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Research Article

Formulation and Evaluation of Pulsatile Drug Delivery System of Telmisartan

Rahul Mante*, R. S. Radke, Aijaz Sheikh, K. R. Biyani

Anuradha College of pharmacy Chikhli, Dist. Buldana, Maharashtra 443201

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ABSTRACT

The present study was undertaken to develop and evaluate pulsatile tablets of Telmisartan designed to release the drug after a specific lag time, synchronized with the circadian rhythm of hypertension, particularly addressing the early morning surge in blood pressure. Core tablets were prepared using direct compression method and formulated with varying concentrations of superdisintegrants—Croscarmellose Sodium and Sodium Starch Glycolate. Among the batches, C2, containing 4% Croscarmellose Sodium, demonstrated the most rapid disintegration (28 sec) and highest drug release at 15 minutes (98.84%), indicating it as the optimal core formulation. Press-coated pulsatile tablets were developed using the optimized core (C2) and a coating of HPMC K100M and HPMC E5 in different ratios. The lag time and drug release profile varied with polymer composition. Formulation F4, with a 3:1 ratio of HPMC K100M to HPMC E5, exhibited the desired lag phase of approximately 5 hours followed by rapid drug release, aligning with the target for morning dosing. All pre-compression and post-compression parameters of both core and coated tablets were within acceptable limits, ensuring good flow properties, mechanical strength, and uniformity. The in-vitro drug release followed Korsmeyer-Peppas kinetics, suggesting anomalous (non-Fickian) drug release behavior, governed by both diffusion and erosion mechanisms. Stability studies conducted on the optimized formulation (F4) under accelerated conditions showed no significant changes in drug content, appearance, or release profile, indicating good stability over 3 months. The developed press-coated pulsatile tablets of Telmisartan successfully achieved a controlled lag phase and targeted drug release, potentially improving therapeutic outcomes and patient compliance in hypertensive patients with a circadian rhythm-based symptom pattern.

INTRODUCTION

Pulsatile drug delivery systems (PDDS) are designed to release drugs in a pulsating manner, offering a distinct approach from continuous release systems. These systems are valuable when a drug needs to be released at a specific time or synchronized with the body's natural rhythms.[1]

***Corresponding Author:** Rahul Mante
Address: *Anuradha College of pharmacy Chikhli, Dist. Buldana, Maharashtra 443201*
Email : rahulmante597@gmail.com
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Key characteristics of PDDS include a lag time before drug release and a subsequent rapid release of the drug. Such systems are particularly beneficial in conditions where symptoms exhibit time-dependent variation, such as hypertension, asthma, arthritis, and cardiovascular diseases.[2] Telmisartan, an angiotensin II receptor antagonist, is widely used in the treatment of hypertension and related cardiovascular conditions. Its therapeutic effectiveness can be enhanced by delivering it in a pulsatile manner, especially since blood pressure typically rises sharply in the early morning hours a phenomenon known as the "morning surge." Conventional immediate-release or sustained-release formulations of Telmisartan may not provide optimal control of this early morning rise in blood pressure. A pulsatile release system can be designed to delay drug release until the early morning hours, thus offering targeted therapeutic action, minimizing drug wastage, and reducing side effects.[3,4] The formulation of pulsatile tablets involves the use of time-dependent or pH-sensitive polymers that form a protective barrier around the core drug, allowing for a delayed and controlled release. Techniques such as press coating, compression coating, or multi-layered tablets are employed to develop these systems. This study aims to formulate and evaluate pulsatile tablets of Telmisartan that can provide a controlled lag phase followed by a burst release, thereby enhancing patient compliance and therapeutic efficacy by synchronizing drug release with the body's natural rhythms.[5,6]

MATERIALS AND METHODS

Materials

Telmisartan was reveived as gift sample from Glenmark Pharmaceuticals, Goa. HPMC K100M and HPMC E5 was purchased from S. D. Fine Chemicals. All other solvents and reagents were of analytical grade.

