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Formulation And Evaluation of Telmisartan Gastro Retentive Drug Delivery Systems

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Abstract:

Pulsatile drug delivery systems are a novel drug delivery system that is gaining a lot of attention because they deliver the drug to the right site of action at the right time and in the right amount, providing spatial and temporal delivery and increasing patient compliance, enhancing bioavailability and prolonging residence time in the stomach, and holding out good prospects for helping patients with chronic conditions like arthritis, asthma, hypertension, and others. The goal of the current study was to create a floating pulsatile drug delivery system that would achieve no drug release when floating and then pulsed, fast medication release. These systems were created to work with the body's natural circadian cycle. Compression coated floating pulsatile medication delivery for Telmisartan was the focus of the current research project. The floating pulsatile concept was used to extend the stomach residence time of a dose form with a lag phase and burst release. Due to the increased risk of heart attacks in people with hypertension in the morning, drug delivery systems that release medications in the morning and offer effective treatment were required. Rapid release core tablets were directly compressed into tablet form, and the core tablets were then top-coated with a buoyant coating of HPMC. For the layer of pulsatile coating, different grades of HPMC polymer were employed. Physical features of the produced formulations were assessed using DSC and XRD Studies on in vitro dissolution, floating lag time, floating time, release lag time, and drug content. The technique demonstrated a superb lag phase, which was followed by a burst release in the distal small intestine. This allows for site- and time-specific delivery of Telmisartan, which acts as chronotherapy for the treatment of hypertension.

Index Terms - Floating, Pulsatile, Circadian rhythm, compression, gastric retention

I. INTRODUCTION:

The primary goal of research investigations is to create an understanding of floating pulsatile medication delivery systems. The pulsating and floating combination is ideal for a particular location and time. Pulsatile drug delivery is the brief, fast release of a predetermined quantity of drug molecules immediately following a predetermined off-release interval. Drug distribution through pulsatile is location- and time-specific. It offers customized and timely distribution, improving patient compliance. This system was created using the body's circadian cycle.1 in which a gastro-retentive drug delivery mechanism is used to require delayed drug release. Floating Pulsatile Drug Delivery System: For medications that dissolve poorly or are unstable in intestinal fluids, floating oral drug delivery systems (FDDS) are effective because they are retained in the stomach. Floating drug delivery systems (FDDS) float in the stomach without slowing down the gastric emptying rate since their bulk density is lower than that of gastric fluids. The medicine is slowly withdrawn from the system at the desired rate while the body is floating on the contents of the stomach. The stomach's residual system is emptied after the medication has been released. These outcomes lead to an improved ability to manage variations in plasma drug concentration and an increase in GRT.[2] Floating drug delivery systems (FDDS) float in the stomach without slowing down the gastric emptying rate since their bulk density is lower than that of gastric fluids. The medicine is slowly withdrawn from the system at the desired rate while the body is floating on the contents of the stomach. The stomach's residual system is emptied after the medication has been released. A floating chamber with air, vacuum, or inert gas can be used to make amedication delivery system float in the stomach.[3] These systems are particularly advantageous for drugs that are specifically absorbed from the stomach or the proximal part of the small intestine. The controlled,slow delivery of drug to the stomach provides sufficient local therapeutic levels and limits the systemic exposure to the drug. This reduces side effects that are caused by the drug in the blood circulation. In addition, the prolonged gastric availability from a site directed delivery system may also reduce the dosingfrequency. [4, 5]

Pulsatile Drug Delivery System: The oral controlled-release system exhibits a characteristic drug release pattern in which the drug concentration is kept in the therapeutic window for an extended period of time, guaranteeing the sustained therapeutic activity. Therefore, there are some circumstances in which such a release pattern is inappropriate. These situations call for the medicine to be released after a delay means that during the first stage of dosage form administration, no medication should be released at all. Pulsatile or pulse release is the name for this type of release pattern.6 Pulsatile drug delivery systems are attracting a lot of attention since they provide spatial and temporal delivery as well as increased patient compliance by delivering the drug at the right location of action at the right time and in the right amount. The Pulsatile Drug Delivery System is a time-controlled drug delivery system that controls the lag time independently of the environment, including pH, enzymes, GIT motility, etc. The pulsatile systems are made for chrono pharmacotherapy, a form of medicine based on the body's circadian cycle. Drug administration in chrono pharmacotherapy (timed drug therapy) is coordinated with biological rhythms to maximize therapeutic impact while minimizing adverse effects on the patient. A good drug delivery system should be capable of supplying enough medication for an extended period of time for its optimum therapeutic activity.7 The technique can provide the right dosage of

