DEVELOPMENT AND VALIDATION OF A UV SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF LISINOPRIL BOTH IN BULK AND MARKETED DOSAGE FORMULATIONS

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Development and validation of a UV spectrophotometric method for the determination of lisinopril both in bulk and marketed dosage formulations

Abstract:

Lisinopril is angiotensin converting enzyme inhibitor widely used in management of blood pressure and congestive heart failure. This study proposes a simple, rapid and economic method of analysis of lisinopril in bulk as well as in formulation using UV spectrophotometer. The present method has been developed in distil water which makes it economic and reproducible. Absorption maxima was obtained at 206nm. The method is validated using ICH Q2R1 guideline for various parameters like precision, accuracy, limit of detection, limt of quantitation etc. Drug follows lineariy in concentration range 10-50 µg/ml with correlation coefficient value (r^2) 0.999. The accuracy study was performed by recovery checking at three different concentrations i.e., 80%, 100% and 120 %. The % recovery was found to be in the range 99.27%– 99.95%. The precision of the method was studied as an intra-day, inter-day variations and repeatability. The % R.S.D. value less than 2 indicate that the method is precise. The proposed method is a cost-effective quality-control tool for routine analysis of lisinopril in pharmaceutical dosage form.

Keywords: Lisinopril, ICH Q2R1, Distill water, UV spectrophotometer.

1. Introduction

Lisinopril is called ACE inhibitors. ACE stands for angiotensin converting enzyme. Lisinopril used in high blood pressure (hypertension), congestive heart failure, and in heart attack.

Lisinopril is the angiotensin converting enzyme (ACE) inhibitor that is used in treatment of hypertension, heart attacks, congestive heart failure also in renal and retinal complications of diabetes. Lisinopril is effective management of hypertension and cardiac diseases. Its onset of action is 1-2 hours. Duration of action is 24 hours .Absorption of the lisinopril is slowly and incompletely from GI tract(oral) and peak plasma concentration obtain after 7 hours. Lisinopril absorption not affected by food material .The drug distribution is up to 25%. Lisinopril does not undergo metabolism and excreted by urine in unchanged form. The drug is given orally in case of hypertension. Adult dose is initially 5-10 mg daily given at bedtime. Dose of drug in renovascular hypertension, volume depletion, severe hypertension; Initially 2.5-5 mg once daily. In diuretic patients 5 mg once daily. Maintenance of the dose i.e. 20 mg once daily up to 80 mg daily may be used . In case of children ≥6 years: initially up to 0.07 mg/kg(up to 5 mg once daily) can be given. Bioavailability of the drug is approximately up to 25%, but wide range of 6-60% is also reported.

Properties of lisinopril:

Lisinopril is a white, crystalline powder, having a molecular weight of 441.52 and molar mass of 40.488g/mol. It is soluble in water and sparingly soluble in methanol and practically insoluble in ethanol, acetone, acetonitrile and chloroform.

Table 1 Properties of Lisinopril

content	values
water soluble value	13 g/m
Density	1.21gcm^3
Log P	-0.9
PKa	3.85
Melting point	160^{0c}

IUPAC name of lisinopril is *N*2-[(1*S*)-1-carboxy-3-phenylpropyl]-L-lysyl-L-proline, is Official in IP. BP and USP[1-5].It is most popular antihypertensive agent. It was first developed by the Merck Index as ACE inhibitor. Used in single or in combination with other anti-hypertensive or diuretics like chlorthiazide. There are various methods of analysis for Lisinopril are reported in literature.

2. Materials and methods

2.1 Apparatus

A UV-visible spectrophotometer (Shimadzu, model 1800) with 1 cm quartz cells was used for the absorbance measurements.

2.2 Materials

Lisinopril in the form of powder was provided by Lupin, Aurangabad, which was used as the reference standard.

2.3. Determination of wavelength of maximum absorption

A standard stock solution of Lisinopril (100 µg/ml) was prepared using distil water as diluents and 1 to 5 ml of standard solution was then diluted to obtain 10 ml with water to obtain 10 to 50 µg/ml lisinopril reference solution. An UV spectroscopic scanning (200– 400 nm) was carried out to determine the λ max. Water used as blank.

2.4. Linearity and range

For linearity study, five different concentrations (10, 20, 30,40,50 µg/ml)were prepared using stock solution, and the obtained data were used for the linearity calibration plot. Limit of detection(LOD)and limit of quantification(LOQ) were also calculated .

