Available online on 15.12.2024 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

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Research Article

Comparative Dissolution Studies on Various Brands of Telmisartan Tablets

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Article Info:

Article History:

Received 20 Sep 2024
Reviewed 09 Nov 2024
Accepted 05 Dec 2024
Published 15 Dec 2024

Cite this article as:

Pande A, Kumar V, Prabhakar D, Lala RR, Gurjar AS, Gianani P, Patil S, Ghatge S, Comparative Dissolution Studies on Various Brands of Telmisartan Tablets, Journal of Drug Delivery and Therapeutics. 2024; 14(12):92-98 *DOI: http://dx.doi.org/10.22270/jddt.v14i12.6904*

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Abstract

Background: Telmisartan's low solubility limits its bioavailability, leading to poor dissolution, reduced efficacy, and decreased patient compliance. This study assesses the dissolution and quality control of various commercially available 40 mg telmisartan IP tablets, all marketed as bioequivalent.

Methods: The study analyzed various marketed formulations containing Telmisartan. Both the marketed products and Tazloc were evaluated through dissolution studies (drug release), with drug quantification performed using ultraviolet visible spectroscopy (Jasco UV-730) at λmax values of 291 nm and 296 nm.

Results: Tazloc demonstrated a drug release of 65% in 60 minutes in pH 1.2 HCl, outperforming other commercial tablets. In comparison, Brand A, Brand B, and Brand C each showed less than 60% release within the same period. Additionally, Tazloc exhibited the highest release—over 10% more than the other brands—in pH 4.5. In vitro release studies in pH 6.8 revealed that Tazloc achieved 95% release in 60 minutes, while Brand A, Brand B, and Brand C reached 91%, 82%, and 62%, respectively. Similarly, in pH 7.5 phosphate buffer, the cumulative drug release after 60 minutes was 99% for Tazloc, followed by 96% for Brand A, 94% for Brand B, and 93% for Brand C.

Conclusion: Tazloc, utilising ODCA technology, exhibits superior dissolution and solubility compared to conventional brands, ensuring enhanced bioavailability and optimal blood pressure control, leading to improved patient outcomes.

Keywords: cumulative release, dissolution, ODCA, patient compliance, quality.

INTRODUCTION:

Hypertension is a leading cause of premature death worldwide, affecting an estimated 1.28 billion adults aged 30–79 years. The burden is particularly heavy in low- and middle-income countries, where nearly two-thirds of those affected reside. Despite its prevalence, around 46% of adults with hypertension are unaware of their condition, and less than half (42%) of those diagnosed receive treatment[1]. Although antihypertensive drugs are highly effective in controlling blood pressure, patient adherence in clinical settings remains concerningly low, ranging from 20% to 50% [2,3]. Poor BP control is largely influenced by non-compliance, which includes delays in starting treatment, irregular medication use, and discontinuation over time, all of which compromise effective hypertension management [4,5]. Several factors, such as drug safety, ease of use, quality, polypharmacy, cost, and patient education, play a crucial role in treatment success [4]. Maintaining the quality of antihypertensive medications improves BP control, promotes better patient adherence, and supports effective long-term hypertension management.

Telmisartan, a potent and long-lasting ARB, is widely prescribed for treating essential hypertension [6]. Telmisartan, as a biopharmaceutics classification system (BCS) Class II drug, has low solubility (0.078 mg/mL) but high permeability. This class of drugs often faces bioavailability challenges since solubility is the rate-limiting step in their absorption process. Telmisartan, despite its high permeability, has low solubility in the pH range of 3 to 9, limiting its dissolution in the GI tract. As a result, only a fraction of the dose is absorbed, leading to a bioavailability of 42-58%. This limits dissolution and results in non-linear pharmacokinetics, where higher doses lead to disproportionate increases in plasma concentrations. Its pH-dependent dissolution further

limits absorption, affecting bioavailability [7]. Enhancing solubility and dissolution improves absorption, reduces variability, and ensures product quality and efficacy, resulting in better outcomes and increased patient compliance.

