circadian rhythms are self-sustaining, endogenous oscillations that occur with a periodicity of about 24 hr and regulate many body functions like- metabolism, sleep pattern, hormone production etc. PDDS are widely important in such wide spread disease which is mentioned below

- Chronopharmacotherapy of diseases which shows circadian rhythms in their Pathophysiology Confidential
- Extended day time or night time activity
- Avoiding the first pass metabolism e.g., protein and peptides
- Biological tolerance **(**e.g., transversal nitroglycerin)
- For targeting specific site in intestine e.g., colon
- For time programmed administration of hormone and drugs
- Gastric irritation or drug instability in gastric fluid
- For drugs having the short half life
- Lower daily cost to patient due to fewer dosage units are required in therapy
- Reduction in dose size and dosage frequency and also side effects

Classification of chronopharmaceutical drug delivery system

Pre-Programmed Delivery System

Time controlled pulsatile drug delivery system

Principally, timed pulsatile delivery system is capable of providing one or more rapid release pulses at predetermined lag times or at specific sites, results in better absorption with effective plasma concentration-time profile for a therapeutic agent. Due to potential limitations of the dosage form size, and/or polymeric materials and their compositions, a few orally applicable pulsatile release systems are going for approach[2].

Capsular structure based system

The pharmaceutical capsular dosage form that releases its drug content at either at predetermined time or at a specific site (e.g., colon) in the gastrointestinal tract e.g., Pulsincap. The drug formulation consists of insoluble capsular body, swellable and degradable plugs which made up of approved substances such as hydrophilic polymers, lipids and bioactive molecules. After oral administration this capsular system came in contact with the gastrointestinal fluid than hydrogel plug swells and at preprogrammed lag time period, the plug pushes outside and rapid release the drugs. Generally to developed the plug, polymeric substances used such as poly vinyl acetate, polyethylene-oxide, hydroxyl propyl cellulose etc. This delivery system has also be simplify by using erodible tablet in place of hydrogel plug. This erodible tablet is completely fit in a capsule to retard the fluid entry. Top of capsule dissolve than this tablet erodes during release of drug from mouth of capsule[2].

System based on rupturable coating

This is a reservoir-type time-controlled pulsatile release system consists of water insoluble but water permeable polymeric barrier which surrounded to the drug core subject. This drug core is formulated by using osmotic agents or swelling or gas producing effervescent additives. So that from the dosage form the drug is released from a core after the rupture of a surrounding polymer layer because of a hydrostatic pressure build-up within the system when it immersed into the release media. The pressure necessary to rupture the coating can be achieved with gas-producing effervescent excipients, inner osmotic pressure or swelling agents[2].

A time dependent pulsed release system of salbutamol sulfate in nocturnal asthma consisting of an effervescent core surrounded by consecutive layers of swelling and rupturable polymers was prepared and evaluated. This system prepared by direct compression method using different ratios of microcrystalline cellulose and effervescent agent and then coated sequentially with an inner swelling layer containing a hydrocolloid, hydroxypropyl methylcellulose E5 and an outer rupturable layer having Eudragit RL / RS (1:1).

MATERIALS

Telmisartan Procured from Shashi Pharma, Chhatral, Gujarat, India. Provided by Sura Labs, Dilsukhnagar. .Croscarmellose Sodium Loba chemie Pvt. Ltd. Mumbai, India .Sodium Alginate Loba chemie Pvt. Ltd. Mumbai, India. HPMC K100MLoba chemie Pvt. Ltd. Mumbai, India .Chitosan Loba chemie Pvt. Ltd. Mumbai, India .PVP K30 Loba chemie Pvt. Ltd. Mumbai, India .Sodium bicarbonate Loba chemie Pvt. Ltd. Mumbai, India.Magnesium Stearate Loba chemie Pvt. Ltd. Mumbai, India .Microcrystalline cellulose Loba chemie Pvt. Ltd. Mumbai, India

METHODOLOGY

Analytical method development

Preparation of calibration curve in 0.1N HCL

10mg of Telmisartan pure drug was dissolved in 10ml of methanol (stock solution 1). 1ml of solution was taken and makes up with10ml of 0.1N HCL (100µg/ml) stock-2. From this 1ml was taken and make up with 10 ml of 0.1N HCL (10µg/ml) stock-3. The above stock-II solution was subsequently diluted with 0.1N HCL to obtain series of dilutions containing and 10, 20, 30, 40 and 50µg/ml of

solution. The absorbance of the above dilutions was measured at 295 nm for 0.1N HCL by using UV-Spectrophotometer taking 0.1N HCL as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis.

