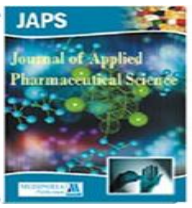
Journal of Applied Pharmaceutical Science 01 (06); 2011: 162-164

Journal of Applied Pharmaceutical Science

Available online at www.japsonline.com



ISSN: 2231-3354
Received: 25-07-2011
Revised on: 27-07-2011
Accepted: 03-08-2011

New Spectrophotometric Methods for Simultaneous Determination of Amlodipine besylate and Lisinopril in Tablet Dosage Forms

Joshi H.V. and Patel J.K.

Joshi H.V.
Research Scholar
Jodhpur National University,
Jodhpur, India.

Patel J.K.
Nootan Pharmacy College,
Visnagar, Gujarat, India

For Correspondence:
Joshi H.V.
Research Scholar
Jodhpur National University,
Jodhpur, India.
Email: hirakjoshi@gmail.com

ABSTRACT

Two simple, accurate, precise, reproducible, requiring no prior separation and economical procedures for simultaneous estimation of Amlodipine besylate (AML) and Lisinopril (LIS) in tablet dosage form have been developed. First method is simultaneous equation method; in this method 360.0 nm and 248.0 nm were selected to measure the absorbance of drugs at both wavelengths. The second method is Q-value analysis based on measurement of absorptivity at 300.0 nm (as an iso-absorptive point) and 360.0 nm. AMD and LIS at maximum wavelength of AML, 360.0 nm and at isoabsorptive point 300.0 nm shows linearity in a concentration range of 5-40 µg/mL. Recovery studies range from >99.82% for AMD and >98.09% for LIS in case of simultaneous equation method and >100% for AMD and >98.45% for LIS in case of Q-analysis method confirming the accuracy of the proposed method. The proposed methods are recommended for routine analysis since it is rapid, simple, accurate and also sensitive and specific (no heating and no organic solvent extraction is required).

Key words: Lisinopril (LIS), Amlodipine besylate (AML), Methanol, UV Spectrophotometer

INTRODUCTION

Amlodipine besylate (David et al, 2006), chemically (R, S) 2-[(2-Aminoethoxy) methyl]-4 -(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylic acid 3-ethyl 3-methyl ester benzene sulphonate, is a Ca-antagonist which blocks the calcium entry by preventing opening of voltage gated L – type and T – type Ca –channels. It mainly affects heart and smooth muscles inhibiting calcium entry caused by depolarization in these tissues. They also dilate coronary vessels, which is important in variant angina. (Budhawari et el, 2006). Lisinopril (Wolters et al, 2007) chemically N2-[(1S)-1-carboxy-3-phenylpropyl]-L-lysyl-L-proline is a drug of the angiotensin-converting enzyme (ACE) inhibitor class that is primarily used in treatment of hypertension, congestive heart failure, and heart attacks, and also in preventing renal and retinal complications of diabetes. Commercially fixed combination of AML (5 mg) and LIS (5 mg) is available in the market as tablet.

Both the drugs are not official in BP and USP and Literature survey reveals several methods such as HPLC (Shah et al,2008) (Chitlange et al, 2008) U.V. spectrosctropy (Wakhede, 2008) Colorimetric (Garg et al, 2008) have been reported for individual drugs as well as in combination with other drugs in formulation. However there is no UV- spectrophotometric method reported so far for the simultaneous estimation of these two drugs from the pharmaceutical formulations. A successful attempt has been made to estimate them simultaneously by spectrophotometric analysis.

MATERIALS & METHODS

A Shimadzu UV/Visible spectrophotometer (Model: UV1700) was employed with spectral bandwidth of 2nm and wavelength accuracy of ± 0.5 nm with automatic wavelength correction with a pair of 10mm quartz cells.

Materials and Reagents

Amlodipine besylate (Glenmark Pharmaceuticals Ltd.) Lisinopril (Sun Pharmaceuticals) and Methanol – AR grade (Qualigens Fine Chemicals, Mumbai) were used in the study.

Method I

Absorption ratio method (Beckett et al 2002) uses ratio of absorbances at two selected wavelengths, one of which is an 'Isoabsorptive point' and other being the λ_{max} of one of the two components. From the overlain spectra (fig 1) of the two drugs it is evident that AML and LIS shows iso absorptive point at 300.0 nm and the λ_{max} of AML is at 360.5 nm. Hence the two wavelengths selected are 300.0 and 360.5nm.

