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DEVELOPMENT OF ANALYTICAL METHOD FOR DETERMINATION OF LISINOPRIL TABLETS USING RP-HPLC METHOD

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ABSTRACT

A high performance liquid chromatographic method was developed, validated and applied for determination of lisinopril in pharmaceutical formulations. A LiChrospher® RP-18 (10 µm, 250x 4 mm) column was used with a mobile phase consisting of acetonitrile: phosphate buffer (30: 70% v/v, pH 2.0), a quantitative evaluation was performed at 215 nm with flow rate of 1 mL/min, and column cooler temperature was maintained at 35 ºC. The retention time was about 6 min. This method is suitable for assay of lisinopril tablets and it can be applied in routine quality control, as it is accurate, precise and simple.

KEYWORDS: Lisinopril, RP-HPLC method, Validation, Quality control

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INTRODUCTION

Lisinopril is a potent, competitive inhibitor of angiotensin-converting enzyme (ACE), the enzyme responsible for the conversion of angiotensin I (ATI) to angiotensin II (ATII). ATII regulates blood pressure and is a key component of the renin-angiotensin-aldosterone system (RAAS). Anti-hypertensive medications can be used alone or in combination[1,2] . Lisinopril is indicated for treatment of hypertension. It may be used alone as an initial therapy or concomitantly with other classes of antihypertensive agents. Lisinopril is indicated as an adjunctive therapy in the management of heart failure with patients who are not responding adequately to diuretics and digitalis. Lisinopril is chemically described as (S)-1-[N^2-(1-carboxy-3-phenylpropyl)-L-lysyl]-L-proline dehydrate[3,4] (Figure1).

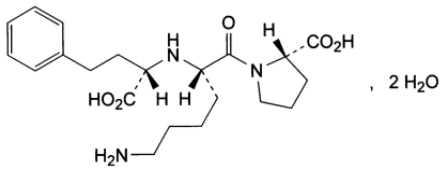

Figure 1
Structure of Lisinopril.

A few spectroscopic[5,6], HPLC[7-9], LC-MS[10], gas liquid chromatography[11] and capillary electrophoresis[12,13] methods were reported earlier for determination of lisinopril in bulk and pharmaceutical dosage forms. We have developed a simple, precise, accurate and specific RP-HPLC method for determination of lisinopril in pharmaceutical dosage forms. As the analytical methods must be validated before being used in the pharmaceutical industry, the proposed HPLC-UV detection method was validated in accordance with the International Conference on Harmonization (ICH) guidelines[14-16], by assessing its specificity, linearity, accuracy, precision, limit of detection and limit of quantification.

MATERIALS AND METHODS

1.1 Reagents and materials

The working standard of lisinopril RS (Purity >99%) was provided by (Sigma-Aldrich). The pharmaceutical preparation of lisinopril (10 mg) was obtained commercially. HPLC grade methanol, acetonitrile and potassium dihydrogen phosphate (Analytical grade) were obtained from Merck (Germany).

1.2 Instrumentation

The HPLC system consists of a Shimadzu DGU-$20A_5$ vaccum degasser, a Shimadzu LC-20AD pump, a Shimadzu SPD-20A UV/VIS detector. The RP-HPLC system was equipped with LC solution software for data processing.

1.3 Chromatographic conditions

The chromatographic separation was achieved on a LiChrospher® RP-18 column packed with octadecylsilyl silica gel 10 µm, 250x 4 mm, under reversed phase partition conditions. The mobile phase was a 30: 70% v/v mixture of Acetonitrile: Phosphate buffer (Dissolved 4.1 g of potassium dihydrogen phosphate in about 900 mL of water in a 1000-mL volumetric flask, pH 2.0 ± 0.1, adjusted with orthophosphoric acid). The flow rate was 1.0 mL/min and the run time was 7 min. Before analysis the mobile phase was degassed by using a sonicator and filtered through a 0.25 µm filter. The column cooler temperature was maintained at (35±2)ºC. The injection volume was 20 µL and the wavelength of detector at 215 nm.

1.4 Preparation of stock solution of lisinopril

About 54 mg of lisinopril was accurately weighed and transferred into 100 mL volumetric flask and dissolved in a mixture of methanol-water (1 : 4 v/v). The final drug concentration of 100 µg/mL was obtained by dissolving the appropriate amount from this standard stock solution in the above said

mixture. Calibration standards of lisonpril were prepared by making serial dilutions of the stock solution at concentrations of 27, 54, 108, 162, 216 µg/mL.

