Asian Journal of Chemistry Vol. 19, No. 5 (2007), 3721-3726

Simultaneous Spectrophotometric Estimation of Losartan Potassium and Atenolol in Bulk and Two Component Formulation

ASHA THOMAS*, MANISHA PATANKAR, K.R. DESHMUKH, LATA KOTHAPALLI, SUMITRA JANGAM, P.R. PATANKAR, S.A. KANDGAONKAR and A.D. DESHPANDE
Department of Pharmaceutical Chemistry, Padmashri Dr. D.Y.Patil Institute of Pharmaceutical Sciences and Research, Pimpri, Pune-411 018, India
E-mail: dypharmachem@yahoo.co.in

Two simple, accurate and economical spectrophotometric methods, derivative spectroscopy method and absorption correction method have been developed for the simultaneous estimation of Losartan potassium and atenolol in their combined dosage formulation. Losartan potassium shows absorbance maxima at 205 nm while atenolol shows at 225.5 nm in double distilled water. The first method employs first order derivative spectroscopy to eliminate spectral interferences. The second method is the absorption correction method using 225.5 and 250 nm as the two sampling wavelengths. The methods allow rapid analysis of binary pharmaceutical formulation with accuracy. Both the drugs exhibit linearity with absorbances in the concentration ranges employed for the methods. Results of the methods were validated statistically and by recovery studies.

Key Words: Estimation, Losartan potassium, Atenolol, UV-visible spectrophotometer.

INTRODUCTION

Losartan potassium (LST), chemically 2-butyl-4-chloro-1-[*p*-(*o*-1H-tetrazol-5-ylphenyl)benzyl]imidazole-5-methanol monopotassium salt][1] is a prototype drug of a new antihypertensive class-non-peptide angiotensin II receptor antagonist[2]. It is not official in any pharmacopoeia. Atenolol (ATL), chemically benzene acetamide, 4-[2'-hydroxy-3'-[(1-methylethyl) amino]propoxy][3] is a selective β1-blocker[2]. It is official in IP[4], BP[5] and USP[6]. Losartan potassium (LST) and atenolol (ATL) are known to have a synergistic therapeutic effect in essential hypertension.

Literature survey reveals several methods such as HPLC[7-9], UV spectrosctropy[10,11], colorimetric[12], eletrophoresis[13,14], flame photometry[15], biological fluids[16,17], gas chromatography[18] and HPTLC[19] have been reported for the estimation of individual drugs as well as in combination with other drugs.

No UV or HPLC method is however reported for the simultaneous analysis of LST and ATL in their combined dosage form. Combination of 50 mg of LST and 50 mg of ATL is now available in the market. So the need was felt to develop new methods to analyze the drugs simultaneously.

EXPERIMENTAL

Shimadzu UV-1601 (Japan) spectrophotometer was employed with a spectral bandwidth of 2 nm, wavelength accuracy of ± 0.5 nm, with automatic wavelength correction and employing a pair of quartz cells. A Shimadzu electronic analytical balance (AX-200) was used for weighing the sample. An ultrasonic cleaner (Art No.400014CL) was used for sonicating the tablet sample solution. Losartan potassium, atenolol (SUN Pharmaceuticals, Baroda) and double distilled water were used in the study.

Preparation of standard stock solution: Standard stock solutions (100 μg/mL) of LST and ATL were prepared by dissolving separately 10 mg of drug each in double distilled water. LST and ATL exhibited λ_{max} at 205 and 225.5 nm, respectively. For analysis by derivative spectroscopy, solutions of 10 μg/mL concentrations of LST and ATL were prepared separately.

Preparation of sample stock solution: 20 Tablets (LOSAR-BETA manufactured by Unichem Laboratories Ltd., Mumbai, India) were weighed and crushed to a fine powder. An accurately weighed powder sample equivalent to 10 mg of LST and ATL each was transferred to a volumetric flask and dissolved in *ca.* 25 mL of double distilled water. After immediate dissolution, the volume was made up to the mark with double distilled water. The solution was sonicated for *ca.* 20 min, filtered through Whatmann filter paper no. 41 and then suitably diluted to obtain a final concentration of 10 μg/mL of LST and ATL each.