Formulation development of Tablets

Formulation of core tablets by direct compression

The inner core tablets were prepared by using direct compression method as shown in the table 7.3. Powder mixtures of Telmisartan, microcrystalline cellulose, CCS, talc, ingredients were dry blended for 20 min. followed by addition of Magnesium Stearate. The mixtures were then further blended for 10 min., 60mg of resultant powder blend was manually compressed using , Lab press Limited, India with a 6mm punch and die to obtain the core tablet.

Formulation of mixed blend for barrier layer

The various formulation compositions containing Sodium Alginate, HPMC K100M and Chitosan, magnesium stearate, talc and microcrystalline cellulose. Different compositions were weighed dry blended at about 10 min. and used as press coating material to prepare press-coated pulsatile tablets respectively by direct compression method.

Preparation of press-coated tablets

The core tablets were press-coated with 120 mg of mixed blend as given in Table.No7.4. 120 mg of barrier layer material was weighed and transferred into a 7mm die then the core tablet was placed manually at the center. The remaining of the barrier layer materiel was added into the die and compressed by using Lab press Limited, India.

Table1: Formulation development of core tablets

Ingredients	C1	C2	C3
Telmisartan	20	20	20
Croscarmellose sodium	20	40	60
Microcrystalline cellulose	Q.S	Q.S	Q.S
PVP k 30	10	10	10
Magnesium stearate	3	3	3
Talc	1	1	1
Total weight	100	100	100

Table 2: Formulations for press coated tablets

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Sodium Alginate	10	20	30	-	-	-	-	-	-
HPMC K100M	-	-	-	10	20	30	-	-	-
Chitosan	-	-	-	-	-	-	10	20	30
PVP K30	15	15	15	15	15	15	15	15	15
Sodium bicarbonate	10	10	10	10	10	10	10	10	10
Magnesium Stearate	3	3	3	3	3	3	3	3	3
Microcrystalline cellulose	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Talc	1	1	1	1	1	1	1	1	1
Total weight	200	200	200	200	200	200	200	200	200

RESULTS AND DISCUSSION

Present study was done on pulsatile tablets with different formulations F1 to F9. Formulations had weight ratio of polymers like Sodium Alginate, HPMC K100M and Chitosan. This section gives detailed description of the results and discussion on pulsatile Telmisartan tablets.

Preformulation Studies

Standardization method for estimation of Telmisartan

Standard curves of Telmisartan were prepared in 0.1N HCL.

Table 3: Calibration data of Telmisartan in 0.1N HCL

Concentration [µg/ml]	Absorbance
0	0
10	0.126
20	0.249
30	0.364
40	0.478
50	0.599

