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Simultaneous Estimation of Losartan Potassium and Hydrochlorothiazide in Tablet Dosage form by UV Spectroscopy

Sowmya CH, Priya M L, Manoj Kumar M, Saranya P K, Priya T S, Prasanthi T and Lakshmana Rao A*

Department of Pharmaceutical Analysis, V. V. Institute of Pharmaceutical Sciences, Gudlavalleru, A.P., India.

***Corresponding Author:**

E-mail: dralrao@gmail.com

Abstract

A simple, specific, accurate and precise method has been developed and validated for the simultaneous determination of Losartan Potassium (LST) and Hydrochlorothiazide (HCT) in tablet dosage forms by UV Spectrophotometry. The wavelength maximum is 226.4 nm for Losartan Potassium and 266.4 nm for Hydrochlorothiazide in 0.1N sodium hydroxide. The linearity was observed in the concentration range of 2-12 µg/ml for both LST and HCT. Percentage recovery was found to be 100.41% for LST and 99.57% for HCT respectively signifies the accuracy of the method. The %RSD values of Losartan Potassium and Hydrochlorothiazide were found to be less than 2. The method was validated statistically and this technique can be employed to analyze the simultaneous estimation of LST and HCT in pharmaceutical dosage forms.

Key words: Losartan Potassium, Hydrochlorothiazide, Estimation, Spectrophotometry, Dosage form.

INTRODUCTION

Losartan Potassium (Fig. 1) is a selective, competitive angiotensin II receptor type 1 (AT_1) antagonist, reducing the end organ responses to angiotensin II. It is chemically 2-butyl-4-chloro-1-[*p*-(o-1*H*-tetrazol-5-ylphenyl)benzyl]imidazole-5-methanol mono potassium salt[1]. Losartan Potassium administration results in a decrease in total peripheral resistance (afterload) and cardiac venous return (preload). All of the physiological effects of angiotensin II, including release of aldosterone, are antagonized in the presence of Losartan Potassium.

Hydrochlorothiazide (Fig. 2) belongs to thiazide class of diuretics. It is chemically known as 6-chloro-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide-1,1-dioxide[2]. Hydrochlorothiazide reduces blood volume by acting on the kidneys to reduce sodium (Na^+) reabsorption in the distal convoluted tubule . The major site of action in the nephron appears on an electro neutral NaCl co-transporter by competing for the chloride site on the transporter. By impairing Na^+ transport in the distal convoluted tubule, Hydrochlorothiazide induces a natriuresis and concomitant water loss[3].

A survey of literature reveals that very few simultaneous analytical methods were available for determination of Losartan Potassium and Hydrochlorothiazide by using spectrophotometric[4-6] and liquid chromatographic methods[7-8]. Hence the objective of the present work is to develop and validate a new, simple, sensitive, specific, precise and accurate UV Spectrophotometric method for the simultaneous determination Losartan Potassium and Hydrochlorothiazide in bulk drug and in pharmaceutical formulations.

MATERIALS AND METHODS

Instrument: Shimadzu UV1800 Double Beam UV-Visible Spectrophotometer was used for spectral studies.

Chemicals and reagents: The reference samples of Losratan Potassium (API) and Hydrochlorothiazide (API) were purchased from Yarrow Chem Products, Mumbai, India. The commercial formulation of Losartan Potassium and Hydrochlorothiazide tablets were procured from the local market. Sodium hydroxide was purchased from Finar Ltd Gujarat, India and was used as diluent.

Preparation of standard stock solution: 100 mg of LST and HCT were accurately weighed and transferred to two separate 100 ml

volumetric flasks and volume made upto mark with 0.1N sodium hydroxide to get concentration of 1mg/ml.

Determination of λmax: The standard solutions of both LST and HCT (10 µg/ml) were scanned in the wavelength region of 200-400 nm and the λ max was found to be 226.4 nm and 266.4 nm for Losartan Potassium and Hydrochlorothiazide respectively. The wavelength spectra of LST and HCT in 0.1N NaOH are shown in Fig. 3 & 4 respectively.

Preparation of calibration curve: From the stock solution concentrations of 2 µg/ml, 4 µg/ml, 6 µg/ml, 8 µg/ml 10 µg/ml and 12 µg/ml solutions were prepared for both Losartan Potassium and Hydrochlorothiazide and absorbances were measured at 226.4 nm and 266.4 nm respectively. Calibration curve was plotted by taking measured absorbances against the concentrations.