Method A: First order derivative spectroscopy: Standard solutions (10 μg/mL) of LST and ATL each were scanned in the spectrum mode of the instrument from 400 to 190 nm. The absorption spectra thus obtained were derivatized from first to fourth order. The first order derivative spectrum was selected for the analysis of both the drugs. From the overlain derivative spectra obtained, the wavelengths were selected in a manner such that at the zero crossing wavelength of one drug the other drug should show substantial absorbance. Thus the first order-overlain spectrum of two drugs (Fig. 1) reveals that LST and ATL show zero absorbance at 205 and 225.5 nm, respectively. Mixed standards of LST and ATL were prepared and their absorbances were measured at the selected wavelengths in the first derivative mode against double distilled water as blank. The absorbances were plotted against concentration to obtain standard calibration curves. LST and ATL exhibited linearity with absorbances in the range of 1-30 and 1-15 μg/mL at their respective selected wavelengths. Coefficient

of correlations were found to be 0.9996 and 0.9995 for LST and ATL, respectively. The optical characteristics and validation data for LST and ATL are presented in Table-1.

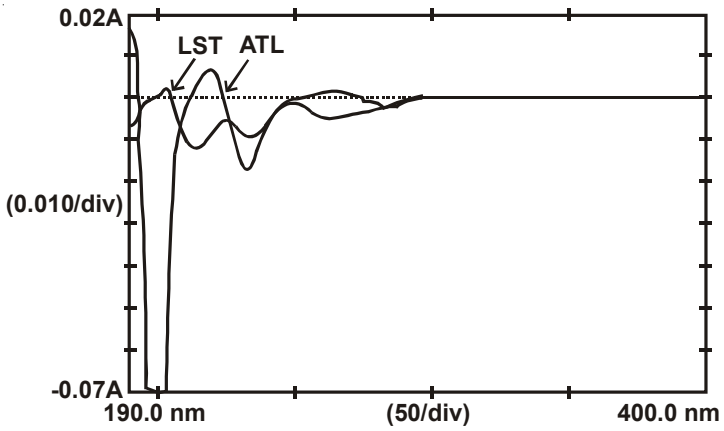

Fig. 1. First order derivative spectra of LST and ATL

TABLE-1
OPTICAL CHARACTERISTICS AND VALIDATION DATA OF LOSARTAN POTASSIUM AND ATENOLOL

Parameters	LST		ATL	
	Method A	Method B	Method A	Method B
Working λ (nm)	225.5	250	205	225.5
Beer-Lamberts Law range (μg/mL)	1-30	5-50	1-15	5-70
Molar absorptivity (L/mol cm)*	-5.714×10^3	9.394×10^4	-1.184×10^4	2.877×10^4
Precision:* Interday Precision	0.9809	0.8247	0.8035	0.8886
Intraday Precision	0.8336	0.6379	0.5045	0.6520
LOD (μg/mL)*	0.0342	0.0054	0.1819	0.0034
LOQ (μg/mL)*	0.1035	0.0163	0.5502	0.0103
Regression Values: Slope*	-0.0013	0.1061	-0.0045	0.0315
Intercept*	0.0003	0.0017	0.0006	-0.1511
Regression coefficient (r^2)*	0.9996	0.9998	0.9995	0.9999

*Average of six estimations;
Method A=First order derivative method, Method B=Absorption correction method.

Estimation from marketed preparation: The tablet sample solution was scanned in the spectrum mode in the range of 400-190 nm. The absorbances of the sample solution were recorded at 205 nm and 225.5 nm in the first order derivative spectra. By using the standard calibration curve, the unknown concentration of the drugs in the sample solutions can be

obtained. The analysis procedure was repeated six times with the same batch of tablets. The results of the tablet analysis and its statistical validation data are given in Table-2.

TABLE-2
STATISTICAL VALIDATION DATA OF FORMULATION

Component	Amount present (mg)	Method	Amount* found (%)	Standard Deviation	Coefficient of variation (%)	Standard error
LST	50	A	100.26	0.6214	0.6215	0.2537
	50	B	100.43	0.7400	0.7402	0.3021
ALT	50	A	99.91	0.8214	0.8210	0.3353
	50	B	100.12	0.4612	0.4610	0.1883

*Average of six determinations.