Drug absorption from solid oral forms depends on drug release, dissolution under physiological conditions, and gastrointestinal permeability. Drug dissolution testing (drug release) is crucial for evaluating product quality, drug release behaviour, and detecting changes in formulation or manufacturing. In-vitro dissolution tests help predict in-vivo performance and are used to assess lot quality, guide new formulation development, and maintain product quality, especially after formulation or process changes. Knowledge of solubility, permeability, and pharmacokinetics is essential for setting dissolution test specifications and ensuring product consistency post-approval [8-10].

Telmisartan's low solubility limits its bioavailability. While several conventional formulations are available, their dissolution remains inadequate, resulting in poor bioavailability and compromised patient outcomes. Insufficient dissolution lowers efficacy, ultimately reducing patient compliance. Therefore, this study evaluates the quality control tests, specifically drug release, of various commercially available brands of telmisartan IP 40 mg tablets, which claim to be bioequivalent.

MATERIALS AND METHODS:

Chemicals and reagents

Potassium dihydrogen phosphate, acetic acid, di-sodium hydrogen phosphate dihydrate, sodium acetate, concentrated hydrochloric acid, and sodium hydroxide were used as received. Whitman Filter Paper (Ashless, Grade 40 circles, 110 mm, 1440-110) and distilled water were employed for the studies. The dissolution media were prepared following the USP procedure. Telmisartan 40 mg tablets from four different brands were obtained from various local retail pharmacists. Products were codified as brand A, brand B, brand C, and Tazloc.

Preparation method of Tazloc

Telmisartan, which is poorly soluble at an intestinal pH of 5.5 to 6.8, is solubilized using a unique process that takes advantage of its solubility at extreme pH levels.

The Optimum Dissolution and Complete Absorption (ODCA) technology is a specific formulation method for Tazloc that ensures each particle of Telmisartan is delivered as a discrete, solubilized entity. The ODCA technology differs from other solubilizing methods by ensuring that each telmisartan particle is delivered in a fully solubilized form, optimizing its dissolution and absorption even within the intestinal pH range of 5.5 to 6.8. This advanced formulation facilitates optimal dissolution and complete absorption, enhancing the drug's bioavailability and therapeutic efficacy.

This unique approach enhances telmisartan's bioavailability, overcoming its poor water solubility (typical BCS class 2 drugs) and providing immediate release. This formulation method is well-suited for telmisartan, as it achieves both high solubility and consistent quality, meeting Indian Pharmacopoeia standards for therapeutic efficacy.

Analytical method development

For the dissolution study, the drug was analysed by ultraviolet (UV) visible spectroscopy (Jasco UV-730) at λmax values of 291 nm and 296 nm, and standard curves were plotted for the respective buffers.

Standard plot of telmisartan

A stock solution of telmisartan (100 µg/mL) was prepared by dissolving 10 mg of the drug in pH 1.2 HCL, pH 4.5 acetate buffer, pH 6.8 phosphate buffer, and pH 7.5 phosphate buffer, each in a 100 mL volumetric flask. Solutions with concentrations ranging from 2 to 20 µg/mL were obtained through dilution. Absorbance was measured at 291 nm for pH 1.2 HCL and 296 nm for the buffer solutions using a UV-visible spectrophotometer. Standard plots of absorbance versus concentration were created, and linear regression analysis was performed for all solutions.

Dissolution profile study or in-vitro release studies

Tablets containing 40 mg of telmisartan were used and compared as per FDA guidelines. The dissolution profiles of four different telmisartan brands (each containing 40 mg of the drug) were analyzed. Dissolution parameters specification is depicted in table 1. The dissolution test utilized the USP paddle apparatus (Type II). 900 ml of dissolution medium was added to each jar, which was placed in the test assembly maintained at 37 ± 0.5°C. The medium was allowed to reach the set temperature, and the rpm was adjusted to 75.