Method

Preparation of Core Tablets of Telmisartan

Core tablets containing 40 mg of Telmisartan were prepared by direct compression. Four different formulations (C1-C4) were prepared, varying the type and concentration of disintegrants Croscarmellose Sodium and Sodium Starch Glycolate, while keeping the total weight at 100 mg using microcrystalline cellulose as a diluent and magnesium stearate and talc as lubricants. The powder blends were prepared by mixing the accurately weighed ingredients, passing them through sieve no. 30, and compressing them using an 8 mm flat face punch on a multi-station tablet punching machine by direct compression method.[7,8,9]

Table 1: Formulation of Telmisartan Core Tablets

Sr. No	Ingredients (Mg)	Batch			
		C1	C2	C3	C4
1	Telmisartan	40	40	40	40
2	Croscarmellose Sodium	2	4	-	-
3	Sodium Starch Glycolate	-	-	2	4
4	Magnesium stearate	1	1	1	1
4	Talc	1	1	1	1
5	Microcrystalline Cellulose	55	54	55	54
6	Total Wt.	100	100	100	100

Formulation of Press Coated Pulsatile Tablet of Telmisartan

Press-coated pulsatile tablets were prepared using the optimized core tablet formulation (C2) and a coating layer composed of HPMC K100M and HPMC E5 in different weight ratios (Table 2). All the ingredients were accurately weighed and passed through sieve no.70 and thoroughly mixed for 5 min. Initially half quantity of the mixture of two polymers HPMC H100M and HPMC E5 with different weight ratio was filled in the die of 12mm diameter and then gently compacted to make a

powder bed with a flat surface. The core tablet was then carefully placed in the centre of powder bed. The die was filled with the remaining of coating mixture so that powder bed was compressed directly using 12mm flat punch to produce desired press coated tablets. 1% of magnesium stearate and talc were used as lubricants in the coating layer.[10,11,12]

Table 2: Composition of Press Coated Tablets

Sr. No	Ingredients (mg)	Batches					
		F1	F2	F3	F4	F5	F6
1	Core Tablet (C2)	100	100	100	100	100	100
2	HPMC K100M	200	-	100	150	160	170
3	HPMC E5	-	200	100	50	40	30
4	Total Wt. (mg)	300	300	300	300	300	300

Evaluation of Powder Blend (Precompression Parameters)

Bulk Density

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

$$Bulk\ Density = \frac{Wright\ of\ Powder}{Volume\ Noted} \dots\dots\dots (1)$$

Tapped Density:

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for multiple times and the tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % in a bulk density apparatus. It is expressed in g/ml and is given by following formula.[13]

$$Tapped\ Density = \frac{Wright\ of\ Powder}{Tapped\ Volume\ of\ Powder} \dots\dots\dots (2)$$

Angle of Repose (Ɵ):

The friction forces in a loose powder can be measured by the angle of repose (Ɵ). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane. The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of powder formed.

Carr's Compressibility Index and Hausner Ratio

The Carr's compressibility index, also known as the Carr's index, is a parameter used to assess the compressibility and flow properties of powdered or granular materials, particularly pharmaceutical powders. It is calculated based on the bulk density and tapped density of the powder and provides insights into its flowability and compaction characteristics. It indicates powder flow properties. It is expressed in percentage and is given by following equation

$$\text{Compressibility Index (\%)} = \frac{Tapped\ Density - Bulk\ Density}{Tapped\ Density} X100 \dots\dots\dots (3)$$

Hausner's ratio, is a parameter used to assess the flowability of powdered or granular materials, particularly pharmaceutical powders. It is calculated based on the tapped density and bulk

density of the powder and provides insights into its flow properties. The Hausner ratio is defined as the ratio of tapped density to bulk density, and it is calculated using the following formula.[14]

$$\text{Hausner Ratio} = \frac{Tapped\ Density}{Bulk\ Density} \ldots\ldots\ldots (4)$$

Evaluation of Core and Pressed Coated Pulsatile Tablets

Weight Variation

The weight variation test is a pharmaceutical quality control test performed on tablets and capsules to ensure uniformity of dosage units within a batch or lot. 20 tablets were selected randomly from the lot and weighted individually to check for weight variation. The average weight per unit is then calculated by dividing the total weight by the number of units in the sample.[15]

Hardness

Tablet hardness, often measured in terms of breaking force or resistance to crushing, provides an indication of the mechanical strength and robustness of the tablet. Hardness testing ensures that tablets can withstand handling, packaging, and transportation without breaking or crumbling, thereby maintaining their integrity and appearance throughout their shelf life. Hardness or tablet crushing strength ie the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in kg/cm2.

