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DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC METHODS FOR SIMULTANEOUS ESTIMATION OF AZELNIDIPINE AND TELMISARTAN IN TABLET DOSAGE FORM USING SIMULTANEOUS EQUATION AND Q-ABSORBANCE RATIO METHODS

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ABSTRACT

Hypertension, a leading cause of global mortality, necessitates effective management to mitigate cardiovascular and renal disease risks. Monotherapy often proves inadequate, with approximately 75% of hypertensive patients requiring combination treatment. Preferred combinations include angiotensin-receptor blockers and calcium channel blockers, with some patients needing triple combination therapy. Recently introduced fixed-dose tablet formulations, such as Azusa T, Uniaz T, Telma-AZ, and Zeblong T, combine Azelnidipine and Telmisartan for hypertension treatment.

Two validated UV spectrophotometric methods, utilizing simultaneous equation and absorbance ratio techniques, have been developed for the simultaneous estimation of Azelnidipine and Telmisartan in pure powder and two-component dosage forms. The methods measure absorbance at 252 nm and 296 nm, and the iso-absorptive wavelength of 268 nm in methanol. Azelnidipine and Telmisartan obeyed Beer's law at their respective λmax, demonstrating linearity in the concentration ranges of 1.6-8 µg/mL and 4-20 µg/mL, with correlation coefficients of 0.9998 for both. Statistical validation adhered to ICH guidelines, confirming the methods' reliability for routine analysis of Azelnidipine and Telmisartan in pharmaceutical formulations.

KEYWORDS:
Azelnidipine; Telmisartan; Simultaneous estimation; absorbance ratio, Validation.

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INTRODUCTION

Treating hypertension has been linked to significant reductions in cardiovascular risk, specifically a 40% decrease in stroke risk and a 15% decrease in myocardial infarction risk. Hypertension is characterized by systolic blood pressure ≥140mmHg and diastolic blood pressure ≥90mmHg. Recently introduced fixed-dose combinations, such as Azusa T, Uniaz T, Telma-AZ, and Zeblong T, combine Azelnidipine and Telmisartan to treat hypertension.

Azelnidipine (AZEL), a calcium channel blocker, has the chemical structure (±)-3-(1-diphenylmethylazetidin-3-yl)5-isopropyl-2-amino-1,4-dihydro-6-methyl-4-(3nitrophenyl)3,5-pyridinedicarboxylate, with a molecular formula $C_{33}H_{34}N_4O_6$ and molecular weight 582.646 g/mol. It appears as a light yellow to yellow crystalline powder, soluble in organic solvents like ethanol, DMSO, and DMF, slightly soluble in methanol, and freely soluble in acetone. Its melting point is 193-195°C, with a pKa value of 7.89.

Telmisartan, an angiotensin II receptor antagonist, has the chemical structure 2-[4-[[4-methyl-6-(1-methylbenzimidazol-2-yl)-2-propylbenzimidazol-1-yl]methyl]phenyl]benzoic acid, with a molecular formula $C_{33}H_{30}N_4O_2$ and molecular weight 514.62 g/mol. It is a white to slight yellowish powder, soluble in organic solvents but practically insoluble in water. Its melting point is 261-263°C, and it exhibits weak acidity with pKa values of 3.5, 4.1, and 6.0.

MATERIALS

All the chemicals and reagents used were of analytical grade.The reference standards of Azelnidipine (AZN) and Telmisartan (TMN) were obtained from Reliable Lab, Jalgaon. Commercially available Telma AZ 16 tablets, containing 16 mg AZN and 40 mg TMN, were utilized for analytical purposes.

EQUIPMENTS

The analytical determination of Azelnidipine and Telmisartan will be performed using a Shimadzu UV 180 UV Spectrophotometer, featuring a spectral band-width of 1 nm. Absorbance measurements will be conducted utilizing 15 mm matched quartz cuvettes, ensuring precise and accurate results.