1.5 Assay of tablet formulation

The contents of twenty commercial tablets were weighed and their mean mass was determined. After grinding the tablets into a fine powder in a glass mortar, an accurately weighed quantity of the tablet powder equivalent to 10 mg of lisinopril was quantitatively transferred into a 100 mL volumetric flask with about 50 mL mixture of methanol-water (1:4 v/v). The contents were sonicated for 15 minutes. The mixture was then made up to 50 mL with the same mixture. The solution was then filtered through a membrane syringe filter (pore size 0.25 µm). The sample solution was injected and the peak area was measured for determination of lisinopril in a tablet formulation.

RESULTS AND DISCUSSIONS

Linearity

Linearity of the method was confirmed by preparing lisinopril standard curve for the analytical range of 27 – 216 µg/mL. The solutions were chromatographed six times, in accordance with the International Conference on Harmonization. Statistical analysis using the least square regression indicated excellent linearity for lisinopril in the mentioned range. A good correlation between lisinopril peak areas and drug concentration was observed with $r^2 \geq 0.99$ (Table 1).

Table 1
Results from study of linearity

Methods	λ, nm	Range (µg/mL)	LR	R	LOD (µg/mL)	LOQ (µg/mL)
RP-HPLC	215	27-216	y=21156302x+472	0.9997	0.05	0.125

Precision

The percentage label claim, present in tablet formulation, was found to be 100.7 %. A typical chromatogram of lisinopril is shown in Figure 2. Precision of the method was confirmed by the analysis of formulation repeated six times (Table 2).

Table 2
Results from assay of tablet formulation

	Assay %
Sample #	Lisinopril
1	100.9
2	99.85
3	99.75
4	101.1
5	100.6
6	101.9
Average	100.7
RSD %	0.804

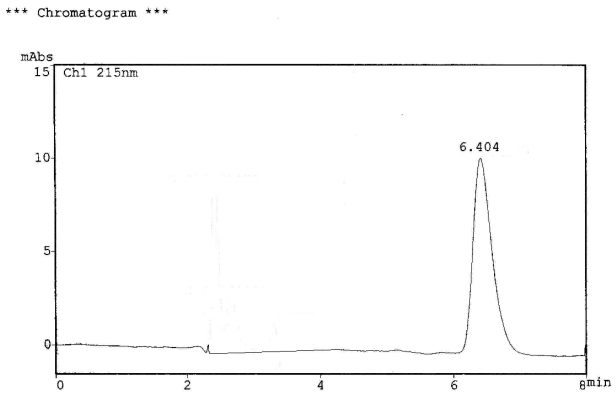

Figure 2
Typical chromatogram of Lisinopril.

Accuracy

To check the accuracy of the developed methods and to study the interference of formulation excipients, analytical recovery experiments were carried out as per ICH guidelines. The results of the recovery studies and their statistical validation data given in Table 3 indicate high accuracy of the proposed method. The percentage recovery was found to be in the range of 98.00-102.0%.

Table 3
Accuracy of Lisinopril

Parameters	% Taken	Mass taken (mg/1 tabl.)	Mass found (mg/1 tabl.)	% Found	% Recovery
			4.99	49.90	99.81
	50.00	5.0	4.92	49.20	98.40
			5.02	50.20	100.4
			10.00	100.0	100.0
	100.0	10.00	9.99	99.00	99.90
			9.89	98.90	98.90
			14.93	149.3	99.53
	150.0	15.0	14.92	149.2	99.47
			15.12	151.2	100.8
X					99.69
SD					±0.729
% RSD					0.731

Robustness

As defined by the ICH, the robustness of an analytical procedure describes its capability to remain unaffected by small and deliberate variations in method parameters. Robustness was performed by small variation in the chromatographic conditions and found to be unaffected by small variations like ± 2% variation in volume of mobile phase composition, ± 0.1 mL/min in flow rate of mobile phase, ±0.1 variation in pH.

Specificity

The specificity of the HPLC method was ascertained by analyzing standard drug and sample solutions. The retention time of lisinopril was confirmed by comparing the retention time with that of the standard.