Thickness

The tablet thickness test is a fundamental quality control measure in pharmaceutical manufacturing, especially for solid oral dosage forms like tablets. Tablet thickness is directly related to the amount of material compressed into each tablet during the manufacturing process. The thickness of the prepared tablets was measured using Digital Vernier calliper. It is expressed in mm.

Friability

The friability test assesses the mechanical strength and resistance to abrasion of tablets during handling, packaging, and transportation. The friability test ensures that tablets maintain their physical integrity and withstand mechanical stress under normal handling conditions. Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at height of 6 inches in each revolution. Pre weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were de dusted using a soft muslin cloth and reweighed and the friability (%) was calculated.[16]

Content Uniformity

Ten tablets were randomly selected and tested for their drug content. Each tablet was powdered and quantity of powder equivalent to 100 mg of drug was taken and transfer it to 10 ml of phosphate buffer pH 6.8. The resulting solution was then diluted appropriately and measured using a UV-Visible spectrophotometer at 296 nm.

Disintegration Test

Tablet disintegration test was carried out on core tablets of telmisartan. The test was performed in the USP disintegration test apparatus. One tablet was placed in each tube and the basket rack was positioned in a 1 liter beaker containing 6.8 phosphate buffer solution at 37 °C ± 1 °C such that the tablet remains 2.5 cm below the surface of the liquid. The time taken for the complete disintegration of the tablets was noted.[17]

In-Vitro Dissolution Study

The in-vitro dissolution study was carried out in USP dissolution test apparatus type II (paddle) with a dissolution medium of 900 ml of phosphate buffer pH 6.8, at 50 rpm (37±0.5ºC). 5 ml aliquot was withdrawn at the specified time interval, filtered through whatman filter paper, and measured spectrophotometrically after suitable dilution at 295 nm using UV-Visible spectrophotometer. An equal volume of fresh medium, which was pre warmed at 37ºC was replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. The results in the form of percent cumulative drug released was calculated.[18,19]

Drug Release Kinetics

The in-vitro drug release data were fitted to various kinetic models: Zero-order, First-order, Higuchi, and Korsmeyer-Peppas to determine the drug release mechanism. The Korsmeyer-Peppas model was further used to determine the release exponent (n) to characterize the drug release mechanism.

Stability Study

Accelerated stability studies were conducted on the optimized formulation by storing the tablets in aluminum foil strips in a stability chamber maintained at 40 °C and 75% RH for 3 months, according to ICH guidelines. The tablets were evaluated for changes in appearance, hardness, disintegration time, drug content, and in-vitro drug release at initial time points and after 3 months.[20]

RESULTS AND DISCUSSION

Precompression Parameters

The micromeritics properties of the powder blend for core tablets of Telmisartan (batches C1 to C4) were evaluated to determine the flow characteristics and packing ability, which are critical for ensuring uniformity in tablet compression. The bulk density of the formulations ranged from 0.50 to 0.52 g/cc, while the tapped density varied from 0.57 to 0.59 g/cc. These values indicate good packing properties and minimal variability between batches. The compressibility index, an indicator of powder flowability and compressibility, ranged from 10.34% to 13.79%. According to standard micromeritics guidelines, a compressibility index below 15% suggests good flow properties, confirming the suitability of these blends for tablet compression. Correspondingly, the Hausner's ratio ranged between 1.11 and 1.16, further supporting the observation that the powder blends exhibit good to excellent flowability, as values below 1.25 indicate desirable flow behavior. The angle of repose, which provides insights into inter-particle friction and cohesion, varied between 25.32° and 27.50° is indicative of good flow properties. The results are shown in table 3.