DERIVATION OF EQUATIONS

Simultaneous Equation Method for analyzingAzelnidipine (AZN) and Telmisartan (TMN) in combination. This method uses absorptivity values to derive equations for determining both drugs in pharmaceutical formulations.

Key Equations:

1. Cx = (A1ax2 – A2ax1) / (ax2ay1 – ax1ay2)
2. Cy = (A2ay1 – A1ay2) / (ax2ay1 – ax1ay2)

Variables:

1. Cx: Concentration of AZN
2. Cy: Concentration of TMN
3. A1 & A2: Absorbance of sample at 252 nm and 296 nm
4.ax1& ax2: Absorptivity of AZN at 252 nm and 296 nm
5. ay1& ay2: Absorptivity of TMN at 252 nm and 296 nm

Absorptivity Values:

1. AZN (252 nm): $0.1246 \times 10^{(-6)}$
2. AZN (296 nm): $0.1322 \times 10^{(-6)}$
3. TMN (252 nm): $0.7397 \times 10^{(-6)}$
4. TMN (296 nm): $0.7433 \times 10^{(-6)}$

Calculations:

1. Cx = (A1 × 0.1322 – A2 × 0.1246) / (0.1322 × 0.7397 – 0.1246 × 0.7433)
2. Cy = (A2 × 0.7397 – A1 × 0.7433) / (0.1322 × 0.7397 – 0.1246 × 0.7433)

This method allows for the simultaneous determination of AZN and TMN concentrations in pharmaceutical formulations.

ANALYSIS OF FORMULATION

Twenty tablets of Telma-AZ (Glenmark) containing 16 mg Azelnidipine (AZN) and 40 mg Telmisartan (TMN) were accurately weighed, and the average weight was determined. The tablets were finely powdered, and an appropriate quantity of powder equivalent to 16 mg AZN and 40 mg TMN was transferred to a 100 mL volumetric flask. Methanol (100 mL) was added, and the mixture was shaken vigorously for 15 minutes, followed by sonication for 5 minutes. The solution was filtered through Whatman filter paper no. 41, and necessary dilutions were made with methanol to achieve final concentrations of 16 µg/mL AZN and 40 µg/mL TMN.

The absorbance of this solution was measured at 252 nm (λmax of AZN), 296 nm (λmax of TMN), and 268 nm (Isoabsorptive Point). The obtained values were substituted into the respective formulae of the simultaneous equation method to calculate the concentrations of AZN and TMN. The results of this analysis are presented in Table 3, demonstrating the successful application of the UV spectrophotometric method for simultaneous determination of AZN and TMN in pharmaceutical formulations.

Method Validation

Calibration curve (linearity of the method)

Calibration curves for Azelnidipine (AZN) and Telmisartan (TMN) were constructed by plotting absorbance against concentrations at their respective λmax values, and regression equations were calculated. The calibration curves were plotted over five different concentrations ranging from 1.6-8 µg/mL for AZN and 4-20 µg/mL for TMN, demonstrating a linear relationship between absorbance and concentration for both drugs (Fig. 2 and Fig. 3). The optical and statistical parameters, including correlation coefficients (r2) close to unity, are summarized in Table 1, indicating the reliability and excellent linearity of the UV spectrophotometric method for quantitative analysis of AZN and TMN.

Accuracy (% Recovery)

The accuracy of the method was determined by calculating recoveries of AZN and TMN by the standard addition method. Known amount of standard of AZN and TMN (80%, 100%, and 120%) were added to the sample solutions of tablet dosage forms. The amounts of AZN and TMN were estimated by equations in method. The results are shown in Table 2. The values prove that the method is accurate. 5.3.

Method Precision (Repeatability)

The precision of the UV spectrophotometric method was evaluated by performing repeated scans (n = 5) of standard solutions of Azelnidipine (AZN) and Telmisartan (TMN) at a concentration of 10 µg/mL. The resulting relative standard deviation (RSD) values were less than 2%, indicating excellent repeatability and precision of the proposed method (Table 2).