medication at the right time and place to have the most impact on the condition, enhancing therapeutic effectiveness and patient compliance. According to the needs and conditions of the patient, it can provide a medication release burst at one or more specified time intervals and allows the release of pharmaceuticals at various places inside the gastro-intestinal tract. The advantages of PDDS extend to drugs with chrono pharmacological behavior, where night time dosing is required, and for various diseases that are influenced by circadian Rhythm since PDDS has a unique mechanism of delivery. Whereby a drug releases rapidly after a lag time, various PDDS is formulated to release a drug after a predetermined lag time in a specific region of the gastrointestinal tract, or as a chronotherapeutic time-dependent release.8 Floating drug delivery system is a strategy to prolong the residence time of various drugs on gastro intestinal fluid. The pulsatile drug delivery system is the rapid and transient release of certain amount of drug molecule within a short time period immediately after a predetermined of release period that is lag time. Drug having maximum absorption in stomach or having problem in intestine are preferred for Floating drug delivery system will be more beneficial for drug which need pulsatile release in stomach thus for disease hypertension. pulsatile drug delivery system is desired but if it will combine with floating action it will be more beneficial for targeting drug in stomach with time dependent release. Heart rate blood pressures are increased in early morning hour (morning or A.M. surge.) The most of hypertension patient, there is rather marked rise in Blood Pressure upon awakening, So there is a constant need for new delivery system that can provide increased therapeutic benefits to the patient by delivering antihypertensive drug at the right time, right place and in right amounts to coincide with circadian rhythm of body and avoid gastric emptying time of antihypertensive drug so it is necessary to us floating pulsatile drug delivery system.

I. DISEASE REQUIRED Gastro Retentive Drug Delivery Systems

Hypertension:

The morning surge, also known as the AM surge, is the early morning increase in heart rate and blood pressure. Afternoon blood pressure starts to drop and reaches its lowest point at midnight. The morning or "A.M." rise in blood pressure that most hypertension patients experience is very noticeable. For the first 4-6 hours after awakening, systolic blood pressure rises at a pace of around 3 mm Hg/hour, whereas diastolic blood pressure rises at a rate of about 2 mm Hg/hour.1

Neoplastic:

As might be expected, normal and cancerous cells' susceptibility to these chemicals may be influenced by the circadian cycles of both healthy and tumor cells. It has been established that normal and malignant tissue may have different "susceptibility rhythms" to drugs. In light of this, better tumor management may arise from the "correct" timing of therapeutic treatment, which also increases maximum drug tolerance and decreases host toxicity10

Myocardial infarction:

Myocardial infarctions tend to start more frequently in the morning, with 34% of incidents taking place between six in the morning and noon. The frequency of acute cardiac arrest and temporary myocardial ischemia is higher in the morning. The release of catecholamine, a rise in cortisol during platelet aggregation, and changes in vascular tone have all been proposed as potential reasons for these findings. If an ACE inhibitor is taken at night, it works better. When used at night, atenolol, nifedipine, and amlodipine are more effective.11,12

Diabetes Mellitus:

Numerous studies on the circadian variation of glucose and insulin in diabetes and their clinical significance in the case of insulin substitution in type I diabetes have been conducted. The purpose of insulin therapy is to emulate the physiological rhythm of continuous basal and meal-stimulated endogenous insulin production in healthy persons.13,14

Lipidemic Disease:

A circadian rhythm occurs during hepatic cholesterol synthesis therefore; cholesterol synthesis is generally higher during the night than during daylight. The maximal production occurs early in the morning, i.e. 12 h after the last meal. Studies with HMG Co-Areductase inhibitor have suggested that evening dosing was more effective than morning.14

II. MATERIALS AND METHODS:

2.1 Organoleptic Properties Determination of Melting Point:

This includes recording of colour, odor and taste of the drug, record of colour is very useful in establishing appropriate of batches. Melting point of Telmisartan was determined by capillary method. Fine powder of Telmisartan was filled in capillary tube (previously sealed at one end). The capillary tube inserted in sample holder of melting point apparatus and a thermometer is also placed in the apparatus. The temperature at which powder melted was noticed.

2.2. Spectroscopic Study:

2.2.1 UV-Visible Spectroscopy: The absorption maxima of the standard solution of drug in phosphate buffer ph 7.5, was determined by scanning between 200-400 nm.

2.2.2 Determination of λ in Phosphate Buffer Ph 7.5: 100 mg Telmisartan was transferred in 100 ml volumetric flask. Then volume was made up to 100 ml by phosphate buffer ph 7.5 (stock 1). after that 2 ml of stock solution was withdrawn from stock 1 and transferred to another 20 ml volumetric flask and volume was made up to 20 ml (100 µg/mL).after that 2 ml solution was withdrawn from stock 2 and transfer to another 20 ml volumetric flask and volume was make up to 20 ml by phosphate buffer 7.5. The resultant solution was subjected to UV spectrophotometric analysis and λ max was determined.