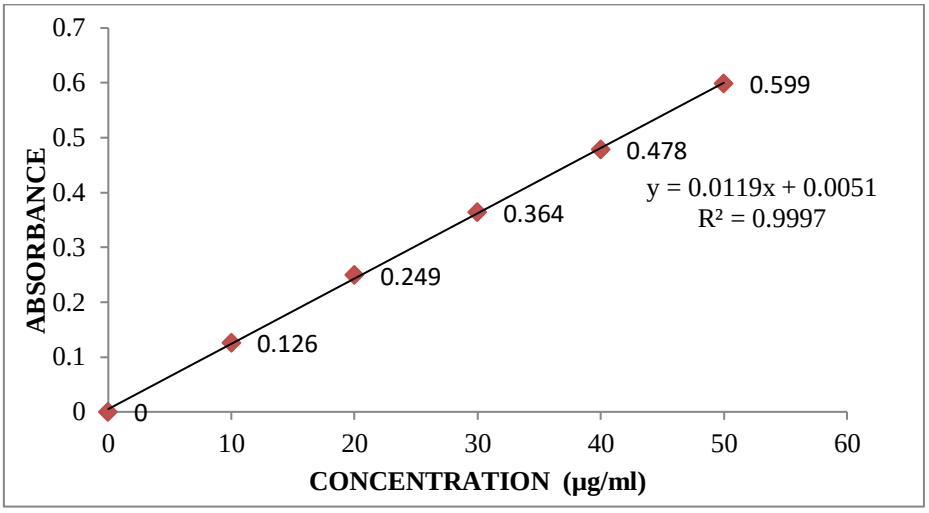

Fig 1: Standard Graph of Telmisartan in 0.1N HCL

Table 4: Pre compression parameters of Cap core tablets

F6	23.10	0.33	0.42	22.35	1.28
C1	26.29	0.34	0.38	10.52	1.11
C2	27.29	0.33	0.38	13.15	1.15
C3	28.29	0.34	0.38	13.14	1.14

Table 5: Post compression parameters of Core tablet

Formulation code	Average Weight (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)	*In vitro* disintegration time (sec)
C1	99.12	3.13	0.24	1.21	98.18	20
C2	100.28	3.25	0.18	1.51	99.27	12
C3	100.77	3.34	0.22	1.60	99.13	16

Table 6: Pre compression Parameters of Telmisartan coated Tablets

Formulation code	Angle of repose (0) *	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	17.10	0.318	0.38	16.31	1.19
F2	28.97	0.342	0.4	15.0	1.176
F3	18.19	0.34	0.43	20.93	1.26
F4	22.61	0.36	0.42	14.28	1.16
F5	26.56	0.33	0.41	19.06	1.24
F7	19.85	0.33	0.41	19.51	1.24
F8	21.80	0.32	0.42	24.70	1.32
F9	17.74	0.33	0.4	17.5	1.21

Table 7: Post compression parameters of Coated tablet

Formulation code	Weight variation (mg)	Hardness (kg/cm^2)	Thickness	Friability (%loss)	Drug content (%)	Floating lag time (min)	Total Floating Time (Hrs)
F1	200.28±0.12	5.82±0.22	2.12±0.78	0.50±0.28	99.28	3.2	5
F2	198.03±0.95	5.66±0.51	2.67±64	0.54±0.34	98.12	3.4	10
F3	199.98±0.74	5.09±0.95	1.85±48	0.62±0.94	99.73	3.8	10
F4	197.57±0.64	5.16±0.46	2.45±32	0.70±0.47	100.01	3.1	5
F5	200.48±0.37	5.77±0.37	1.98±17	0.76±0.85	97.42	3.6	10
F6	196.61±0.56	5.62±0.55	2.12±95	0.82±0.24	99.35	3.2	9
F7	198.38±0.33	5.94±0.48	2.44±81	0.96±0.95	98.75	2.6	8
F8	195.73±0.76	5.81±0.72	2.89±99	0.91±0.81	99.41	2.0	11
F9	200.05±0.84	5.19±0.22	3.18±75	0.52±0.76	99.27	3.4	12

In-Vitro Drug Release Studies of Telmisartan core tablet

Table 8: Drug release of Telmisartan core tablets

Time (min)	C1	C2	C3
0	0	0	0
5	12.82	18.98	7.98
10	22.08	35.48	10.14
15	37.41	55.58	36.98
20	67.66	82.31	58.9
30	91.2	96.88	92.53
45	94.6	98.86	96.66
60	96.92	99.76	98.27

