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Der Pharmacia Lettre, 2012, 4 (4):1080-1084
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Scholars Research Library
ISSN 0975-5071
USA CODEN: DPLEB4

Simultaneous Determination of Azelnidipine and Olmesartan medoxomil by First Derivative Spectrophotometric Method

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ABSTRACT

This paper describes validated First Derivative Spectrophotometric method for the simultaneous estimation of Azelnidipine and Olmesartan medoxomil in synthetic mixture. Quantitative determination of the drugs was performed at 239.4 nm and at 217 nm (N = 1; Δλ = 1) for Azelnidipine and Olmesartan medoxomil, respectively. Proposed method was evaluated for the different validation parameters. The specificity test showed that there was no interference from excipients commonly found in the commercial pharmaceutical formulations at the analytical wavelengths of Azelnidipine and Olmesartan medoxomil. Quantification was achieved over the concentration range of 4 – 32 μg/ ml for Azelnidipine and Olmesartan medoxomil disoproxil fumerate. The mean recovery was 100.48 ± 1.011 and 100.70 ± 1.090 % for Azelnidipine and Olmesartan medoxomil, respectively. This method is simple, precise, sensitive and applicable for the simultaneous determination of Azelnidipine and Olmesartan medoxomil.

Keywords: Azelnidipine and Olmesartan medoxomil, First Derivative Specrophotometry, Method Validation.

INTRODUCTION

Azelnidipine (AZL), (±)-(3)-(1-diphenylmethylazetidin-3-yl)-5- isopropyl-2-amino-1, 4-dihydro-6-methyl-4-(3-nitrophenyl) - 3, 5-pyridinedicarboxylate, is a new dihydropyridine derivative with calcium antagonistic activity [1]. The recommended dosing of AZL is 16 mg per day. A literature survey revealed that AZL is not yet official in any pharmacopoeia. Very few analytical methods have been reported for the determination of AZL includes HPLC [2, 3], LC-MS method [4, 5], LC-ESI -MS [6, 7], HPLC-MS-MS [8].

Olmesartan medoxomil (OLM) 2, 3-dihydroxy-2-butenyl4-(1-hydroxy-1-methylethyl)-2-propyl-1-[p-(o-1Htetrazol-5-ylphenyl)benzyl]imidazole-5-carboxylate,cyclic-2,3-carbonate.Hydrochloro thiazide (HCT) is one of the oldest and widely used thiazide diuretics [9]. A literature survey revealed that OLM is not yet official in any pharmacopoeia. Several analytical methods have been reported for the determination of olmesartan medoxomil in biological fluids includes LC-MS-MS [10], degradation product HPLC [11], HPTLC [12] and Capillary zone electrophoresis [13].

Several clinical trials prove that OLM and AZL gives better therapeutic effect in essential hypertension than in single dosage form [14]. There was not any single method reported for simultaneous determination of the two drugs

by first derivative spectrophotometric method. The aim of the present work was to develop a simple, sensitive, accurate, and precise first derivative spectrophotometric method for routine analysis. The proposed method was validated according to ICH guidelines [15].

MATERIALS AND METHODS

Apparatus

Absorbance was measured, and derivative spectra were recorded over the wavelength range of 200-400 nm in two matched quartz cells with a 1 cm path length using a Shimadzu – 1800 UV – Visible Spectrophotometer.(Shimadzu, Japan).

Reagents and Materials

All the chemicals and reagents used were of AR grade and purchased from ACS Chemicals, India.

Preparation of AZL and OLM Standard Stock Solutions

Standard stock solution of AZL and OLM (10 mg of each) were prepared separately in 100 ml in methanol to get the final concentration of 100 µg/ ml. From the standard stock solution of drugs, different dilutions were prepared to construct the calibration graph.

Selection of wavelength for estimation of AZL and OLM

A standard stock solution of AZL and OLM was diluted appropriately with methanol to obtain solutions containing 4 – 32 µg/ ml for AZL and OLM. Spectra of these diluted solutions were scanned in the spectrum mode between 200 - 400 nm, with the band width of 2 nm against methanol as blank. These zero order spectra of AZL and OLM were treated to obtain corresponding first order and first order derivative spectra with an interpoint distance of 1 nm in the range of 200 – 400 nm. The derivative spectra were recorded by using digital differentiation (convolution method) with a derivative wavelength difference of 1nm in the range of 200 – 400 nm. No smoothing of the spectra was found to be necessary. Using memory channels, the first derivative spectra were overlapped. The wavelength 239.4 nm was selected for the quantification of AZL (where the derivative response for OLM was zero). Similarly, 217 nm was selected for the quantification of OLM (where the derivative response for AZL was zero). A characteristic wavelength (ZCPs) for AZL and OLM were confirmed by varying the concentration of the one component and while the concentration of the other component was constant, and vice versa.

