Research Article

DEVELOPMENT AND VALIDATION OF A STABILITY INDICATING UV-SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF LOSARTAN POTASSIUM IN BULK AND TABLET DOSAGE FORM

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ABSTRACT
A simple, sensitive and reproducible stability indicating UV Spectrophotometric method has been developed for quantitative determination of Losartan Potassium in bulk and pharmaceutical formulations. The UV- spectrum was scanned between 220 to 400 nm and 227.4 nm was selected as maximum wavelength for absorption. Beer's law was obeyed in the concentration range of 2.02-22.22 µg/ml. Good accuracy (98.11-99.85%), precision (RSD 0.303-0.334) and selectivity (= 0.5%) were found, and the method was successfully applied to the pharmaceutical dosage form containing the above-mentioned drug without any interference by the excipients. The method was fast and economical and it was also selective and sensitive for the desirable range. Results of the analysis were validated as per ICH guidelines and by recovery studies. Stability testing study includes the effect of temperature, oxidation, photolysis and susceptibility to hydrolysis across a wide range of pH values.

Key words: Spectrophotometry, Losartan Potassium, Stability Indicating, Validation

INTRODUCTION

Losartan Potassium1.[2-Butyl-4-chloro-1-[2'-(1H-tetrazol-5-yl)-1,1'-biphenyl)-4-yl] methyl]-1H-imidazole-5-methanol,is an angiotensin II receptor antagonist drug used mainly to treat high blood pressure (hypertension). The drug is official in United States Pharmacopoeia 28. In the present study, a simple, sensitive, accurate and validated[2] UV-Spectrophotometric method for the estimation of Losartan Potassium in bulk and tablet dosage forms has been developed using 0.01 N HCl solutions.

The literature survey reveals that the methods available for estimation of Losartan Potassium include RP-HPLC[3], HPLC, HPTLC, derivative spectrophotometry[4] and simultaneous spectrophotometric methods[5-6].

In the present method 0.01 N HCl is used as solvent. HCl (0.01 N) has an advantage of being inexpensive, non-volatile and relatively less hazardous. Moreover the maximum wavelength for both the drugs remains stable by changing the concentration of the drugs.

Stability Indicating Assay Methods (SIAMs) may be defined as validated, quantitated analytical method that can detect the change with timing chemical, physical and microbiological properties of drug substances and drug products, and that are specific so that the content of active ingredients, degradation products and other component of interest can be accurately measured without interference.

MATERIALS AND METHODS

Instrument:

(1) ELICO SL 160 Double beam UV-VIS Spectrophotometer with spectral band width of 1.8 nm, wavelength accuracy of 2 nm and matched quartz cells of 10 mm optical path length.

Table-1: Calibration curve data for Losartan Potassium

S. No.	Conc. (µg/ml)	Abs.*	SD	RSD**
1	2.02	0.078	0.002	1.923
2	4.04	0.160	0.002	1.250
3	6.06	0.243	0.003	1.235
4	8.08	0.346	0.003	0.867
5	10.10	0.432	0.003	0.787
6	12.12	0.515	0.003	0.583
7	14.14	0.578	0.003	0.519
8	16.16	0.661	0.002	0.303
9	18.18	0.766	0.002	0.261
10	20.20	0.835	0.002	0.240
11	22.22	0.940	0.002	0.213
Slope	**0.0006**	**0.0423**	**1.36**	
Intercept	**0.0009**	**0.0057**	**16.08**	
Correlation				

