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GREEN SOLVENT-ASSISTED DEVELOPMENT OF UV-SPECTROPHOTOMETRIC AND RP-HPLC METHODS FOR TELMISARTAN AND EFONIDIPINE HCL ETHANOLATE

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ABSTRACT

Background: Hypertension is a prevalent cardiovascular disorder requiring effective therapeutic strategies. Telmisartan, an angiotensin II receptor antagonist, and Efonidipine HCl Ethanolate, a calcium channel blocker, are often co-administered for synergistic blood pressure control. To ensure the quality and efficacy of pharmaceutical formulations, it is essential to develop simple, precise, and eco-friendly analytical methods for the simultaneous estimation and validation of these formulations in accordance with ICH Q2(R1) guidelines. **Methodology:** Two UV spectroscopic methods and one RP-HPLC method were developed and validated. Method A employed the simultaneous equation approach using absorbance values at 297 nm and 251 nm, corresponding to the λmax of Telmisartan and Efonidipine, respectively. Method B utilized the area under the curve (AUC) method for simultaneous quantification. The RP-HPLC method was performed on an Agilent C18 column (250 × 4.6 mm, 5 µm) with isocratic elution using ethanol and 0.1% orthophosphoric acid in water (85:15 v/v) at a flow rate of 0.9 mL/min, and detection was at 253 nm. **Results and Discussion:** All three methods demonstrated excellent linearity, precision, and accuracy within validated ranges. Recovery studies confirmed reliability, with values within acceptable limits. The UV method (Greenness score 92) is slightly greener than HPLC (Greenness score 88), with both demonstrating excellent eco-friendly performance. The UV methods offer rapid and economical screening, while RP-HPLC ensures high sensitivity and specificity. The use of ethanol as a green solvent supports eco-friendly pharmaceutical analysis. **Conclusion:** Validated UV and RP-HPLC methods were successfully developed for simultaneous estimation of Telmisartan and Efonidipine HCl Ethanolate. These approaches are robust, precise, economical, and environmentally sustainable for routine quality control in pharmaceutical dosage.

INTRODUCTION

Chemically, Telmisartan is recognized as 2-(4-[[4-methyl-6-(1-methylbenzimidazol-2-yl)-2-propylbenzimidazol-1-yl]methyl]phenyl]benzoic acid. Figure 1 shows the structure of telmisartan. It's an angiotensin II type 1 (AT1) receptor

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antagonist that produces an antihypertensive effect [1]. It provides dual action by inhibiting the renin-angiotensin system (RAS) and acting as a specific agonist of peroxisome proliferator-activated receptor gamma (PPARγ), which regulates insulin and glucose metabolism in skeletal muscles. This dual approach offers protective benefits against damage to blood vessels & kidneys caused by diabetes and cardiovascular conditions [1-4]. Chemically Efonidipine HCl Ethanolate is recognized as 2-[Benzyl(phenyl)amino]ethyl 5-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphorinan-2-yl)-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydro-3-pyridinecarboxylate monohydrochloride monoetha- nolate. Figure 2 shows the Efonidipine HCl Ethanolate Structure.

As a dual-acting L-type and T-type calcium channel antagonist, this 1,4-dihydropyridine derivative is indicated for the treatment of hypertension and angina pectoris by rendering reduced automaticity of the heart and vasodilation. The combination of Telmisartan and Efonidipine HCl Ethanolate is used to treat hypertension and provides effective control through synergistic action [5-8]. Based on a review of the literature, several analytical techniques for Telmisartan have been developed using UV spectroscopy [9-10]. UV spectroscopic method was developed for Efonidipine HCl Ethanolate [11-13]. Methods have been developed for drug combination by RP-HPLC and bioanalytical techniques [14-17]. Some analytical methods developed for this combination, involving UV spectroscopy or RP-HPLC, have been documented using green solvents for the simultaneous quantification of Telmisartan and Efonidipine HCl Ethanolate, with greenness assessment [18]. The primary goal of this study is to create and confirm a simple, accurate, precise, and environmentally friendly UV-spectroscopic & RP-HPLC technique to replace costly & dangerous methods for measuring Telmisartan & Efonidipine HCl Ethanolate [19]. UV spectroscopy is an economical, straightforward, and efficient analytical platform. HPLC offers detailed, precise analysis of mixtures.

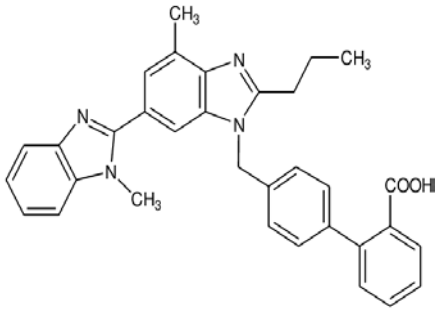


Figure 1: Telmisartan Structure

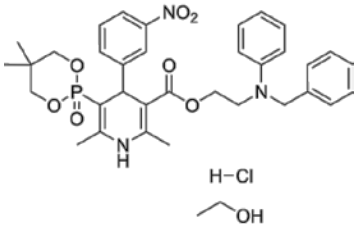


Figure 2: Efonidipine HCl Ethanolate Structure

MATERIAL AND METHODS

Materials

Telmisartan and Efonidipine HCl Ethanolate, as a gift sample, were provided by Swapnroop Drugs and Pharmaceuticals. RP-HPLC-grade ethanol was used as a solvent for quantification by UV spectrophotometry and RP-HPLC. A fixed dose of marketed tablet formulation EFNOCAR-T 40/40 (Zuventus Healthcare Limited), containing Efonidipine hydrochloride ethanolate 40 mg and Telmisartan 40 mg, was procured from the local market. Spectrophotometric measurements were conducted using a Shimadzu UV-1800 double-beam UV-Visible spectrophotometer equipped with UV Probe software and a 1-cm quartz cuvette, operating over the wavelength range of 200-400 nm. An Agilent 1100 equipped with a reciprocating pump (HP-1100) and a UV detector was used for the RP-HPLC analysis. Separation was achieved using ChemStation software with a DAD detector and a reversed-phase Agilent C18 column (4.6 x 250 mm i.d., 5 µm).

