EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 8
Issue: 5
290-294
Year: 2021

FIRST- ORDER DERIVATIVE AND UV-SPECTROPHOTOMETRIC METHODS FOR SIMULTANEOUS DETERMINATION OF TELMISARTAN AND AZELNIDIPINE IN BULK AND TABLET DOSAGE FORM

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Article Received on 04/03/2021 **Article Revised on 24/03/2021** **Article Accepted on 14/04/2021**

ABSTRACT
Two sensitive, precise, accurate for First order derivative and UV- spectrophotometric methods for simultaneous estimation of Telmisartan (TEL) and Azelnidipine (AZEL) in bulk and tablet dosage forms. Method A involved simultaneous equation method, In this method, the two wavelengths 324 nm (λ_{max} of TEL) and 220 nm (λ_{max} of AZEL) were selected. Method B was First order derivative spectroscopy method in which derivative amplitudes were measured at selected wavelengths (220 nm for TEL and 244 nm for AZEL). Linearity was observed in the concentration range of 16-80 µg/ml for TEL and 3.2-16 µg/ml for AZEL by method A and B respectively. The proposed methods have been applied successfully to the analysis of cited drugs in pharmaceutical formulations. Recovery study was performed to confirm the accuracy of the methods. The methods were validated as per ICH guidelines.

KEYWORDS: Telmisartan, Azelnidipine, Simultaneous estimation, First order derivative.

INTRODUCTION
Telmisartan is 2-(4-{[4-methyl-6-(1-methyl-1H-1,3-benzodiazol-2-yl)-2-propyl-1H-1,3 benzodiazol-1-yl]methyl} phenyl) benzoic acid (Fig 1). It is an angiotensin II receptor antagonist (ARB) used in the management of hypertension. Generally, angiotensin II receptor blockers (ARBs) such as telmisartan bind to the angiotensin II type one (AT1) receptors with high affinity, causing inhibition of the action of angiotensin II on vascular smooth muscle, ultimately leading to a reduction in arterial blood pressure. Recent studies suggest that telmisartan may also have PPAR-gamma agonistic properties that could potentially confer beneficial metabolic effects.

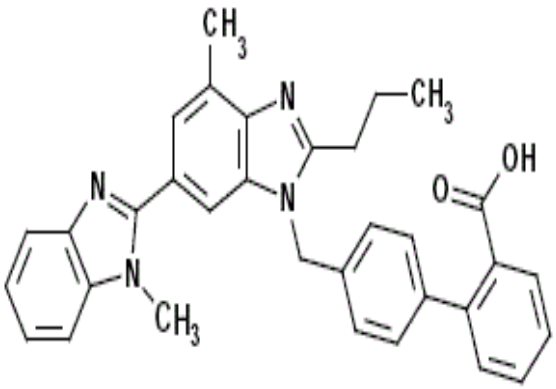

Fig. 1: Structure of Telmisartan.

Azelnidipine (AZEL) is chemically (±)-3-(1-diphenylmethylazetidin-3-yl) 5-isopropy12-amino-1, 4-dihydro-6-methyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylate (Fig 2). It is a dihydropyridine (DHP) type of calcium channel blocker (CCB) used for the treatment of hypertension. AZEL has two enantiomers due to an asymmetric carbon at the 4-position of the DHP ring. The pharmacological action of AZEL resides in the (R)-enantiomer. This is in marked contrast to other CCBs in which the (S)-enantiomer is responsible for the biological activity. The peculiar three-dimensional structure of the active enantiomer of

AZEL may be related to its unique pharmacological features that are not shared by other DHPs such as long lasting reduction in blood pressure, decreased heart rate and antiatherosclerotic effect. AZEL also shows diuretic effect by increasing urine volume and thus reduction in retention of ions.