Assay of tablet dosage form: Twenty tablets were weighed and average weight of tablets was calculated. The tablets are crushed to fine powder. The powder equivalent to 50 mg of Losartan Potassium and 12.5 mg of Hydrochlorothiazide was accurately weighed and transferred into a 50 ml clean dry volumetric flask containing 30 ml of 0.1N sodium hydroxide. The solution was sonicated for 5min and the volume was made up to the mark with a further quantity of the 0.1N sodium hydroxide. The solution was then filtered through Whatmann filter paper. Further pipette 1 ml of the above stock solution into a 10 ml volumetric flask and the volume was made up to the mark with the 0.1N sodium hydroxide. Later pipette out 1 ml of above solution into a 10 ml volumetric flask and the volume was made up to the mark with the 0.1N sodium hydroxide.

RESULTS

A simple, rapid, precise and accurate UV spectrophotometric method was developed for the simultaneous determination of Losartan Potassium and Hydrochlorothiazide from bulk samples and their tablet dosage forms. 0.1N NaOH was selected as a solvent for analysis. The wavelength of maximum absorbance was selected to be 226.4 nm and 266.4 nm for estimation of LST and HCT respectively. The linearity was found satisfactory in the concentration range of 2-12 µg/ml for both LST (Fig. 5) and HCT (Fig. 6). The regression equation for Losartan and Hydrochlorothiazide over its absorbances were found to be y=0.03563x-0.00285 and y=0.07398x+0.00244 (Table 1) respectively with a correlation coefficient (r^2) of 0.99665 for LST and 0.99851 for HCT. Precision of the method was studied by repeated measurements of drug solution and results showed lower %RSD values. The %RSD for intra-day precision and inter-day precision for LST were found to be 0.46% and 0.465% respectively. The %RSD for intra-day precision and inter-day precision (Table 2 & 3) for HCT were found to be 0.30% and 0.20% respectively. This reveals that the method is quite precise. The percent recoveries of the drug solutions of Losartan Potassium and Hydrochlorothiazide were studied at three different concentration levels. Recovery studies of the drug were carried out for the accuracy parameter at three different concentrations levels i.e. multiple level recovery studies. The mean percent recovery of the drugs LST and HCT was 100.41% (Table 4) and 99.5% (Table 5) respectively. The limit of detection (LOD) and limit of quantification (LOQ) for Losartan Potassium were found to be 0.30 µg/ml and 0.92 µg/ml respectively. The limit of detection (LOD) and limit of quantification (LOQ) for Hydrochlorothiazide were found to be 0. 17 µg/ml and 0.53 µg/ml respectively (Table 6). The percentage purity for the assay of LST and HCT were found to be 99.08% and 99.20% respectively (Table 7). The assay results showed that the drug contents of this product to be in accordance with the labeled claims. No interfering peaks were found in the absorption spectrum of the tablet formulation indicating that excipients used in tablet formulations did not interfere with the simultaneous estimation of the drugs Losartan and Hydrochlorothiazide by the proposed UV spectrophotometric method.

CONCLUSION

Present study describes an UV spectrophotometric method for the

simultaneous determination of Losartan Potassium and Hydrochlorothiazide in bulk sample and pharmaceutical formulations. The satisfying recoveries, low correlation coefficient and assay results confirmed the suitability of proposed method for the routine quality control analysis for simultaneous determination of LST and HCT in pharmaceutical formulations. The standard and %RSD calculated for proposed method was within limits and indicates high degree of precision. To conclude, the proposed UV spectrophotometric method is conveniently used for analysis of Losartan Potassium and Hydrochlorothiazide in combined pharmaceutical dosage forms.

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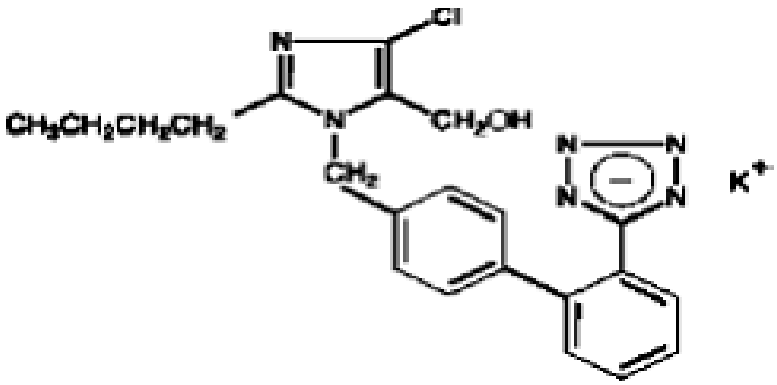