Methods

Selection of solvent

Choosing the right solvent is fundamental to developing methods, significantly influencing analyte solubility, absorbance, and resolution. To attain high recovery and consistent sensitivity, it is essential to select the best solvent. An appropriate solvent maintains column integrity and reduces background noise, leading to accurate results. Solubility studies of each drug were conducted in a multiple range of solvents, including distilled water, methanol, ethanol, and acetonitrile. Both drugs show optimal solubility in Ethanol [6].

RP-HPLC METHOD

Mobile Phase Preparation

A 0.1% (v/v) Orthophosphoric Acid (OPA) solution was prepared by transferring 1 mL of OPA into a 1000 mL volumetric flask, then diluting to the mark with RP-HPLC-grade water. To remove dissolved gases, the resulting solution was degassed for 10 min in an ultrasonic water bath, then filtered through a 0.45 µm filter.

Chromatographic conditions

Chromatographic separation was done on RP-HPLC using an Agilent 1100 HPLC series equipped with an Agilent C18 column with internal dimensions of 250 mm x 4.6mm, 5µm, a reciprocating pump, and a UV detector (DAD) for simultaneous quantification of Telmisartan and Efonidipine HCl Ethanolate. The mobile phase consisted of ethanol and 0.1% OPA water in an 85:15 (v/v) ratio, delivered at 0.9 ml/min at ambient temperature (25-28°C) [4]. The wavelength of 253 nm was chosen as a compromise because it provides adequate absorbance for both Telmisartan (λmax 297 nm) and Efonidipine (λmax 251 nm). This ensures simultaneous detection with balanced sensitivity for both drugs. Selecting this midpoint enhances method reliability and robustness in RP-HPLC analysis. Chromatographic conditions for RP-HPLC were shown in Table 1. The Chromatogram of RP-HPLC Telmisartan & Efonidipine HCl is shown in Figure 3.

Preparation of Standard stock solution

Accurately weighed 10 mg of Telmisartan and 10 mg of Efonidipine HCl Ethanolate were transferred to a 100 ml amber-colored volumetric flask, and 50 ml of ethanol was added. The mixture was sonicated for 10 min to ensure dissolution, and the volume was made up to 100 ml with ethanol. The prepared solution was subsequently filtered through a Whatman filter paper. This resulted in the preparation of 100 µg/ml solutions of Telmisartan and Efonidipine HCl Ethanolate, respectively, and a standard stock solution of known concentration. The standard solution was later diluted to prepare various concentrations from 10-50µg/ml of Telmisartan and Efonidipine HCl Ethanolate separately.

Table 1: Chromatographic conditions for RP-HPLC

Parameter	Chromatographic conditions
Column	Agilent C18 (4.6 x 250 mm, 5µm)
Mobile phase	Ethanol:0.1% OPA water(85:15v/v)
Flow rate	0.9 ml/min
Detection wavelength	253 nm
Injection volume	20 µl
Temperature	25-28°C

Preparation of sample solution

A total of 20 tablets were randomly selected and weighed precisely to calculate the mean weight. The tablets were then ground to a powder using a mortar and pestle. From the resulting powder, the powder equivalent to 10 mg of Telmi and EFNO was precisely weighed and placed into a 100 mL amber-colored volumetric flask. 50 mL of ethanol was added to the volumetric flask and sonicated for 10 min. After sonication, the volume was made up using ethanol, giving a 100 µg/ml solution. The obtained solution was then filtered through a 0.45 µm filter. Further dilutions were made using this sample to obtain solutions of 10-50 µg/ml concentration.

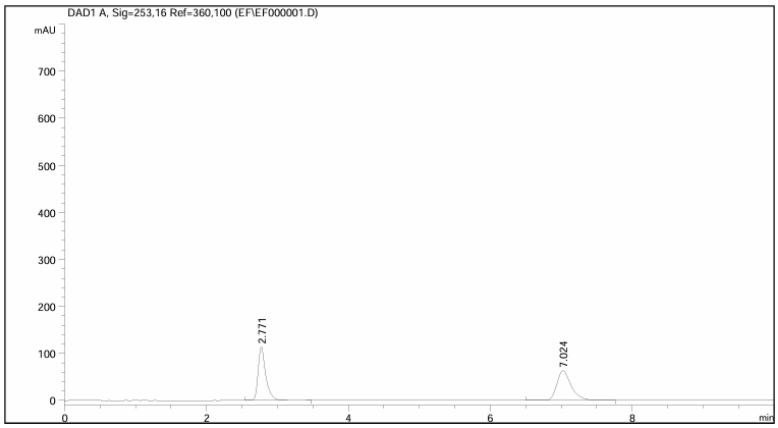


Figure 3: Chromatogram of RP-HPLC Telmisartan & Efonidipine HCl

UV Method

Preparation of Standard stock solution

10 mg of both Telmi and EFNO were accurately weighed and transferred to a 100 mL amber-colored volumetric flask, dissolved in ethanol, and sonicated for 10 min. The volume was made up to the mark with ethanol, resulting in a 100 µg/ml solution. The standard solution was later used for the preparation of sample solutions of concentration 5-25µg/ml [22].

Preparation of sample solution

The weight of 20 tablets was measured precisely, and the average weight was determined. Using a mortar and pestle, the tablets were crushed, and from this powder, an equivalent weight of 10 mg Telmi and EFNO was precisely weighed and placed into the 100 ml amber coloured volumetric flask. This resulted in a 100 µg/ml conc. solution. The resulting solution was then used for further dilutions to make concentration 5-25µg/ml.

Selection of wavelength

The working standard solutions of both Telmisartan and Efonidipine HCl Ethanolate were scanned over the range of 200-400 nm, using ethanol as a blank, to determine the absorption maxima. Telmisartan shows the maximum absorption at 297 nm (λ1), while Efonidipine HCl Ethanolate shows the maximum absorption at 251 nm(λ2). Overlay spectra of Telmisartan & Efonidipine HCl Ethanolate are shown in Figure 4.