Table 1: Protocol for dissolution studies

Apparatus used	USP Type II Apparatus (Paddle Type)
Volume of dissolution	900ml
Temperature	37 ± 0.5 °C
Speed	75 rpm
Aliquot withdrawn	5 ml
Dissolution media	pH 1.2 Hydrochloric acid, pH 4.5 Acetate Buffer, pH 6.8 Phosphate buffer, pH 7.5 Phosphate buffer
Sampling time	5, 10, 15, 20, 30, 45, 60 mins
Method of Analysis	pH 1.2 Hydrochloric acid: λmax= 291 nm and for other buffers: λmax= 296 nm UV Vis Spectrophotometer.
No. of tablets	6

After introducing the test sample into the dissolution jar, the assembly was lowered to its static position, and the medium was stirred at 100 rpm. At various time points (5, 10, 15, 20, 30, 45, and 60 mins), 5 mL samples were withdrawn using a graduated pipette and transferred to clean, dried, and labeled test tubes. After each sampling, an equal volume of fresh dissolution medium was added to maintain consistent conditions. The withdrawn samples were diluted by a factor of 10 with buffer, and Drug release was measured at various time intervals using a UV-visible spectrophotometer absorbance was measured at 291 nm for 0.1N HCL and 296 nm for acetate buffer at pH 4.5, phosphate buffer at pH 6.8 and 7.5. The cumulative percentage of released is calculated using the formula

$$Concentration\ of\ drug\ (\mu g/mL) = (slope\ \times\ absorbance) \pm\ intercept$$

$$Cumulative\ \%\ release = \frac{Volume\ of\ the\ sample\ withdraw\ (mL)}{Bath\ volume\ (v)} \times P\ (t-1)\ +\ Pt$$

Where,

Pt= Percentage release at time t'

P (t-1) = Percentage release previous to 't'

Dissolution profile of various brands of telmisartan

The reference product was telmisartan (40 mg) tablets, marketed by USV Pvt. Ltd. To evaluate the similarity between two dissolution profiles, two fit factors are commonly used: f1 (difference factor) and f2 (similarity factor). For two dissolution profiles to be considered similar and bioequivalent, the f1 value should range from 0 to 15, while the f2 value should be between 50 and 100. An f1 value above 15 indicates significant dissimilarity, whereas an f2 value greater than 50 signifies substantial similarity.

$$f1 = \left\{\frac{\sum_{t=1}^{n}(R_t - T_t)}{\sum_{t=1}^{n} R_t}\right\} \times 100$$

$$f2 = 50.\ log\left\{\left[1 + \frac{1}{n}\sum_{t=1}^{n}(R\ t\ -\ T\ t)^2\right]^{-0.5} \times 100\right\}$$

Here, Rt and Tt represent the cumulative percentage dissolved at each of the selected time points (n) for the reference and test products, respectively. (Table 2)

Table 2: Similarity factor (f2) for dissolution profiles of telmisartan

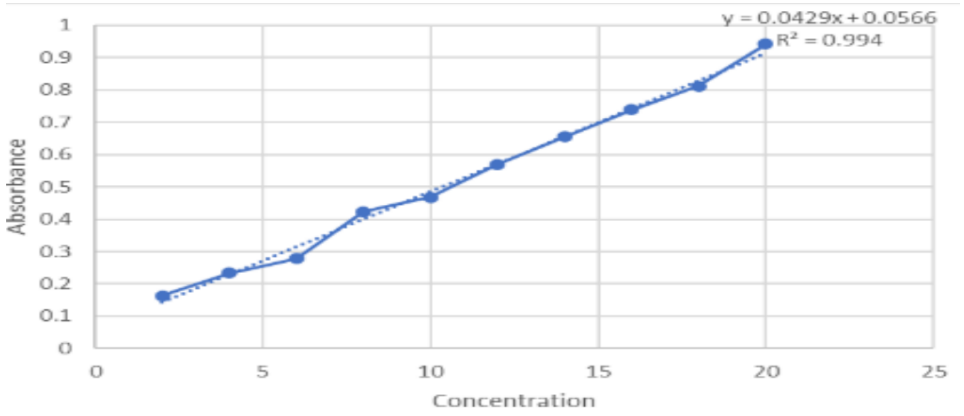
Brand	pH 1.2 Hydrochloric acid		pH 4.5 Acetate Buffer		pH 6.8 Phosphate Buffer		pH 7.5 Phosphate Buffer	
	f1	f2	f1	f2	f1	f2	f1	f2
Brand A	21.40	45.32	13.62	87.32	7.45	59.77	10.39	49.89
Brand B	32.18	48.61	37.54	59.67	21.98	37.03	21.33	34.95
Brand C	31.7	44.30	41.53	54.71	48.59	59.92	16.79	40.3

