Research Article

Development and Validation of UV Spectrophotometric Method for the Estimation of Lisinopril in Bulk and Pharmaceutical Formulation

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Accepted on: 09-01-2014; **Finalized on:** 28-02-2014.

ABSTRACT

To develop simple, economical, precise and less time consuming UV method for the estimation of Lisinopril in bulk and pharmaceutical formulations. Though HPLC methods are official in Pharmacopoeias some Non chromatographic methods developed by chemical modification of Lisinopril or simple coupling reactions were equally competent. The method is based on UV spectroscopic technique. Lisinopril shows the maximum absorbance at 218nm in absorption maxima method. Drug followed the linearity in the range of 2-12µg/ml for this method with correlation coefficient (r^2) of 0.9994. The results of analysis have been validated statistically and recovery studies confirmed the accuracy of the proposed method. The method was validated as per the International Conference on Harmonization (ICH) guidelines. The proposed method is recommended for routine analysis since it is rapid, simple, accurate and sensitive.

Keywords: Absorption maxima method, HPLC, Lisinopril, UV spectrophotometry.

INTRODUCTION

Lisinopril[1-2]is chemically named as N2-[(1S)-1-carboxy-3-phenylpropyl]-L-lysyl-L-proline, is official in IP, BP and USP.[3-7] This most popular antihypertensive agent first developed by the Merck Index as ACE inhibitor and used in single or in combination with other anti-hypertensive or diuretics like Chlorthiazide.[8] Drug Regimen Prescribed for the hypertensive patients of Lisinopril is 1.1%. Literature review shows that there are developed methods including spectrophotometric, atomic absorption, HPLC and LC-MS method for the estimation of Lisinopril.There are developed Spectrophotometric methods [9-11] of analysis in single or in combination. Lisinopril shows absorption in UV-visible range in alkaline media produced by sodium hydroxide was measured in absorption maxima method. The spectrofluioremetric[12-13] methods of analysis were developed to estimate Lisinopril present in small quantities i.e., in nanogramms in blood or plasma. In the present investigation simple and sensitive UV spectrophotometric method have been developed for the quantitative estimation of Lisinopril in bulk and its marketed formulations with good accuracy and economy.

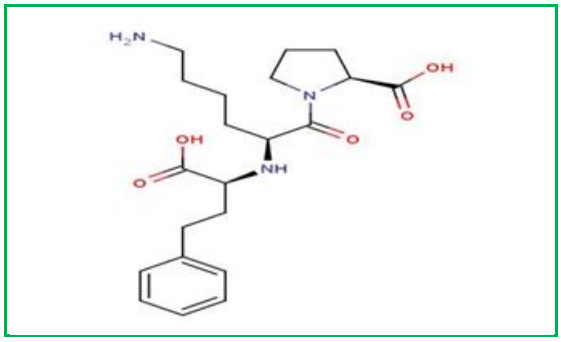

Figure 1: Structure of Lisinopril

MATERIALS AND METHODS

All the chemicals used during the experimental work are of Analytical grade. Lisinopril standard was procured from Chandra labs, Kukatpally, Hyderabad. Tablet formulation containing Lisinopril-2.5 mg was obtained commercially. NaOH pellets were procured from Merck Ltd.

Instrumentation

Analytical balance of Shimadzu type BL-220 and Shimadzu UV-1800 UV/VIS Spectrophotometer was used with 1cm matched quartz cells. The equipment was controlled by a PC installed properly with the UV probe software.

Preparation of standard solution

The pure drug of about 10 mg was weighed and transferred in to a 10ml volumetric flask. The drug was dissolved completely in a few ml of 0.1N NaOH and made up to the final volume with NaOH to get a stock solution of concentration 1000µg/ml. Aliquots of standard stock solution were pipette out and diluted suitably with water to get the final concentration of standard solutions.

Absorption maxima method

The solutions were scanned in the range of 400-200 nm against 0.1N NaOH as reference, and the peaks were observed in the spectra at 218nm. The wavelength selected for analysis of drug was 218nm. The drug obeys the lamberts law in the range of 2-12 µg/ml. By using linearity plot the quantification was carried out.

Optical characteristics

Optical characteristics such as Beer's law limit (µg/mL), Correlation coefficient, Regression equation, Slope (m), and Intercept (c) were calculated.

