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Development and validation for determination of lisinopril dihydrate in bulk drug and formulation using RP-HPLC method

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ABSTRACT

A simple, reproducible and efficient reverse phase high performance liquid chromatographic method was developed for Lisinopril in bulk drug and formulation. A column having 150 × 4.6 mm in isocratic mode with mobile phase containing acetonitrile: phosphate buffer (70:30; adjusted to pH 3.0) was used. The flow rate was 0.8 ml/min and effluent was monitored at 216 nm. The retention time (min) and linearity range (μg/ml) for Lisinopril was (1.510) and (10-35). The developed method was found to be accurate, precise and selective for determination of Lisinopril in bulk and formulation.

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INTRODUCTION

Lisinopril (Figure 1) is an orally bioavailable, long-acting angiotensin-converting enzyme (ACE) inhibitor with antihypertensive activity. Lisinopril, a synthetic peptide derivative, specifically and competitively inhibits ACE, which results in a decrease in the production of the potent vasoconstrictor angiotensin II and, so, diminished vasopressor activity. In addition, angiotensin II-stimulated aldosterone secretion by the adrenal cortex is decreased which results in a decrease in sodium and water retention and an increase in serum potassium [1–3]. Literature survey reveals the availability of several methods by using various Mobile phases but no method was available on this Mobile phase that is acetonitrile: phosphate buffer (70:30; adjusted to pH 3.0) which was a unique method with better results [4–6].

MATERIALS AND METHODS

Chemicals and reagents

The reference sample of Lisinopril was supplied by wockhardt Pharmaceutical Industries Ltd., Aurangabad. HPLC grade water and acetonitrile were purchased from Merck (India) Ltd., Mumbai. Potassium dihydrogen phosphate and orthophosphoric acid of AR Grade were obtained from, Research Lab (India) Ltd [7, 8].

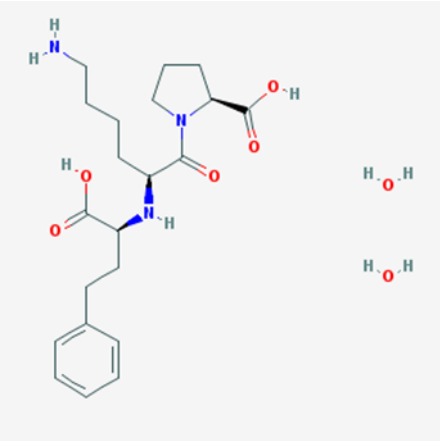

Figure 1: Structure of Lisinopril dihydrate

Chromatographic conditions

The analysis of the drug was carried out on a Waters HPLC system equipped with a reverse phase Xterra C18 column (150mmx4.6mm; 5μm), a 2695

Table 1: Calibration data of lisinopril

Concentration(μg/ml)	Mean peak area (n=6)
10	742315
15	1419822
20	2121436
25	2810895
30	3531268
35	4265201

Table 2: Precision studies for lisinopril

Concentration of lisinopril (10μg/ml)	Peak area	
	Intra-day	Inter-day
Injection-1	1021546	1052530
Injection-2	1020125	1075203
Injection-3	1030560	1061251
Injection-4	1019832	1081789
Injection-5	1047695	1078415
Injection-6	1021346	1084812
Average	1026851	1072333
Standard Deviation	10965.24	12691.25
% RSD	1.067852	1.183517

Table 3: Accuracy studies for lisinopril

% Concentration	Amount added (mg)	Amount found (mg)	% Recovery	% Mean recovery
80	18	17.95	99.72	99.64
100	20	19.80	99.00	
120	22	22.05	100.22	

Table 4: System suitability parameters

Parameter	Result of lisinopril
Linearity (μg/ml)	10-35
Correlation coefficient	0.999
Tailing factor	1.6
LOD (μg /ml)	0.010024
LOQ (μg /ml)	0.030374
Specificity	Specific
Precision	Intra-day 1.067852 Inter-day 1.183517
Accuracy	99.64