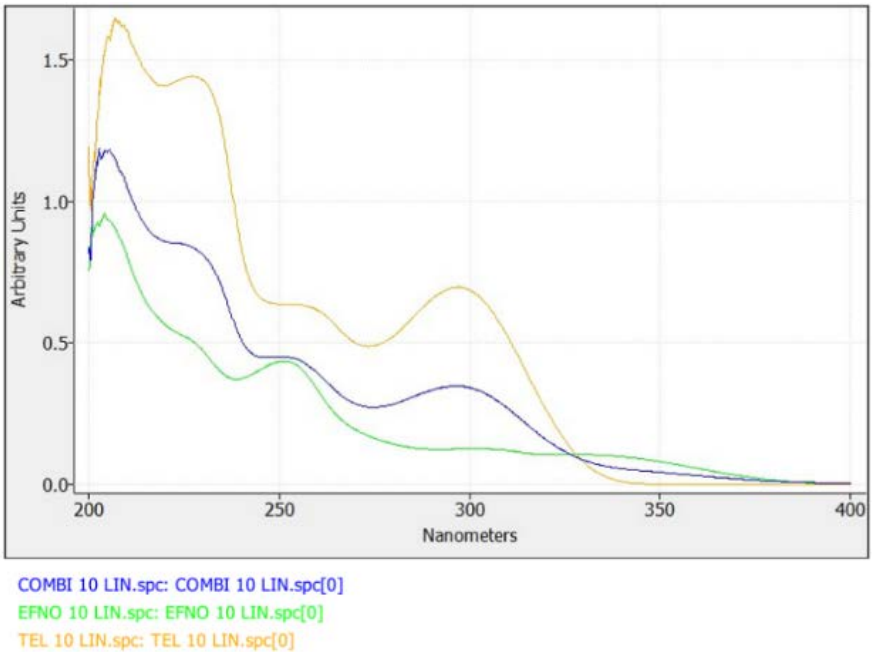


Figure 4: Overlay spectra of Telmisartan & Efonidipine HCl Ethanolate

METHOD A: Simultaneous Equation Method

The simultaneous equation method (SEM), also known as Vierprdt's method, is a UV-spectrophotometric method used to analyze multi-component mixtures and quantify two or more drugs with overlapping spectra without requiring physical separation. This approach relies on measuring the absorbance at the λ_{max} of each drug and using Beer-Lambert's law to solve simultaneous equations to determine their concentrations. This technique is based on the absorption of both analytes at the maximum wavelength (λ_{max}). The responses of Telmisartan and Efonidipine HCl Ethanolate were noted at 297nm & 251nm, respectively [22]. This method is evaluated by using the following simultaneous mathematical expressions:

$$Cx = \frac{A2ay1 - A1ay2}{ax2ay1 - ax1ay2}$$

$$Cy = \frac{A1ax2 - A2ax1}{ax2ay1 - ax1ay2}$$

Where, Cx = Conc. of Telmi, Cy = Conc. of EFNO, A1 = Absorbance of Telmisartan at λ_1 (298 nm), A2= Absorbance of Efonidipine HCl Ethanolate at λ_2 (251 nm), ax1= Absorptivity of Telmisartan λ_1, ax2= Absorptivity of Telmisartan at λ_2 (251 nm), ay1= Absorptivity of Efonidipine HCl Ethanolate at λ_1, ay2= Absorptivity of Efonidipine HCl Ethanolate at λ_2.

METHOD B: AREA UNDER CURVE

The Area Under Curve (AUC) method is a UV-spectrophotometric technique used in analytical method development, particularly when drugs exhibit broad spectra or lack a sharp, distinct spectrum. Unlike the simultaneous equation method, which uses single-point absorbance values over a specified wavelength range. Telmisartan and Efonidipine HCl Ethanolate working solutions were prepared in ethanol and scanned on a UV spectrophotometer over the 200-400 nm range. The wavelengths 287-307 nm and 241-261 nm were selected from the spectra to represent the spectra of Telmisartan and Efonidipine HCl Ethanolate, respectively, as shown in Figure 5 by Area under the curve. This method determines drug concentrations using these two spectral regions.

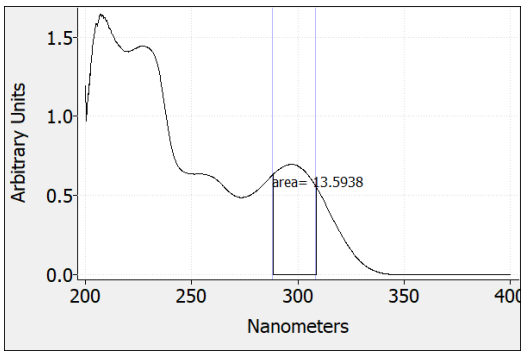


Figure 5: A) UV Area under the curve spectrum of TELMI

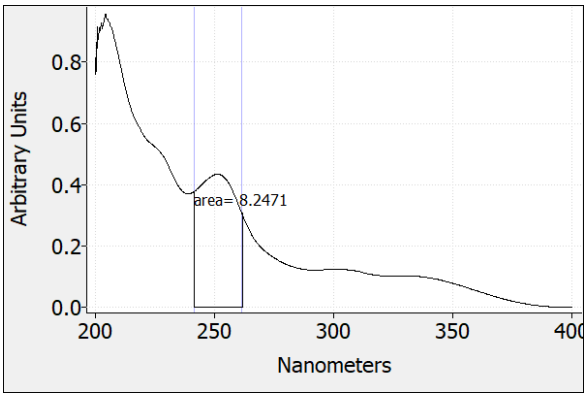


Figure 5: B) UV Area under the curve spectrum of EFNO

METHOD VALIDATION

Method validation is carried out using system suitability studies, Linearity, precision, LOD, LOQ, Accuracy, Robustness, and Ruggedness [20,21].

System suitability studies

The system suitability of RP-HPLC was evaluated to ensure proper chromatographic performance. Standard solutions of Telmisartan and Efonidipine HCl Ethanolate at 10 µg/mL were used to assess system suitability parameters, including retention time, tailing factor, Theoretical plates, peak area, and resolution. The system suitability was determined to be within acceptable parameters.