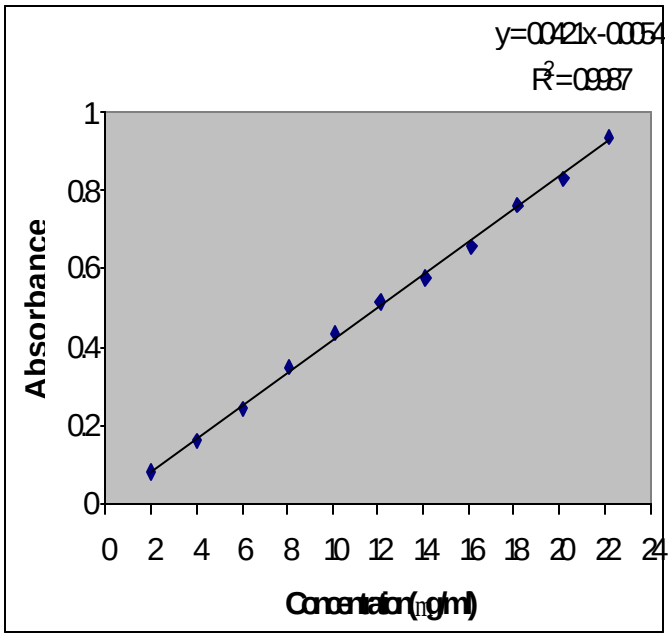
* Data represents mean of triplicate determina tions.
** % desired < 2 %; Specified limit < 5.3%.

Table 2: Summary of Analytical parameters of Losartan Potassium

S. No.	Parameters	Losartan Potassium
1.	**lamda (max.) nm**	227.4
2.	**Beer's law limit (µg/ml)**	2.02-22.22
3.	**Sandell's sensitivity**	0.0239
4.	**Molar absorptivity**	19.235 x 10^3
5.	**Regression equatio**	Y = 0.0421x -0.0054
6.	**Slope:**	0.0421
	-test for slope	154.61[a]
	-SD	0.0001
	-Confidence interval	± 0.001
9.	**Intercept:**	0.0054
10.	-test of intercept	1.55[b]
11.	-SD	0.0008
	-Confidence interval	± 0.008
	Correlation- coefficient	0.9993

a: passes the test of slope, slope being significantly (p = 0.05) different from zero.
b: passes the test of intercept, intercept being not significantly (p = 0.05) different from zero.

Figure 1: Calibration curve for Losartan Potassium at 227.4 nm



* Graph is plotted using mean of triplicate determinations.

Table 3: Summary of Validation parameters of Losartan Potassium

S. No.	Parameters	Losartan Potassium
1.	**Specificity :**	
	-% interference	< 0.5
	-% agreement	100.4-100.6
2.	**Range (μg/ml):**	
	-Working range	0.472-22.22
	-Linearity range	4.04-22.22
	-Target range	10.50-15.7
	-Test conc. (100%)	13.13
3.	**Precision :**	
	-Repeatability(n = 7)	0.387
	-Intraday (n=3)	0.303
	-Interday (3 days)	0.334
4.	**Accuracy %**	98.11-99.85
5.	**LOD (μg/ml)**	0.156
6.	**LOQ (μg/ml)**	0.472

Table 4: Results of Estimation of Losartan Potassium in Tablet Dosage Form

Brand	Labeled amount	Amount found[a]	%Labeled amount	RSD
Losacar-50	50 mg	49.50 ± 0.255	99.00 ± 0.509	0.515
Losar-50	50 mg	49.56 ± 0.337	99.134 ± 0.673	0.679

a: average of three readings

Table 5: Result of forced degradation study of Losartan Potassium

S. No.	Conditions applied	Conc. taken (μg/ml)	Conc. found Average (μg/ml)	Observation
1.	**Acidic hydrolysis (0.1-1.0 N)**	20.0 μg/ml	19.8 μg/ml	No appreciable change
2.	**Basic hydrolysis (0.02-0.1 N)**	20.0 μg/ml	48.81 μg/ml	Degraded
3.	**3% H_2O_2**	20.0 μg/ml	Change in lamda max	Degraded
4.	**Thermal stress (60°C, 24 hrs.)**	20.0 μg/ml	16.6 μg/ml	Degraded
5.	**UV-treatment (7 days & 4 hrs daily)**	20.0 μg/ml	15.2 μg/ml	Degraded

(2) GR 200 Analytical weighing balance (AND Company).
(3) pH meter (Aminco Pvt. Ltd.).

