Research Article

SIMULTANEOUS DERIVATIVE SPECTROPHOTOMETRIC DETERMINATION AND VALIDATION OF LOSARTAN POTASSIUM IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

A literal and specific first derivative UV- spectrophotometric method was raised for the estimation for Losartan potassium in solid pharmaceutical dosage form. Development and validation of an 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. The λ-max of losartan potassium was found to be 234nm to both crude and marketed sample and is analyzed using Beer-Lamberts law. Beer's law was obeyed at the concentrations ranging 4-8 mcg/ml. Based on the spectrophotometric characteristics of Losartan potassium, a signal at 234 nm of the derivative spectrum (234) was found adequate for quantification. The linearity between signal of derivative spectrum (234) and concentration of Losartan potassium in the range of 4.00 - 8.00 mcg/ml in aqueous solutions presents a square correlation coefficient (r^2) of 0.992. The mean recovery percentage was 100.56. In addition, the proposed method is simple, easy to apply, low-cost, does not use polluting reagents and requires relatively inexpensive instruments.

Keywords: Losartan potassium, UV-visible spectrophotometer, Derivative spectrometric determination.

INTRODUCTION

Losartan is a 2-n-butyl-4-chloro-5-hydroxymethyl-1-((2'-(1H-tetrazol-5-yl)(biphenyl-4-yl)methyl) imidazole potassium salt, is a strong antihypertensive agent, non-peptide, and exerts its action by specific blockade of angiotensin-II receptors (fig 1). It develops a gradual and long-lasting effect as antihypertensive, becoming a new alternative to this frequent chronic disease treatment. Losartan potassium is a light yellow solid, molecular weight is 461, melting point is 183.5-/184.5 8C, soluble in water (3.3 mcg/ml at pH 7.8), pKa value is 4.9, and exhibits highly variable and low oral bioavailability (approximately 33%). Losartan is, therefore, considered class 3 in the biopharmaceutics classification system, because it has high solubility and low permeability. It is in the pharmaceutical market in the form of tablets.[1]
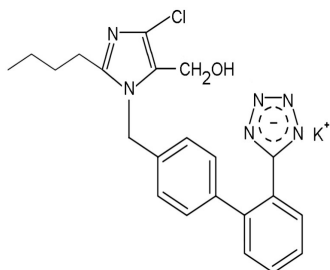

Figure 1: Chemical structure of losartan potassium

We propose and validate a new procedure to determine Losartan potassium drug substance when it is as a single active principle in tablets based on UV derivative spectrophotometry. An analytical method to control the quality of a pharmaceutical form should be under systematical evaluation to verify its usefulness in relation to the purposes of the design. The aim of this work was to develop a method that could be used for the individual analysis of tablets and fulfilling the requirements of analytical quality necessary to be applied to the content uniformity tests indicated by The USP XXIV, for finished pharmaceutical products.

MATERIALS AND METHODS

Instruments

01**.** UV-Vis, Jasco-V 630 with 1 cm quartz cells

02. Ultrasonic bath, Dolphin 3.5L (100H)

03. Analytical Balance, Shimadzu-AY220

Chemicals

Losartan potassium, 1M sodium hydroxide solution, distilled water, 0.1 M phosphoric acid, 0.1 M acetic acid and 0.1 M boric acid.

Methods[2-4]

Preparation of Standard Stock Solution

A standard stock solution (1000 mcg/ml) was prepared by dissolving accurately 50 mg of crude losartan potassium in dist. water. This stock solution was used to prepare further standard solutions of the drug. And a 100 mcg/ml solution was prepared by dissolving 1 ml of standard stock solution in 10ml of distilled water.

Marketed Sample solution

A commercially available 50 mg Losartan potassium tablet was dropped into a 100 ml volumetric flask and some distilled water was added. It was treated in ultrasonic

bath for 10 min and then distilled water was added to complete the volume, filtered through Whatman filter paper. Some supernatant was used for the determination and further dilutions are made.

Spectrophotometric measurements

The absorbance of the solutions containing Losartan potassium at 5.00 mcg/ml was determined in the UV range 200-270 nm. The derivative spectra were obtained by instrumental electronic differentiation in the range of 220-260 nm. The amplitude values obtained in the first derivative spectra were arbitrary units of the distance from the central zero base line to the negative peak obtained at 234 nm (fig 2).

