Simultaneous spectrophotometric estimation of amlodipine and valsartan in capsule formulation

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ABSTRACT

This work deals with the simultaneous determination of amlodipine besylate (AMLB) and valsartan (VAT) in a binary mixture form by two different methods. The first method of analysis is Derivative spectroscopy to eliminate spectral interference by measuring absorbance at two wavelengths 250nm and 237.5nm for AMLB and VAT respectively. The second method involves the application of Absorbance corrected for interference method at the wavelengths 250nm and 360nm. The linearity range was 10-50mcg/ml and 10-80mcg/ml for AMLB and VAT respectively. The proposed methods were successfully applied for the simultaneous determination of both drugs in commercial capsule preparation. The methods were validated statistically and recovery studies were performed to confirm the accuracy of method.

Key words: Amlodipine, Valsartan, Pharmaceuticals.

INTRODUCTION

Amlodipine besylate (AMLB), 2-[(2-amino ethoxy)-methyl]-4-(2-cholophenyl)-1, 4-dihydro-6-methyl-3, 5-pyridine dicarboxylic acid 3-ethyl-5-methyl ester, benzosulfonate, is a potent dihydro calcium channel blocker[1].Valsartan (VAT), N-(1-Oxopentyl)-N-[[2'-(1H-tetrazol-5-yl) [1, 1'-biphenyl]-4-yl] methyl]-L-valine, is a potent angiotensin receptor blocker[1]. Literature survey reveals various methods such as HPLC[2], RP-HPLC[3], HPTLC[4], LC-MS/MS[5], LC-MS[6] and simultaneous UV-spectrophotometric methods[7, 8]are reported for the estimation of AMLB alone or in combination with other anti-hypertensive agents. Methods such as HPLC[9], Capillary electrophoresis[10], and simultaneous UV- spectrophotometric methods[11, 12] are reported for estimation of VAT alone or in combination with other drugs, but no method till date has been reported for simultaneous determination of both AMLB and VAT in combined dosage form. The analysis of AMLB is of prime importance since AMLB is present in very small quantity relative to VAT. Therefore, the aim of this paper was to explore the possibility of using techniques of first order derivative and absorbance corrected for interference methods for quantifying AMLB and VAT simultaneously in their mixture form.

EXPERIMENTAL

Material and Methods
Instrument

A dual beam Shimadzu UV-visible spectrophotometer 1700 was used as instrument. Reagents and chemicals: Methanol of analytical grade was used as solvent. AMLB and VAT were obtained as gift samples from Glenmark Pharmaceuticals Limited, Nashik and Lupin Laboratories Ltd, Pune respectively. The commercial formulation of AMLB and VAT is available in ratio of 1:32{Valzaar- sm (2.5/80mg)} as capsules.

Procedure

Spectral characteristics of AMLB and VAT*:* Standard stock solutions of AMLB and VAT of

100μg/ml each were prepared in methanol. Aliquot portions equivalent to 20mcg/ml of VAT and AMLB were accurately transferred into two 10ml volumetric flasks and the volume was completed with methanol. The absorption spectra were recorded (fig. 1), lmax for AMLB was found to be 237.5 and 360nm. VAT was found to have 250nm as the λmax. The zero order spectra was derivatized to first order and zero crossing for AMLB and VAT was observed at 237.5nm and 250nm respectively (fig. 2). The calibration data for both drugs is summarized in table 1.

Application of the proposed methods for the determination of AMLB and VAT in capsules: A

total of 20 capsules were uncapped and the contents of the capsules were accurately weighed. An amount equivalent to one capsule (containing 2.5mg of AMLB and 80mg of VAT) was weighed and dissolved in about 50ml of methanol, stirred for 30min, and final volume was made up to 100ml with methanol. The solution was filtered through Whatman filter paper no.41, and first few drops were rejected.

15.5ml of standard stock solution of AMLB (100μg/ml) was added to 1ml of the filtered solution in a 50ml volumetric flask, to make the solution of equal concentration for both the drugs, final volume was made upto the mark with methanol. The

Table 1: Calibration data for AMLB and VAT

Calibration	First order derivative method		Absorbance corrected for interference method			
Data	AMLB	VAT	AMLB		VAT	
Wavelength selected	250nm	237.5nm	360nm	250nm	360nm	250nm
Slope	-0.0013	-0.0011	0.0132	0.0218	0	0.0303
Intercept	-0.0004	0.0003	0.0039	-0.0016	0	0.0142
Linearity range(mcg/ml)	10-50	10-80	10-50	10-50	0	10-80
Correlation Coefficient	0.9992	0.9982	0.9996	0.9986	0	0.9995

Table 2: Precision of spectrophotometric methods developed for analysis of Capsules (n=6)

Calibration	First order derivative method		Absorbance corrected for interference method	
Data	AMLB	VAT	AMLB	VAT
Repeatability				
% Mean±S.D	100.21±0.896	99.64±0.838	100.48±0.652	99.85±0.827
%RSD	0.899	0.841	0.6481	0.828
Intraday				
% Mean±S.D	100.02±0.898	99.91±0.858	99.66±0.471	100.43±0.411
% RSD	0.8980	0.8580	0.472	0.4100
Interday				
% Mean±S.D	100.03±1.023	99.11±0.644	99.5±0.361	100.63±0.842
% RSD	1.019	0.649	0.363	0.836

S.D: Standard deviation, RSD: Relative standard deviation, S.E: Standard error.

concentration of both AMLB and VAT were determined.