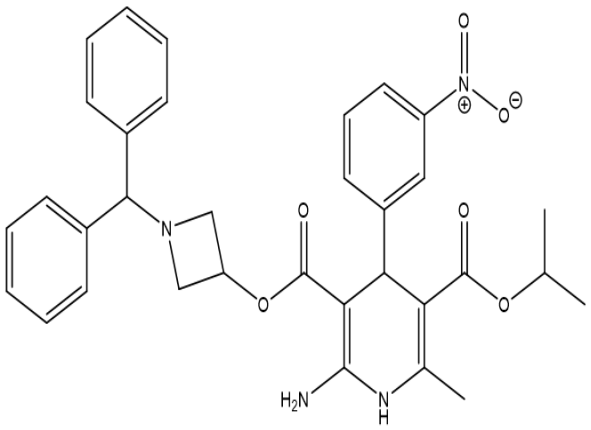

Fig. 2: Structure of Azelnidipine.

Literature survey revealed that there are some methods reported for the simultaneous estimation of these drugs, some methods for estimation of individual drugs.[3-7] or with other drugs,[8-13] UV-Spectrophotometry,[14-15] RP-HPLC.[16-20] There is no first order derivative spectrophotometric method available in the literature for Simultaneous estimation Telmisartan and Azelnidipine. So we have decided to develop and validate a new simple, rapid, accurate, specific and highly sensitive and economical first order derivative and simultaneous determination for the estimation of Telmisartan and Azelnidipine. The developed method was validated as per ICH norms.[21]

MATERIALS AND METHODS

Instrumentation

The instrument used in the present study was UV-Visible spectrophotometer (Lab India-UV 3000^{+}) with spectral band width of 1 nm. All weighing was done on electronic balance (Model Shimadzu AUX -220).

Reagents and chemicals

TEL and AZEL reference standards were kindly provided by Pure Chem Pvt.Ltd, Ankleshwar, Gujarat. Pharmaceutical dosage form Telma-AZ tablets (Glenmark Pharmaceuticals Ltd) containing telmisartan 40mg, azelnidipine 8mg was obtained from the local market. Methanol was used as a solvent.

Determination of absorptivity values

Standard stock solutions of TEL (4000 µg/ml), AZEL (800 µg/ml) were prepared in methanol. For the selection of analytical wavelength solutions of TEL (160µg/ml), AZEL (32µg/ml) were prepared separately by appropriate dilution of standard stock solution with methanol and scanned in the spectrum mode from 200 to 400 nm. From the overlain spectra of these drugs (Fig 3), wavelengths 324 nm (λmax of TEL), 220 nm (λmax of AZEL) were selected for analysis.

The calibration curves (Fig 4, 5) for TEL and AZEL were prepared in the concentration range of 16-80 µg/ml, 3.2-16 µg/ml respectively at the selected wavelengths.

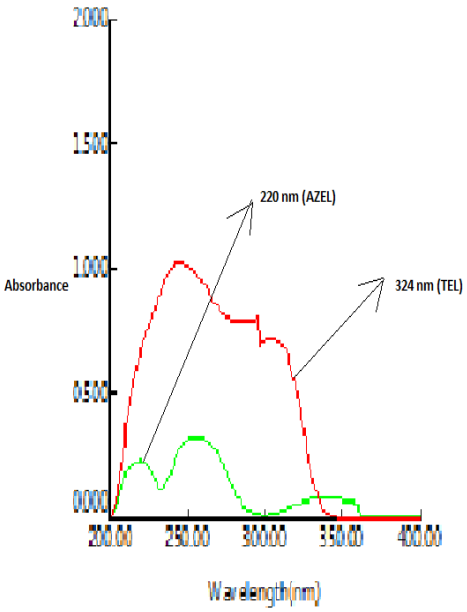

Fig. 3: Overlay spectrum of AZEL and TEL.

