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Spectrophotometric Determination of Losatan Potassium in Pure Form and in tablet dosage form.

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Abstract: Development and validation of analytical UV derivative spectrophotometric method to quantify Losartan potassium used as a single active principle in pharmaceutical forms were done. A study was carried out of all the parameters established by USP XXIV to validate an analytical method for a solid pharmaceutical form, i.e. linearity, range, accuracy, precision and specificity. Based on the spectrophotometric characteristics of the Losartan Potassium respective λmax 232nm shows linearity in a concentration range of 2-12 µg/ml and in aqueous solutions presents a square correlation coefficient (r^2) of 0.9998. The mean % recovery was found to be 99.50, 100.092 and 100.34.[1] The precision expressed as relative standard deviation (%R.S.D.) 0.9243%. In addition, the proposed method is simple, easy to apply, low-cost, does not use polluting reagents and requires relatively inexpensive instruments.[1] Then, it is a good alternative to existing methods for determining Losartan potassium in tablets provided that the pharmaceutical dosage form does not contain hydrochlorothiazide as second drug.
Keyword: Losartan Potassium, UV spectrophotometer, Validation.

Introduction

Hypertension is one of the best established independent risk factors for cardiovascular disease and is common in all populations and all ethnic groups. Hypertension remains a major clinical challenge, because of both the direct consequences of high blood pressure (cerebral haemorrhage, hypertensive heart failure, and progressive renal failure) and the secondary consequence of accelerated atherosclerosis and its complications in the aorta, coronary and cerebral arteries. In developed countries, heart disease and stroke are, respectively, the first- and third- ranked causes of morbidity and mortality.[1, 2] Losartan potassium, an angiotensin II receptor antagonist is the agent to be introduced for the treatment of hypertension. The chemical structure of losartan potassium is shown in Figure 1.

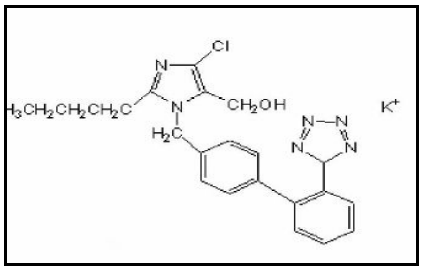

Fig. 1 Losartan potassium

Losartan (I, 2-n-butyl-4-chloro-1-[p-(o-1 H-tetrazol- 5-ylphenyl) benzyl imidazole 5methanol

Monopotassium salts) is a highly selective, orally active, non-peptide angiotensin II receptor antagonist indicated for the treatment of hypertension. It has a more potent active metabolite EXP3174 (II, 2-n-butyl-4-chloro-1-[2-(1H-tetrazol-5 yl) biphenyl- 4-yl) methyl] imidazole-5-carboxyl acid) 1. The determination of Losartan has been carried out in tablets by HPLC, capillary electrophoresis and super-critical fluid chromatography 2, 3, in urine by gas chromatography- mass spectrometry4 and, simultaneously with its active metabolite in biological fluids, by HPLC5- 10.[3]

Materials and Methods:

Material

Spectral runs were made on a Shimadzu UV-Visible spectrophotometer, model- 1700 (Japan) was employed with spectral bandwidth of 0.5 nm and wavelength accuracy of ± 0.3 nm with automatic wavelength corrections with a pair of 10 mm quartz cells. Glassware's used in each procedure were soaked overnight in a mixture of chromic acid and sulphuric acid rinsed thoroughly with double distilled water and dried in hot air oven.[4,5] Losartan Potassium reference standard was kindly provided by Concept Pharmaceutical Ltd., Aurangabad (M. S.) The pharmaceutical preparations of Losartan Potassium that is Losar*-50 (Unichem Laboratories Ltd.) and Losacon-50 (Concept Pharmaceutical Ltd., Aurangabad). All the solutions were protected for light and were analyzed on the day of preparations.

Determination of standard calibration curves and analytical method for the assay of Losartan potassium

In order to determine the standard calibration curve of losartan potassium in distilled water, a stock solution of 50 mg/100 ml in distilled water was prepared. Then dilutions were made to prepare a series of solutions containing losartan potassium in different concentrations.[6] In these solutions absorbance values at 232 nm were determined UV spectrophotometrically and by plotting the concentration values (x) versus absorbance values (y) a calibration curve of losartan potassium in distilled water was obtained.

