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Development and validation of an UV derivative spectrophotometric determination of Losartan Potassium in Tablet

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ABSTRACT

A simple, sensitive and accurate, low cost and requires relatively inexpensive instrument, then it is good alternative *to existing method for determination losartan potassium in tablet . Pharmacopeias have not yet provided an official method for its quantification. Losartan potassium, the method employed is a first derivative spectroscopy a signal at 234 nm of the first derivative spectrum was found adequate for quantification. The linearity between signal 1D234 and concentration of Losartan potassium in the range of 4.00-14µg/ml in aqueous solutions presents a square correlation coefficient (r2) of 0.9996, .the recovery studies confirm accuracy of proposed method and low values of standard deviationconfirm precision of the method, the method is validated as per ICH guideline.*

Keywords: Losartan potassium; Derivative spectrophotometric determination; Tablets

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INTRODUCTION

Losartan Potassium is a member of class I antihypertensive agent It is effectively usedfor the treatment of hypertension and heart disease either singly or sometime with thecombination of diuretics. It is also recommended for the patient having type II diabeticdisease with proteinuria and stroke prevention. This drug is white crystalline, soluble inaqueous medium, selective, non-peptide and angiotensin II receptor antagonist.

The IUPAC name of Losartan Potassium is (monopotassium salt) 2-butyl -4-chloro-1-[[2´ - (1H- tetrazol-5-yl) [1, 1´- biphenyl] -4-yl] methyl] – 1H –imidozole -5- methanol, with thefollowing structure.

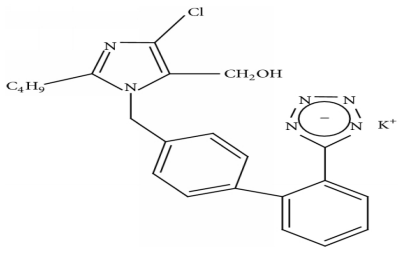

Figure 1. Losartan potassium

Literature reveals that the several analytical methods have been used for the qualitative studies of Losartan Potassium such as high performance liquid chromatography (HPLC), high performance thin layer chromatography (HPTLC) electrochemical radioimmunoassay , reverse phase high pressure liquid chromatography (RP- HPLC). Spectroscopic method was also conducted for determination of Losartan Potassium and UV spectroscopic method has been used for the simultaneous estimation of Losartan Potassium and Hydrochlorothiazide (HCT).[(1)]

Losartan potassium is pharmaceutical market in the form tablet. United State Pharmacopeia [(2)] has not yet incorporated in analytical monograph.

The propose and validate a new procedure to determine Losartan potassiumdrug substance when it is as single active in tablet, based on UV derivative spectrophotometry, which is recommended for losartan potassium in tablet [(3)], but the recommended linear range of the method is very narrow (4 6 µg/ml) and the result was not compared to standard method such as HPLC. The aim of this work was to develop an alternative analytical method that could be used for individual analysis of tablet and fulfilling the requirementsof analytical quality necessary to be applied to the content uniformity test including by for finished pharmaceutical products.

MATERIALS AND METHODS

Reagents and chemical

Losartan potassium salt (99.86 % purity) from GPT INDIA, Methanol highly grade from Scharlaue, SPAN.

Apparatus

UV 1800 spectrophotometry (SHIMADZU), double beam, JAPAN,analytical balance Sartorius CPA2245, GERAMAN and OSCAR ULTRASONIC micro clean -109, INDIA.

Solubility determination

Solubility of Losartan potassium was determined in different solvents. Losartan was found to be soluble in water and methanol.

Stock solution and standard

A standard stock solution 1000µg/ml was prepared by dissolving accurately4.63mg of losartan potassium in 50ml volumetric flask, completed with 50% methanol, this solution was used to prepare further standard solution of the drug.10µg/ml of Losartan potassium, of stock solution were scanned in the range of 200 to 400nm, using methanol 50% as blank.

Selection of Detection Wavelength

Spectrophotometric analysis were performed on Jasco, V-630 spectrophotometer, with 1.00cm quartz cell. The optimized operating condition for recording the first derivative spectra were: scan speed 400nm/min; spectral slit width, 1.5nm; data interval 1nm; Accessory USE -753; an ordinate maximum of -0.02 to 0. 03 measurement were carry out usingfirst derivative of the absorbance spectra.