Intermediate Precision (Reproducibility)

The intermediate precision of the UV spectrophotometric method was evaluated through intra-day and inter-day studies, assessing standard solutions of Azelnidipine (AZN) and Telmisartan (TMN) at three concentration levels. Each concentration was analyzed in triplicate on the same day (intra-day) and on three consecutive days (inter-day). Results, expressed as relative

standard deviation (RSD), demonstrated excellent reproducibility, with RSD values consistently below 2% (Table 2), confirming the method's reliability and robustness.

Robustness

The stability of Azelnidipine (AZN) and Telmisartan (TMN) solutions in methanol was evaluated over a 24-hour period at ambient temperature. The results showed negligible degradation, with absorbance variations of less than 1%, indicating excellent solution stability.

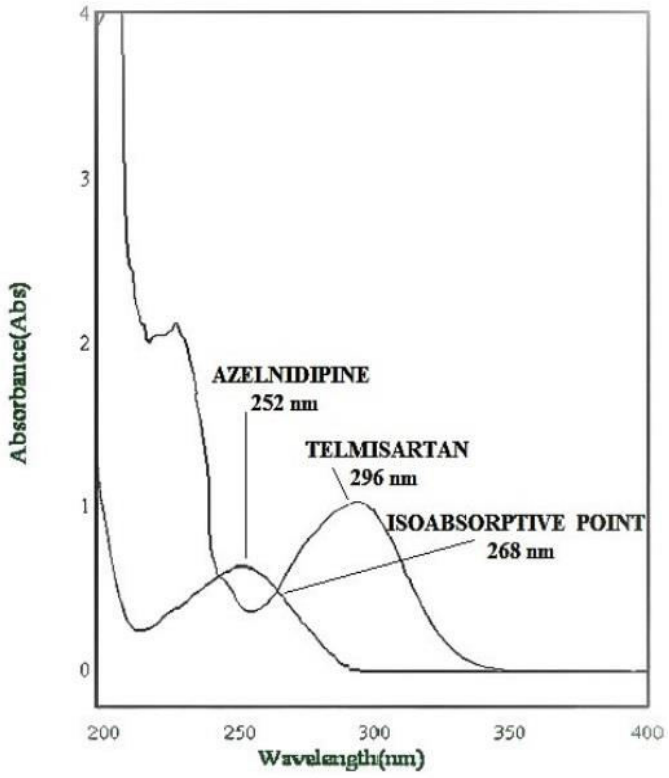

Fig. 1: Overlay Spectrum of AZN and TMN

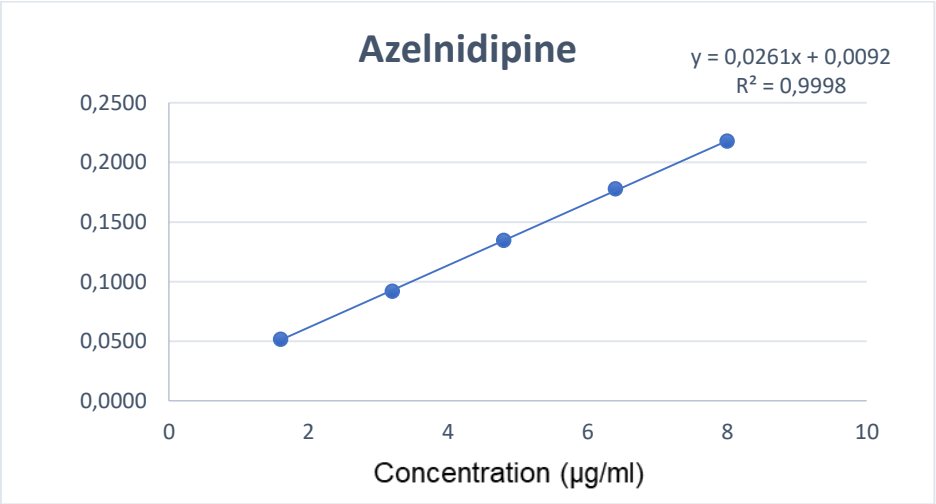

Fig. 2: Calibration curve of AZN.