Validation:

The method was validated according to ICH Q2B guidelines for validation of analytical procedures in order to determine the linearity, sensitivity, precision, Limit of Detection (LOD) and Limit of Quantification (LOQ) and accuracy for the analyte.[7, 8]

Accuracy:

To ascertain the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%). Percent recovery for Losartan Potassium, by both the methods, was found in the range of 99.50, 100.092 and 100.34%.[7, 8]

Linearity:

The linearity of measurement was evaluated by analyzing different concentration of the standard solution of Losartan Potassium. For simultaneous equation method and Q analysis, the Beer- Lambert's concentration range was found to be 2-12 µg/ml for Losartan Potassium.

Precision:

Precision was studied to find out intra and inter-day variations in the test method of Losartan Potassium. Calibration curves prepared in medium were run in triplicate in same day and for three days. %RSD (relative standard deviation) were calculated which should be less than 2 %. The results are tabulated in Table 3.[7, 8]

Limit of Detection (LOD) and Limit of Quantification (LOQ):

The LOD and LOQ of losartan potassium were determined by using standard deviation of the response and slope approach as defined in International Conference on Harmonization (ICH) guidelines. The LOD and LOQ were found to be 0.0412µg/ml and 0.1371 µg/ml.

Table 1: **Linear regression analysis of calibration curves with their respective absorptivity values.**

Parameter	Standard drug
Maximum absorbance	232 nm
Beer's law limit (µg/ml)	2-12 µg/ml
Correlation coefficient (r)	0.9998
Molar absorptivity (lit/mole/cm)	42942.37
Slope	0.0137
Intercept	-0.0022

Table 2: Results of analysis of laboratory samples.

Analyte	Standard drug	Losar*-50	Losacon-50
% Conc. Estimated _ (Mean)	101.87%	99.97%	100.78%
Coefficient of variance	0.018	0.086	0.0174
Label Claim	--------	50mg	50mg
% Label Claim ± R. S. D.	--------	100.025±0.2091	101.015±0.1325

Table 3: Results of intermediate precisions.

Day	% Label claim estimated (Mean ± % R.S.D.)% Label claim estimated		
	Standard drug	**Losar*-50**	**Losacon-50**
Intraday	102.42±0.3544	100.125±0.2133	99.65±0.2229
Interday	102.725±0.1795	101.375±0.1137	99.40±0.3317

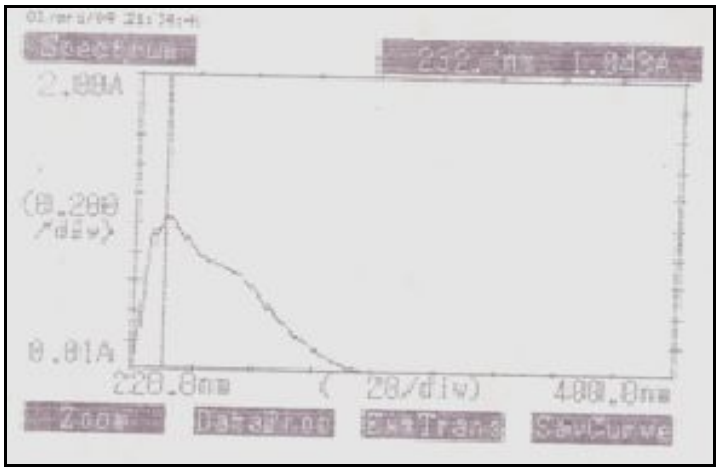

Fig.2. Spectra of Losartan Potassium.

Results and Discussion:

The spectra of Losartan Potassium exhibit λmax 232nm. This wavelength was selected for analysis and it is assume to be sensitive wavelength. Standard calibration curves for Losartan Potassium were linear with correlation coefficients (r) values in 0.9998 at the selected wavelengths.[9] The calibration curves were repeated three times in a day and the average % RSD was found to be 0.9243%, similarly the method was repeated for three different days and average % RSD was found to be 0.8491.[10, 11] The LOD and LOQ were found to be 0.0412µg/ml and 0.1371µg/ml. The accuracy of the method was confirmed by recovery studies from tablet at three different levels of standard additions; recovery in the range of 99.50 to 100.34% justifies the accuracy of method.

Conclusions:

The developed method was found to be simple, sensitive, accurate, precise, reproducible, and can be used for routine quality control analysis of losartan potassium in bulk and pharmaceutical formulation.

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