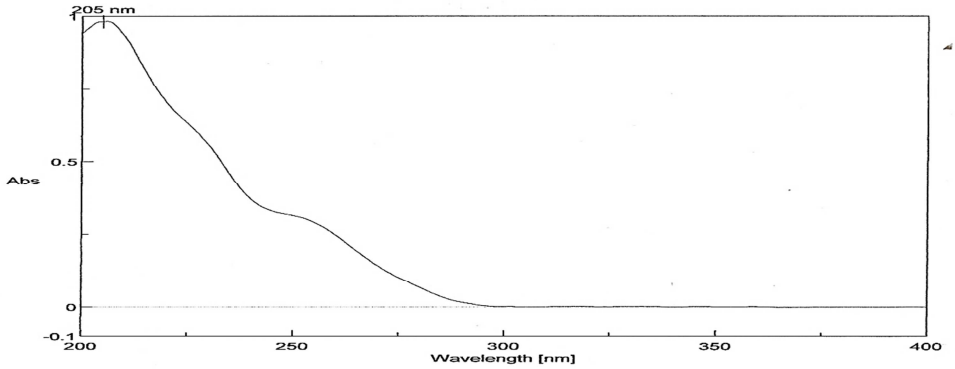

Figure 2. Losartan potassium zero order

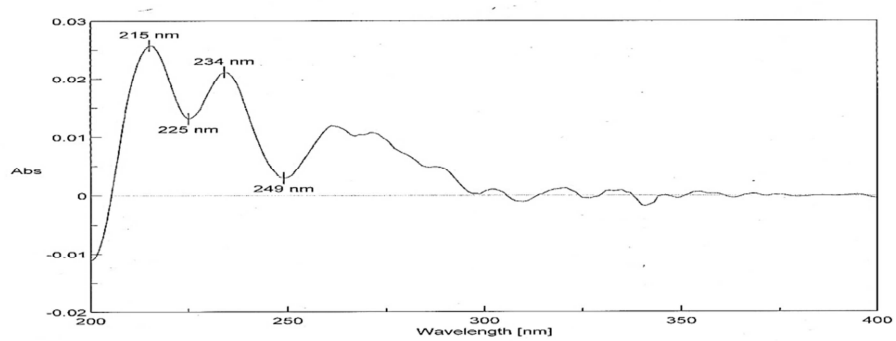

Figure 3. Losartan potassium ID_{234}

Established of optimal level of various parameters:
Standard stock solution of losartan potassium was diluted to yield different concentrations of 4-14 µg/ml.The absorbance was measured at 234nm, the standard curve was plotted against concentration versus absorbance ofdilution,

Market sample analysis
Twenty tablets were weighed and powdered a quantity equivalent to 50mg of losartan potassium was weighted accurately and transfer into dry clean 100ml volumetric flask dissolved in 50% methanol, filtered through whatmann filter paper and made up to the volume.10µg/ml of sample was measured at 234nm.

Recovery studies
To study the accuracy and repeatability of the proposed method, recovery experiments were carried outby adding a known amount of drug to preanalysed sample and the percentage recovery was calculate.

RESULTS AND DISCUSSION

Quantitative analysis of losartan potassium tablets

Table 1. Assay of Losartan potassium in tablet dosage form

Drug	Batch No	Label claim mg/Tablet	Amount * found	%Recovery	%RSD
LOSACAR India	GP1933C	50	50.26	100.52	0.36
Amilosan Sudan	TNS001	50	49.64	99.28	0.49
NILOSAAR Sudan	2NZ02	50	48.95	98.00	0.80
Cozal Sudan	4161	50	50.02	100.04	0.37
ZYLTAN India	Z10528	50	50.92	101.84	0.10

**Average of three determination*

Calculations
LOD (LIMIT OF DETECTION)
It is the lowest amount of analyte, in sample that can be detected. Limit test merely sustained that the amount of analyte is above or below a certain level.

DL =3.3/s.d.s

LOQ (LMIT OF QUANTIFICATION)

It is the lowest concentration of analyte in sample that can be determined with acceptable accuracy and precision.

QL =10/s.d.s

SANDELL' S SENSITIVITY
It is useful to detect the metals present in the sample; it's mainly used for colored compounds

Sensitivity:
The sensitivity is expressed as Sandell's sensitivity:

Concentration of drug/ Absorbance X 0.001

Sensitivity is the concentrationof analyte(in μgmL^{-1}) which will give an absorbance of0.001 in a cell of path length 1cm and expressed as μgcm^{-2}.

Table 2.Sensitivity data of Losartan potassium

Concentration µg/ml	ABS at 234nm	Sandell's sensitivity
4	0.220	0.1818
6	0.324	0.1851
8	0.423	0.1891
10	0.541	0.1848
12	0.637	0.1884
14	0.740	0.1891

Determination of Absorptivity
Molar absorptivity (Ɛ) was calculated from the formula

Ɛ =A/C

Where A = absorbance,

C = Concentration of sample concentration in moles/liter

Table 3.Molar absorptivity of Losartan potassium

Concentration.µ g/ml	ABS	Ɛ
4	0.2204	181.88
4	0.2204	
4	0.2197	
6	0.3239	185.07
6	0.3238	
6	0.3249	
8	0.4229	189.12
8	0.4238	
8	0.4234	
10	0.5405	184.84
10	0.5416	
10	0.5428	
12	0.6363	188.38
12	0.6383	
12	0.6368	
14	0.7409	189.18
14	0.7409	
14	0.7393	

The concentration obeyed beer law .And square correlation coefficient was found to be 0.9996.