Fig. 1: Molecular structure of Losartan Potassium

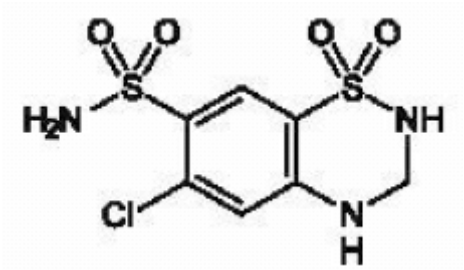

Fig. 2: Molecular structure of Hydrochlorothiazide

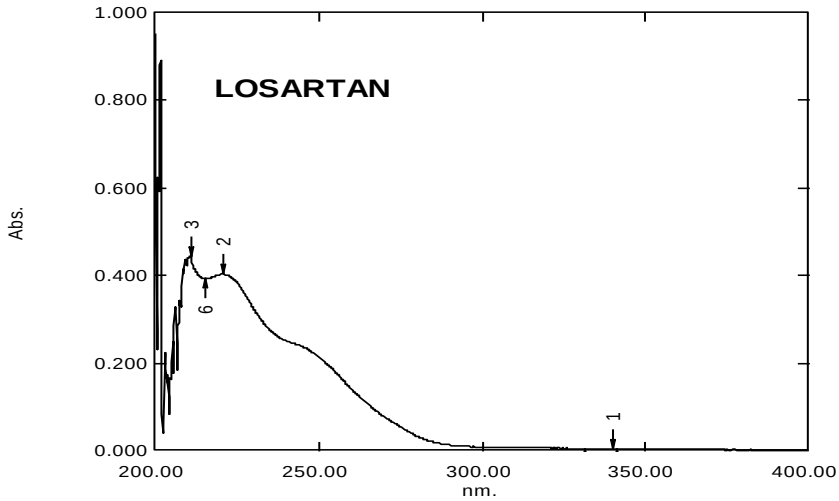

Fig. 3: UV Spectrum of Losartan Potassium

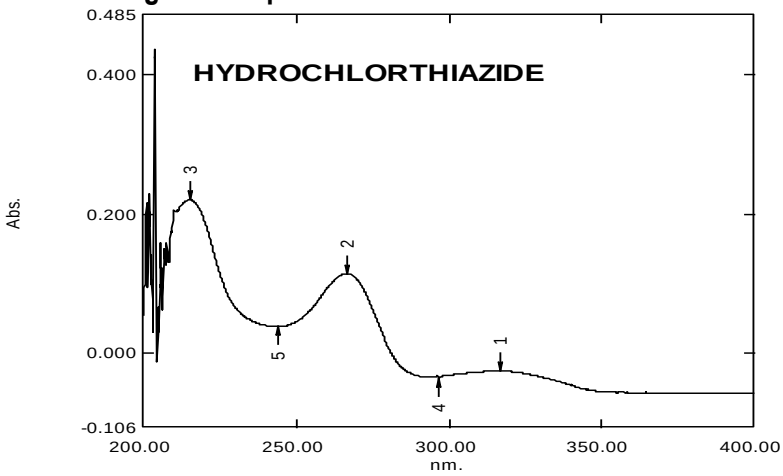

Fig. 4: UV Spectrum of Hydrochlorothiazide

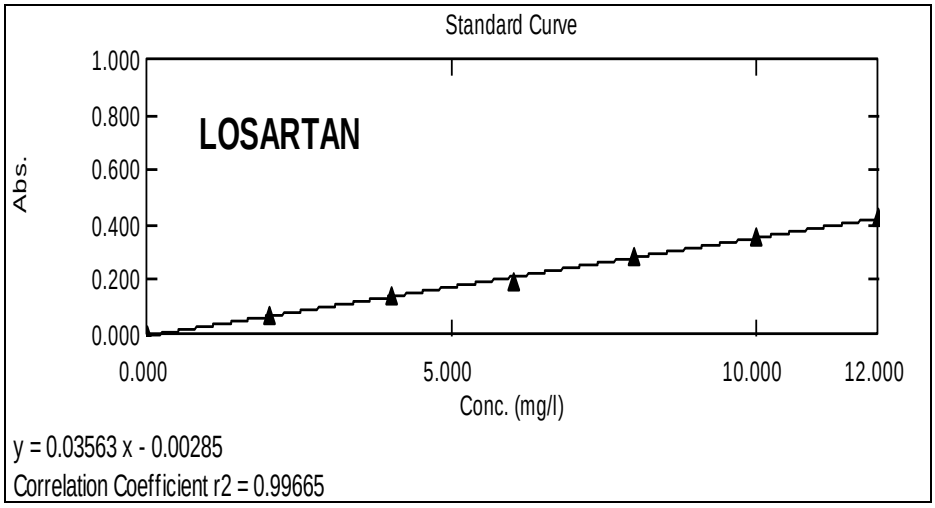

Fig. 5: Calibration curve of Losartan Potassium

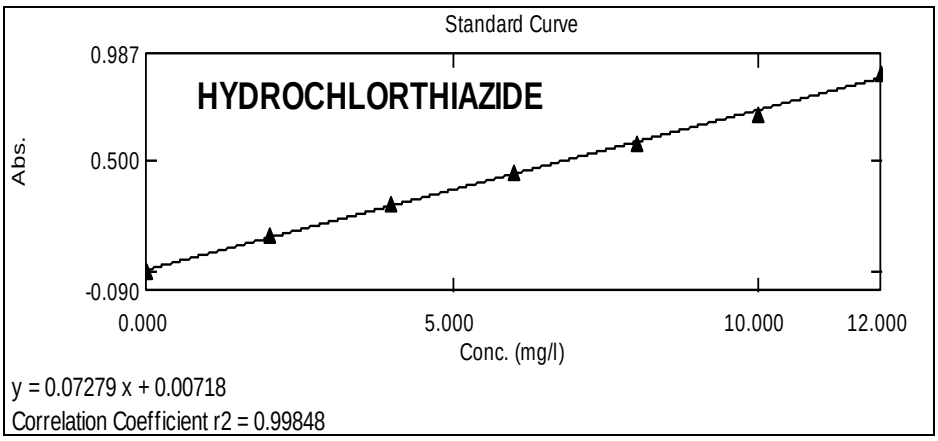

Fig. 6: Calibration curve of Hydrochlorothiazide

Table 1: Linearity results of Losartan Potassium and Hydrochlorothiazide

S. No.	Concentration (µg/ml)	Losartan Absorbance	Hydrochlorothiazide Absorbance
1	2	0.072	0.163
2	4	0.141	0.305
3	6	0.191	0.445
4	8	0.287	0.582
5	10	0.360	0.716
6	12	0.424	0.897
Slope		0.03563	0.07398
Intercept		-0.00285	0.00244
Regression Equation(y)		0.03563x-0.00285	0.07398x+0.00244
Correlation Coefficient(r^2)		0.99665	0.99851

Table 2: Intra-day precision results of Losartan Potassium and Hydrochlorothiazide

S. No.	Time (Hours)	LST Absorbance	HCT Absorbance
1	0	0.191	0.440
2	1	0.193	0.442
3	2	0.190	0.445
4	3	0.194	0.440
5	4	0.191	0.443
6	5	0.193	0.445
7	6	0.192	0.442
	Mean	0.450	0.442
	SD	0.008	0.00013