Preparation and analysis of Sample solutions

Twenty tablets were weighed and powdered. Quantity of powder equivalent to 16 mg of AZL and 20 mg of OLM was transferred in a 100 ml measuring flask and dissolved in methanol with sonication for 20 minutes. The solution was filtered through whatman filter paper no. 41 and the residues were washed thoroughly with methanol. The filtrate and washings were combined in a 100 ml volumetric flask and diluted to the mark with methanol to obtain final solutions of 20 µg/ml of OLM and 16 µg/ml of AZL. The absorbance was recorded at 239.4 nm and 217 nm. Concentrations of both drugs were calculated from corresponding calibration curves.

Validation

The method was validated for linearity, accuracy, precision, repeatability, selectivity, and specificity in accordance with ICH guidelines. Accuracy was studied by measurement of recovery at three different levels of the amount expected in the formulation. Precision was measured both intra-day and inter-day. In the intra-day study the concentrations of all three drugs were calculated three times on the same day at intervals of an hour. In the inter-day study the concentrations of all three drugs were measured on three different days. Specificity of the method was confirmed by loading the excipients used in tablet formulation with preweighed standard drugs and the absorbance was measured. The limits of detection and quantitation of the method were studied to detect the lowest amount of analyte and quantitative determination of analyte in a sample, respectively.

RESULTS AND DISCUSSION

The zero order spectra of standard solutions of AZL and OLM were found to be similar in nature when overlaying. It was observed that AZL and OLM contribute significantly at their corresponding λmax values of absorption. Therefore, it was thought that a derivative graphical method could be used to estimate AZL and OLM in the presence of each other. The derivative spectra of different orders were obtained from the zero order spectra using

digital differentiation. The principle advantages of derivative spectroscopy are the improvement of resolution of overlapping absorption bands and the accuracy and precision compared to UV absorption methods; therefore, derivative spectroscopy has been used in quantitative analysis when the analyte to be determined present in admixture with other components. Fig. 1 & 2 shows that the over layered first derivative spectra could be used for determination of AZL and OLM. The spectra present well defined bands for determination of the analytes, and the sensitivities are greater. Thus first derivative was selected and the other derivatives were discarded because they showed insufficient resolution and do not present analytical advantages. The type of solvent, degree of deviation, range of wavelength, and N value were chosen in order to optimize the conditions. The solvent selected was methanol because it allowed sufficient spectral resolution to be obtained for the application of the peak zero method. The derivative wavelength difference depends on the measuring wavelength range and N values. Generally, the noise decreases by increasing Δλ. The optimal wavelength range should be chosen because broad peaks become sharper, the ratio of signal-to-noise(S/N) increases, and the sensitivity of the method increases by the degree of low pass filtering or smoothing. Therefore, a series of N value (N = 1 – 9) was tested in the first order UV spectrum of AZL and OLM in methanol. Optimum results were obtained in the measuring wavelength range 200 – 400 nm, N = 1(Δλ = 1) for first derivative method. The first derivative spectra of AZL and OLM were found to be appropriate for the determination of AZL and OLM by having separated zero crossing points in methanol. The first derivative spectrum of AZL has zero absorption at 217 nm, where OLM gives significant derivative response, while spectrum of OLM has zero absorption at 239.4 nm, where AZL gives the significant derivative response. Therefore, 239.4 nm was selected for estimation of AZL and 217 nm was selected for the estimation of OLM.

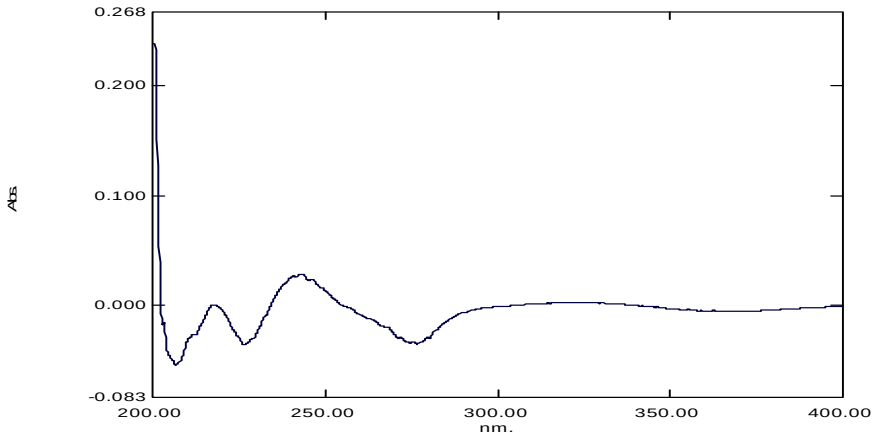

Figure I: First derivative spectra of Azelnidipine (Zero crossing point 217 nm)