Method B: Absorption correction method: Suitable dilutions of both the drug solutions (10 µg/mL LST and 10 µg/mL ATL) were scanned between 400 to 190 nm using the spectrum mode of the instrument. The overlain spectrum of the two drugs (Fig. 2) indicated that LST showed λ_{max} at *ca.* 205 nm. However it exhibited significant absorption at 250 nm, at which ATL showed zero absorbance. Hence 250 nm was selected for the determination of LST without any interference of ATL. However both the drugs exhibited strong absorbance at about 225.5 nm. The Beer's law is obeyed by ATL over the concentration range of 5-70 µg/mL at 225.5 nm with a co-efficient of correlation of 0.9998. LST exhibited linearity over a concentration range of 5-50 µg/mL both at 225.5 and 250 nm. The co-efficients of correlation were found to be 0.9998 and 0.9999 for LST at 225.5 and 250 nm, respectively.

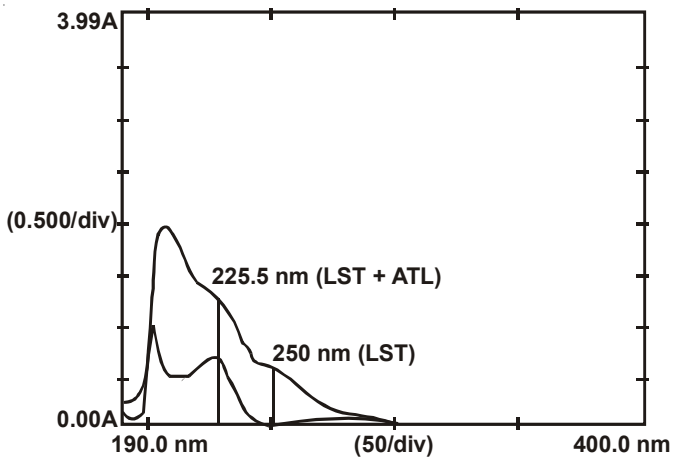

Fig. 2. Overlain spectra of LST and ATL

Absorbances of both the drugs recorded were found to be practically additive at 225.5 nm. An accurate estimation of ATL at 225.5 nm has been achieved after correction for absorption by LST.

The molar absorptivity values for each drug at the selected wavelengths were calculated. Since ATL does not absorb at 250 nm, the concentration of LST at 250 nm is given by the formula[20] -

$$A_{LST\ 250} = \in_{LST\ 250} \times b \times c_{LST\ 250}$$

$$c_{LST\ 250} = A_{LST\ 250}/29 \times 1 \quad (1)$$

The absorbance of LST at 225.5 nm was calculated as,

$$A_{LST\ 225.5} = \in_{LST\ 225.5} \times b \times c_{LST\ 225.5}$$

$$A_{LST\ 225.5} = 58.7 \times 1 \times c_{LST\ 225.5} \quad (2)$$

The corrected absorbance of ATL at 225.5 nm was found to be-

Corrected absorbance of ATL at 225.5 nm = $A_{225.5} - A_{LST\ 225.5}$, where

$$A_{ATL\ 225.5} = 30.7 \times 1 \times c_{ATL\ 225.5} \quad (3)$$

where, $A_{LST\ 250}$ and $A_{LST\ 225.5}$ - Absorbances of LST at 250 and 225.5 nm, respectively, $\in_{LST\ 250}$ and $\in_{LST\ 225.5}$ - Molar absorptivity of LST at 250 and 225.5 nm, respectively, $c_{LST\ 250}$ and $c_{LST\ 225.5}$ - Concentration of LST at 250 and 225.5 nm, respectively, A_{250} and $A_{225.5}$ - Absorbance of standard mixture at 250 and 225.5 nm, respectively, $A_{ATL\ 225.5}$ - Absorbance of ATL at 225.5 nm, $\in_{ATL\ 225.5}$ - Absorptivity of ATL at 225.5 nm, $c_{ATL\ 225.5}$ - Concentration of ATL at 225.5 nm.

Estimation from marketed preparation: Suitable dilutions of tablet sample solution were scanned in the range of 400-190 nm and its absorbances were recorded at wavelengths selected for this method. The concentration of each drug in the sample solution was then calculated using eqns. 1-3. The results of the tablet analysis and its statistical validation data of tablet formulations are given in Table-2.