RESULTS AND DISCUSSION:

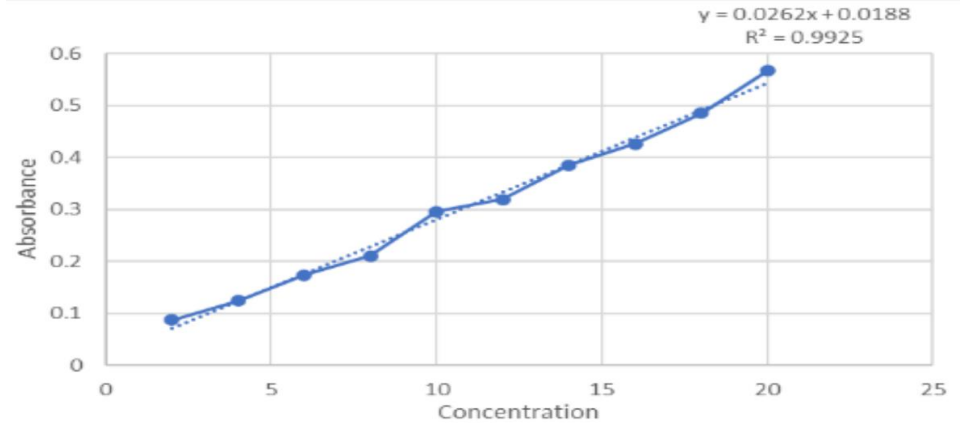
Linearity

Telmisartan exhibited maximum absorbance at 291 nm in pH 1.2 HCL and at 296 nm in various buffer solutions, within a concentration range of 2-20 µg/mL, as illustrated in Figure 1. Linearity was observed across this concentration range, with absorbance measured at 291 nm for pH 1.2 HCL and 296 nm for the buffer solutions using a UV-Vis spectrophotometer. The regression coefficients were found to be 0.994 for pH 1.2 HCL, 0.9925 for pH 4.5 acetate buffer, 0.999 for pH 6.8 phosphate buffer, and 0.9991 for pH 7.5 phosphate buffer, as shown in Figure 1.