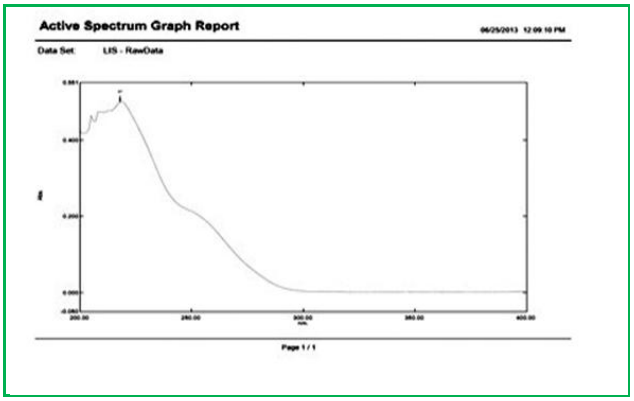

Figure 2: Absorption maxima spectrum of Lisinopril

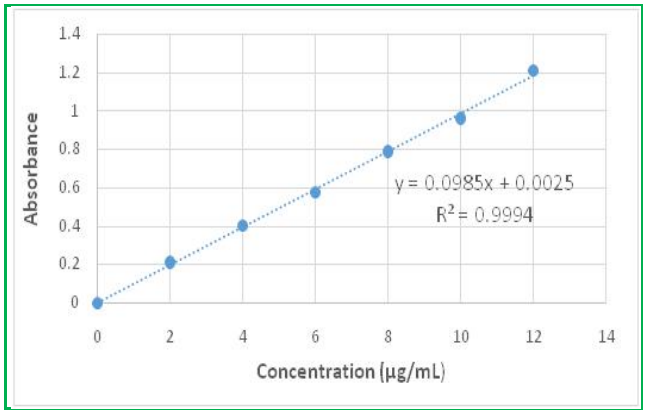

Figure 3: Calibration curve of Lisinopril at 218nm

Table 1: Optical characteristics

Optical characteristics	Method A
Beer's law limit (µg/ml)	2-12
Correlation coefficient (r^2)	0.9994
Regression equation	y = 0.0985x + 0.0025
Slope (a)	0.0985
Intercept (b)	0.0025
LOD	0.085µg/ml
LOQ	0.257µg/ml

Analysis of tablet formulation

For the estimation of Lisinopril in pharmaceutical formulation by above method, 10 tablets of LIPRIL-2.5 brand were weighed and triturated to a fine powder. Tablet powder equivalent to 10mg was weighed and transferred to 100ml volumetric flask and dissolved in few ml of 0.1N NaOH with the aid of ultra-sonication for 15min; this was filtered through whatman filter paper no. 41 to get the stock solution of 100 µg/ml various dilutions were prepared from tablet solution and analyzed for six times and the concentration for both the methods was calculated by using calibration curve.

Validation of Analytical Methods

The analytical methods were validated according to ICH validation parameters.[14]

Linearity

Fresh aliquots were prepared from standard stock solution ranging from 2-12 µg/ml and the absorbance values of each concentration was recorded at 218nm for this method using NaOH as blank. The drug shows linearity between 2-12 µg/ml for this method.

Table 2: Analysis of Formulation

Drug	Label Claim (mg/ Tablet)	Amount* Found (mg/ Tablet)	% Amount Found	% RSD
Lisinopril	2.5	2.54	101.6	1.18%

*Mean of three readings

Table 3: Linearity of Lisinopril

Concentration in µg/ml	Absorbance
	UV Method
2	0.211
4	0.403
6	0.575
8	0.790
10	0.964
12	1.211

Precision

In intraday study, concentration of replicates of drug was calculated on the same day for three times. In inter-day study the concentration of drug were calculated on three successive days which expresses the laboratory variation in different days. In both intra and inter day precision study for the methods %RSD was calculated.

Accuracy

Accuracy of the developed method was confirmed by performing recovery studies at three different concentration ranges 80%, 100%, 120% each one in triplicate. From the recovery studies it was clear that the method is very accurate for quantitative estimation of tablet as the statistical results were within the acceptance range.

Limit of Detection and Limit of Quantification

The limit of detection and limit of quantification of Lisinopril by proposed methods were determined using calibration graphs. LOQ and LOD were calculated as;

$$LOD = 3.3 \times S.D/S$$

$$LOQ = 10 \times S.D/S$$

Where S is the slope of the calibration curve and SD is the standard deviation of response of least concentration of calibration curve in three replicates.

Robustness

Robustness of the method was determined by carrying out the analysis at five different wavelengths (±0.5nm).

The respective absorbance was noted and the result was indicated by % RSD.

Ruggedness

Ruggedness of the method was determined by carrying out the analysis by two different analysts and the respective absorbance was noted. The result was indicated by % RSD.

RESULTS AND DISCUSSION

The developed method was found to be precise as the %RSD values for intra-day and inter-day were found to be less than 2%. Good recoveries (98.75% to 100.45%) of the drug were obtained at each added concentration, which indicates that the method was accurate. The LOD and LOQ were found to be in sub-microgram level, which indicates the sensitivity of the method. The method was also found to be robust and rugged as indicated by the %RSD values which are less than 2%. The results of assay show that the amount of drug was in good agreement with the label claim of the formulation as indicated by % recovery (101.6%).

Table 4: Accuracy studies of Lisinopril

Method	Amount of µg/ml		% of drug added	Amount recovered	% Recovered	% RSD
	Tablet	Pure drug				
UV	4.0	3.2	80	7.18	99.72	0.86
	4.0	4.0	100	7.98	98.75	
	4.0	4.8	120	8.84	100.45	

Table 5: Summary of validation

Parameter	Result
Linearity indicated by correlation coefficient	0.9994
Precision indicated by %RSD	0.86%
Accuracy indicated by % recovery	98.75-100.45 %
Limit of detection (LOD), µg/mL	0.085
Limit of quantitation (LOQ), µg/mL	0.257
Linear regression equation	y = 0.0985x + 0.0025
Robustness indicated by %RSD	0.67
Ruggedness indicated by %RSD	0.57
Assay indicated by % purity	101.6%

CONCLUSION

The proposed methods are simple, sensitive, and cost-effective. Validated in terms of precision, linearity and accuracy. The results are reproducible, and can be used successfully for the estimation of Lisinopril in bulk and its pharmaceutical formulations.

Acknowledgement: The author is thankful to Prof. A.Prameela Rani and University College of pharmaceutical sciences, Acharya Nagarjuna University, Guntur for providing necessary laboratory facilities.

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Source of Support: Nil, **Conflict of Interest:** None.