2.3 Thermal Analysis:

2.3.1 Differential Scanning Calorimetric (DSC) Study: By Differential scanning calorimetric study measures the heat loss and gain resulting from physical and chemical change within a sample as a function of temperature. It is used for assessment of purity, polymorphism, degradation and excipient compatibility. DSC studies were performed using a Mettler DSC 1 (Mettler Toledo, Germany). The instrument was calibrated with an indium standard. Accurately weighed sample (5-10mg) were placed in closed, pierced, flat bottom aluminum pans. DSC scan were recorded at a constant heating rate of 10oC/min. from 30 to 3500C. Nitrogen gas was pumped at a flow rate of 80ml/min. The melting points,peak maxima, appearance any new peak and change in peak shape were noted.

2.4. Preparation of Core Tablet (CT):

2.4.1 Direct Compression Tablet of Telmisartan were made by direct compression method. All ingredients were weighted accurately and mix well for 15 min. sodium starch glycolate used as disintegrating and magnesium stearate were used as lubricant and microcrystalline cellulose used as diluents and PVP as binder. The resultant powder mixtures were then compressed into tablets using KBR machine (die diameter 8mm).

Method of Preparation of Tablet:

INGREDIENTS (Mg)	C1	C2	C3	C4	C5
Telmisartan	40	40	40	40	40
Sodium Starch glycolate	8	10	12	14	16
Magnesium stearate	2	2	2	2	2
Microcrystalline cellulose	140	138	136	134	132
Polyvinylpyrrolidone	10	10	10	10	10
Total	**200**	**200**	**200**	**200**	**200**

Table no.1 Formulation of CT of Telmisartan

2.4.2. Formulation of The Floating Pulsatile Release Tablet by Direct Compression (FPRT): Dry coated Floating pulsatile tablet was prepared by placing HPMC excipient layer in 12 mm die and core tablet was placed on it. Then, the remaining quantity of floating pulsatle release layer wasadded in the die so as to cover core tablet and finally compressed 800mg tablet by using KBR tablet machine. (Die Diameter 12 mm).

2.5 Micromeritic Properties:

2.5.1: Bulk Density, Tap Density: The term bulk density refers to a measure used to describe a packing of particles. It is (gm/ml) and was determine using a balance and measuring cylinder. An accurately weighed amount of powder should be introduced in 100 ml measuring cylinder. Note the initial volume, then the cylinder should

be tapped 100 times on a plane hard surface and Tapped density is determined by placing a graduated cylinder containing same mass of powder on a mechanical tapper tapped volume of packing should be recorded. Bulk Density (BD) and Tapped Density (TD) should be calculated by using following formula.

$$\text{Bulk Density} = \frac{\text{Weight of the powder}}{\text{Bulk volume}}$$

$$\text{Tap Density} = \frac{\text{weight of the powder}}{\text{Tapped volume}}$$

2.5.2 Carr's Index:

Compressibility index of powder can be determined by following carr's compressibility index (%) carr's index calculated by suitable formula to determine flow properties of powder. The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is a measure of the relative inter-particulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater inter-particle interactions, and a greater difference between the bulk and tapped densities will be observed.

Table no 2: Flow properties of powders according to cars index

Sr. no	Carr's index (%)	Flow
1	5-15	Excellent
2	12-16	Good
3	18-21	Fair to passable
4	23-35	Poor
5	33-38	Very poor
6	>40	Extremely poor

2.5.3. HAUSNER'S RATIO Hausner's ratio is an index of ease of powder flow. It is calculated by the following formula:8

$$\text{Hausne's ratio} = \frac{\text{Tap density}}{\text{Bulk density}}$$

Table no 3: Hausners ratio no

Sr. no	Hausner's ratio	Flow
1	1.05-1.18	Excellent
2	1.14-1.20	Good
3	1.22-1.26	Fair to pass
4	1.30-1.54	Poor
5	1.50-1.61	Very poor
6	1.67	Very very poor

2.5.4 Determination of Angle of Repose:

Angle of repose is the tan inverse of angle between height (h) of pile of powder and the radius (r) of the base of conical pile. It can be obtained between the freestanding surface of the powder heap and the horizontal plane. The fixed funnel that is secured with its tip at a given height h, above graph paper, placed on the flat horizontal surface. Powder is carefully poured through funnel until the apex of conical pile just touches the tip of funnel. Different ranges of flow ability in terms of angle of repose are given bellowTable no 4: Determination of Angle of Repose

Sr. no	Flow property	Angle of Repose(degrees)
1	Excellent	25-30
2	Good	31-35
3	Fair-aid not needed	36-40
4	Passable may hang up	41-55
5	Poor must agilate,vibrate	46-55
6	Very poor	56-65
7	Very very poor	>66

2.6. Evaluation Parameter of Core Tablet

2.6.1 In-Vitro Disintegration Time The U.S.P. device to test disintegration uses 6 glass tubes that are 3" long; open at the top and 10 mesh screens at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37 ± 20 C such that the tablet remain 2.5cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet. According to the test the tablet must

disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass.