Linearity and Range

Linearity confirms that an instrument's output is directly proportional to the quantity of analyte present. The range specifies the particular concentration interval from minimum to the maximum levels within which this direct relationship is maintained with accuracy and precision. The linearity of TELMI & EFNO was determined by scanning solutions of different concentrations using the UV-vis spectroscopic method over a range of 5-25 µg/ml, whereas for RP-HPLC, solutions ranging from 10-50 µg/ml were used.

The selection of concentration ranges for UV spectrophotometry and HPLC was guided by the intrinsic performance characteristics of each technique rather than an attempt to enforce uniformity. UV spectrophotometry provides consistent linearity and reliable absorbance readings at lower concentrations (5–25 µg/ml), where measurements remain within the optimal detection window and avoid saturation. Conversely, HPLC achieves superior peak resolution and reproducibility at slightly higher concentrations (10–50 µg/ml), ensuring stable chromatographic behavior and minimizing baseline noise. Applying a single concentration range across both methods would compromise accuracy—either by pushing UV readings into non-linear regions or by restricting HPLC to unnecessarily low levels, thereby reducing chromatographic stability. Therefore, the ranges were intentionally tailored to each method's strengths to ensure valid sensitivity assessments and robust statistical comparisons, rather than imposing uniformity that could introduce bias or diminish reliability. The pictogram illustrating the relationships between concentration and peak area, as well as between concentration and absorbance, was plotted for RP-HPLC and UV-Vis Spectroscopy, yielding a regression equation. UV-Visible Spectroscopic overlay of Telmisartan & Efonidipine HCl Ethanolate was shown in Figure 6.

RESULT

System suitability

The reproducibility of the chromatographic system was evaluated using parameters such as tailing factor, theoretical plate count, resolution, retention time, and peak area. The system suitability parameters TELMI & EFNO by the RP-HPLC method are summarized in Table 2. Together, these metrics provide a clear picture of the system's consistency and reliability across repeated injections. The consistently low tailing factors (0.63 for EFNO and 0.70 for TELMI) confirm symmetrical peak shapes, which are essential for accurate integration and quantification. Theoretical plate values of 3776 and 6439, well above the minimum requirement of 2000, highlight the column's high efficiency and its ability to deliver sharp peaks even after multiple runs. TELMI's resolution of 16.0, far exceeding the acceptance limit of >2.0, demonstrates excellent separation from adjacent peaks, ensuring that quantification is not compromised by co-elution. In addition, retention times and peak areas remained stable across different injections, reinforcing the system's reproducibility.

Consistent retention times reflect precise control over mobile-phase composition, flow rate, and column performance, while stable peak areas confirm a reliable detector response and consistent sample preparation. Taken together, these findings establish that the chromatographic system is not only suitable but also highly reproducible, capable of delivering dependable results under routine laboratory conditions. Such reproducibility is critical in pharmaceutical analysis, as it ensures compliance with regulatory standards and supports the reliable quality control of Telmisartan and Efonidipine HCl ethanolate.

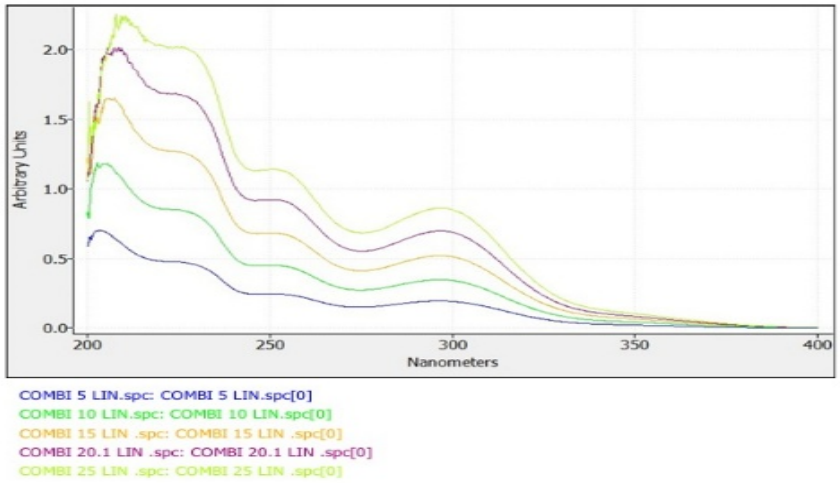


Figure 6: UV-Visible Spectroscopic overlay of Telmisartan & Efonidipine HCl Ethanolate

Table 2: System suitability parameters TELMI (10 µg/ml) & EFNO (10 µg/ml) by proposed RP-HPLC method

Parameters	EFNO	TELMI	Acceptance criteria
Retention Time	2.771	7.024	-
Tailing Factor	0.63	0.70	≤ 2.0
Theoretical Plate	3776	6439	>2000
Peak Area	847.36	879.31	-
Resolution	-	16.00	>2.0

Linearity

The linearity study of TELMI and EFNO across five concentration levels shows that both RP-HPLC and UV-spectrophotometric methods are dependable. For TELMI, RP-HPLC covered a wide range (10–50 µg/ml) with a steep slope (49.24) and an almost perfect correlation (r^2 = 0.9999). This proves that the detector is highly sensitive to concentration changes, making RP-HPLC ideal for accurate measurement even at higher levels. The UV methods (simultaneous equation and area under curve), tested over a smaller range (5–25 µg/ml), gave slightly lower slopes but still strong correlations ($r^2 \approx 0.998$). This means they are reliable for routine checks, though less sensitive than RP-HPLC. For EFNO, all three methods showed excellent linearity, with correlation values of 0.9998, 0.9983, and 0.998. Again, RP-HPLC showed the steepest slope (42.079), confirming its higher sensitivity. Since all r^2 values are very close to 1.0, the response is directly proportional to conc., ruling out issues like non-linearity or detector saturation. Linearity studies for EFNO and TELMI by RP-HPLC and UV spectroscopic methods are shown in Table 3, and Linearity graphs of TELMI and EFNO by RP-HPLC, simultaneous equation method, and Area under the curve are shown in Figures 7A- 7F. In practice, RP-HPLC is the best choice when precision and sensitivity are critical, such as in complex formulations or bioanalytical studies. UV-spectrophotometry, on the other hand, is faster and more suitable for routine quality control. Overall, the linearity findings confirm that the validated methods are strong, flexible, and capable of delivering accurate results across different pharmaceutical applications.