Method validation [4, 5]
Linearity:
From the standard stock solution of losartan potassium, pipette out sample to obtain concentration range from (4, 6, 8, 10, 12, and 14µg/ml).

Table 4.Data of calibration curve

Concentration µg/ml	ABS	%RDS
4	0.220	0.18
6	0.324	0.18
8	0.423	0.10
10	0.541	0.21
12	0.637	0.16
14	0.740	0.12

Accuracy:
Accuracy was assessed using over 3 concentration levels covering the specific range (80 -120%).Accuracy was reported as percent recovery by the assay of known added amount of analyte in the sample.

Table 5. Recovery studies:

Sample Added µg/ml	Amount of drug recovered µg/ml	Amount of drug	%recovery
1	4	4.07	101.75
2	6	5.98	99.70
3	8	7.84	98.00
4	10	9.98	99.80
5	12	11.80	98.33
6	14	13.85	98.93

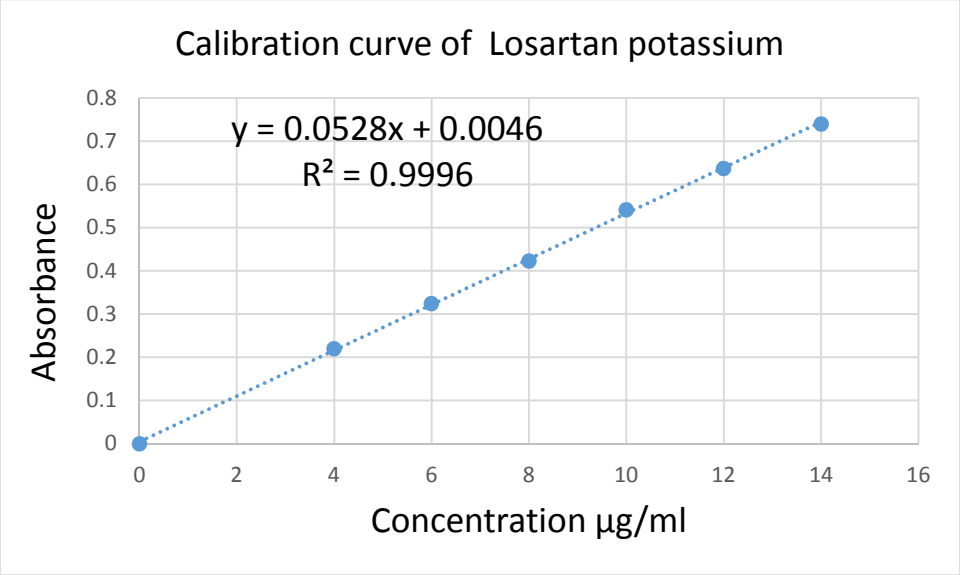

Figure 4. Plotting of data of calibration curve of LOP vs ID_{234} value

Precision:

The precision of the assay were performed by repeatability (intraday) and intermediate precision, sample 10µg/ml and reported as RSD%

Repeatability precision:

Table 6. Repeatability of Losartan potassium

Repeatability precision		Run	Absorbance at 234nm	Assay	% RSD N=6
Sample	Concentration				
Losartan potassium	10µg/ml	1	0.5385	99.89	0.102
		2	0.5393	100.04	
		3	0.5399	100.15	
		4	0.5386	99.90	
		5	0.5397	100.11	
		6	0.5390	99.98	

Intermediate precision:

Intermediate precision of the assay was determined for 10µg/ml concentration at 6 runs.

Table 7.Dataof inter- day intermediate precision

Intermediate precision		Run	Absorbance at 234nm	Assay	% RSD N=6
Sample	Concentration				
Losartan potassium	10µg/ml	1	0.5407	100.15	0.18
		2	05404	100.10	
		3	0.5406	100.13	
		4	0.5397	99.96	
		5	0.5380	99.65	
		6	0.5400	100.02	

Table 8. Validation parameters of Losartan potassium calcium absorption at ID_{234}

Parameters	Results	
Linear range	to14µg/ml	
Molar absorptivity	186.41	
Sandell sensitivity	0.18641	
Regression equation	Y =0.0528x+0.0046	
Correlation coefficient(r^2)	0.9996	
Slope	0.0528	
Intercept	0.0046	
LOD µg/ml	0.317	
LOQ µg/ml	0.9615	

CONCLUSION

The zero order spectra of pure losartan potassium was found to be difficult because it's shows a maximum absorption close to 202 nm and an ill-defined shoulderband featureless , extended from 225 to 240nm, figure 2. This behavior precluded the analytical use zero order absorbance.

The calibration curve plot for the method was linearover the concentration range of 4 -14µg/ml. The determination of coefficients (r2) was found 0.9995, the method was found to be precise and the % RSD value for intra-day 0.102 and inter-day 0.18 respectively it was less than 1%.

Recovery percentage (98.0-101.75) was foundto begood at each added concentration, indicating that the method was accurate. The result of assay showed that the amount of losartan potassium was good agreement with the label claim of formulation as indicated by % assay(99.93).

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