Derivative method

First order derivative spectra revealed that AMLB and VAT showed zero absorbances at 237.5 and 250nm respectively. As at the zero crossing point of one drug, the other drug showed substantial absorbance, hence these two wavelengths could be effectively employed for estimation of both drugs. Absorbance corrected for interference[13]: If the

identity, concentration and absorpitivity of the one of the absorbing component are known, the concentration of other absorbing component is then calculated from the corrected absorbance (total absorbance minus the absorbance of the one of the component). The absorbances were taken at 250nm and 360nm for both the drugs. The absorbitivity (A1%, 1cm) values for VAT was 37.41 at 250nm and 0 at 360nm and for AMLB was 18.84 at 250nm and 11.36 at 360nm.

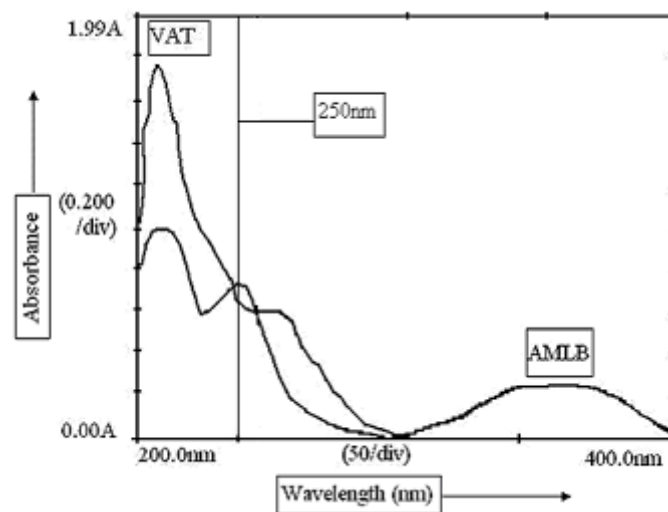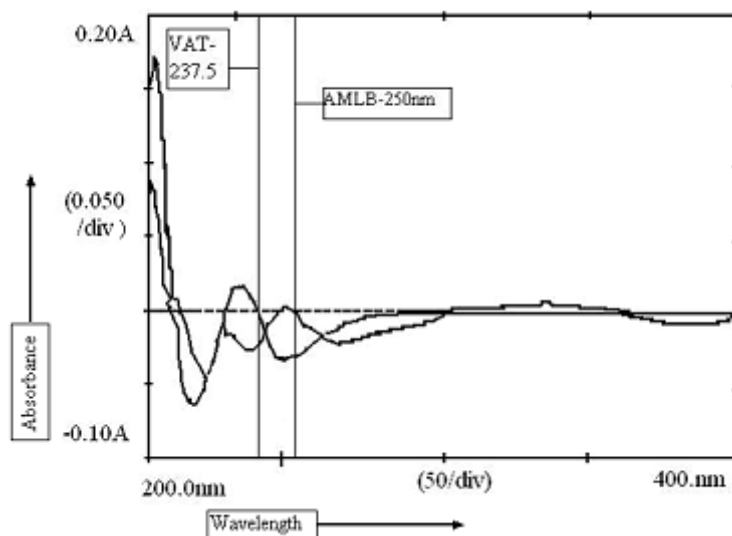**Fig.1: Absorption spectra of AMLB and VAT**

Fig. 2: First order derivative spectra of AMLB and VAT

RESULTS AND DISCUSSION

AMLB and VAL obeyed Beer's law in the concentration range of 10-50mcg/ml and 10-80mcg/ml respectively. For First order derivative method wavelengths selected were 250nm and 237.5nm and the percentage composition in capsule formulation was found to be 100.10% (SD ±1.043) and 99.33% (SD ±0.8798) for AMLB and VAT respectively. For Absorbance corrected for interference the wavelength selected were 250nm and 360nm and the percentage composition in capsule formulation was found to be 100.17% (SD±1.213) and 99.3% (SD±0.9658) for AMLB and VAT respectively.

Validation of methods[14]

Methods were validated as per ICH guidelines. The data evaluated are summarized in Table 2. Accuracy of the method was found out by recovery study from pre analyzed synthetic mixture at three levels of standard addition, from 80% to 120% and the percentage recovery of the three concentrations was found to be close to 100%.

CONCLUSION

The proposed methods i.e., the First order derivative method and Absorbance corrected for interference can be used for the simultaneous determination of AMLB and VAT either in the binary mixture form or in their capsule preparation. The proposed methods are precise, accurate, and simple to perform. They are rapid and do not require any expensive or sophisticated instruments. Hence, proposed methods can be used for the routine analysis of AMLB and VAT.

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