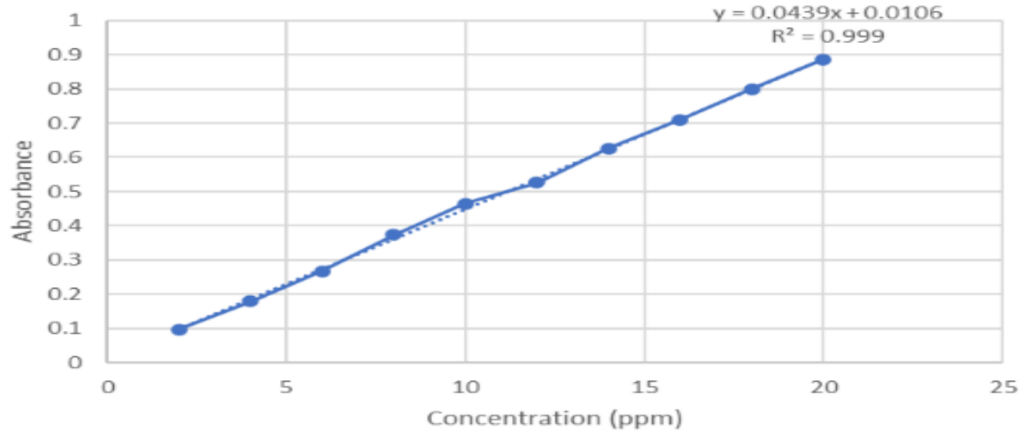
a] pH 1.2 HCL



b] pH 4.5 acetate buffer



c] pH 6.8 phosphate buffer



d] pH 7.5 phosphate buffer

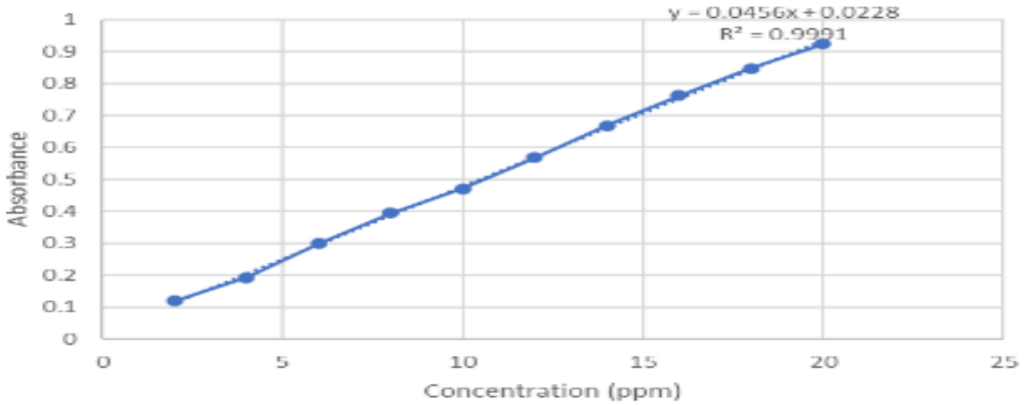


Figure 1: Linearity curve / Standard curve of telmisartan

Dissolution Test

Dissolution studies (In vitro drug release)

The in-vitro drug release characteristics of the developed marketed tablets were analyzed. Dissolution data from all experiments showed high reproducibility, so only the average values were plotted. Both IP and USP state that not less than 75% of drugs must be released in 30 minutes.

pH 1.2 Hydrochloric acid

The in vitro drug release of telmisartan tablets is shown in Figure 2a.

Tazloc showed a release of 65% in 60 mins as compared to other commercial tablets in pH 1.2 HCL. brand A, brand B, and brand C, showed less than 60 % drug release in 60 min.

pH 4.5 acetate buffer

In vitro release of different brands containing telmisartan in pH 4.5 acetate buffer is shown in figure 2b.

The Tazloc showed maximum release as compared to brands A, B and C, respectively (less than 10%) in 60 mins. Telmisartan alone in pH 4.5 acetate buffer has low solubility as shown in the standard curve figure 1b. All dissolution curves obtained did not show further release from 15 min onwards. This may be caused by the limited solubility of telmisartan at pH 4.5 acetate buffer.