Table 3: Micromeritics Properties of Powder Blend of Core Tablets of Telmisartan Formulation (C1 to C4)

Batch	Bulk Density (g/cc)	Tapped Density (g/cc)	Compressibility Index (%)	Hausner's Ratio	Angle of Repose (Θ)
C1	0.52 ± 0.05	0.59 ± 0.06	11.86 ± 0.07	1.13 ± 0.02	25.32
C2	0.51 ± 0.06	0.59 ± 0.05	13.55 ± 0.09	1.15 ± 0.02	25.62
C3	0.50 ± 0.04	0.58 ± 0.08	13.79 ± 0.05	1.16 ± 0.04	27.50
C4	0.52 ± 0.05	0.57 ± 0.04	10.34 ± 0.07	1.11 ± 0.05	26.30

Post Compression Parameters of Core Tablets of Telmisartan

Table 4: Post Compression Parameters of Core Tablets of Telmisartan (C1 to C4)

Batch	Weight Variation (mg)	Hardness (Kg/cm²)	Friability (%)	Thickness (mm)	Drug Content (%)	Disintegration Time (sec)
C1	100 ± 1.4	3.5 ± 0.48	0.90 ± 0.16	3 ± 0.06	97.56 ± 0.81	34 ± 1.12
C2	101 ± 1.2	3.5 ± 0.61	0.86 ± 0.20	3.1 ± 0.04	99.16 ± 0.74	28 ± 1.51
C3	100 ± 1.6	3.4 ± 0.52	0.88 ± 0.18	3.2 ± 0.03	96.72 ± 0.66	38 ± 0.74
C4	101 ± 1.4	3.6 ± 0.56	0.87 ± 0.23	3 ± 0.04	98.45 ± 0.60	32 ± 0.64

The weight variation for all batches was within the acceptable limits, with values ranging from 100 ± 1.4 mg to 101 ± 1.4 mg. This indicates uniformity in tablet weight, which is essential for dose accuracy. The hardness of the tablets remained consistent at approximately 3.5 ± 0.48 to 3.6 ± 0.56 Kg/cm², indicating adequate mechanical strength to withstand handling and packaging without compromising tablet integrity. Friability values ranged from 0.86±0.20% to 0.90±0.16%, which are within acceptable limits (below 1%), ensuring that the tablets possess sufficient mechanical resistance without excessive brittleness. The thickness of the tablets varied slightly, ranging from 3.0 ± 0.03 mm to 3.2 ± 0.04 mm, which is within the standard tolerance limits, indicating uniformity in compression. The drug content analysis showed uniform drug distribution in all batches, with values between 96.72% and 99.16%, which complies with standard pharmacopeial limits (90-110%). This ensures that the patients receive the correct therapeutic dose. The disintegration time for the core tablets varied from 28 ± 1.51 sec to 38 ± 0.74 sec, indicating rapid disintegration within acceptable limits, which is essential for ensuring effective drug release and absorption. Among the formulations the batch C2 showed lowest disintegration time of 28 sec formulated using 4% of Croscarmellose Sodium as superdisuntegrants.

In-Vitro Dissolution Study of Core Tablets

The dissolution profile of the Telmisartan core tablets was assessed to determine the impact of different superdisintegrants on drug release. At the 5-minute mark, batch C2 (Croscarmellose Sodium 4%) exhibited the highest drug release (52.26%), followed by C4 (48.66%), C3 (44.72%), and C1 (41.15%). This indicates that a higher concentration of Croscarmellose Sodium enhances the initial drug release. At 15 minutes, C2 achieved almost complete dissolution (98.84%), while C4 (90.12%) and C3 (70.02%) followed. The increase in Croscarmellose Sodium concentration significantly accelerated drug release compared to Sodium Starch Glycolate. By 20 minutes, both C1 and C3 had comparable release profiles (~86%), whereas C4 achieved 98.69% dissolution, suggesting that a higher concentration of Sodium Starch Glycolate improves overall drug release. At 30 minutes, almost complete drug release was observed in C1 (97.56%) and C3 (98.61%). The dissolution results confirm that the type and concentration of superdisintegrants significantly influence drug release. Croscarmellose Sodium at 4% (C2) demonstrated the fastest and most complete dissolution, making it the most effective superdisintegrant among the tested formulations. Sodium Starch Glycolate at 4% (C4) also showed high drug release but required slightly more time than C2. Lower concentrations of superdisintegrants (C1 and C3) exhibited slower drug release rates, indicating that higher concentrations contribute to better disintegration

and dissolution. These findings suggest that selecting an optimal superdisintegrant and its concentration is crucial for achieving rapid and complete drug release, which is essential for ensuring the therapeutic efficacy of Telmisartan tablets. Data for in vitro drug release of core tablets was shown in figure 1.