2.5. Intra-day precision (repeatability) and inter-day precision study (intermediate precision)

Prepare stock solution of 100 µg/ml of Lisinopril The five different aliquots were then diluted 10ml to obtain the concentrations of 10, 20 to 50 µg/ml.This procedure was repeated in the following days.

Table 2 Intra-day precision determined for five different concentrations of lisinopril

Concentration (µg /ml)	Absorbance measured (Mean ± SD)	RSD (%)
10	0.3616±0.0004	0.130
20	0.6910±0.0008	0.118
30	1.1176±0.0021	0.193
40	1.4470±0.0037	0.258
50	1.7226±0.0009	0.054

Table3 Inter-day precision determined for five different concentrations of lisinopril

Concentration (µg /ml)	Absorbance measured (Mean ± SD)	RSD (%)
10	0.4573±0.0004	0.103
20	0.7823±0.0009	0.120
30	1.2203±0.0012	0.102
40	1.5323±0.0012	0.081
50	1.7906±0.0028	0.160

2.6. Stability study

Samples prepared for repeatability study were preserved for 24 h at room temperature and analyzed on the following day to test for short-term stability.

Table 4 Stability study

Conc (µg /ml)	Mean±SD(µg /ml)	RSD%
10	0.3616±0.0004	0.130
20	0.6910±0.0008	0.118
30	1.1176±0.0021	0.193
40	1.447±0.0037	0.258
50	1.722±0.0009	0.054

2.7. Accuracy/recovery study

Lisinopril tablets were finely powdered and the sample stock solution of 100µg/ml was prepared. To preanalyzed sample solution, a known amount of standard stock solution was added at different level i.e. 80%, 100% and 120%.

Table 5 Accuracy study

Dosage form	Label claim	Amount added (%)	Recovery(%)
Brand 1	10 mg	80	99.951
		100	99.27
		120	98.02
Brand 2	10 mg	80	99.66
		100	100.42
		120	98.19

3. Results and discussion

3.1. Method development and optimization

Lisinopril is water soluble drug use distill water for dilution. The wavelength of lisinopril was found to be (λ max) was 206nm.

3.2. Method validation

3.2.1. Linearity and range

The calibration curve obtained was evaluated by its correlation coefficient .The absorbance of the samples in the range of 10–50µ g/ml was linear with a correlation coefficient (R2) 0.999.The LOD and LOQ were calculated as 0.079206 µ g/ml and0.23824 µ g/ml respectively.

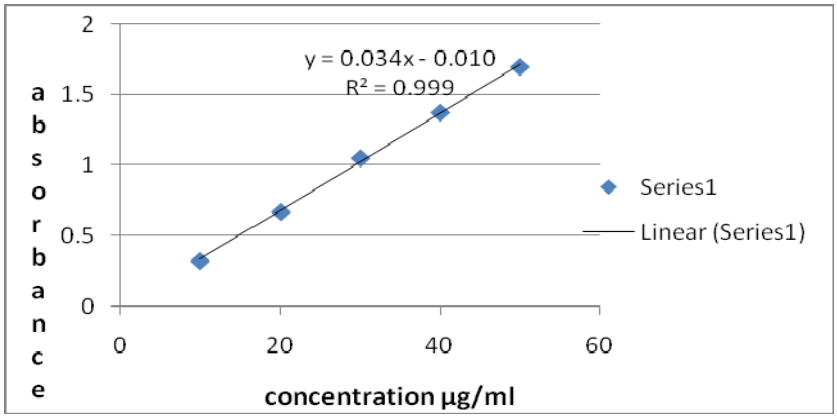

Figure 1 Calibration Curve of Lisinopril

Table 6 Concentration of Lisinopril

Concentration µg/ml	Absorbance
10	0.325
20	0.672
30	1.053
40	1.376
50	1.689

3.2.2. Intra-day and inter-day precision

The intra-day and inter-day precision stud confirmed adequate sample stability and method reliability where all the RSDs were <2%.

3.2.3. Stability

Stability study's results were within the acceptance range and indicated the samples stability over 24h (short-term).

3.2.4. Accuracy/recovery

Results within the range of 98.0% to 102.0% ensure an accurate method as well as indicate non-interference with the excipient of formulation.

4. Conclusion

The present method is simple, reproducible and economic for routine analysis of lisinopril in bulk and dosage form. This method is proved to be specific for determination of lisinopril in presence of excipients and related substances.

Analytical method development mainly involves method which is precise, simple, accurate and having advantages over existing methods. For this purpose literature survey was carried out which was found to be beneficial further developing a method. Literature survey revealed no reported UV –Visible spectrophotometric method till date reported to the best of our knowledge.

Acknowledgment

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