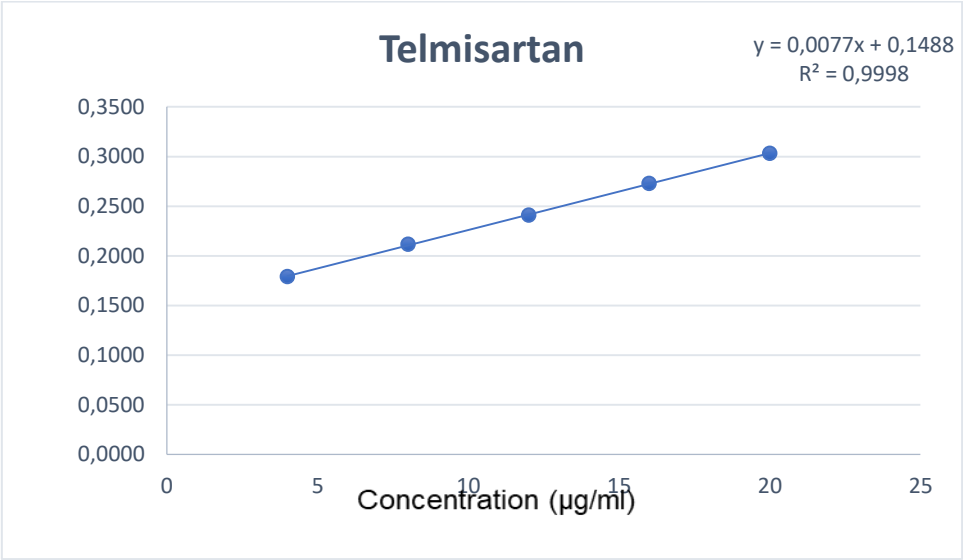

Fig.3.Calibration curve of TMN.

Table 1: Optical Characteristics Data.

PARAMETERS	SIMULTANEOUS EQUATION METHOD	
	AZN	TMN
Working λmax	252nm	296nm
Beer's law limit	1.6-8 µg/ml	4-20µg/ml
Correlation coefficient	0.9998	0.9998
Intercept	0.0092	0.1488
Slope	0.0261	0.0077
Regression equation	Y=0.0261x + 0.0092	Y=0.0077x + 0.1488

Table 2: Summary of Validation Parameters for the Proposed Methods

Sr. No.	Parameters	AZN	TMN
1	Precision . Repeatability (n=6) 2. Intra-day precision (n=6) 3. Inter-day precision (n=6)	 0.59% 0.43-0.76 0.27-0.96	 0.20% 0.11-0.20 0.11-0.30
2	Accuracy (% Recovery)	99.88-101.99%	100.21-100.75%
3	Limit of Detection (LOD)	0.088	0.3
4	Limit of Quantification (LOQ)	0.2681	0.9090

Table 3: Compilation of results of commercial formulation

Tablet	Label Claim	Amount of Recovered ± S.D.	% Assay ± S.D.	%RSD
Telma-AZ	AZN 16mg	15.92±0.7	99.50±0.46	0.46
	TMN 40mg	48.03±0.15	100.08±0.38	0.38

CONCLUSION

This study presents convenient and accurate methods for simultaneous estimation of Azelnidipine (AZN) and Telmisartan (TMN) using UV spectrophotometry. Two methods were developed: Simultaneous Equation and Q-Analysis. For both methods, linearity was observed in the concentration ranges of 1.6-8 µg/mL (AZN) and 4-20 µg/mL (TMN). Absorptivity coefficients were calculated and used to determine concentrations in tablet dosage forms. The percent label claim for AZN and TMN in tablets was accurately determined using both methods. Recovery studies confirmed the methods' accuracy. These methods are suitable for routine quality control analysis of AZN and TMN in combined dose formulations.