Losartan potassium standard solution with excipients (500mcg/ml)

50.20 mg Losartan potassium standard and 106.5 mg of an excipient mixture (containing 1.7% magnesium stearate, 42.7% cellulose microcrystalline, 42.7% lactose, 12.8% talc) were transferred to a 100-ml volumetric flask and treated in ultrasonic bath for 10 min and then dist. water was added to complete the volume, filtered through Whatman filter paper. Lastly further dilutions are made.

Effect of pH on the spectrophotometric behavior of Losartan potassium solution

The 1 ml aliquots of Losartan potassium standard stock solution were transferred to the respective100 ml volumetric flasks and volume was completed with 0.1 M Britton-/Robinson buffer previously adjusted to the required value with a 1 M sodium hydroxide solution. A blank solution of the correspondent buffer was used in the measurement. The spectra of Losartan potassium between pH 2 and 9 were registered. First derivative spectra of 5.00 mcg/ml aqueous solutions of Losartan potassium adjusted at pH from 2 to 9 with Britton-Robinson buffer solution. A blank solution of the corresponding B-R buffer was placed in the reference beam of the spectrophotometer.

0.1M Britton-Robinson buffer solution

0.1M Britton-Robinson buffer solution was prepared by using 0.1 M phosphoric acid, 0.1 M acetic acid and 0.1 M boric acid in equal volumes.[6]

Method Validation[5-9]

Determination of linearity and range

Five aliquots of Losartan potassium standard stock solution were taken in triplicate and transferred to respective 100 ml volumetric flasks in such amounts as to obtain final concentrations of 4.00, 5.00, 6.00, 7.00 and 8.00mcg/ml of Losartan potassium. Volume was made with distilled water and each flask content was measured to determine first derivative spectrum (234) value (table 1, fig 2 and 3).

Table 1: Experimental data of losartan potassium

Concentration (mcg/ml)	Absorbency			
	1st time	2nd time	3rd time	Mean
4	0.0690	0.0695	0.0696	0.0693
5	0.0777	0.0789	0.0778	0.0781
6	0.0847	0.0838	0.0848	0.0844
7	0.0920	0.0929	0.0928	0.0925
8	0.1028	0.1038	0.1034	0.1033
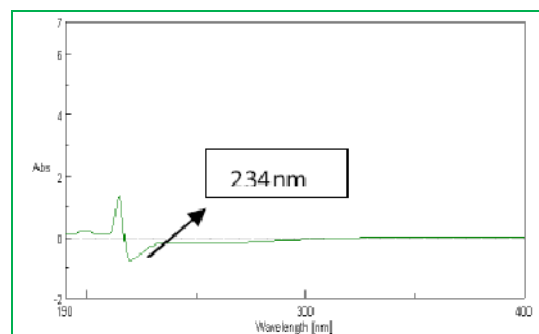
Figure 2: λ-max of Losartan Potassium

$y = 0.008x + 0.036$
$R^2 = 0.992$

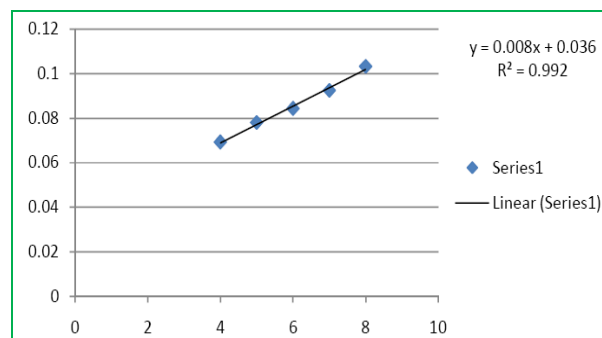**Figure 3:** Linearity graph of Losartan potassium.

Determination of precision

Five 1 ml aliquots of Losartan potassium standard solution with excipients were transferred to respective 100-ml volumetric flasks and volume was completed with distilled water. A portion of each of these solutions was transferred to the sample cuvette of the spectrophotometer and the values first derivative spectrum (234) were measured and recorded.