2.7 Evaluation Parameter of Floating Pulsatile Tablet:

❖ Weight variation

❖ Thickness

❖ Hardness

❖ Friability

❖ Floating time and floating lag time

2.7.1. Weight Variation Test:

Twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity. The percent deviation was calculated using the following formula.

% Deviation = (Individual weight – Average weight / Average weight) × 100

Table no 5; Pharmacopoeia specifications for tablet weight variation:

Average weight of tablets (mg) (IP)	**Average weight of tablets (mg) (USP)**	**Maximum percentage difference allowed**
Less than 80	Less than 130	10
80-250	130-324	7.5
More than 250	More than 324	5

2.7.2. Thickness Test: The thickness in millimetres (mm) was measured individually for 10 pre-weighed tablets by using a Vernier Callipers. The average thickness and standard deviation were reported.

2.7.3 Hardness: Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under conditions of storage, transportation and handling before usage depends on its hardness. For each formulation, the hardness of 10 tablets was determined using Pfizer hardness tester and the average was calculated and presented with standard deviation.

2.7.4 Friability Test: Twenty (20) tablets were selected from each batch and weighed. Each group of tablets was rotated at 25 rpm for 4 minutes (100 rotations) in the Roche friabilator. The tablets were then dusted and re-weighed to determine the loss in weight. Loss in the weight of tablet is the measure of friability and is expressed in percentage as:

$$\% \text{ Friability} = [(W1 - W2) / W1] \times 100$$

Where W1 = Initial weight of 20 tablets

W2 = Weight of the 20 tablets after testing

2.8 In Vitro Buoyancy Studies:

The in vitro buoyancy was determined by floating lag time, as per the method described by Rosa et al. The tablets were placed in a beaker containing 100 mL of 0.1N hydrochloric acid. The time required for the tablet to rise to the surface and float was determined as floating lag time. The duration of time for which the dosage form constantly remained on the surface of medium was determined as the total floating time.

2.9 In Vitro Dissolution Study of Floating Pulsatile Release Tablet (FPRT):

Tablet was introduced in dissolution test apparatus (paddle) and apparatus was set in motion and rotate with 75 rpm and 5 ml sample was withdrawn after 1 hour, and dilute to 25 ml volumetric flask, with phosphate buffer ph 7.5 after that 2nd dilution was taken i.e. 0.1 ml in 10 ml volumetric flask. Sample withdrawn were analysed by UV spectrophotometer at 296 nm wavelength using phosphate buffer ph 7.5.

III. RESULT AND DISCUSSION:

3.1 Preformulation:

SR. NO	EXPERIMENT	RESULT
1.	**Physical Properties** a) Color b) Odor	a) A white to off-white crystalline powder b) odorless
2	**Solubility** a) Sparingly soluble b) Slightly soluble c) Practically insoluble	Sparingly soluble in Dichloromethane Slightly soluble in Methanol Practically insoluble in Water
3	**Melting Point**	The reported melting point of Telmisartan is in the Range of 265°C-272°C the observed melting point is270^0c.

Table No 6: Pre formulation

Preformulation is the first step in rational development of any Pharmaceutical dosage form ofa new drug. Preformulation study focuses on Physiochemical Property of new drug compound that can affect drug performance and development of effective dosage form. The reported melting point of pure drug Telmisartan is the range of 265oC-272oC and the observed melting point at 270o c. It confirmed that given powdered drug is in pure in nature and it confirmed that given power is Telmisartan.

3.2 Thermal Analysis:

Differential Scanning Calorimetric (DSC) Study:

Fig No 1: Differential Scanning Calorimetric Graph

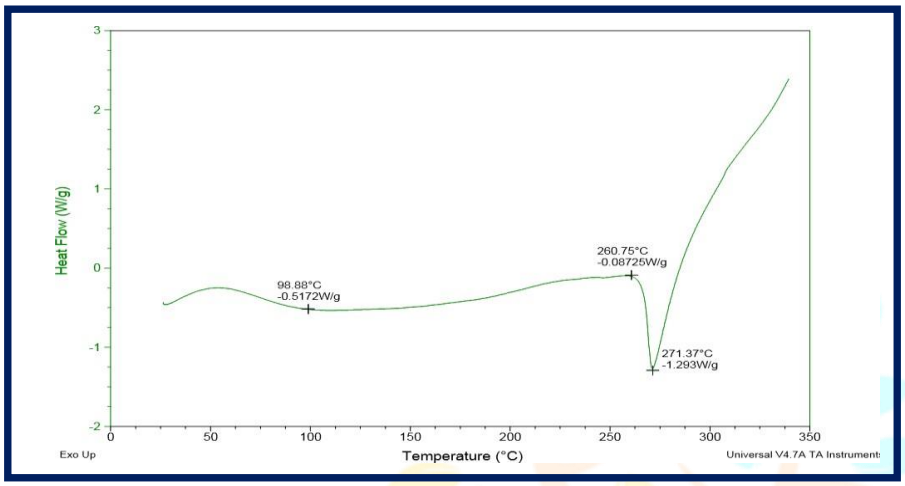
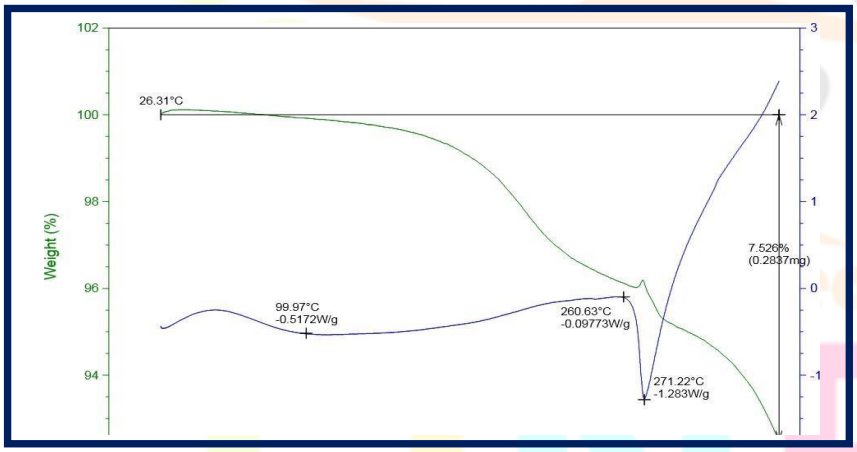


Fig No 2: Differential Scanning Calorimetric Graph



DSC studies were performed using a Mettler DSC 1 (Mettler Toledo, Germany). The instrument was calibrated with an indium standard. Accurately weighed sample (5-10mg) were placed in closed, pierced, flat bottom aluminium pans. DSC scan were recorded at a constant heating rate of 10oC/min from 30 to 350oC. Nitrogen gas was pumped at a flow rate of 80ml/min. The melting points, peak maxima, appearance any new peak and change in peak shape were noted. DSC was used to assess the thermal behaviour of the drug Telmisartan. In the fig. 1 DSC Thermogram of Telmisartan shows a single sharp characteristic endothermic peak (T peak=271.37oC) corresponding to the melting point of Telmisartan. And a single peak indicates that the drug sample is free from impurities.

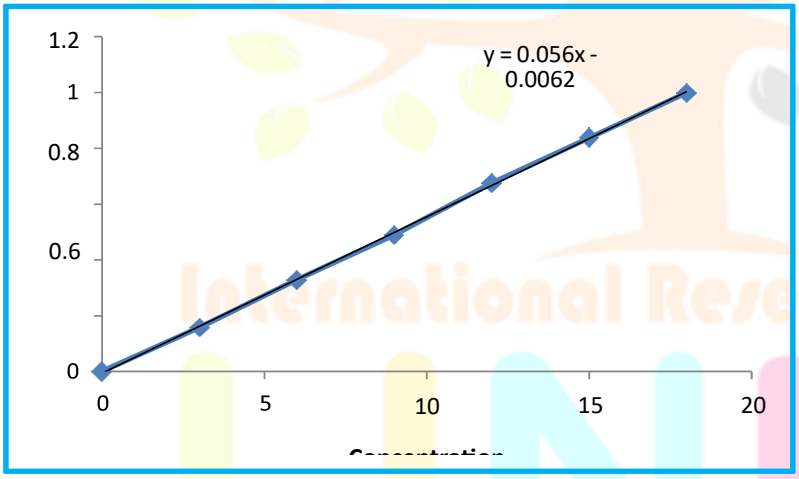
3.3 Calibration Curve of Telmisartan:

Calibration curve of Telmisartan in phosphate buffer pH 7.5 was found to be linear in range of 3 to 18 µg/ml and coefficient was found to be 0.999

Table No.7: Reading of Calibration Curve of Telmisartan in Phosphate Buffer Ph 7.5

Sr. No	Concentrationµg/ml	Absorbance
1	3	0.157
2	6	0.328
3	9	0.489
4	12	0.675
5	15	0.838
6	18	0.999

Fig No. 3: Calibration Curve of Telmisartan in Phosphate Buffer Ph 7.5



The λ max of pure drug Telmisartan was found to be 296nm. It indicates that given sample of drug is pure in nature and it confirmed that the given powder is Telmisartan. The calibration curve of telmisartan is as per beers law the slope was found 0.006 and R 2=0.999. Hence from calibration curve and λ max it is clear that given sample of powder drug is Telmisartan and itis pure in nature.