Chemicals and Reagents:

Concentrated HCl available in Lab. was mixed in double distilled water to prepare a 0.01 N HCl solution and used in the present method.

Drug sample:

Standard Losartan Potassium was obtained as gift sample from M/S Intas Pharmaceuticals Pvt. Ltd., Ahmedabad (Gujarat).

Marketed formulations:

Losacar-50 (Zydus Medica) and Losar-50 (Unichem) tablets, both containing 50 mg of Losartan Potassium were procured from local market.

Preparation of standard Losartan Potassium solution:

Losartan Potassium (10.1 mg) was accurately weighed and dissolved in 100 ml of 0.01 N HCl to give a stock solution of concentration 101µg / ml.

Preparation of calibration curve for Losartan Potassium:

Aliquots (0.2, 0.4, …. 2.2 ml) from standard solution of Losartan Potassium were pipetted out in to a series of eleven, 10 ml volumetric flasks and the volume was made upto 10 ml with 0.01 N HCl. The absorbances were measured in triplicate at 227.4 nm against reagent blank. The calibration curve was constructed by plotting absorbance v/s concentration (µg/ml). Correlation coefficient was also measured. The Calibration curve data and the summary of analytical parameters are presented in Table 1 and Table 2 respectively.

ESTIMATION OF LOSARTAN POTASSIUM IN TABLET DOSAGE FORM:

For the analysis of Losartan Potassium in tablets, two different brands of 50 mg strength [Losacar-50 (Zydus Medica), Losar-50 (Unichem)] were taken. Twenty tablets each of Losacar-50 and Losar-50 were weighed and powdered. The tablets powder equivalent to 50 mg of Losartan Potassium was accurately weighed for both brands and transferred to, two 100 ml volumetric flasks. 25 ml of 0.01 N HCl was added to both flasks and sonicated for 15 minutes, finally the volume was made up to 100 ml with the same solvent. These solutions were filtered through Whatmann filter paper no. 40. From these stock solutions, test dilutions were prepared by appropriate dilutions to get concentrations with in the range of Beer's law limits. The absorbances of these solutions were measured in triplicate at 227.4 nm against blank. The results are shown in Table 4.

Recovery studies and validation of the method according to I.C.H Q2B guidelines:

Recovery studies were carried out at 80%, 100% and 120% of target concentration. From the amount found, percentage recovery was calculated. Precision of the method was studied by carrying out intraday, interday analysis and expressed as Relative Standard Deviation[4] and are reported in Table 3. The results of recovery studies were found to be satisfactory and are reported in Table 4.

Stability studies of Losartan Potassium:

Stability studies were performed by forced degradation study of Losartan Potassium and it includes the study of effect of temperature, oxidation, photolysis and susceptibility to hydrolysis across a wide range of pH values. For acidic hydrolysis 1.0 N HCl, for basic hydrolysis 0.1 N NaOH, for **oxidation study 3%** H_2O_2 was used. For carrying out photolysis studies the drug was treated with UV light for 4 hrs a day for7 days and thermal stress was applied by heating the drug at 60^0C for 24 hrs. The results are shown in Table 5.

DISCUSSION:

The proposed method for determination of Losartan Potassium showed molar absorptivity of 19.23×10^3 Lt. $mole^{-1}$ cm^{-1} and Sandell's sensitivity of 0.0239 mg/cm^2/ 0.001 absorbance units. Linear regression of absorbance on concentration gave the equation y = 0.0421x-0.0054 with a correlation coefficient (r) of 0.9993. % relative standard deviation for intraday and interday analysis was found to be 0.279 and 0.362 respectively. Limit of detection and limit of quantitation were found to be 0.156 mg/ml and 0.472 mg/ml respectively. The higher percentage recovery value indicates that there is no interference of the excipients present in the formulation. The stability studies indicates that appreciable changes were observed by treating the drug with UV light, Thermal stress, oxidation and basic hydrolysis, however there was no appreciable change with acidic hydrolysis. Thus the method is useful for the determination of Losartan Potassium in bulk and pharmaceutical formulations.

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