Determination of accuracy

Aliquots of Losartan potassium standard solution with excipients obtained after centrifugation were transferred to 100 ml volumetric flasks, in triplicate, for preparing solutions of 4.00, 5.00, 6.00, 7.00 and 8.00mcg/ml. Spectrophotometric measurements were taken and values of first derivative spectrum (234) for each solution were determined and recorded (table 2). Also Losartan potassium standard stock solution prepared and from this Losartan potassium standard stock solution prepared 8.00, 10.00, 12.00, 14.00 and 16.00 mcg/ml. After shaking carefully, values of first derivative (234) were measured. This operation was done in also triplicate (table 3).

Assay of pharmaceutical samples

A 50 mg Losartan potassium tablet was dropped into a 100 ml volumetric flask. Then aliquots were measured

and the first derivative was obtained. Losartan determination was performed by means of a calibration curve.

The final drug content was calculated by the formula:

mg of Losartan content/dosage form = (First derivative$_{234}$ – a)/b*10

Where,

First derivative$_{234}$ - spectrophotometric measurement of the sample;

a - The intercept of the calibration curve first derivative spectrum (234) versus conc. of Losartan potassium;

b - The slope of the calibration curve first derivative (234) versus conc. of Losartan potassium;

10 - Dilution factor.

Table 2: Recovery results for Losartan potassium solution with excipients

Concentration (mcg/ml)	Found* (mcg/ml)	Recovery (%)	R.S.D. (%)
4	4.09±0.02	102.25	0.42
5	5.05±0.04	101.00	0.22
6	5.98 ±0.02	99.66	0.35
7	7.01±0.01	100.14	0.77
8	7.98±0.02	99.75	0.47

R.S.D – Relative standard deviation; * data presented as mean±SD

Table 3: Recovery results for Losartan potassium standard solution

Concentration (mcg/ml)	Found* (mcg/ml)	Recovery (%)	R.S.D. (%)
8	8.02±0.02	100.25	0.12
10	10.04±0.02	100.40	0.23
12	11.96±0.04	99.66	0.43
14	13.98±0.03	99.85	0.17
16	16.01±0.01	100.06	0.22

R.S.D – Relative standard deviation; * data presented as mean±SD

Determination of content uniformity of tablets

Each one of the three pharmaceutical forms (doses of 50 mg) was treated and aliquots were measured and recorded (table 4). The acceptance criteria correspond to those established by USP XXIV.[10]

Table 4: Content uniformity of Losartan potassium tablets

Name of formulation	Label claim (mg)	Amount found (mg)	% Label claim
Losar	50	50.22	100.44
Cozaar	50	51.20	102.40
Ovance	50	49.31	98.62

RESULTS AND DISCUSSION

The UV spectrum in aqueous solution of Losartan potassium shows an absorbance maximum close to 200 nm and extending from 220 to 260 nm. This behavior precludes the analytical use of absorbance if the aim is optimization of parameters of analytical quality. Otherwise, the first derivative spectrum shows an intense maximum at 234 nm with evidently useful characteristics from the analytical viewpoint. Variation in pH from 5 to 9 of aqueous Losartan potassium solution did not alter the spectral characteristics, thus it is unnecessary buffering, since an aqueous solution is sufficient as is shown by the recovery assay in the accuracy determination. The linearity of spectrophotometric measurement for Losartan potassium solutions within the concentration range 4.00 - 88.00 mcg/ml, equivalent to 80-120% of the nominal value of a tablet, was satisfactory. The accuracy studied by means of assays of recovery in Losartan potassium solutions and Losartan potassium with excipients gave mean values of 99.66 and 102.25%, respectively. The results are shown in tables. It can be seen that the excipients used in the preparation of the pharmaceutical form (magnesium stearate, cellulose microcrystalline, lactose and talc) do not interfere in the determination. So, this spectrophotometric method is appropriate to determine content uniformity of Losartan potassium when this is the only active principle in pharmaceutical forms. Finally, content uniformity test was performed in accordance with the requirements of USP XXIV with tablets of commercial brand. Three tablets, individually processed as indicated in solution were found to contain between 98.62 and 102.40% of the nominal value, meeting values with the requirements. In relation to the other methods to determine Losartan potassium in tablets mentioned in literature, this derivative spectrophotometric method presents a similar accuracy and precision and a lower sensitivity, but enough for the proposed goals.

CONCLUSION

The developed method is an alternative to determine Losartan potassium in pharmaceutical dosage forms that contain it as unique active principle with quite satisfactory results for the specific purposes of its design. Its advantages over other existing methods are its simplicity, fastness, low-cost and non-polluting conditions.

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