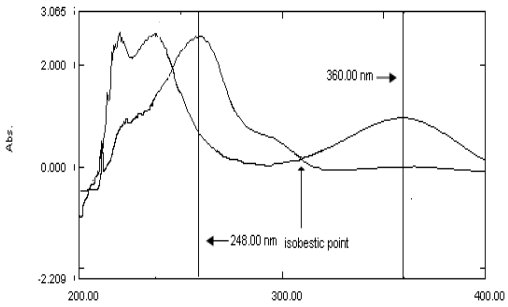


Fig 1: Overlay spectra of LIS and AML.

Six standard solutions of each drug having concentrations 5, 10, 20,30, 40, 50µg/ml were prepared separately in methanol and absorbances at 300.0 nm and 360.5 nm were measured and absorptivity coefficients were calculated using calibration curve. Mixed standards containing 10µg/ml for AML and 10µg/ml (n=6) for LIS were prepared and absorbances at 300.00 nm and 360.5 nm were measured. From the absorbance values the concentration of drug in the pure mixed standard was determined using following formula,

For AML,

$$C_1 = Q_0 - Q_2 / Q_1 - Q_2 \times A/a_1$$

For LIS,

$$C_2 = Q_0 - Q_1 / Q_2 - Q_1 \times A/a_2$$

Where,

Q_0 = Absorbance of mixed standard at 300.0 nm/absorbance of mixed standard at360.5nm

Q_1= Absorbance of AML 300.5nm / Absorbance of AML 360.5

Q_2= Absorbance of LIS 300.0 nm / Absorbance of LIS at 360.5nm

A = Absorbance of mixed standard at isoabsorptive point

a_2 and a_2 = Absorptivities of AML and LIS respectively.

Analysis of tablet formulation

Twenty tablets were weighed and ground to a fine power. An accurately weighed powder sample equivalent to 5 mg of AML and 5 mg of LIS was transferred to a 100 ml volumetric flask, dissolved in methanol and volume was made up to the mark with methanol. The solution was kept for the sonication for 20 minutes, filtered through Whatmann filter paper No. 41. Aliquot of this solution was diluted to produce the concentration of 10µg/ml for AML and 10µg/ml for LIS (n=6). The absorbances of sample solutions at 300.00 nm and 360.5 nm were measured and amount of drug present in the sample solution was calculated in the same manner as that of pure mixed standard solution.

The results of analysis and statistical validation for the marketed tablet formulation are reported in Table-1 and Table-2 respectively. The results of recovery studies conducted by the addition of different amounts of pure drugs at 80%, 100% and 120% levels to a tablet solution were found to be satisfactory and are given in the Table-3.

Table 1: Analysis of tablet formulation.

Method	Label claim (mg/tab)		Amount Found* (mg/tab)		Label claim (%)	
	AML	LIS	AML	LIS	AML	LIS
I	5	5	4.98	5.01	99.66	101.12
II	5	5	4.99	4.97	99.97	100.33

Table 2: Statistical validation of tablet formulation.

Method	Standard Deviation		% coefficient of variation		Standard error	
	AML	LIS	AML	LIS	AML	LIS
I	0.5483	0.9693	0.55	0.96	0.2239	0.3957
II	0.3882	0.5715	0.39	0.57	0.1585	0.2333

Table 3: Statistical validation of recovery studies.

Method	Type of Recovery in %	Mean ±S D*		Coefficient of variation*		Standard Error*	
		AML	LIS	AML	LIS	AML	LIS
I	80	99.50±0.4330	100.38±0.8314	0.44	0.83	0.2500	0.4800
	100	99.97±0.3753	101.46±0.7744	0.38	0.76	0.2167	0.4471
	120	100.10±0.2179	100.61±1.166	0.22	1.16	0.1258	0.6730
II	80	100.00±0.5292	100.06±0.2309	0.53	0.23	0.3055	0.1333
	100	100.26±0.3055	99.96±0.2082	0.30	0.20	0.1764	0.1202
	120	99.87±0.3055	100.10±0.1000	0.30	0.09	0.1764	0.0577

Method II

Two wavelengths selected for the method are 360.0 nm and 248.0 nm that are absorption maxima of AMD and LIS respectively in methanol. The stock solutions of both the drugs were further diluted separately with methanol to get a series of standard solutions of 5 -30 µg /mL concentrations. The absorbances were measured at the selected wavelengths and absorptivities (A 1%, 1 cm) for both the drugs were determined as mean of six independent determinations. Concentrations in the sample were obtained by using following equations.