RESULTS AND DISCUSSION

The results of the analysis of tablet formulations are in good agreement with the label claim of the formulations. The value of the standard deviation and coefficient of variation calculated for both the tablet analysis and recovery studies were satisfactorily low, indicating the high degree of precision of the proposed methods. Also the results of the recovery studies give in Table-3 indicate high degree of accuracy of the proposed methods.

TABLE-3
RECOVERY STUDIES AND ITS STATISTICAL VALIDATION DATA

Recovery (%)	Component	Amount present (mg)	Amount of standard added (mg)	Recovery* ± SD (%)		Coefficient of variation* (%)		Standard error*	
				A	**B**	**A**	**B**	**A**	**B**
80	LST	50	40	100.38 ±0.7687	99.70 ±0.1000	0.766	0.100	0.44	0.06
	ATL	50	40	99.90 ±1.143	100.13 ±0.1041	1.144	0.104	0.66	0.06
100	LST	50	50	99.38 ±1.068	100.13 ±0.1002	1.075	0.100	0.61	0.05
	ATL	50	50	99.43 ±0.2291	99.36 ±0.3547	0.2304	0.357	0.13	0.20
120	LST	50	60	99.51 ±0.8372	99.56 ±0.6500	0.8413	0.653	0.18	0.37
	ATL	50	60	100.46 ±0.8036	99.78 ±0.4072	0.780	0.408	0.60	0.23

*Average of three determinations at each level of recovery.

REFERENCES

1. S. Budavari, The Merck Index, Merck and Co., Inc., Whitehouse Station, NJ, edn. 12, p. 863, 5604 (1996).
2. P.N. Bennett and M. J.Brown, Clinical Pharmacology, Churchill Livingstone, edn. 9, p. 469, 480 (2003).
3. K. Florey, Analytical Profiles of Drug Substances, Academic Press, Vol. 13, pp. 1-23 (1984).
4. Indian Pharmacopoeia, The Controller of Publications, Government of India, Ministry of Health and Family Welfare, New Delhi, Vol. 2, edn. 3, pp. 72-75 (1996).
5. British Pharmacopoeia, International Edition, HMSO Publications Centre, London, Vol. 2, p. 179 (2004).
6. United States Pharmacopoeia, + (USP_{27} + NF_{22}), United States Pharmacopeial Convention, pp. 184-185 (2004).
7. N. Erk, *J. Pharm. Boimed. Anal.*, **24**, 603 (2001).
8. S.V. Erram and H.P. Tipnis, *Indian Drugs*, **29**, 436 (1992).
9. G.V. Kanumula and B. Raman, *Indian Drugs*, **37**, 38 (2000).
10. C.V. Prasad, C. Parihar, K. Sunil and P. Parimoo, *J. Pharm. Biomed. Anal.*, **17**, 877 (1998).
11. N.R. Lande, B.M. Shetkar, S.S. Kadam and S.R. Dhaneshwar, *Indian J. Pharm. Sci.*, **63**, 66 (2001).
12. A.H. Prabhakar and R. Giridhar, *J. Pharm. Biomed. Anal.*, **27**, 861 (2002).
13. R.C. Williams, M.S. Alasandro, V.L. Fasone, R.J. Boucher and J.F. Edwards, *J. Pharm. Biomed. Anal.*, **14**, 1539 (1996).
14. A. Shafati and B.J. Clark, *J. Pharm. Biomed. Anal.*,**14**, 1547 (1996).
15. M.N. Reddy, J.M. Krishna, V.R. Kumar, K.V.K. Rao and D.G. Shankar, *Acta. Cienc. Indica.*, **26**, 31 (2000).
16. M.A. Ritter and C.I. Furtek, *J. Pharm. Biomed. Anal.*, **15**, 1021 (1997).
17. R.B. Miller, *J. Pharm. Biomed. Anal.*, **9**, 849 (1991).
18. J.H. Peng, J.S. Tu and J.D. Xin, *J. China Pharm. Uni.*, **26**, 344 (1995).
19. A.P. Argekar and S.G. Powar, *J. Pharm. Biomed. Anal.*, **21**, 1137 (2000).
20. A.H. Beckett and J.B. Stenlake, Practical Pharmaceutical Chemistry, Part II, CBS Publishers and Distributors, New Delhi, edn. 4, pp. 280-286 (2002).

(*Received*: 20 May 2006; *Accepted*: 5 March 2007) AJC-5473