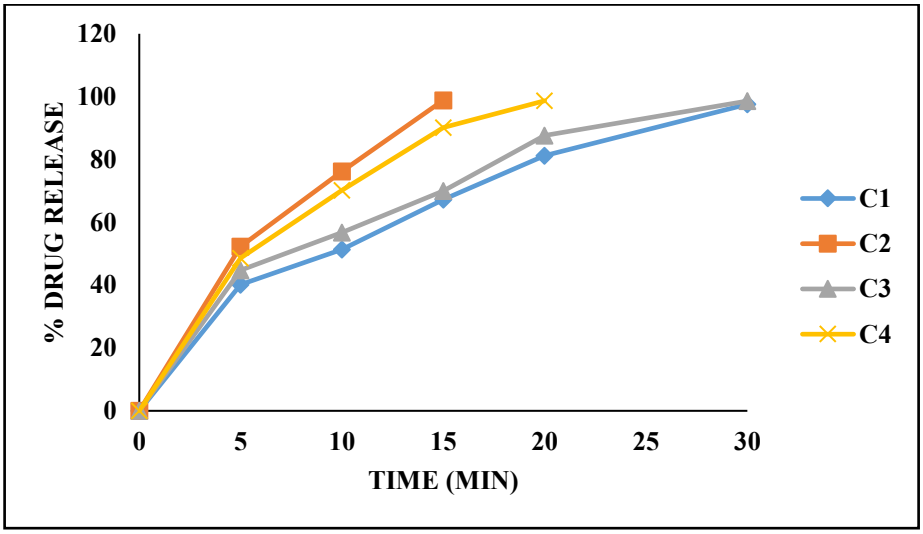

Figure 1: In Vitro Drug Release Profile of Telmisartan Core Tablets Formulation

Evaluation of Press-Coated Pulsatile Tablet of Telmisartan

The formulated Telmisartan press-coated pulsatile tablets (F1 to F6) were evaluated for various parameters, including weight variation, hardness, friability, thickness, drug content, and lag time. The results are shown in table 5.

Weight Variation:

The weight of the formulated tablets ranged between 300 mg to 302 mg, with minimal deviation (± 0.22 to ± 0.57), indicating uniformity in tablet weight across all formulations. The consistency in weight variation ensures proper content uniformity and dosage accuracy, complying with pharmacopoeial standards.

Hardness:

The hardness of the tablets varied from 5.3 to 5.6 kg/cm², which ensures mechanical strength sufficient to withstand handling and transportation. The values indicate that the tablets have adequate strength for processing without being too brittle or excessively hard.

Friability:

Friability values for all formulations ranged between 0.50% and 0.62%, remaining well below the acceptable limit of 1%. These results confirm that the tablets possess good mechanical resistance and can endure stress during handling and packaging without breaking or chipping.

Thickness:

The thickness of the formulated tablets ranged between 4.50 mm to 4.53 mm, with minor variations observed among different formulations. The uniformity in thickness suggests a controlled compression process and consistency in formulation.

Drug Content:

The drug content across all formulations was within the acceptable range, varying between 96.30% and 99.36%. The highest drug content was

observed in F4 (99.36%), while F5 showed the lowest (96.30%). These results indicate uniform drug distribution within the tablets, ensuring consistent dosing.

Lag Time:

A key parameter for pulsatile drug delivery is lag time, which varied among the formulations. Formulations F2 and F3 exhibited no lag time (0 hours), indicating that the drug release was immediate. In contrast, F1, F4, F5, and F6 demonstrated a lag time of 5 hours, suggesting that these formulations successfully achieved the desired pulsatile release profile. The variation in lag time may be attributed to differences in polymer composition and coating thickness. From the data it was observed that, the evaluation results indicate that formulations F1, F4, F5, and F6 successfully exhibited a lag time suitable for pulsatile drug release, making them ideal candidates for chronotherapeutic treatment of hypertension with Telmisartan. However, F2 and F3 failed to achieve the intended lag time, releasing the drug immediately instead. These findings highlight the importance of optimizing the coating composition to achieve the desired pulsatile effect.