Table 3: Linearity studies by RP-HPLC and UV-spectroscopy methods

Parameters	RP-HPLC	Simultaneous equation method (A)	Area under curve method (B)
TELMI			
Linearity range(µg/ml)	10-50	5-25	5-25
Regression equation	y=49.24x+1097.3	Y=0.0727x-0.0094	y=1.3719x+0.3355
Slope	49.24	0.0727	1.3719
Intercept	1097.3	0.0094	0.3355
Correlation coefficient(r^2)	0.9999	0.998	0.9983
EFNO			
Linearity range(µg/ml)	10-50	5-25	5-25
Regression equation	Y= 42.079 + 1113.4	y=0.0696x-0.0375	y=0.9175x-0.6561
Slope	42.079	0.0696	0.9175
Intercept	1113.4	0.0375	0.6561
Correlation coefficient(r^2)	0.9998	0.9983	0.998

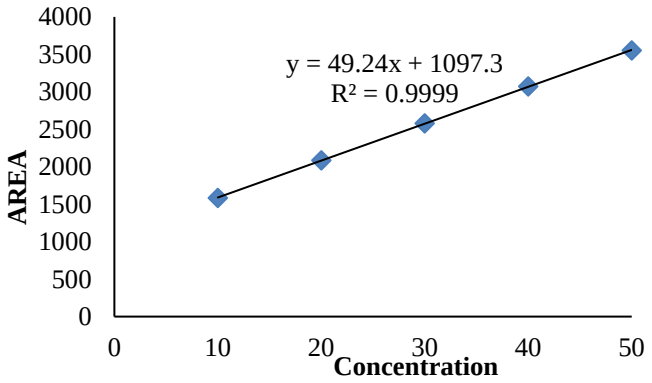


Figure 7(A): Linearity graphs of TELMI by RPHPLC

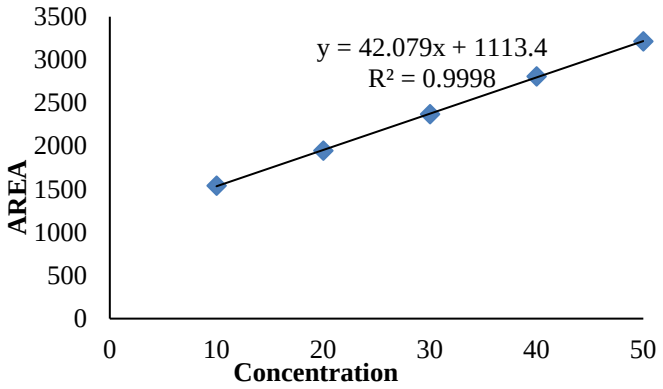


Figure 7(B): Linearity of EFNO by HPLC method

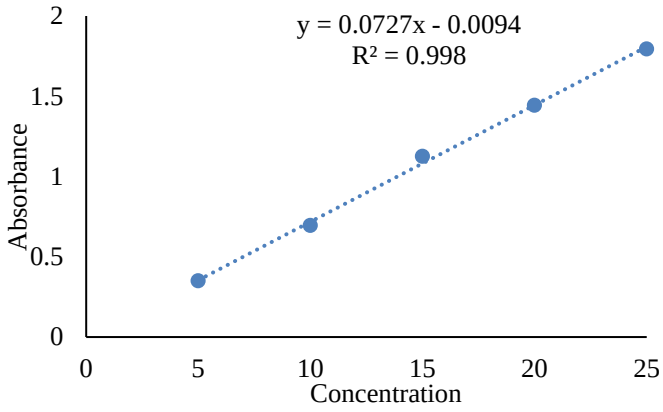


Figure 7(C): Linearity graphs of TELMI by SEM

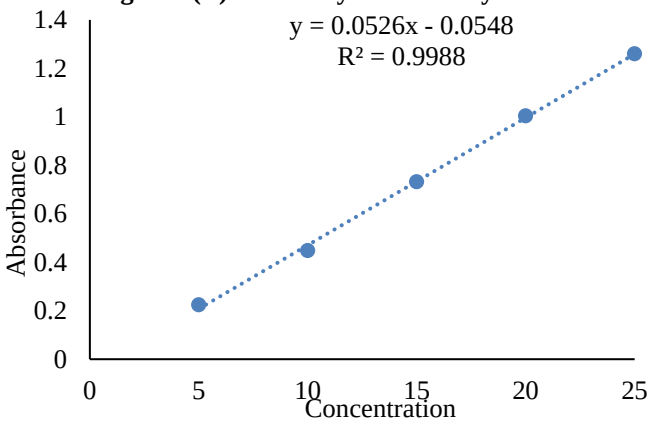


Figure 7(D): Linearity of EFNO by SEM

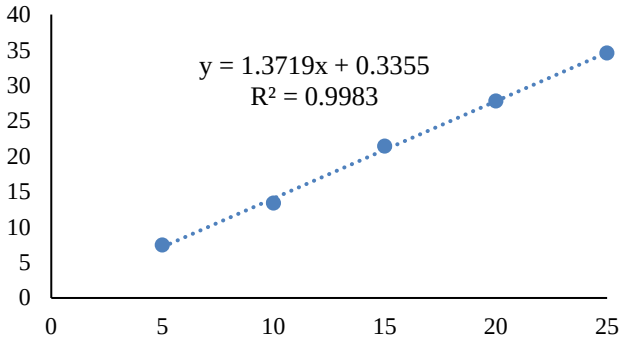


Figure 7(E): Linearity graphs of TELMI by AUC

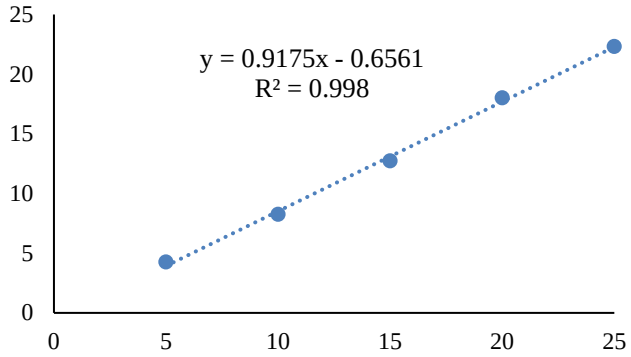


Figure 7(F): Linearity of EFNO by AUC

LOD & LOQ

The measurement of LOD (limit of detection) and LOQ (limit of quantification) for TELMI and EFNO across three methods highlights the sensitivity of each technique. RP-HPLC showed the lowest values (TELMI: LOD 0.147 µg/ml, LOQ 0.447 µg/ml; EFNO: LOD 0.178 µg/ml, LOQ 0.539 µg/ml), indicating that it can detect and measure very small amounts of the drug. This makes RP-HPLC especially useful for studies that require trace-level detection, such as stability testing, impurity checks, or bioanalysis. The area under the curve method showed the highest values (TELMI: LOD 1.430 µg/ml, LOQ 4.334 µg/ml; EFNO: LOD 1.614µg/ml, LOQ 4.891µg/ml) compared to the simultaneous equation and RP-HPLC method, which means it shows lower sensitivity, as seen from its higher LOD/LOQ values compared to Method A and HPLC. Even so, laboratories may still select Method B because it is straightforward, requires less advanced equipment, and is more economical for routine testing where very low detection limits are not critical.

It also offers faster operation and reduced solvent use, which supports eco-friendly practices. Therefore, while Method A and HPLC are better suited for high-sensitivity applications, Method B remains a practical choice when cost, simplicity, or sustainability are the main priorities. Table 4 shows the LOD & LOQ values determined by UV spectrophotometry and RP-HPLC for TELMI and EFNO.

Table 4: LOD & LOQ of EFNO and TELMI by UV Spectrophotometer & RP-HPLC method.

Method	Simultaneous equation method		Area under curve method		RP-HPLC	
	TELMI	EFNO	TELMI	EFNO	TELMI	EFNO
LOD	0.0984	0.17624	1.43015	1.6139	0.147363	0.177886
LOQ	0.2983	0.53408	4.3338	4.8908	0.446557	0.53905

Precision

Both the repeatability and interday precision of developed techniques for the determination of Telmisartan and Efonidipine HCl Ethanolate simultaneously were evaluated as per ICH Q2(R1) guidelines. % RSDs of repeatability and interday precision for the developed methods of both drugs were found to be less than 2%. Interday and Intraday studies were shown in Table 5.

Table 5: Interday and Intraday Precision study