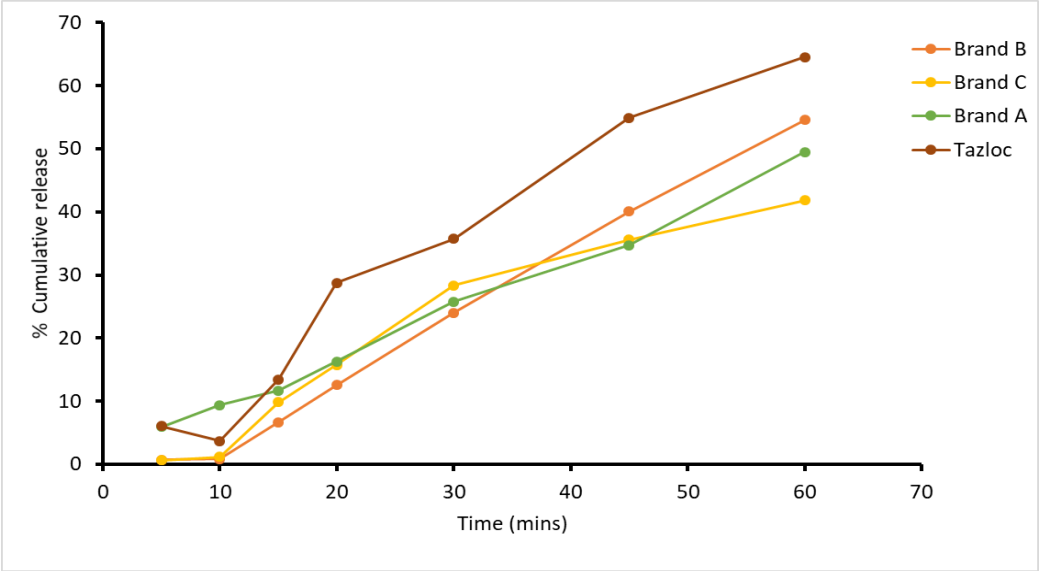
pH 6.8 phosphate buffer

In vitro, release in pH 6.8 of different brands containing telmisartan is shown in Figure 2c. Brand A, brand B, brand C, and Tazloc showed 91%, 82%, 62% and 95% respectively in 60 mins.

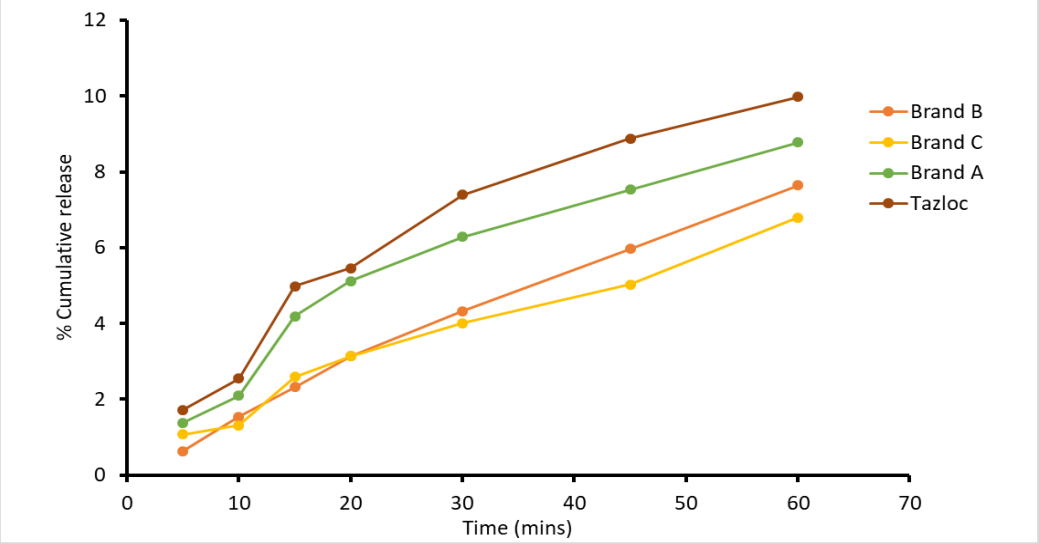
pH 7.5 phosphate buffer

In vitro, release patterns of telmisartan tablets are shown in Figure 2d. Both IP and USP state that not less than 75% of the drug must be released in 30 minutes. In pH 7.5 phosphate buffer Cumulative release of 96%, 94%, 93%, and 99% were observed in 60 mins for brand A, brand B, brand C, and Tazloc, respectively.