3.4 COMPATIBILITY STUDY:

FTIR Spectra of Pure Drug Telmisartan:

Fig. No. 4: FTIR Spectra of Pure Telmisartan.

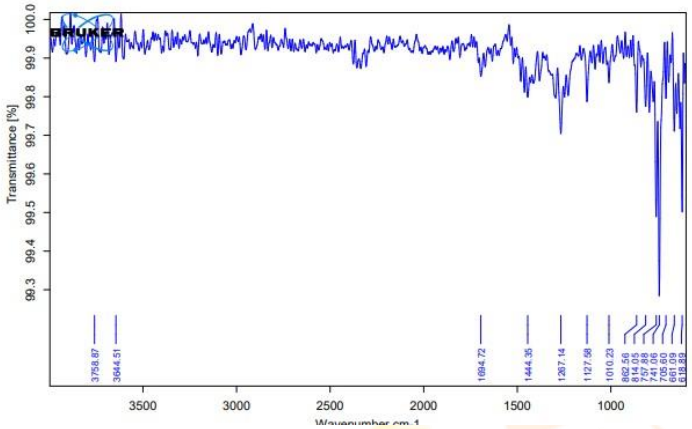


Table. No. 8: FTIR Spectra of Pure Telmisartan.

Functional group	Theoretical Wave number (cm^{-1})	Peaks(cm^{-1})	Indication
C-H	2850-3000	2866.137	Alkanes (stretch)
C-N	1080-1360	1295.330	Amines (stretch)
C=C	1620-1680	1686.404	Alkenes (stretch)
O-H	2500-3300	2735.455	Carboxylic acid (stretch)

FTIR Spectra of Drug With Excipients:

Fig No: 5 FTIR Spectra of Drug and Excipient

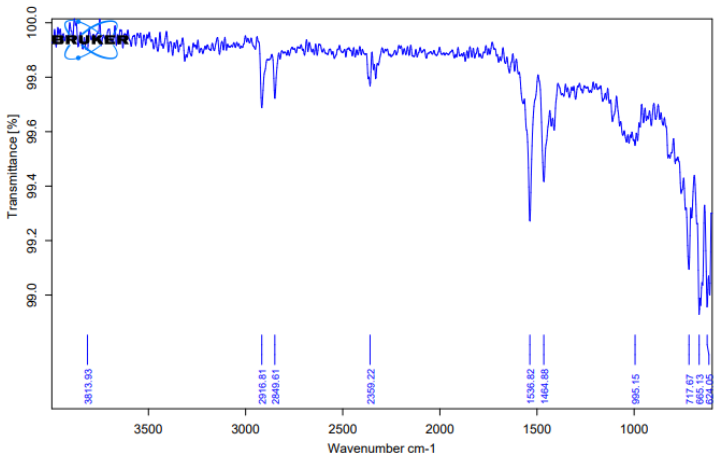


Table No 9: FTIR Values Of Drug and Excipients

Functional Group	Theoretical Wave number (cm^{-1})	Peaks(cm^{-1})	Indiction
C-H	2850-3000	2916.124	Alkanes (stretch)
C-N	1080-1360	1264.526	Amines (stretch)
C=C	1620-1680	1638.471	Alkenes (stretch)
O-H	2500-3300	2849.054	Carboxylic acid (stretch)

Infrared spectra of pure Telmisartan and Physical mixture were recorded using Fourier transform infrared spectroscopy (Agilent carry 630). By this clear it is clear that the drug remained its normal value even in its formulation along with polymer and other excipients. By this observation it is clearly indicate that there is no interaction of drug with polymer and excipient used in present study

3.5 Pre-Compression and Post Compression Parameter:

Table No 10: Pre-Compression Parameters of CT

BATCH CODE	BULK DENSITY (g/ml)	TAPPED DENSITY (g/ml)	HAUSNER'S RATIO	CARR'S INDEX (%)	ANGLE OF REPOSE θ
C1	0.39±0.07	0.44±0.06	1.11± 0.03	11.62±1.07	21.1± 0.40
C2	0.43±0.06	0.48±0.08	1.12± 0.02	12.5±1.18	22.02±1.09
C3	0.35±0.010	0.40±0.07	1.11± 0.08	10± 0.59	31.15± 0.25
C4	0.41±0.06	0.51± 1.09	1.15± 0.04	13.28±0.35	24.17± 0.30
C5	0.44± 0.08	0.50±0.06	1.11± 0.07	10± 0.54	25.14± 0.38

The tablets of different formulations were subjected to various evaluation tests, such as thickness, uniformity of weight, hardness, friability, and drug content the result was shown in table.