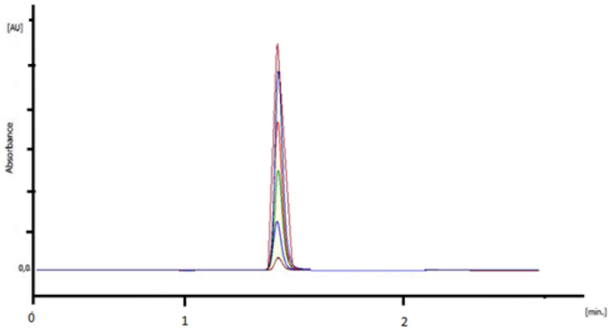

Figure 2: Linearity peak of lisinopril

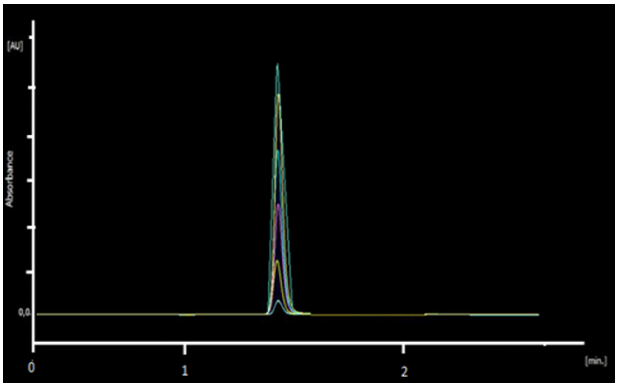

Figure 3: From the instrument linearity peak of lisinopril

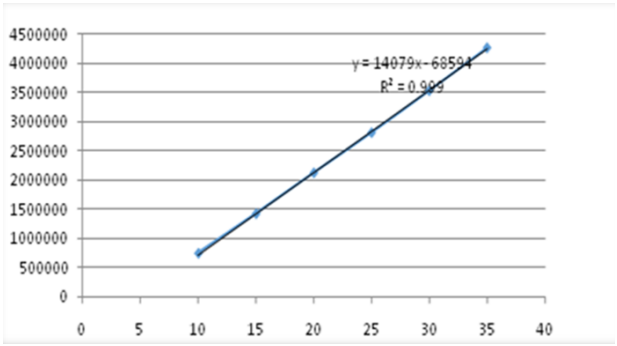

Figure 4: Linearity curve of lisinopril

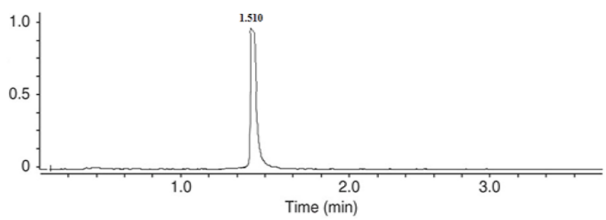

Figure 5: Typical chromatogram of lisinopril

binary pump, a 20μl injection loop and a 2487 dual absorbance detector and running on Waters Empower software. The UV spectrum of the drugs was taken using a shimadzu 1800 UV/VIS double beam spectrophotometer.

Preparation of phosphate buffer (pH 3.0)

7 gm of KH_2PO_4 was weighed into a 1000 ml beaker, dissolved and diluted to 1000 ml with HPLC water and pH adjusted to 3.0 with orthophosporic acid.

Preparation of mobile phase and diluents

300 ml of the phosphate buffer was mixed with 700ml of acetonitrile. The solution was degassed in an ultrasonic water bath for 5 minutes and filtered through 0.45 μ filter under vacuum.

Procedure

A mixture of buffer and acetonitrile in the ratio of 30:70 v/v was found to be the most suitable mobile phase for lisinopril. The solvent mixture was filtered through a 0.45 μ membrane filter and sonicated before use. It was pumped through the column at a flow rate of 0.8 ml/min. The column was maintained at ambient temperature. The pump pressure was set at 900 psi. The column was equilibrated by pumping the mobile phase through the column for at least 30 min prior to the injection of the drug solution. The detection of the drug was monitored at 216 nm. The run time was set at 9 min. Under these optimized chromatographic conditions the retention time obtained for the drugs lisinopril was 1.510 min [9, 10].

Calibration plot

About 100 mg of lisinopril was weighed accurately, transferred into a 100 ml volumetric flask and dissolved in 50 ml of a 30:70 v/v mixture of phosphate buffer and acetonitrile. The solution was sonicated for 15 min and the volume made up to the mark with a further quantity of the solvent to get a 1000 μg/ml solution. From this, a working standard solution of the drugs (10μg/ml for lisinopril) was prepared by diluting the above solution to 10 ml in a volumetric flask. Further dilutions ranging from 10-35 μg/ml for lisinopril was prepared from the solution in 10ml volumetric flasks using the above diluents. 20μl of each dilution was injected six times into the column at a flow rate of 0.8 ml/min and the corresponding chromatograms were obtained. From these chromatograms, the average area under the peak of each dilution was computed. The calibration curve constructed by plotting concentration of the drug against peak area was found to be linear in the concentration range of 10-35μg/ml for lisinopril. The relevant data are furnished in Table 1 and Typical Chromatogram was shown inFigures 2,

3 and 4. The regression equations of this curves was computed.