	%RSD	0.85	0.30

Table 3: Inter-day precision results of Losartan Potassium and Hydrochlorothiazide

S. No.	Time (Days)	LST Absorbance	HCT Absorbance
1	1	0.191	0.445
2	2	0.193	0.440
3	3	0.191	0.445
4	4	0.190	0.443
5	5	0.192	0.442
6	6	0.190	0.443
	Mean	0.191	0.443
	SD	0.00089	0.00089
	%RSD	0.465	0.20

Table 4: Recovery studies for Losartan Potassium

Level	Standard conc. (µg/ml)	Conc. added (µg/ml)	Conc. found (µg/ml)	% Recovery	% Mean recovery
80%	10	8	7.95	99.37	100.41
100%	10	10	10.23	102.3	
120%	10	12	11.95	99.58	

Table 5: Recovery studies for Hydrochlorothiazide

Level	Standard conc. (µg/ml)	Conc. added (µg/ml)	Conc. found (µg/ml)	% Recovery	% Mean recovery
80%	10	8	7.96	99.50	99.57
100%	10	10	10.09	100.9	
120%	10	12	11.8	98.33	

Table 6: LOD and LOQ of Losartan Potassium and Hydrochlorothiazide

Parameter	Losartan Potassium Measured value (µg/mL)	Hydrochlorothiazide Measured value (µg/mL)
Limit of detection	0.30	0.17
Limit of quantification	0.92	0.53

Table 7: Assay results of Losartan Potassium and Hydrochlorothiazide formulations

Formulation		Label claim	Amount found	%Assay
LOSAR H	Losartan Potassium	50 mg	49.54 mg	99.08%
	Hydrochlorothiazide	12.5 mg	11.85 mg	99.20%