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Research Article

SIMULTANEOUS ESTIMATION OF LOSARTAN POTASSIUM AND HYDROCHLOROTHIAZIDE FROM TABLETS BY FIRST ORDER DERIVATIVE SPECTROSCOPY

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ABSTRACT

Losartan Potassium and hydrochlorothiazide are used in combination for treatment of hypertension. The present work deals with simple spectrophotometric method development for simultaneous estimation of Losartan Potassium (LOS) and Hydrochlorothiazide (HCT) in two component tablet formulation. The method employed is a first order derivative spectroscopy. For determination of sampling wavelength, 20 µg/ml of each of LOS and HCT were scanned in 200-400 nm range and sampling wavelengths were 257 nm for LOS where HCT showed zero crossing point and 243 nm for HCT where LOS showed zero crossing point in first order derivative spectroscopy. For this method linearity observed in the range of 10-90 µg/ml for LOS and 2.5-22.5 µg/ml for HCT. The recovery studies confirmed accuracy of proposed method and low values of standard deviation confirmed precision of method. The method is validated as per ICH guidelines.

Keywords: Losartan Potassium, Hydrochlorothiazide, Derivative spectroscopy

INTRODUCTION

Losartan Potassium (LOS) is chemically described as [4(2hydroxy3isopropylaminopropoxy) phenylacetamide] and is competitive antagonist and inverse agonist of A-II, and Hydrochlorothiazide (HCT) is 6-Chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7- sulfonamide 1,1-dioxide used as diuretic (1). In the chemical analysis of multicomponent dosage form one drug may interfere with estimation of other drug. Hence analytical methods are developed to estimate all the drugs simultaneously in multi-component formulations (2-8).

Many analytical methods like HPLC, HPTLC, electrochemical, radioimmunoassay were reported for determination of LOS (9-14) and HCT (13-17) alone and combination with other antihypertensive drugs. The RP-HPLC method has been reported for simultaneous estimation of LOS and HCT (13).

However no first order (18-19) derivative spectrophotometric method is reported till date for simultaneous determination of these drugs. In this communication we report a new UV spectrophotometric method using derivative spectroscopy.

MATERIALS AND METHODS

Materials

Instruments

Spectrophotometric analysis was carried out on a JASCO UV-spectrophotometer V- 630 using a 1 cm quartz cell. The instrument settings were zero order and first derivative mode and band width of 2 nm in the range of 200–400 nm.

Reagents and Chemicals

Losartan Potassium and hydrochlorothiazide supplied by Cipla Pvt. Ltd. India. All solvents of spectrophotometric grade were procured from LOBA CHEM. Water used in analysis was purified by glass distillation apparatus.

Methods

Calibration Curve

The stock solutions were prepared separately in water: methanol (50:50) to obtain 100 µg/ml of both drugs. The nine working mixed standard were prepared by dilution of stock solution in same solvent system in concentration range 10-90 µg/ml of LOS and 2.5-22.5 µg/ml for HCT. Losartan Potassium and hydrochlorothiazide initially scanned for determining sampling wavelength in range 200-400 nm. Sampling wavelengths were 257 nm for LOS where HCT showed zero crossing point and 243 nm for HCT where LOS showed zero crossing point (Figure 1). Calibration graphs were constructed from the absorbance values of drugs at respective wavelength.

Analysis of Tablet Formulation

Marketed tablet formulation containing LOS (50 mg) and HCT (12.5) mg were analyzed using this method. From the contents of 20 tablets, an amount equivalent to 10 mg of LOS and 5 mg of HCT was weighed and dissolved in 60 ml of solvent in 100 ml volumetric flask. The solution was filtered through Whatmann filter paper no. 41 and then final volume of the solution was made up to 1000 ml to get stock solution containing 100 µg/ml of LOS and 50 µg/ml of HCT.

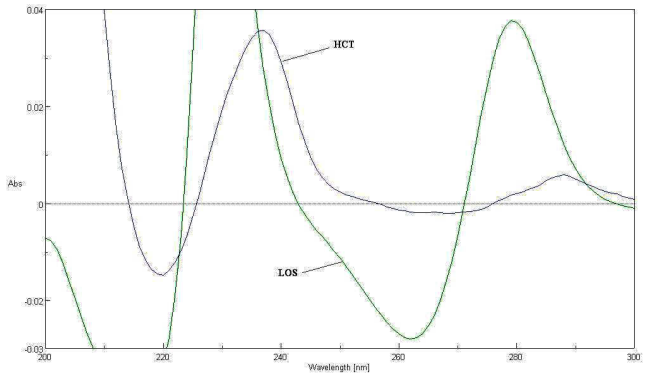

Fig. 1: Overlain Spectra of LOS and HCT in First Order Derivative Mode.

After appropriate dilutions, the absorbances were measured and the concentration of each analyte was determined with the equations generated from calibration curve for respective drugs (9-10). The results of Tablet analysis are shown in Table 2.

The developed method was validated by following ICH Q2B (R1) guidelines (20). The following parameters were studied for validation.

Accuracy

Recovery studies were performed by standard addition method at three levels i.e., 80%, 100% and 120%. Known amounts of pure LOS and HCT were added to pre-analyzed sample of marketed formulation and they were subjected to analysis by the proposed method. Results of recovery studies are shown in Table 1.