Table 5: Evaluation of Telmisartan Press Coated Pulsatile Tablets

Batch	Weight Variation (mg)	Hardness (Kg/cm^2)	Friability (%)	Thickness (mm)	Drug Content (%)	Lag Time (Hr)
F1	301 ± 0.23	5.4 ± 0.42	0.62 ± 0.34	4.50 ± 0.52	97.61 ± 0.23	5
F2	300 ± 0.41	5.5 ± 0.32	0.51 ± 0.30	4.53 ± 0.33	98.02 ± 0.67	0
F3	302 ± 0.57	5.6 ± 0.57	0.50 ± 0.27	4.50 ± 0.35	96.42 ± 0.19	0
F4	300 ± 0.22	5.5 ± 0.21	0.58 ± 0.25	4.52 ± 0.47	99.36 ± 0.26	5
F5	302 ± 0.25	5.3 ± 0.36	0.54 ± 0.38	4.51 ± 0.64	96.30 ± 0.30	5
F6	301 ± 0.38	5.4 ± 0.30	0.58 ± 0.36	4.52 ± 0.31	97.41 ± 0.53	5

In Vitro Drug Release of Press Coated Pulsatile Tablets

The dissolution profile of Telmisartan press-coated pulsatile tablets prepared using HPMC K100M and HPMC E5 showed distinct release patterns based on polymer composition. Batch F1 prepared with HPMC K100M alone, exhibited a controlled release, with 21.32% drug release at 8 hours, indicating a sustained drug release profile. HPMC K100M is high viscosity grade polymer and hence showed very slow drug release with lag time of 5 hrs. Batch F2 formulated with HPMC E5 alone, showed an immediate release, reaching 99.3% drug release at 4 hours. Batch F2 gives lag time of 0 hrs, making it unsuitable for pulsatile delivery. No lag time from formulation may be due to low viscosity grade of HPMC polymer which colud no able to hold the drug for longer time. Batch F3 formulated using combination of HPMC K100M and HPMC E5 in equal ratio give the lag time of 0 hrs and demonstrated a moderate release, achieving 92.26% release at 8 hours, suggesting partial pulsatile release. Batch F4 formulated using combination of HPMC K100M and HPMC E5 (150:50mg), gave lag time 5 hrs, exhibited effective pulsatile release, with 98.61% drug release at 8 hours, making it a promising formulation for chronotherapeutic drug delivery. Batch F5 prepared with HPMC K100M and HPMC E5 (160:40mg) gives lag time of 5 hrs, showed an extended release, achieving 88.27% drug release at 8 hours, suggesting controlled drug delivery. Batch F6 prepared with HPMC K100M and HPMC E5 (170:30 mg) gives lag time 5 hrs,

giving 80.34% of the drug released at 8 hours, showing the slowest release rate among all formulations, making it ideal for sustained drug release.

From the dissolution study it was noted that formulations F1, F4, F5, and F6 successfully exhibited a lag time suitable for pulsatile drug release, making them potential candidates for chronotherapeutic treatment of hypertension with Telmisartan. However, F2 and F3 did not achieve the intended lag time, as they released the drug immediately. Among the tested formulations, F4 emerged as the most promising, as it achieved effective pulsatile release with complete drug release at 8 hours. The combination of HPMC K100M and HPMC E5 released in modulating the drug release profile, influencing the lag time and sustaining drug release over time. The % cumulative drug release versus time data for all formulations batch is shown in figure 2.