parameters	Simultaneous Equation Method		Area Under Curve Method		RP-HPLC Method		Acceptance Criteria
	TELMI	EFNO	TELMI	EFNO	TELMI	EFNO	
Repeatability	0.1153	0.5439	1.22	1.31	0.34	0.18	≤ 2%
Interday	0.4189	0.3953	1.4659	0.9390	0.63	0.38	

Accuracy

The accuracy study showed that both UV-Visible spectrophotometry and RP-HPLC methods yield reliable recovery values for TELMI and EFNO, demonstrating their suitability for quantitative analysis in pharmaceutical formulations. In the UV method, TELMI recoveries ranged from 99.97% to 101.18% with %RSD below 2%, while EFNO recoveries ranged from 100.01% to 100.58% with %RSD below 1.3%. These results confirm that the UV method yields values very close to the true concentration, with little variation, indicating good precision & accuracy.

RP-HPLC showed slightly better precision, with TELMI recoveries ranging from 98.82% to 99.96% and EFNO recoveries from 98.22% to 100.65%, all with %RSD values well below 1%. This demonstrates the strong reproducibility and robustness of RP-HPLC, making it especially useful when high sensitivity and precision are required. Overall, both methods are reliable. UV-spectrophotometry offers a simple and efficient option for routine quality control, while RP-HPLC provides greater precision for more demanding analytical tasks. Accuracy data for UV and RP-HPLC methods are shown in Table 6.

Table 6: Accuracy data for UV and RP-HPLC techniques

Method	Drug	Level	Conc. Present (µg/ml)	Spiked Conc.(µg/ml)	Total Conc.Taken (µg/ml)	Amount of standard recovery (µg/ml)	%Recovery ± SD (n=3)	%RSD
UV-Visible Spectro. method	TELMI	80%	10	8	18	18.033	99.97	0.182
		100%	10	10	20	20.577	101.18	1.70
		120%	10	12	22	21.632	101.14	1.25
	EFNO	80%	10	8	18	17.898	100.58	1.17
		100%	10	10	20	19.864	100.01	1.27
		120%	10	12	22	21.973	100.26	0.50
RP-HPLC Method	TELMI	80%	10	8	18	17.89	98.96	0.113
		100%	10	10	20	20	99.96	0.006
		120%	10	12	22	21.86	98.82	0.627
	EFNO	80%	10	8	18	17.87	98.22	0.135
		100%	10	10	20	20.06	100.65	0.357
		120%	10	12	22	22	100.02	0.299

Robustness

The robustness study showed that the developed RP-HPLC method for TELMI and EFNO is highly dependable, even when small changes were made to key parameters such as detection wavelength, flow rate, and mobile phase composition. In all tested conditions, %RSD values stayed well below the 2% limit, and peak areas remained consistent. This proves that the method is unaffected by minor variations that often occur in routine laboratory work. In practice, this means the method can deliver accurate and precise results even when slight differences arise between analysts, instruments, or laboratories. The Robustness studies for EFNO and TELMI by RP-HPLC and UV methods are shown in Tables 7 and 8**.**

Table 7: Robustness studies for EFNO and TELMI by Rp-HPLC method

Factors	Chromatographic changes	TELMI		EFNO	
		Peak Area	%RSD	Peak Area	%RSD
Wavelength of detection	252	3022.4	0.13	2917.1	0.02
	254	2954.04	0.15	2736.72	0.30
Flow rate	0.8	3369.2	0.00	3177.3	0.03
	1	2685.25	0.07	2542.57	0.09
Mobile phase	84% Ethanol + 16% (0.1% OPA Water)	2978.8	0.10	2831	0.04
	86% Ethanol + 14% (0.1% OPA Water)	2994.32	0.07	2827.24	0.03

Table 8: Robustness data of UV method.