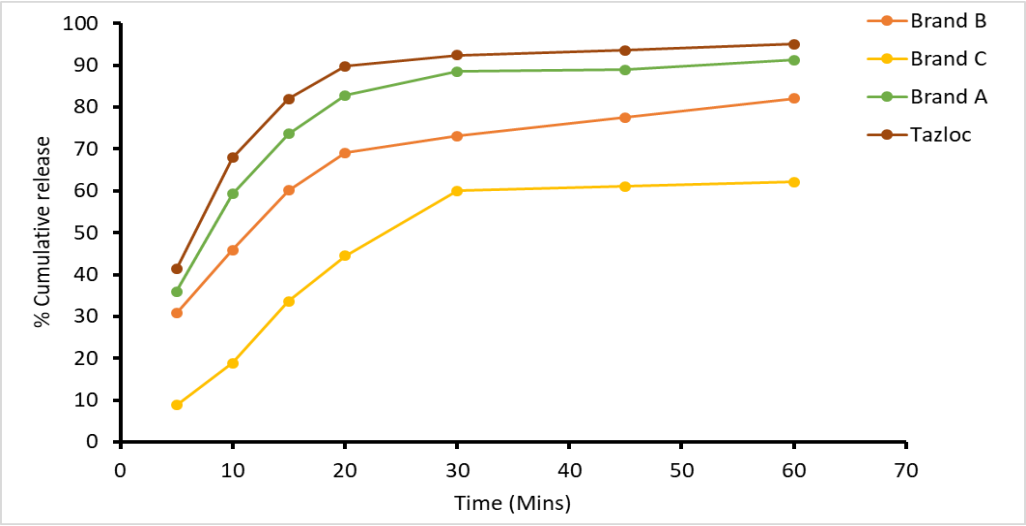
a] pH 1.2 hydrochloric acid



b] pH 4.5 acetate buffer



c] pH 6.8 phosphate buffer



d] pH 7.5 phosphate buffer

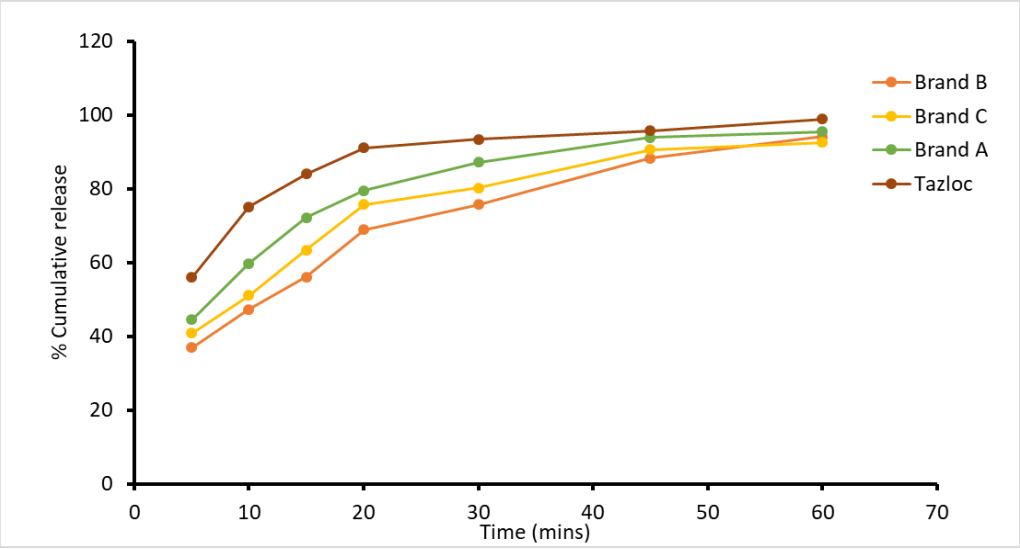


Figure 2: In vitro drug release of various telmisartan brands

A comparison of the in vitro release of different brands of telmisartan tablets is illustrated in Figure 3. Although the brands met the dissolution test specifications outlined in the IP and USP, significant differences were found in their drug release as seen by the f1 and f2 values for the dissolution data.