CONCLUSION

A simple isocratic RP-HPLC method with UV detection has been developed for determination of lisinopril. The method was validated for accuracy, precision, specificity, robustness and linearity. The run time is relatively short (7 min), which enables rapid quantification of many samples in routine and quality control analysis of tablets.

REFERENCES

1. Devika GS, Sudhakar M and Venkateshwara Rao J, RP-HPLC method for simultaneous estimation of metolazone and ramipril in oral solid dosage form, Int J of Parma and Bio Sciences, 3 (4): 193-200, (2012).
2. Mullaicharam AR, Shummo PM and Muthuprasanna P, Sustained release matrix metoprolol tartrate with inlay hydrochlorothiazide tablet, Int J of Parma and Bio Sciences, 1 (2): 1-10, (2010).
3. Patchett A, Harris E, Tristram E, Wyvratt M, Wu M, Taub D, Peterson E, Ikeler T, Broeke J, Payne L, Ondeyka D, Thorsett E, Greenlee W, Lohr N, Hoffsommer R, Joshua H, Ruyle W, Rothrock J, Aster S, Maycock A, Robinson F, Hirschmann R, Sweet C, Ulm E, Gross D, Vassil T and Stone C, A New Class of Angiotensin-Converting Enzyme Inhibitors, Nature, 288 (5788): 280-283, (1980).
4. Martindale, The Complete Drug Reference, 33rd Edn., Pharmeceutical Press, London: 921-923, (2002).
5. Jamakhandi C, Javali C, Disouza J, Chougule US, Mullani AK, Spectrophotometric Determination of Lisinopril Dosage Form by condensation reaction, J Pharm Pharm Sci, 3 (2): 185-187, (2011).
6. Permender R, Sushila R, Shyama T, Vikash K, Simultaneous estimation of Amlodipine Besylate and Lisinopril Dihydrate as A.P.I. and in tablet dosage forms by modified form of simultaneous equation method using derivative UV-Spectrophotometry, Int J Pharm Tech Res, 2 (1): 556-562, (2010).
7. El-Emam AA, Hansen SH, Mohamed AM, El-Ashry SM, El-Sherbiny DT, Determination of lisinopril in dosage forms and spiked human plasma through derivatization with 7-chloro-4-nitrobenzo-2-oxa-1,3-diazole (NBD-Cl) followed by spectrophotometry or HPLC with fluorimetric detection, J Pharm Biomed Anal, 34 (1): 35-44, (2004).
8. Beasley CA, Shaw J, Zhao Z, Reed RA, Development and Validation of a stability indicating HPLC method for determination of lisinipril, lisinopril degradation product and parabens in the lisinopril extemporaneous formulation, J Pharm Biomed Anal, 37 (3): 559-567, (2005).
9. El-Gindy, Ashour A, Abdel-Fattah L, Shabana MM, Spectrophotometric, spectrofluorimetric and LC determination of lisinopril, J Pharm Biomed Anal, 25 (5-6): 913-922, (2001).
10. Zhou N, Liang Y, Chen B, Wang P, Chen X, Lu F, Development and validation of LC-MS method for the determination of lisinopril in human plasma and its application in a bioequivalence study, J Chromatogr Sci, 46 (10): 848-853, (2008).
11. Avadhanulu B and Pantula R, Gas liquid chromatographic estimation of lisinopril in its pharmaceutical dosage forms, Indian Drugs, 30(12): 646-649, (1993).
12. Qin XZ, Nguyen DST, Ip DP, Separation of lisinopril and its RSS diastereoisomer by micellar electrokinetic, J Liq Chromatogr, 16(17): 3713-3734, (1993).
13. Hillaret S, Grauwe K and Bossche W, Simultaneous determination of hydrochlorothiazide and several inhibitors of angiotensin-converting enzyme by capillary electrophoresis, J Chromatogr A, 924 (1-2): 439-449, (2001).
14. ICH Q2A; Guidelines on validation of analytical procedure; Definitions and terminology, Federal Register, 1995, 60, 11260.
15. ICH Q2B; Guidelines on validation of analytical procedure; Methodology, Federal Register, 1996, 60, 27464.
16. Sukhdev S, Jasbir S, Development of accelerated stability protocol for sildenafil tablets – a European perspective Review, Int J of Parma and Bio Sciences, 1 (4): 27-34, (2010).