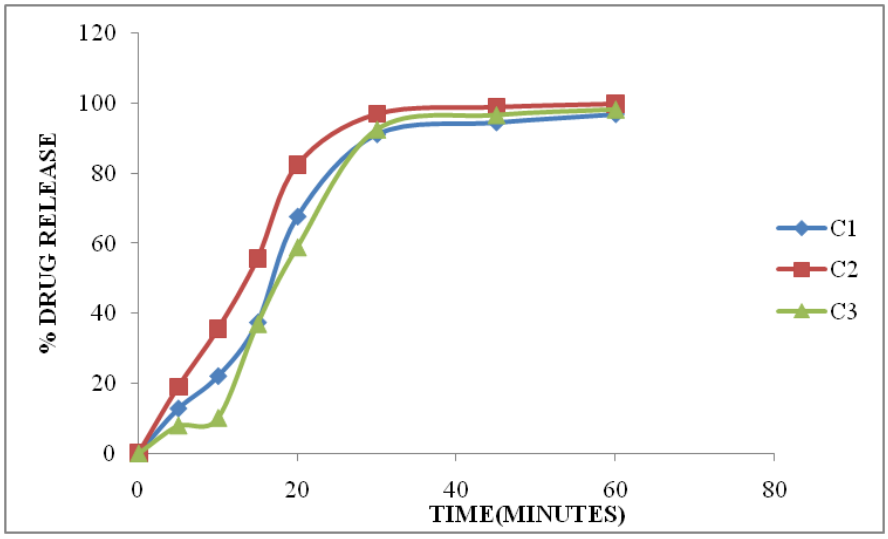

Fig 2: Cumulative % drug released of Telmisartan core tablets

In vitro drug release study of Telmisartan pulsatile tablets

Table 9: Cumulative % drug Release of Coated Telmisartan Tablets containing Sodium Alginate

Time (hr)	F1	F2	F3
0	0	0	0
0.5	0.14	0.13	0.12
1	0.18	0.19	0.22
2	0.25	0.21	5.43
3	28.54	25.29	15.68

4	50.34	30.18	24.32
5	98.37	41.72	30.62
6		51.31	39.57
7		60.34	44.28
8		72.48	50.02
9		88.68	61.25
10		100.64	77.31
11			84.92
12			95.45

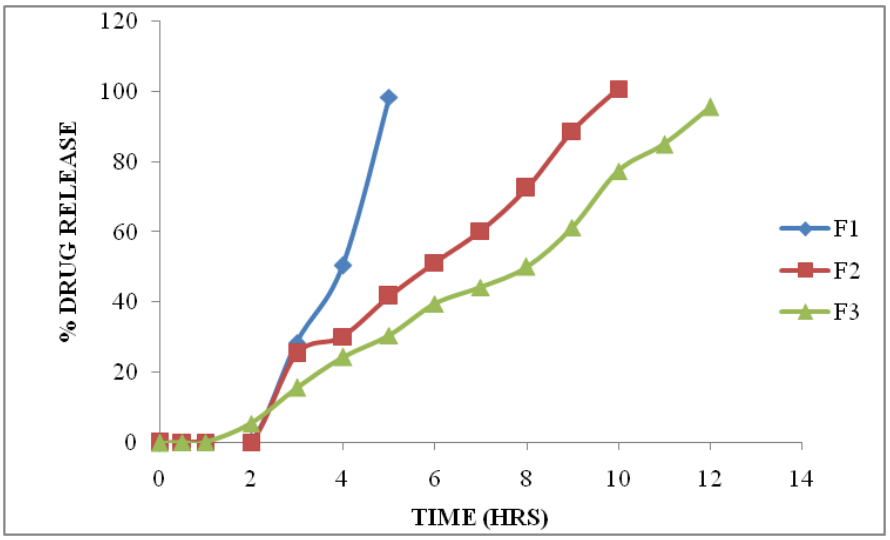

Fig 3: Cumulative % drug release study of Telmisartan pulsatile tablets (F1, F2 & F3)

Table 10: Cumulative % drug Release of Coated Telmisartan Tablets containing HPMC K100M

Time (Hr)	F4	F5	F6
0	0	0	0
0.5	0.28	0.12	0.11
1	12.56	0.19	0.17
2	28.18	1.95	1.35
3	50.34	10.12	9.38
4	85.17	21.23	20.38
5	90.61	30.22	28.39
6	99.76	39.15	35.59
7		43.52	40.38
8		49.06	52.12
9		55.79	64.21
10		75.34	74.86
11		94.25	80.67
12			94.76