REFERENCES

1. Gorostidi, M., & de la Sierra, A. (2013). Combination therapy in hypertension. Advances in Therapy, 30(4), 320-336.
2. Collins, R., Peto, R., MacMahon, S., Hebert, P., Fiebach, N. H., &Eberlein, K. A. (1990). Blood Pressure, Stroke and Coronary Heart Disease. Part 2: Short Term Reductions in Blood Pressure: Overview of Randomized Drug Trials in Their Epidemiologic Context. Lancet, 335, 827-838.
3. Dabhade, M. G., &Dabhade, P. S. (2012). Review on Simultaneous Determination of Antihypertensive Analytes in Pharmaceutical Dosage Form by Different Analytical Methods. International Journal of Pharmacy Research & Technology, 2(2), 09-15.
4. Indian Pharmacopoeia (2018). Azelnidipine. Indian Pharmacopoeial Commission, Ghaziabad, India.
5. Indian Pharmacopoeia (2010). Ministry of Health & Family Welfare, Vol-II & III, 6th edn. Indian Pharmacopoeial Commission, Ghaziabad, India, 1076-77, 2186-88.
6. British Pharmacopoeia (2010). Vol-I & II, 6th Edn. The Stationery Office, London, 484-85, 2042-44.
7. United States Pharmacopoeia (2011). National Formulary-29, Vol. II & III, 34. The United States Pharmacopoeial Convention, Rockville, MD, USA, 2321-22, 4357-58.
8. Raskpur, K. (2011). UV-Spectrophotometric Method Development and Validation for Determination of Azelnidipine in Pharmaceutical Dosage Form. International Journal of Pharmacy and Pharmaceutical Sciences, 4(1), 238-240.
9. Prabhakar, D., &Jayaveera, K. N. (2018). Method Development and Validation of Azelnidipine by RP-HPLC. International Journal of ChemTech Research, 11(1), 7-12.
10. Gore, M., &Dabhade, P. (2016). RP-HPLC Method Development and Validation of Azelnidipine. International Journal of Pharmaceutical Sciences and Research, 7(12), 5111-5114.
11. Ganduri, R., Jayachandra, & Reddy, P. P. (2014). Stability Indicating Liquid Chromatographic Method for the Simultaneous Determination of OlmesartanMedoxomil and Azelnidipine in Combined Tablet Dosage Form. International Journal of Pharma Sciences and Research, 5(6), 275-282.
12. Patel, J. K., & Patel, N. K. (2014). Validated Stability-Indicating RP-HPLC Method for the Simultaneous Determination of Azelnidipine and Olmesartan in Their Combined Dosage Form. ScientiaPharmaceutica, 82(3), 541-554.
13. Santosh Kumar, M., &Jupally, V. R. (2017). Development and Validation of a Stability Indicating RP-HPLC Method for Simultaneous Determination of Telmisartan and Amlodipine in Combined Dosage Form. Asian Journal of Pharmaceutical and Clinical Research, 7(1), 32-35.
14. Rupareliy, & Joshi, H. (2013). Stability Indicating Simultaneous Validation of Telmisartan and Cilnidipine with Forced Degradation Behavior Study by RP-HPLC in Tablet Dosage Form. ISRN Chromatography, 6.
15. Lakshmi Surekha, M., Kumar Swamy, G., & Lakshmi Ashwini, G. (2012). Development and Validation of RP-HPLC Method for the Estimation of Telmisartan in Bulk and Tablet Dosage Form. International Journal of Drug Development and Research, 4(4), 200-205.
16. International Conference on Harmonisation of Technical Requirements for Human Use (2005). Validation of Analytical Procedure: Text and Methodology Q2 (R1). ICH Harmonized Tripartite Guidelines.