Method	Variables	Variables		TELMI	EFNO
		TELMI	EFNO	%RSD	
Simultaneous equation Method	Wavelength (nm)	296	250	0.28	0.32
		298	252	0.31	0.34
Area Under Curve		288-308	240-260	0.298	0.3245
		286-306	242-262	0.321	0.3457
Simultaneous equation Method	Temperature variation (°C)	24°C	24°C	0.357	0.389
		26°C	26°C	0.364	0.417
Area Under Curve Method		24°C	24°C	0.362	0.418
		26°C	26°C	0.37	0.431

Greenness assessment

The greenness evaluation revealed that both UV-Visible spectrophotometry and RP-HPLC methods are environmentally acceptable, with analytical eco-scale scores of 92 and 88, respectively, indicating excellent compliance with green chemistry principles. The UV method incurred fewer penalty points (8) than HPLC (12), mainly due to lower energy consumption and simpler instrumentation, thereby ranking slightly higher in terms of eco-friendliness. RP-HPLC, while marginally less green, still demonstrated strong sustainability performance with acceptable waste generation and occupational safety. Complementary assessment tools such as GAPI, NEMI, and AGREE further confirmed that both methods align well with green analytical practices, validating their suitability for routine pharmaceutical analysis with minimal environmental impact. Assessment of the greenness values of the analytical methods using AGREE, GAPI, NEMI & Eco-Scale is shown in Table 9.

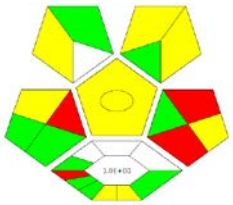
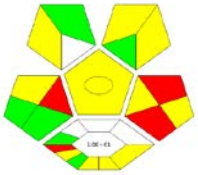
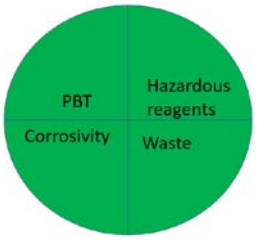
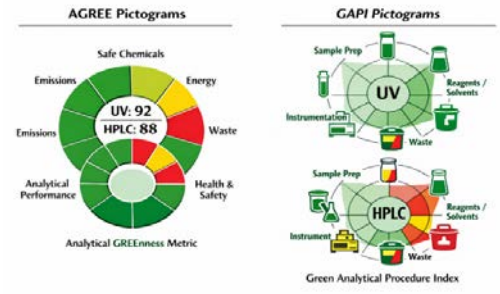
DISCUSSION

This study demonstrates the robustness and reliability of ethanol-assisted UV-spectrophotometric and RP-HPLC methods for the analysis of Telmisartan (TELMI) and Efonidipine HCl ethanolate (EFNO). Both techniques were carefully validated, and the results confirm their suitability for routine pharmaceutical quality control. By evaluating system suitability, linearity, accuracy, precision, and robustness, the study provides strong evidence that these methods can consistently deliver dependable results under varied laboratory conditions. The proposed method clearly demonstrates superiority over Darji H's approach by integrating sustainability into analytical practice without compromising reliability. Darji H's protocols, while strong in precision, recovery, and system suitability, rely on acetonitrile and methanol—solvents that are toxic and pose significant disposal challenges, thereby increasing the environmental burden. In contrast, the present method employs ethanol and orthophosphoric acid water for HPLC and ethanol alone for UV analysis, offering a biodegradable, safer, and eco-friendly alternative that aligns more closely with the principles of green analytical chemistry. Although slightly higher %RSD values and lower theoretical plate counts are observed compared to Darji's results, the method still maintains acceptable accuracy and recovery. This balance between analytical validity and ecological responsibility makes the present approach more suitable for laboratories aiming to reduce chemical hazards and minimize environmental impact, thereby advancing the broader goal of sustainable analytical science. System suitability parameters were the first step in confirming method reliability. The tailing factors obtained (0.63 for EFNO and 0.70 for TELMI) suggest minor peak fronting rather than tailing.

This behavior is most likely linked to the green mobile-phase composition, which modifies analyte–stationary-phase interactions compared with conventional solvents. Despite the fronting, peak symmetry was adequate and did not interfere with

accurate integration. Therefore, the low tailing factors can be attributed to the eco-friendly solvent system and do not represent a limitation of the developed method. Theoretical plate counts of 3776 and 6439 showed high column efficiency, meaning the column produced sharp peaks and effective separation. TELMI's resolution value of 16.0 far exceeded the minimum requirement of 2.0, ensuring clear separation from adjacent peaks and eliminating the risk of co-elution. Retention times and peak areas, though not part of formal acceptance criteria, were consistent across repeated runs, further supporting reproducibility. Together, these values confirm that the chromatographic system is stable and reliable.

Table 9: Assessment of greenness values of analytical method by AGREE, GAPI, NEMI & Eco-Scale.

Green Evaluation tools	UV		HPLC	
Eco-Scale Assessment	Ethanol	4	Ethanol	4
	Instrument	1	0.1%Orthophosphoric Acid Water	1
	Energy Used	0	Instrument	2
	Waste	3	Energy Used	2
	Occupational Hazard	0	Waste	3
	Total Penalty Points	8	Occupational Hazard	0
	Analytical Eco Scale	92	Total Penalty Points	12
			Analytical Eco Scale	88
Green Analytical Procedure Index (AGREE)				
GAPI				
NEMI				
				

Linearity studies across three methods—RP-HPLC, simultaneous equations, and area under the curve—yielded strong correlation coefficients ($R^2 > 0.998$). This shows that detector response was directly proportional to concentration, eliminating concerns of non-linearity or saturation. TELMI exhibited a wide linear range (10–50 µg/ml) with a steep slope

(49.24) in RP-HPLC, indicating high sensitivity. UV-based methods, though tested over narrower ranges (5–25 μg/ml), still maintained strong correlations (≈0.998), confirming their reliability for routine quantification. EFNO showed similar consistency, with RP-HPLC again yielding the steepest slope (42.079), highlighting its superior sensitivity. These outcomes establish that both methods are analytically sound and reproducible, meeting ICH Q2(R1) guidelines for validation.