3.5.1 Hausner's Ratio: In the result of Hausner's ratio of various batches was shown in table no 22. It shows that all batch show excellent flow properties. All Batches were in the range of1.11±0.03 to 1.16±0.04.

3.5.2 Carr's Index: Carr's index was carried out and result was shown in table no 05. It was found that all batches shown good and excellent flow properties. All batches were in the range of 10±0.54 to 14.28±0.35

3.5.3Angle of Repose: The angle of repose of core tablet was carried out and the result was shown in table no 05. It shown that batch C1 and C2 has excellent flow properties and batch C3, C4, C5 shown good flow properties. Angle of repose was found to be in the range of 21.1±0.40 to31.15±0.25

Evaluation of Disintegration Time and Drug Content of Core Tablet:

Table No 11: Evaluation of Disintegration and Drug Content Core Tablet

BATCH CODE	DISINTEGRATION TIME (SEC)	DRUG CONTENT
C1	197±1.10	97± 0.046
C2	165±1.24	97±0.57
C3	135±1.18	98±0.88
C4	93 ±0.40	97±1.19
C5	65 ±0.78	99±0.35

3.7 Disintegration Time and Drug Content of Core Tablet: The tablet to become fully available for absorption, the tablet must first disinigrate and discharges the drug to the body fluid for dissolution. The disintegration time of core tablet batch C1 to C5 obtained 199±1.10, 162±1.24, 130±1.18, 97±0.40, 60±0.78 respectively. In that increase the concentration of disintegrating agent of sodium starch glycolate, there are decrease the disintegration time. Reading of the drug content is in prescribed limit.

3.8 Post Compression Parameter of FPRT:

Table No 12: Post Compression Parameter Of FPRT:

Batch Code	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm3)	Friability(% loss of weight)
C1	790± 1	7.3± 0.02	6.2± 0.12	0.5± 0.02
C2	796± 3.4	6.9± 0.02	7.5± 0.11	0.62 ± 0.02
C3	800±1	7.2 ±0.2	7.1± 0.1	0.54± 0.01
C4	809±3	7.2± 0.10	7± 0.24	0.62± 0.03
C5	807 ±2.8	7± 0.11	7.3±0.11	0.60±0.03

3.8.1 Weight Variation Test- The percentage weight variation of all formulation was shown in table no. 27 All batch posses weight variation test within pharmacopeial limit and it was found between 790±1 and 809±3.

3.8.2Thickness- The thickness of BPRT tablet is shown in table. The thicknesses of BPRT tablets were measured by verniarcaliper. In that all of formulation shown uniform thickness. The thickness of all formulation ranged between 6.9±0.02 to7.3±0.02 mm. The thickness should be controlled within a ± 5% variation of standard.

3.8.3 Hardness Test- The hardness of batches of BPRT tablet was found to be range between6.2±0.12 to 7.5±0.11 kg/cm3

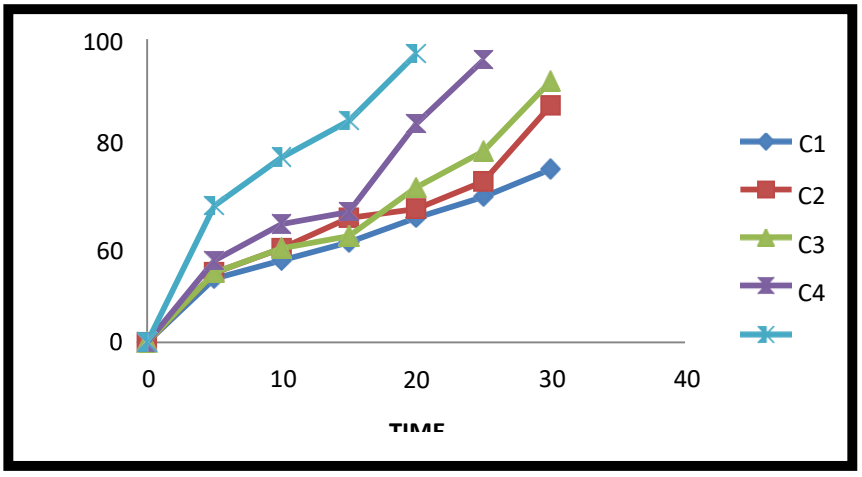
3.8.4 friability Test The batches of all formulation of friability test were shown in table all tablet insuring that the tablet were mechanically stable. According to B.P specification, the total loss should not excide than 1 %

