RESEARCH PAPER

Accepted 10 January 2003
Revised 18 November 2002
Received 15 July 2002
Indian J. Pharm. Sci., 2003, 65(2): 167-170

Simultaneous Spectrophotometric Determination of Losartan Potassium and Hydrochlorothiazide in Tablets

M. B. SHANKAR*, F. A. MEHTA, K. K. BHATT, R. S. MEHTA AND M. GEETHA
A. R. College and G. H. Patel Institute of Pharmacy, P.O. Box 19, Vallabh Vidyanagar-388 120.

Two simple, accurate and precise methods for simultaneous estimation of losartan potassium and hydrochlorothiazide in combined dosage form have been described. First method employs formation and solving of simultaneous equations using 206.6 nm and 270.6 nm as two analytical wavelengths. Second method is dual wavelength method, which uses the difference of absorbance values at 206.6 and 261.4 nm for the estimation of losartan and absorbance values at 270.6 nm for the estimation of hydrochlorothiazide. Both the methods allow the simultaneous determination of losartan and hydrochlorothiazide in the concentration ranges employed for this purpose with the standard deviation of <1.0% in the assay of tablets.

The combination of hydrochlorothiazide (HCZ) and losartan potassium (LP) is widely used in the treatment of hypertension. Monographs of various pharmacopoeias described the assay of hydrochlorothiazide. Reports are available for estimation of hydrochlorothiazide in combined formulations using HPLC[1,2], spectrophotometry[3-5] and quantitative TLC[6]. For estimation of losartan potassium, a spectrophotometric method was reported[7]. Recently reports appeared which described simultaneous estimation of losartan and hydrochlorothiazide using spectrophotometry[8,9], HPLC[10-12] and HPTLC[9]. In the spectrophotometric estimations that were described, Gandhimathi *et al.*[8] used simultaneous equation with methanol as solvent while Shah *et al.*[9] used derivative spectroscopy with methanol and water as the solvent. This paper describes two spectrophotometric methods for simultaneous estimation of hydrochlorothiazide and losartan potassium using 0.1 M HCl as solvent. HCl (0.1 M) has an advantage of being inexpensive, non-volatile, and relatively less hazardous. Moreover, in the dissolution tests for hydrochlorothiazide tablets, various pharmacopoeias prescribe 0.1 M HCl as dissolution media. Considering these facts we selected the proposed spectrophotometric methods with 0.1 M HCl.

*For correspondence
E-mail: mbs_mg@yahoo.co.in

MATERIAL AND METHODS

UV/Vis double beam spectrophotometer, model Spectrascan UV-2600 (Chemito Instruments limited) and Lamda 19 of Perkin Elmer, USA with 1 cm UV matched quartz cells were used.

Preparation of solutions:

Losartan potassium standard stock solution (0.2 mg/ml) was prepared by taking a 50 mg portion of LP (Cadila Pharmaceuticals Ltd. Ahmedabad) standard was accurately weighed and transferred to a 100 ml volumetric flask and volume was made up with 0.1M HCl. From this, 10 ml was withdrawn and transferred to a 25 ml volumetric flask, 0.1 M HCl was added to volume to give a concentration of 200 μg/ml.

Hydrochlorothiazide standard stock solution (0.05 mg/ml) was prepared by taking a 12.5 mg portion of HCZ (Unichem Pharmaceuticals Ltd., Mumbai) standard was accurately weighed and sonicated with some 0.1 M HCl for 3 min and then transferred to a 250 ml volumetric flask and 0.1M HCl was added to volume to give a concentration of 50 μg/ml.

Simultaneous equations method (Method 1):

Selection of analytical wavelengths was done by tak-

ing pure drug samples of LP and HCZ, which were separately dissolved in 0.1M HCl to give two solutions of 8.0 ppm. They were then scanned in the wavelength range of 200 to 330 nm. Wavelengths 206.6 and 270.6 nm were selected for the formation of the simultaneous equations. For constructing calibration curves, two series of different concentrations of LP were prepared from the stock solutions.