Precision

Precision study was performed to find out intra-day and inter-day variations. The results of precision studies are reported in Table 2 and values of standard deviation less than 2% indicates high degree of precision.

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

The LOD and LOQ were separately determined based on the calibration curves. The standard deviation of the y-intercepts (σ) and slope of the regression lines (S) were used. These values were calculated using following formula

$$LOD = 3.3 \times \sigma / S \quad LOQ = 10 \times \sigma / S$$

Robustness

The robustness of method was studied by changing composition of solvent system. The results of robustness studies are reported in Table 3.

Ruggedness

The ruggedness study was carried out by using different instruments and analyst. The results are as shown in Table 3.

Table 1: Results of Tablet Analysis and Recovery Study

Drug	Label Claim (mg/Capsule)	%Label Claim Estimated Mean[a]± SD[b]	Amount Added (mg)	% Recovery Estimated Mean[a]± SD[b]
LOS	50	99.25±1.257	40	99.76±1.266
		101.91±1.965	50	100.87±1.186
		98.78±1.032	60	99.92±1.601
HCT	12.5	98.21±1.034	10	98.04±0.9143
		98.75±1.289	12.5	99.84±0.7453
		99.31±1.712	15	99.55±0.9560

a: Average of Three Determinations b: Standard Deviation.

Table 2: Results of Precision Studies

Analyte	Precision		Amount of Pure Drug Added in mg	% concentration Found (Mean[a] ± SD[b])
LOS	Intra-Day	T1	40	99.04 ±1.2422
		T2	50	99.55 ± 0.5152
		T3	60	99.60 ±0.6613
	Inter-Day	D1	-	1001.11±0.6739
		D2	-	100.02±0.9637
		D3	-	100.04 ± 1.2422
HCT	Intra-Day	T1	10	98.33 ± 1.1558
		T2	12.5	99.40 ± 1.2844
		T3	15	98.56± 1.4750
	Inter-Day	D1	-	98.75±1.2897
		D2	-	99.31±1.71258
		D3	-	99.59 ± 0.27678

a: Average of Three Determinations b: Standard Deviation.

Table 3: Result of Robustness and Ruggedness Study

Parameter	Modification	% Recovery Mean[b] ± SD[c]	
		LOS	HCT
Robustness Study			
Solvent System Ratio	45:55	99.91±1.9658	99.21 ± 1.0107
(Water: Methanol)	48:52	98.78±1.0328	100.39 ± 0.3644
	50:50[a]	99.59 ±0.5015	98.21±1.0346
	52:48	99.72 ± 0.5042	98.75±1.2897
	55:45	99.87 ± 0.8311	99.31±1.71258
Ruggedness Study			
Instrument	UV-530	100.09±0.73	100.39±0.37
	UV-630	100.10 ± 0.87	100.68 ± 0.94
Analyst	I	99.72 ± 0.50	99.31 ± 0.32
	II	99.45 ± 0.51	99.37 ± 1.10

a: Optimized Parameter for Developed Method b: Mean of Three Readings

c: Standard Deviation

RESULTS AND DISCUSSION

The zero order spectra of pure drugs were found to be overlapping making their simultaneous determination difficult. The first derivative spectrophotometric method was considered to be ideal to facilitate their quantitative determination. It was observed during initial study that first derivative spectra have ideal zero-crossing points for the estimation of LOS and HCT in their combined dosage form. The method utilizes nine mixed standard solutions which were scanned in a wavelength range of 200-400 nm against methanol:

water (50:50 % v/v) as blank. The first order derivative spectra were obtained by instrumental electronic differentiation in the range of 200nm to 400nm. There was no interference of HCT at a wavelength of 257 nm of first derivative spectrum of LOS, thus this wavelength was selected for quantitation of LOS, while no interference of LOS at a wavelength of 243 nm of first derivative spectrum of HCT due to zero crossing point, thus this wavelength was selected for quantification of HCT.

Linear regression data showed a good linear relationship over a concentration range of 2.5-22.5 µg/ml for HCT and 10-90 µg/ml for LOS. For both the drugs nine point calibration curves were generated. Data obtained from interday and intraday studies showed high degree of repeatability of an analytical method under normal operational conditions. Result of tablet formulation showed percent relative standard deviation values in the average range of 0.7995 for LOS and 0.8137 for HCT, which indicates repeatability of method. The results indicated excellent recoveries ranging 99.00 to 101.11 % for HCT and 99.16-100.55% for LOS. Recoveries obtained for two drugs do not differ significantly from 100 % showed that there was no interference from common excipients used in formulation indicating accuracy and reliability of method

Lower limit of detection for LOS and HCT was found to be 1.4235and 1.0137 µg/ml respectively. While limit of quantitation for LOS and HCT were found to be 4.3136 and 3.0718 µg/ml respectively. Average percent RSD values for tablet analysis by using methanol: water (60:40%v/v) was found to be 0.7142 for LOS while 0.7613 for HCT which proves the ability of the method to remain unaffected by small deliberated changes in conditions of analysis.

CONCLUSION

The proposed method for simultaneous estimation of losartan potassium and hydrochlorothiazide in their combined dosage form is accurate, precise and reproducible.

Moreover the method is economic, simple and rapid, hence can be employed for routine analysis in quality control laboratories. The further optimization of method will make it useful for pharmacokinetic and biopharmaceutical studies.

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