Cx = (A2ay1-A1ay2)/(ax2ay1-ax1ay2)

Cy = (A1ax2-A2ax1)/(ax2ay1-ax1ay2)

Where A1 and A2 are absorbances of mixture at 360.0 nm and 248.0 nm respectively, ax_1 and ax_2 are absorptivities of AML at λ_1 and λ_2 respectively and ay_1 and ay_2 are absorptivities of LIS at at λ_1 and λ_2 respectively. Cx and Cy are concentration of AML and LIS respectively.

Analysis of tablet formulation

Tablet sample solution was made as per the method described in Method – I and solution was diluted to get a final concentration equivalent to 10µg/ml of AML and 10µg/ml of LIS (n=6) and from the overlain spectra the absorbances were measured at 360.0 nm for AML and 248.0 nm for LIS in spectrophotometric mode of an instrument . Amount of drug present in the sample solution was obtained from the simultaneous equation.

The results of analysis and statistical validation for the marketed tablet formulation are reported in Table-1 and Table-2 respectively. The results of recovery studies conducted by the addition of different amounts of pure drugs at 80%, 100% and 120% levels to a tablet solution were found to be satisfactory and are given in the Table-3.

RESULTS AND DISCUSSION

The absorption ratio method, also called as Q – analysis, employs the absorption ratio at two selected wavelengths and can be employed for the routine analysis of the two drugs in the combined dosage forms using simple instrument unlike the second method, which requires more accuracy. Second method is used to eliminate the spectral interference from one of the two drugs as the wavelength for estimation of the other drug. This method requires spectral data processing and hence can be performed only on recording spectrophotometers with such facilities.

The amount found from the proposed methods was in good agreement with the label claim of the formulation. Also the value of standard deviation and coefficient of variation calculated were satisfactorily low, indicating the suitability of the proposed methods for the routine estimation of tablet dosage forms.

ACKNOWLEDGEMENTS

Author wishes to thanks to Nootan Pharmacy College, Visnagar for providing the Instrumental and Chemicals facility. Authors are also thankful to Sun Pharmaceuticals PVT LTD, Baroda and Glenmark Pharmaceuticals LTD, Mumbai for providing the gift samples of Lisinopril and Amlodipine Besylate respectively.

REFERENCES

A Wolters Kluwer. Drugs Facts and Comparisons. 57th edition. (2003) 519, 625.

Beckett A. H and Stenlake J.B. Practical Pharmaceutical Chemistry. 4th ed. CBS Publishers and distributors, (2002) 281-300.

Budawari, S. The Merck Index.13th Ed. Merck & Co. Whitehouse Station, NJ,(2001); 488.

D.A Shah, KK Bhatt, RS Mehta. Stability indicating RP-HPLC estimation of atorvastatin calcium and amlodipine besylate in pharmaceutical formulations. in Indian Journal of Pharma Sci and Res. 2008;70: 754-760.

Devid A. Willians and Thomas L. Lemke. Foye's Principles of Medicinal Chemistry. 5th ed.(2006) 507.

Garg, G., S. Saraf and S. Saraf .Development and validation of simultaneous estimation of Enalapril maleate and Amlodipine besylate in combined dosage forms. Trends Applied Sci. Res.2008;3: 278-284.

Goodman and Gilman. The pharmacological basis of therapeutics. 10th ed. 984.

H.P.Rang, M.M. Dale, J.M. Ritter, P.K. Moore. Pharmacology. 5th ed. 282-283.

K. Raja Rajeswari, G.G. Sankar, AL Rao, J.N. Seshagirirao. RP-HPLC method for the simultaneous determination of Atorvastatin and Amlodipine in tablet dosage form. Indian Journal of Pharma Science and Research. 2006; 68: 275-277.

Remington, The science and practice of pharmacy. 19th ed. MACK Publishing Company. (1995) 593-598.

SB Wankhede, SB Wadkar, KC Raka, SS Chitlange. Simultaneous estimation of amlodipine besilate and olmesartan medoxomil in pharmaceutical dosage form. Ind. Jou of Pharm Sci and Res.2009;71: 563-567.

Sohan S Chitlange, Mohammed Imran, Dinesh M Sakarkar. RP-HPLC method for Simultaneous estimation of Amlodipine and Metoprolol in tablet formulation. Asian Journal of Pharmaceutics.2008;2: 232-234.

Willard, Merritt, Dean, Settle. Instrumental Methods of Analysis. 7th ed. CBS Publisher and distributors, 169-178.