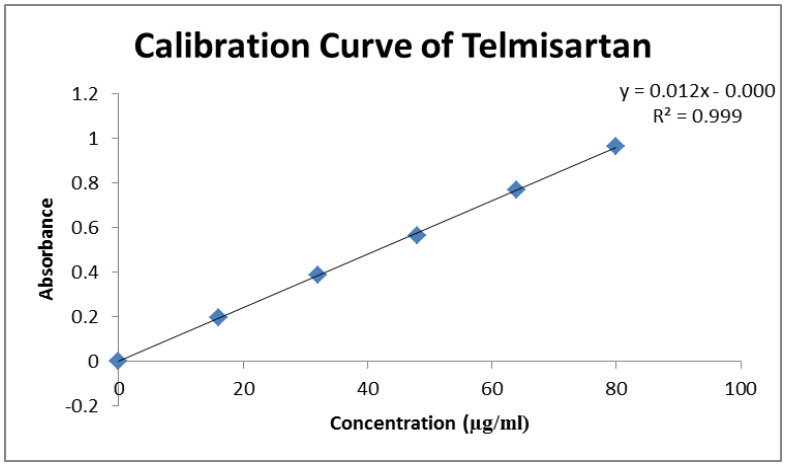

Fig. 4: Calibration curve of TEL.

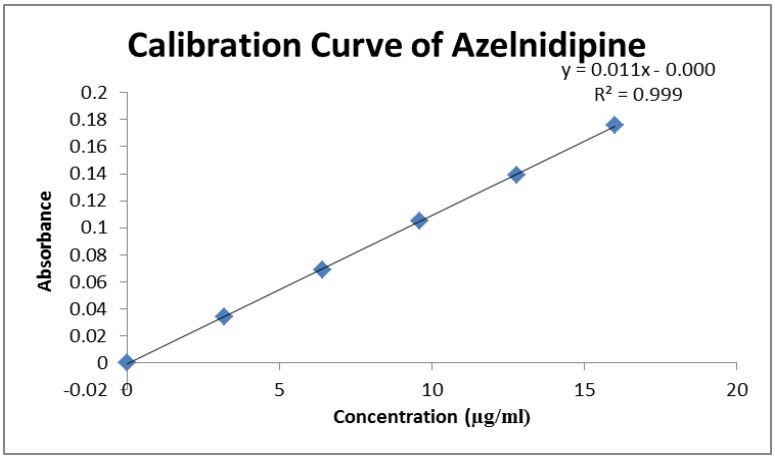

Fig. 5: Calibration curve for AZEL.

Linearity

The work in standard solutions were obtained by dilution of the stock solution in methanol. Series of solutions with concentration of 16- 80 µg/ml and 3.2– 16 µg/ml of TEL and AZEL respectively were used to determine linearity by two methods.

Formulation analysis

For estimating TEL and AZEL in tablet formulation, Twenty tablets were weighed and average weight was calculated. The tablets were crushed to obtain fine powder. Tablet powder equivalent to 40 mg of TEL and 8 mg of AZEL was transferred to 10 ml volumetric flask. 7ml of methanol was added and sonicated for 15 min and volume was made up to the mark with methanol. The solution was then filtered though Whatmann filter paper No. 41. Appropriate aliquots were taken for further analysis.

Method A: simultaneous equation method

Sample stock was appropriately diluted with methanol to obtain final concentration of 80 µg/ml for TEL and 16 µg/ml for AZEL. Absorbance of diluted sample solution was measured at selected wavelengths 324 nm for TEL and 220 nm for AZEL.

Method B: first order derivative spectroscopy

Standard solutions of both drugs (32 µg/ml and 6.4 µg/ml) were scanned separately in the range of 200- 400 nm. These spectrums were converted to first order derivative spectra by using derivative mode. For this method, 220 nm and 244 nm were selected as wavelengths of measurements for TEL and AZEL respectively. There was proportionate increase in amplitude at 220 nm and 244 nm for TEL and AZEL respectively.