3.9 Dissolution Study of Core Tablet:

Table No 13: Post Compression Parameter Of FPRT:

Time (MIN)	C1	C2	C3	C4	C5
5	21± 0.23	23± 0.29	23± 1.2	27± 0.9	45± 0.2
10	27 ± 0.73	31± 0.82	31± 0.4	39± 1.3	61± 0.8
15	33 ± 0.08	41± 0.36	35± 0.7	43± 0.5	73± 1.2
20	41± 0.46	44± 0.99	51± 1.2	72± 0.6	95 ± 0.9
25	48± 1.11	53± 0.36	63± 0.8	93 ± 0.8	_
30	57 ± 0.26	78± 0.12	86 ± 0.7	_	_

Fig. No 6: % Drug Release Batches C1 to C5:

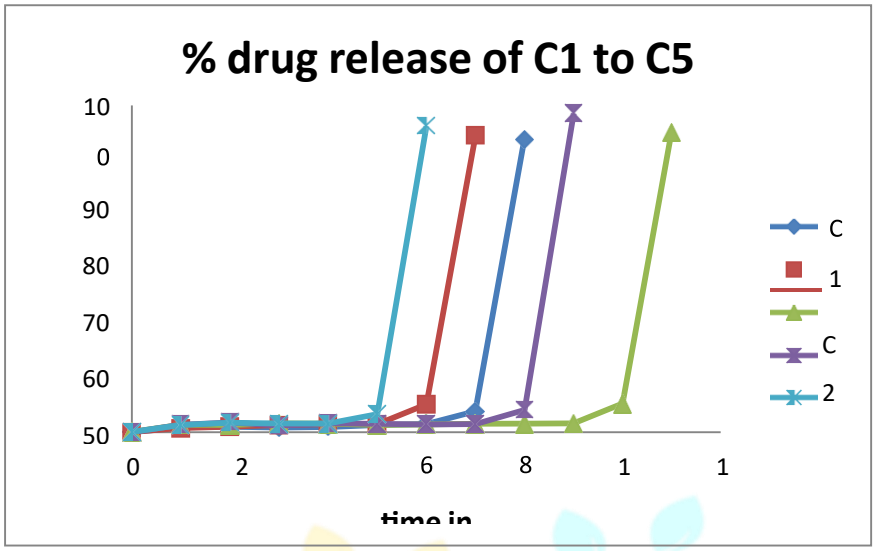


3.10 Dissolution Study of FPRT Tablet:

Table No 14: Dissolution Study of FPRT Tablet:

Time (Hrs)	A1	A2	A3	A4	A5
1	1.48±0.001	1.14±0.005	2.22±0.0011	2.31±0.0015	2.11±0.00020
2	1.69±0.0013	1.62±0.0012	2.07±0.0033	2.99±0.0056	2.77±0.00025
3	1.44±0.0012	2.07±0.004	2.62±0.0011	1.99±0.0014	2.54±0.0013
4	1.62±0.002	2.34±0.0060	2.53±0.009	2.69±0.0006	2.53±0.0003
5	2.20±0.0020	2.33±0.003	2.1±0.0081	2.45±0.0026	5.44±00011
6	2.49±0.0013	8.46±0.0045	2.32±0.00066	2.39±0.0033	93.56±0.0028
7	6.33±0.0011	90.8±0.0099	2.46±0.001	2.44±0.0032	-
8	89.52±0.005	-	2.52±0.0081	6.83±0.009	-
9	-	-	2.61±0.0033	97.56±0.0051	-
10	-	-	8.71±0.0022	-	-
11	-	-	91.77±0.0015	-	-

Fig. no 7: Graph of Drug Release of floating pulsatile tablet



IV. CONCLUSION:

In the dissolution study of Floating pulsatile release tablet the percent drug release from batch C1 to C5 was found to be 89.52±0.005, 90.8±0.0099, 91.77±0.0015, 97.56±0.0051, 93.56±0.0028 respectively. In that batch no. C4 show more drug release compared to other batches. For the treatment of hypertension it is necessary to release of tablet in morning (AM surge) hence there are required release of drug after lag time that is C 8 hrs. Graph of drug release show that in the batch no C4 release of drug after 8 hrs. Because of more drug release of batch no C4 that is 97.56±0.0051 and release of drug after 8 hrs. Which is concerned with circadian rhythm of disease of hypertension, hence batch no C4is optimized batch.

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