Validation of the proposed method

The specificity, linearity, precision, accuracy, limit of detection, limit of quantification, robustness and system suitability parameters were studied systematically to validate the proposed HPLC method for the determination of lisinopril. Solution containing 10μg/ml for lisinopril was subjected to the proposed HPLC analysis to check intra-day and inter-day variation of the method and the results are furnished in Table 2. The accuracy of the HPLC method was assessed by analyzing solutions of lisinopril at 80%, 100% and 120% concentrated levels by the proposed method. The results are furnished in Table 3. The system suitability parameters are given in Table 4.

Linearity

LOD and LOQ studies of lisinopril

The limit of detection and limit of quantification for lisinopril was found to be 0.0101 and 0.0303 respectively, which indicate the sensitivity of the method.

Specificity studies of lisinopril

The specificity of the method was ascertained by analyzing standard drug and sample. The spot for lisinopril in sample was confirmed by comparing the Rf and spectra of the spots with that of standards indicating no interference of any another peak of mobile phase, impurity.

Precision studies for lisinopril

Precision of the method was performed by intra-day and inter-day studies. The % RSD values obtained from peak area for lisinopril was 1.067852 intra-day and 1.183517 inter-day. The developed method was found to be precise as the RSD values for repeatability and inter-day precision studies were <2%, respectively, as recommended by ICH guidelines and Shown in the Table 2.

Estimation of lisinopril in tablet dosage forms

Commercial brand of tablets was chosen for testing the suitability of the proposed method to estimate lisinopril in tablet formulations. Twenty tablets were weighed and powdered. An accurately weighed portion of this powder equivalent to 100 mg of lisinopril was transferred into a 100 ml volumetric flask and dissolved in 25 ml of a 30:70 v/v mixture of phosphate buffer and acetonitrile. The contents of the flask were sonicated for 15 min and a further 25 ml of the diluent was added, the flask was shaken continuously for 15 min to ensure complete solubility of the drug. The volume was made-up with the diluent and the solution was filtered through a 0.45 μ membrane filter. This solution was further diluted to get the required concentrations. The solution containing 10μg/ml of lisinopril was injected into the column six times. The average peak area of the drug was computed from the chromatograms and the amount of the drug present in the tablet dosage form was calculated by using the regression equation obtained for the pure drug [11–13].

Accuracy studies for lisinopril

Accuracy of the method was obtained by performing recovery studies by the standard addition method at different levels of standard drug i.e. 80%, 100% and 120% of lisinopril to analyzed tablet powder sample and mixture were reanalyzed by the proposed method. From the amount of drug found percentage recovery was calculated. The relevant results are furnished in Table 3.

RESULTS AND DISCUSSION

In the proposed method, the retention time of lisinopril was found to be 1.510 min. Quantification was linear in the concentration range of 10- 35μg/ml for lisinopril. The regression equation of the linearity plot of concentration of lisinopril over its peak area was found to be y = 14079x - 68594 (r^2=0.9990) for lisinopril, where X is the concentration of lisinopril (μg/ml) and Y is the corresponding peak area. The limit of detection and limit of quantification for lisinopril was found to be 0.010024l and 0.030374 respectively, which indicate the sensitivity of the method. The use of phosphate buffer and acetonitrile in the ratio of 30:70 v/v resulted in peak with good shape and resolution. The high percentage of recovery indicates that the proposed method is highly accurate. No interfering peaks were found in the chromatogram of the formulation within the run time indicating that excipients used in tablet formulations did not interfere with the estimation of the drug by the proposed HPLC method. Figure 5 shows typical chromatogram of lisinopril. All the parameter result of lisinopril was shown in Table 4.

CONCLUSION

The proposed HPLC method is rapid, sensitive, precise and accurate for the determination of lisinopril can be reliably adopted for routine quality control analysis of lisinopril bulk and in its tablet dosage forms.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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