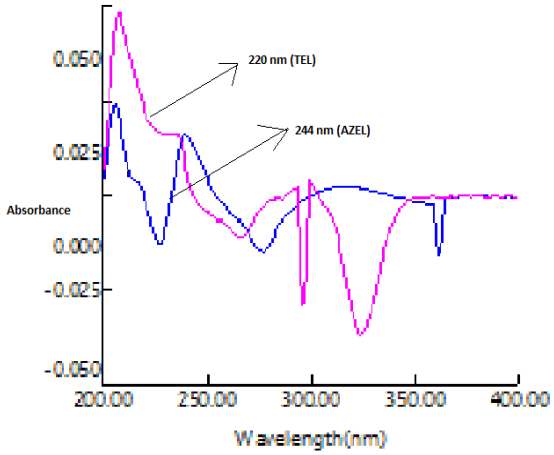

Fig. 6: Overlay First order derivative spectra of TEL and AZEL

RESULTS AND DISCUSSION

The proposed methods for simultaneous estimation of TEL and AZEL in combined dosage form were found to be accurate, simple and rapid which can be well understood from validation data as given in Table 3. Linearity was observed by linear regression equation method for TEL and AZEL in different concentration range. The Correlation coefficient of these drugs for TEL was 0.99948 and AZEL was 0.99987, indicating good linearity. The assay results obtained by proposed methods as shown in Table 2 are in fair agreement, hence it can be used for routine analysis of two drugs in combined dosage forms. There was no interference from tablet excipients was observed in these methods. It can be easily and conveniently adopted for routine quality control analysis. These methods are accurate, simple, rapid, precise, reliable, sensitive, reproducible and economic and are validated as per ICH guidelines.

Table 1: It shows calibration data for TEL and AZEL for both the methods.

PARAMETER	TELMISARTAN	AZELNIDIPINE
λ_{max} (nm)		
Simultaneous method	324	220
First order derivative	220	244
Linearity (µg/ml)		
Simultaneous method	16-80	3.2-16
First order derivative	16-80	3.2-16
Correlation coefficient (r^2)		
Simultaneous method	0.99948	0.99987
LOD (µg/ml)	2.00624	0.19831
LOQ (µg/ml)	6.01872	0.59493

Table 2: It shows assay results for the determination of TEL and AZEL in its tablets by the proposed methods.

Drug	Label claim (mcg/ml)	Amount found (mcg/ml)	% Label claim	S.D (±)	Amount found(mcg/ml)	% Label claim	S.D (±)
		Method A			Method B		
TEL	40	39.15	99.68	0.42	39.25	100.24	0.35
AZEL	8	7.85	99.88	0.38	7.83	100.75	0.32

Table 3: It shows result of recovery studies by the proposed methods.

Level of % Recovery	Mean (% Recovery)		±SD		%RSD	
	TEL	AZEL	TEL	AZEL	TEL	AZEL
50%	99.42	99.97	1.5811	1.2536	1.5930	1.2529
100%	99.86	100.15	1.8659	1.1577	1.8681	1.1545
150%	100.15	100.40	0.7246	1.0073	0.7046	1.0066

CONCLUSION

Simple UV spectrophotometric methods were developed for the simultaneous determination of Telmisartan and Azelnidipine in bulk and tablet formulation without any interference from the excipients. To the best of our knowledge, the present study is the first report for the purpose. The present methods succeeded in adopting a simple sample preparation that achieved satisfactory extraction recovery and facilitated its application in coformulated formulation.

The results of our study indicate that the proposed UV spectroscopic methods are simple, rapid, precise and accurate. Statistical analysis proves that, these methods are repeatable and selective for the analysis of TEL and AZEL. It can therefore be concluded that use of these methods can save much time and money and they can be with accuracy.

ACKNOWLEDGEMENTS

The authors would like to thank pure chem pvt.ltd for providing the sample of telmisartan and azelnidipine. We are grateful to Adhiparasakthi College of Pharmacy, Melmaruvathur, Tamilnadu for providing all neccesary facilities and support to carry out this work.

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