The first series contained LP in the range of 4-12 μg/ml and the second series contained 3-8 μg/ml, their absorbance measured calibration curves were plotted at 270.6 and 206.6 nm, respectively. Another two series of different concentrations of HCZ were prepared from the stock solutions. The irst series contained HCZ in the range of 4-10 μg/ml and the second series contained 4-12 μg/ml, their absorbance measured calibration curves were plotted at 270.6 and 206.6 nm, respectively. The absorptivities (A 1%, 1 cm) of both the drugs at both the wavelengths were determined. These calculated values were the mean of five independent determinations.

The absorbance and absorptivity values at the particular wavelengths were calculated and substituted in the following equations to obtain the concentrations: $C_x=A^2a^1_y-A^1a^2_y / a^2_xa^1_y-a^1_xa^2_y$ (1) and $C_y=a^2_xA^1-a^1_xA^2/a^2_xa^1_y-a^1_xa^2_y$ (2), where A1, A2 are abosrbances of the mixture at 1 and 2, respectively, a^1_x and a^2_x are absorptivities of X at 1 and 2, respectively, a^1_y and a^2_y denote absorptivities of Y at 1 and 2 respectively, C_x is the concentration of the LP, and Cy is the concentration of the HCZ.

Dual wavelength calculation method (Method 2):

From the overlain spectra of LP and HCZ, 270.6 nm was taken as the wavelength for estimation of HCZ. The wavelengths used for estimation of LP are 206.6 and 261.4 nm. The former is the λ_{max} of LP, whereas later is the wavelength which shows equal absorbance as that at 206.6 nm on the spectra of HCZ. A series of mixed standard solutions were prepared of different concentrations. Concentration range of LP was 6.4-19.2 μg/ml and that of HCZ was 1.6-4.8 μg/ml. Calibration curve for HCZ was plotted between absorbance at 270.6 nm versus concentration and for LP difference of absorbance values between 206.6 and 261.4 nm were plotted against the concentration.

Estimation from tablets:

Twenty tablets of two brands, Tablet 1-Nusar (Nucron Labs, label claim- 50 mg of LP and 12.5 mg of HCZ,) and Tablet 2-Losartas HT (Micro Labs, label claim- 50 mg of LP and 12.5 mg of HCZ), were weighed and finely powdered. Appropriate quantity of powder from each tablet was accurately weighed and sonicated for 5 min with 60 ml of 0.1 M HCl. This was transferred to 250 ml volumetric flask; volume was made up with 0.1 M HCl and filtered. Necessary dilutions of filtrate were made with 0.1 M HCl to achieve the final concentrations of 13.76 μg/ml of LOS and 3.44 μg/ml of HCZ for Tablet 1., 9.0 μg/ml of LP and 2.25 μg/ml of HCZ for Tablet 2. Calibration curves were used to obtain concentration of drug in formulation using above methods.

RESULTS AND DISCUSSION

The overlain spectra of both drugs (spectra not shown) showed that the peaks are well resolved thus satisfying the criteria for obtaining maximum precision based on absorbance ratios[13]. The criteria being the ratios $(A^2/A^1)/(a^2_x / a^1_x)$

TABLE 1: REGRESSION ANALYSIS OF THE CALIBRATION CURVES.

Method	Drug	Wavelength (nm)	Concentration Range (μg/ml)	Intercept (RSD)	Slope	r^2
Method 1	LP	206.6	3-8	0.0014 (2.14)	0.0974	0.9999
		270.6	4-12	0.0046 (3.29)	0.0106	0.9998
	HCZ	206.6	4-12	0.009 (3.04)	0.0517	0.9997
		270.6	4-10	-0.0097 (1.18)	0.0777	0.9996
Method 2	LP	206-261.4*	6.4-19.2	0.241 (2.84)	0.0803	0.9990
	HCZ	270.6	1.6-4.8	0.0014 (2.69)	0.1253	0.9993

Method 1 is the simultaneous equation method while Method 2 is the dual wavelength method, RSD is relative standard deviation while r^2 is correlation coefficient,* indicates difference of absorbance of LP between 206.6 and 264.1 nm.