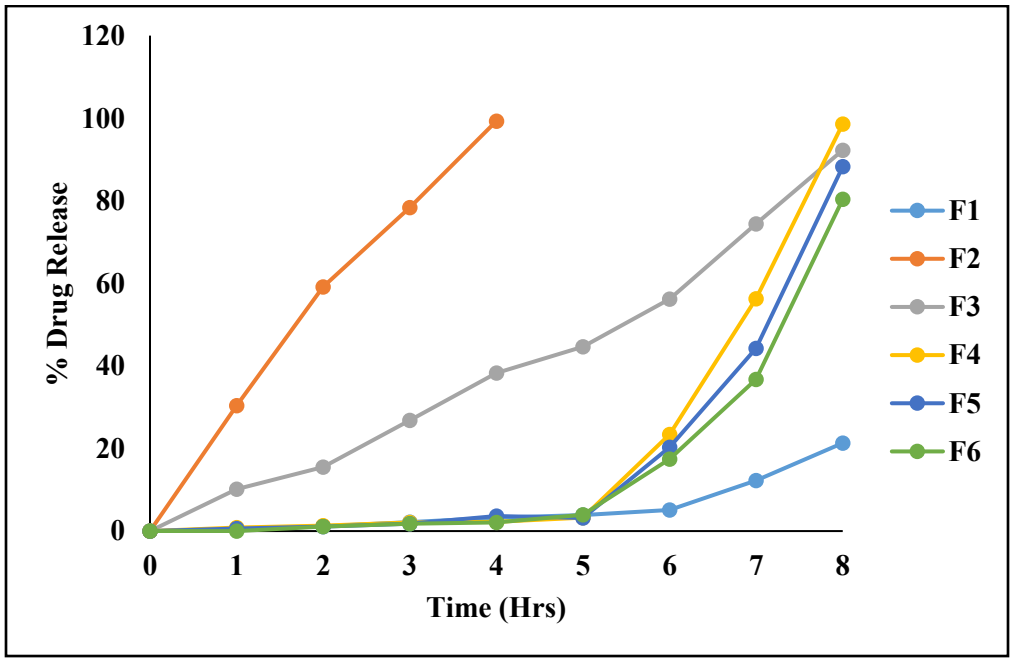

Figure 2: Comparative Dissolution Profile of Pressed Coated Tablets Formulation F1 to F6

Drug Release Kinetics

The drug release data of Telmisartan pulsatile tablet formulations (F1 to F6) were evaluated using various kinetic models: Zero Order, First Order, Higuchi, and Korsmeyer-Peppas. The model that best fits each formulation was determined based on the correlation coefficient (R^2), while the release exponent (n) from the Korsmeyer-Peppas model provided insight into the drug release mechanism. Among all the models applied, the Korsmeyer-Peppas model exhibited the best fit for all six formulations, with the highest R^2 values, indicating that drug release followed a diffusion and polymer relaxation-based mechanism rather than simple concentration-dependent or diffusion-only kinetics.The optimized batch formulation F4, showed a relatively lower Peppas R^2 value (0.74), but a very high n value of 2.23, again indicative of Super Case II transport, dominated by swelling and polymer erosion. Although the R^2 value is slightly lower, the high n value supports the controlled pulsatile behavior desired in the optimized formulation.

Table 6: Model Fitting Release Profile of Formulations F1 To F6

Formulation	Zero Order	First Order	Higuchi	Korsmeyer-Peppas		Best Fitting Model
	R^2	R^2	R^2	R^2	('n' Value)	
F1	0.725	0.701	0.526	0.916	1.61	Peppas
F2	0.989	0.774	0.957	0.995	0.85	Peppas
F3	0.975	0.773	0.84	0.978	1.07	Peppas
F4	0.642	0.427	0.429	0.740	2.23	Peppas
F5	0.632	0.488	0.423	0.801	2.28	Peppas
F6	0.62	0.5	0.413	0.735	2.06	Peppas

CONCLUSION

This study successfully developed and evaluated a pulsatile drug delivery system for Telmisartan using a press-coated tablet strategy. The core tablets formulated with 4% Croscarmellose Sodium (Batch C2) displayed superior disintegration and dissolution profiles, qualifying it as the optimal core. The press-coating layer composed of varying concentrations of HPMC K100M and E5 significantly influenced the lag time and drug release kinetics. The formulation F4 (HPMC K100M:E5 in a 150:50 mg ratio) emerged as the most effective pulsatile system, offering controlled lag time of 5 hours, near-complete drug release (98.61% at 8 hours), consistent physical characteristics, and adequate drug content uniformity. The study underscores the critical role of polymer viscosity and ratio in designing chronotherapeutic drug delivery systems. By aligning drug release with the circadian rhythm of hypertension, the pulsatile formulation enhances therapeutic outcomes, reduces side effects, and improves patient compliance. Overall, the optimized pulsatile formulation of telmisartan holds significant potential for targeted and time-specific hypertension therapy. Further in vivo studies would be beneficial to confirm its clinical effectiveness and establish its superiority over conventional dosage forms.

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