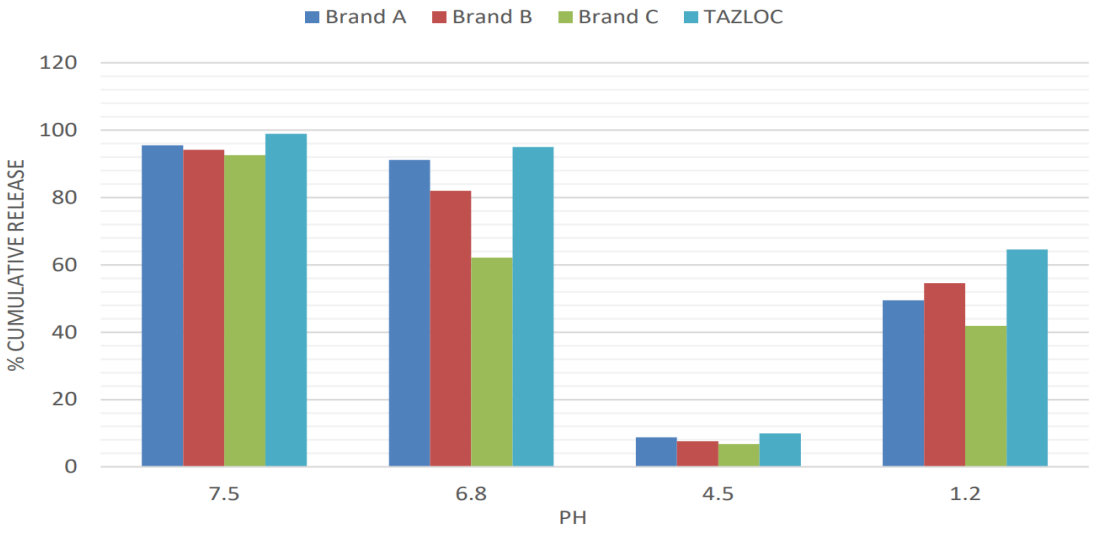


Figure 3: Comparison of in-vitro drug release profile in various pH media

Tazloc tablets are manufactured using ODCA technology, designed to enhance the dissolution and absorption of Telmisartan. Telmisartan belongs to the BCS Class 2, characterized by low solubility but high permeability. This poses challenges for achieving optimal bioavailability. ODCA technology addresses these challenges by ensuring that each particle of telmisartan is in a solubilized form, improving dissolution and absorption. Telmisartan dissolves only at extreme pH levels, so a highly alkaline solvent base is used to solubilize the drug. A key advantage of this process is that it allows telmisartan to dissolve within the intestinal pH range of 5.5 to 6.8, overcoming its usual solubility limitations in that environment, thereby improving its bioavailability and therapeutic effectiveness.

Limitation: As the evaluations are experimental, there may be errors related to instrumental constraints or technical issues. Given the study's in vitro nature, further in vivo studies are recommended to confirm that enhanced drug release correlates with improved bioavailability and clinical outcomes.

CONCLUSION:

In vitro dissolution methods assessed the in vivo potential of solid oral dosage forms and served as quality control for drug performance. Studies on the in vitro drug release of marketed tablets, including Tazloc, demonstrated high reproducibility. Tazloc tablets, produced with ODCA technology, enhanced the drug release and absorption of telmisartan within the intestinal pH range of 5.5 to 6.8, improving bioavailability and therapeutic effectiveness. Compared to other formulations, Tazloc showed superior dissolution and solubility, ensuring high quality and enhanced bioavailability. The improved dissolution of Tazloc, made possible by ODCA technology, leads to enhanced bioavailability of telmisartan, ensuring a more consistent and effective therapeutic response. This reliable dissolution allows Tazloc to reach optimal plasma concentrations more predictably, which in turn stabilizes blood pressure more effectively than conventional formulations.

Funding: This study was conducted by USV Private Limited., India.

Conflict of disclosure: Sagar Patil and Shweta Ghatge are employees of USV Private Limited. All other authors have nothing to disclose.

Acknowledgment: The medical writing support was provided by Shital Kolhe (Sqarona Medical Communications LLP, Pune).

Data Availability: All data used during the present study will be available from the corresponding author if deemed necessary.

Funding statement: No funding.

Ethical approval: N/A

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