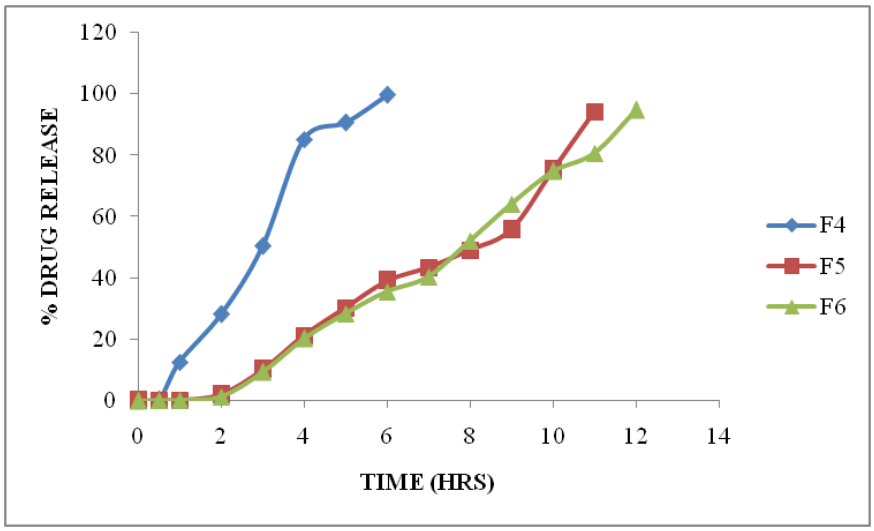

Fig 4: Cumulative % drug release study of Telmisartan pulsatile tablets (F4, F5 & F6)

Table 11: Cumulative % drug Release of Coated Telmisartan Tablets containing Chitosan

Time (hr)	F7	F8	F9
0	0	0	0
0.5	0.19	0.16	0.12
1	0.65	0.54	0.54
2	1.95	1.84	0.59
3	5.39	14.74	19.74
4	13.73	20.38	25.38
5	27.37	38.48	36.48
6	41.38	47.48	45.48
7	63.83	50.29	52.29
8	80.29	61.27	66.27
9	96.38	79.38	71.38
10		86.39	78.39
11		96.28	86.28
12			99.58

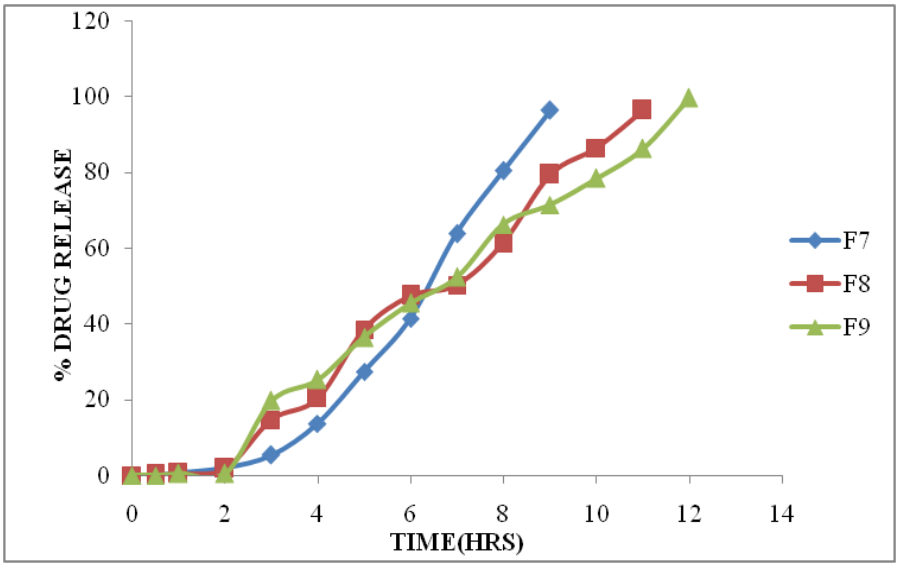

Fig 5: Cumulative % drug release study of Telmisartan pulsatile tablets (F7, F8, F9)