for drug y and $(a^2_y / a^1_y)/(A^1/A^2)$ for drug x should lie outside the range of 0.1-2.0. Where A^1, A^2 represent abosrbances of the mixture at λ_1 and λ_2, a^1_x and a^2_x represent absorptivities of X at λ1 and λ2, and a^1_y and a^2_y denote absorptivities of Y at λ1 and λ2, respectively. In the present context the above criteria was found to be satisfied for LP (x) and HCZ (y) where λ1 is 206.6 nm and λ2 is 270.6 nm. The overlain spectra of HCZ of different concentration show two distinct peaks, one at around 224 nm and other at 270.6 nm. Only the second peak showed change in absorbance proportional to concentration of drug. Hence, for simultaneous equations method, this peak was used for determination of HCZ. Since only one prominent peak exists for LP at 206.6 nm, the same was used for its determination. Absorbance was determined at both the wavelengths, calibration curves were plotted and regression analysis was carried out (Table 1). The absorptivity was then calculated and along with absorbance values were substituted in the equations 1 and 2 to obtain concentration of drugs.

Dual wavelength calculation method is applicable where, out of the two spectra, one should show two wavelengths with equal absorbance. The spectra of LP and HPZ when overlaid indicated that the spectra of HCZ satisfied this condition while that of LP did not. Hence, 270.6 nm was used for the estimation of HCZ while the difference in the absorbances between 206.6 nm and 261.4 nm was considered for estimation of LP.

TABLE 2: ASSAY RESULTS OF LOSARTAN AND HYDROCHLOROTHIAZIDE IN COMMERCIAL FORMULATIONS BY METHOD 1 AND 2.

Tablet	Method 1		Method 2	
	%LP	%HCZ	%LP	%HCZ
Tablet 1	99.8±0.64	100.9±0.70	100.2±0.74	101.2±0.61
Tablet 2	99.2±0.84	100.4±0.89	100.1±0.83	100.9±0.74

Method 1 is the simultaneous equation method while Method 2 is the dual wavelength method. Values for recovery are mean ± s.d. for three determinations.

TABLE 3: SUMMARY OF VALIDATION PARAMETERS.

Parameters	Method 1		Method 2	
	LP	HCZ	LP	HCZ
Linearity range (μg/ml)	0-20	0-20	1-20	1-20
Correlation coefficient (r^2)	0.9999	0.9997	0.9990	0.9993
Precision (%CV)				
Intra day (n=3)	0.64-2.95	0.689-2.38	2.75-3.15	0.61-0.70
Inter day (n=3)	0.67-3.08	0.759-2.6	2.88-3.22	0.83-0.89
Accuracy (%)	99.0-100.2	99.0-101.0	99.3-100.8	100.3-101.0
Repeatability (RSD, n=7)	0.00423 for (206.6 nm)	0.00816 for (206.6 nm)	0.00269	0.00225
	0.0373 for (270.6 nm)	0.00478 for (270.6 nm)		
Reproducibility	Reproducible	Reproducible	Reproducible	Reproducible
Specificity	Specific	Specific	Specific	Specific

Method 1 is the simultaneous equation method while Method 2 is the dual wavelength method, RSD is the relative standard deviation while r^2 is the correlation coefficient, CV is the coefficient of variation.

Both the methods were successfully used to estimate the amounts of losartan potassium and hydrochlorothiazide present in two of the marketed tablet formulations containing losartan potassium and hydrochlorothiazide. The assay values for tablets 1 and 2 by both methods are in the range 99.2-100.1% and 100.4-101.2% for losartan and hydrochlorothiazide, respectively. The results obtained were comparable with the corresponding labelled amounts, (Table 2).

By observing the validation parameters (Table 3), both the methods were found to be specific, accurate, precise, repeatable and reproducible. However, dual wavelength method has an advantage of simpler calculation over the simultaneous equations method. Hence, both the methods can be employed for routine analysis of tablets for assay as well as in dissolution testing.

ACKNOWLEDGEMENTS

The authors thank Cadila Pharmaceuticals Ltd. (Ahmedabad) for the sample of pure losartan potassium and Unichem Pharmaceuticals Ltd. (Mumbai) for the pure sample of hydrochlorothiazide.

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