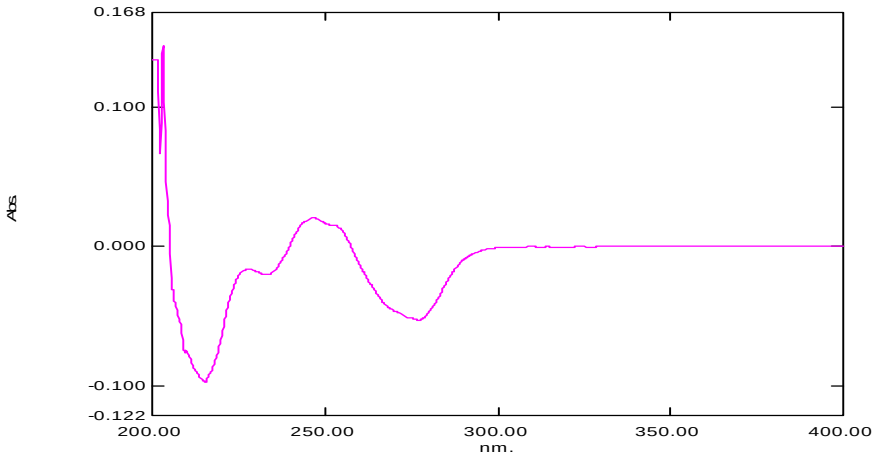

Figure II: First derivative spectra of Olmesartan (Zero crossing point 239.4 nm)

Validation of Proposed Method

Linearity

Linear correlation was obtained between absorbance and concentration of AZL and OLM in the range of 4 – 32 µg/ ml for AZL and OLM. Data of regression analysis are summarized in Table1.

Accuracy

The recovery experiments were carried out by the standard addition method. The recoveries obtained were 100.48 ± 1.011 and 100.70 ± 1.090 % for AZL and OLM, respectively. The high percentage recovery and low % RSD values indicate that methods are accurate.

Method Precision

The RSD values for AZL and OLM were found to be 1.00 and 0.852 %, respectively. The RSD values were found to be below 2% which indicate that the proposed method is repeatable.

Intermediate Precision

The RSD values were found to be below 2% which indicate that the proposed methods are reproducible (Table 2).The proposed validated method was successfully applied to determine AZL and OLM in their tablet dosage forms. The results obtained for AZL and OLM were comparable with the corresponding labeled amounts (Table 3).

Table 1: Regression analysis of calibration curves for AZL and OLM for the proposed First Derivative Spectrophotometric method

Sr.No.	Parameters	AZL	OLM
1	Concentration Range (µg/ ml)	4-32	4-32
2	Slope	0.001	0.002
3	Intercept	0.001	0.001
4	Correlation Coefficient	0.995	0.996

Table 2: Summary of validation parameters for the proposed method

Sr.No.	Parameters	AZL	OLM
1	LOD[a] (µg/ ml)	0.286	0.238
2	LOQ[a] (µg/ ml)	0.867	0.721
3	Accuracy (%)	100.48 ± 1.011%	100.70 ± 1.090 %
4	Repeatability (%RSD[c] n[d] = 6)	0.23	0.35
5	Interday Precision (n = 3)	1.56-1.900	0.69-1.546
6	Intraday Precision (n = 3)	0.957-1.04	0.69-1.015

a LOD = Limit of detection. b LOQ = Limit of quantification. c RSD = Relative standard deviation. d n = Number of determination

Table 3: Assay results for the combined dosage form using the proposed method

Drug	Amount taken(mg)	Amount Found (mg)	Assay	% RSD
Azelnidipine	16	15.983	99.895±1.552	1.553
Olmesartan	20	19.98	99.916±1.772	1.773

CONCLUSION

Proposed method was found to be precise and accurate. The methods can be used for the routine simultaneous analysis of AZL and OLM in synthetic mixture. Moreover, the proposed method has the advantages of simplicity, convenience and quantification of AZL and OLM in combination and can be used for the assay of their dosage form.

Acknowledgments

The authors wish to thank department of pharmaceutical sciences, Hemchandracharya North Gujarat University for their kind help and providing all necessary facilities.

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