Drug – Excipient compatibility studies

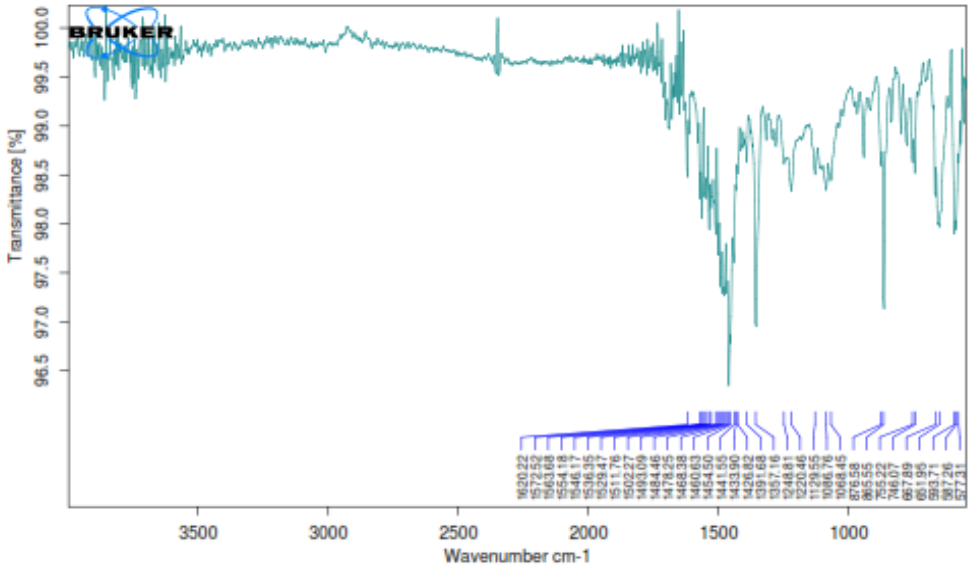

Fig 6: FTIR spectra of Telmisartan pure drug

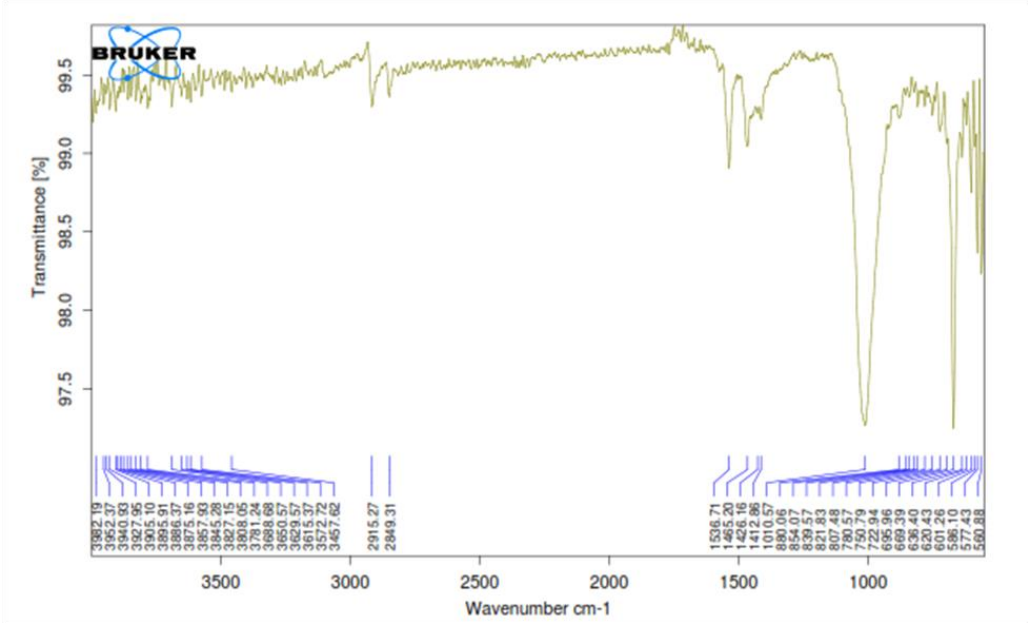

Fig 7: FTIR spectra of Optimized Formulation

CONCLUSION

Telmisartan Pulsatile dosage form was formulated by press coating technique. The lag time and time-controlled release behavior of Telmisartan from press coated tablets could be modulated by varying the concentration of polymer in outer coating layer and thickness if compression coating. From formulation C1-C3 Telmisartan core tablets, C2 showed faster drug release than the other formulations. Faster drug release can be correlated with the less disintegration time. So, C2 formulation was selected as best formulation for further press coating and enteric coating formulations. Among All Formulations F9 was showed maximum % drug release 99.58% at 12 hours. Hence F9 Formulation was considered as optimized Formulation.

REFERENCES

1. J.ravi kumar reedy,m.veera jyothsna,t.s.mohamed saleem,c.madhu sudhana chetty. Pulsatile drug delivery systems. J Pharm Sci Res. 2009;1(4):109-11.
2. Ramesh d, parmar rk, parikh g. vidyasagar,dhaval. Pulsatile drug delivery systems. Int J Pharm Sci Nanotechnol. 2009;3:605-11.
3. Nobuhiko Y, Teruo O, Yasuhisa S. Yui n, okano t and Sakurai y. In flammation responsive degradation of cross linked hyaluronic acid gels. J Control Release. 1992;22(2):105-16. doi: 10.1016/0168-3659(92)90195-W.