Accuracy and precision studies further confirmed the reliability of both techniques. In UV-spectrophotometry, TELMI recoveries ranged from 99.97% to 101.18% with %RSD values below 2%, while EFNO recoveries were between 100.01% and 100.58% with %RSD under 1.3%. RP-HPLC demonstrated slightly better precision, with TELMI recoveries ranging from 98.82% to 99.96% and EFNO recoveries from 98.22% to 100.65%, all with %RSD values well below 1%. The recovery values for Telmisartan obtained by the UV method (101.18% at 100% level and 101.14% at 120% level) are slightly higher than those from RP-HPLC (~99%) because UV spectrophotometry directly measures absorbance and is more prone to matrix effects. Excipients or formulation components may absorb at similar wavelengths, causing a minor positive bias in recovery. In contrast, RP-HPLC separates the analyte from excipients before detection, reducing interference and yielding values closer to the true content.

A comparison of the two techniques highlights their complementary nature. UV-spectrophotometry is simple, cost-effective, and energy-efficient, making it particularly useful for rapid screening and high-throughput analysis. Although it is less sensitive than RP-HPLC, its efficiency and ease of use make it ideal for routine applications where speed and minimal resource use are prioritized. RP-HPLC, on the other hand, demonstrated superior resolution and selectivity, enabling precise quantification even in complex formulations or biological matrices. This dual-method approach ensures flexibility, allowing laboratories to select the most appropriate technique depending on analytical requirements—whether rapid screening or detailed quantification.

The use of ethanol as a solvent represents a significant advancement in analytical methodology. Conventional solvents such as acetonitrile and methanol, widely used in RP-HPLC, are associated with toxicity, disposal challenges, and higher environmental impact. Ethanol, being biodegradable, renewable, and less hazardous, reduces ecological burden while maintaining chromatographic efficiency. Greenness assessment confirmed that both methods minimize hazardous waste generation and energy demand, aligning with the principles of green analytical chemistry. This substitution supports the broader sustainability agenda in pharmaceutical sciences, where reducing environmental footprint is increasingly prioritized. By integrating ethanol into analytical workflows, the study demonstrates that sustainability can be achieved without compromising analytical performance.

Comparative literature analysis strengthens these findings. Previous studies on Telmisartan and other antihypertensive drugs often relied on acetonitrile-based mobile phases, reporting similar accuracy and precision but at the expense of environmental safety. The present work shows that ethanol can serve as a viable alternative without compromising analytical performance. Moreover, the dual validation of UV and RP-HPLC methods provides a more comprehensive framework than single-method approaches reported earlier. This ensures that laboratories have access to both rapid screening and high-resolution quantification methods, enhancing flexibility and reliability in pharmaceutical analysis.

From a regulatory perspective, ethanol-assisted methods enhance compliance with evolving sustainability guidelines in pharmaceutical quality control. Regulatory agencies increasingly emphasize eco-friendly practices, and the demonstrated robustness of both methods ensures their applicability in routine laboratory settings. The UV method, with a greenness score of 92, demonstrates slightly greater eco-friendliness than HPLC, which has a score of 88. Both techniques, however, fall within the category of excellent green performance, reflecting minimal environmental impact. The difference in scores highlights UV's marginal advantage in sustainability, yet both remain commendable choices for eco-conscious analytical practices. This comparison underscores the growing emphasis on greener methodologies in pharmaceutical and chemical analysis.

CONCLUSION

UV & RP-HPLC methods have been developed and validated for the determination of TELMI & EFNO in their pharmaceutical dosage forms. The developed methods are straightforward, reliable, precise, quick, and specific. The

validation of the developed techniques was conducted in accordance with the ICH Q2(R1) guidelines. Both methods may simultaneously evaluate TELMI & EFNO in a fixed-dose combination without interference. The efficacy of green analytical chemistry was demonstrated by both methods. The UV-spectrophotometric approach is more appropriate for high-throughput screening in pharmaceutical research, as it allows rapid measurements, requires minimal sample handling, and consumes less solvent, making it efficient for large-scale preliminary testing.

In contrast, RP-HPLC is better suited for regulatory compliance and routine quality control, as it offers higher sensitivity, reproducibility, and detailed impurity profiling that align with international validation standards such as ICH and FDA guidelines. High-throughput screening (HTS) is recognized as the preferred approach for rapid, large-scale compound evaluation in areas such as drug discovery, toxicology, and genomics. This method relies on automated assays that can efficiently test thousands of compounds in parallel, making it invaluable for accelerating research and development.

In contrast, regulatory compliance refers to adhering to established laws, official rules, and industry standards. It is the appropriate term when discussing conformity with legal or professional requirements, ensuring that processes and outcomes meet mandated guidelines. Presenting this distinction will enhance the study's industrial relevance by clearly indicating which method to adopt based on operational requirements.

ABBREVIATIONS

TELMI: Telmisartan; EFNO: Efonidipine HCl Ethanolate; LOD: Limit of detection; LOQ: Limit of quantification; UV: Ultraviolet spectroscopy; RP-HPLC: Reverse phase High performance Liquid chromatography; SD: Standard Deviation; %RSD: Percentage relative standard deviation; ICH: International conference on Harmonization; OPA: Ortho phosphoric acid; AUC: Area under curve; SEM: Simultaneous equation method.

FINANCIAL ASSISTANCE

NIL

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

R. K. Godge and M. S. Kotkar contributed to conceptualization, methodology design, supervision, manuscript writing, and final approval of the draft. S. B. Dighe, M.F. Ansari, and S.P. Mankar conducted experimental work, collected data, and reviewed the literature.

DECLARATION OF USE OF AI TOOLS

The authors used Copilot in selected sections of the manuscript for improving readability. All content, analysis, and conclusions were reviewed and verified by the authors. The authors take full responsibility for the originality, accuracy, and integrity of the work.

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