4. Chaudhari Hs, Lohar ms, Amritkar as, Jain dk, dheeraj t. baviskar. Pulsatile drug delivery system. Int J Pharm Sci Rev Res. 2011;8(2):160-9.
5. El-Maradny HA. Modulation of a pulsatile release drug delivery system using different swellable / rupturable materials. Drug Deliv. 2007;14(8):539-46. doi: 10.1080/10717540701606574, PMID 18027184.
6. Keerthi S, reddy vb. gopal muralidharan1, l. v.g nargund1. Formulation and evaluation of pulsatile drug delivery system of anti-asthmatic drug. Am. J. Pharmtech res. 2014;4(1):797-809.
7. Dubey J, Verma N. Floating drug delivery system: a review. IJPSR. 2013;4(8):2893-9.
8. Chikhalikar SS, Wakade RB. Floating drug delivery system – an approach to oral controlled drug delivery. Int J PharmTech Res. 2012;4(4):1812-26.
9. Tripathi GK, Singh S. Formulation and in vitro evaluation of pH sensitive oil entrapped polymeric blended buoyant beads of amoxicillin. Scholars research library. 2010;2(2):131-38.
10. Burns SJ, Attwood D, Barnwell SG. Assessment of a dissolution vessel designed for use with floating and erodible dosage forms. Int J Pharm. 1998;160(2):213-18. doi: 10.1016/S0378-5173(97)00312-8.
11. Baumgartner S, Kristl J, Vrecer F, Vodopivec P, Zorko B. Optimisation of floating matrix tablets and evaluation of their gastric residence time. Int J Pharm. 2000;195(1-2):125-35. doi: 10.1016/s0378-5173(99)00378-6, PMID 10675690.
12. Kharia AA, Hiremath SN, Singhai AK, Omray LK, Jain SK. Design and optimization of floating drug delivery system of acyclovir. Indian J Pharm Sci. 2010;72(5):599-606. doi: 10.4103/0250-474X.78527, PMID 21694992.
13. Bhowmik D, Chiranjib B, Margret C, Jayakar B, Kumar KPS. Floating drug delivery system-A review. Scholars research library. 2009;1(2):199-18.
14. narang N. An updated review on: Floating Drug Delivery System (Fdds).
15. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating drug delivery systems: a review. AAPS PharmSciTech. 2005;6(3):E372-90. doi: 10.1208/pt060347, PMID 16353995.
16. Chien YW. Rate-control drug delivery systems: controlled release vs. sustained release. Med Prog Technol. 1989;15(1-2):21-46. PMID 2530424.
17. Chien YW. Oral drug delivery and delivery system in novel drug delivery systems, ed. Vol. 50. NY: Marcel Dekker publication; 1992.
18. Patel GM. Floating Drug Delivery System: an Innovative Approach to Prolong Gastric Retention; 2007. Available from: http://www.pharmainfo.net.
19. Koner P, Saudagar RB, Dharwal J. Gastro-retentive drugs a novel approach towards floating therapy in http://www.pharmainfo.net/exlusive/reviews/gastro-retentive drugs a novel approach towards floating therapy/, 2007.
20. Mathur P, Verma N. Floating drug delivery system: an innovative acceptable approach in gastroretentive drug delivery. Scholars research library. 2010;2(2):257-70.
21. Chandel A, Chauhan K, Parashar B, Kumar H, Arora S. Floating drug delivery systems: A better approach. Int Curr Pharm J. 2012;1(5):110-18.
22. Shah SH, Patel JK, Patel NV. Stomach specific floating drug delivery system: a review. International journal of pharmaceutical. Technology Publishing and Research 2009; 1(3): 623-33.
23. Gopalakrishnan S, Chenthilnathan A. Floating drug delivery system: a review. J Pharm Sci Technol. 2011;3(2):548-54.
24. Vedha H, Chaudhary J. The recent developments on gastric floating drug delivery system: an overview. Journal of pharmaceutical. Technology Publishing and Research 2010; 2(1); 524-34.