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RESEARCH ARTICLE

DEVELOPMENT AND VALIDATION OF HPLC METHODFOR THE SIMULTANEOUS ESTIMATION OF LISINOPRILAND HYDROCHLOROTHIAZIDETABLET DOSAGE FORM

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ABSTRACT

This work describes a new, fully validated, simple, rapid, selective, and sensitive HPLC method with UV detection for the direct determination of Lisinopril and Hydrochlorothiazide tablet dosage form The mobile phase consisted of Phosphate buffer: Methanol (85:15) adjust pH 4.5 with orthophosphoric acid. The linearity range of Lisinopril was found to be 4-20 µg/ml and Hydrochlorothiazide 5-25 µg/ml. Detection was done at 291 nm and the retention time of Lisinopril was found to be 3.1 min and Hydrochlorothiazide 4.6 min with the flow rate of 0.8 ml/min. The method was found to be simple, linear, rapid, accurate, precise, reproducible and robust.

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INTRODUCTION

High-Performance Liquid Chromatography (HPLC): High-performance liquid chromatography (HPLC) is an advanced form of liquid chromatography used in separating the complex mixture of molecules encountered in chemical and biological systems, in order to understand better the role of individual molecules. Among different chromatographic methods, high performance liquid chromatography (HPLC) offers a greater variety of stationary phases, which there by allows selective interactions and more possibilities for separation[1, 2]. In HPLC the separation is about 100 times faster than the conventional liquid chromatography due to packing of particles in the range of 3-10 m. In HPLC mobile phase composition is changed in a programmed fashion to increase the efficiency of separation. Depending on the unique affinity of each component (referred to as the analyte) between the mobile phase and the stationary phase, each analyte migrates along the column at different speeds and emerges from the column at different times, thus establishing a separation of the mixture. Analytes with higher affinity for the mobile phase migrate faster down the column, whereas those with higher affinity for the stationary phase migrate slower. This migration time (referred to as retention time) is unique for each analyte and can be used in its identification. With the appropriate use of a detection method after the column, each analyte can also be quantified for analysis.Smaller column particle size can improve chromatographic resolution, but increased solvent delivery pressure is needed. Further reduction of column particle size can allow for higher solvent flow rates, reducing analysis time without sacrificing resolution[3, 4].

Method Development: The goal of the HPLC methods is try to separate and quantify the main active drug, any reaction impurities, all available synthetic inter-mediates and any degradants. The number of drugs introduced into the market is increasing every year. These drugs may be either new entities or partial structural modification of the existing one. Very often there is a time lag from the date of introduction of a drug into the market to the date of its inclusion in pharmacopoeias[5, 6]. This happens because of the possible uncertainties in the continuous and wider usage of these drugs, reports of new toxicities (resulting in their withdrawal from the market), development of patient resistance and introduction of better drugs by competitors. Under these conditions, standards and analytical procedures for these drugs may not be available in the pharmacopoeias. Thus it becomes necessary, to develop newer analytical methods for such drugs and their combination[7, 8].

Need and Steps in Analytical Method Development: Method development in chromatography is the setting up of an analytical procedure that will be appropriate for the analysis of a particular sample. In industries, new measurement technologies can only be adopted if a sound scientific rationale for the application has been developed, proven, justified and the developed method has been approved by internal company procedures. Newer analytical methods are developed for these drugs or drug combinations because of the following reasons.

- The drug or drug combination may not be official in any Pharmacopoeia. A literature search may not reveal an analytical method for the drug or its combinations.
- Analytical methods may not be available for the drug combination due to the interference caused by excipients.

- Analytical methods for the quantification of drug or drug combination from biological fluid may not be available[9].
- Analytical methods for a drug in combination with other drugs may not be available.

There are various aspects which should be kept in mind while developing a method for HPLC such as:

- Selection of the HPLC method which includes choosing either of the two, reverse phase or normal phase HPLC depending upon the nature of the sample, for example, for polar analytes the reverse phase HPLC is used to obtain better retention and resolution and for low or medium polarity samples, generally normal phase chromatography is preferred.
- Selection of proper mobile phase for the analyte is the most crucial stage in developing a method for HPLC. A mobile phase which has the capability of pulling the analyte from the column is chosen. When dealing with weak acids and bases, pH should be adjusted which has effect on the retention of the analyte?
- A stationary phase is generally C18 bonded in the case of reverse phase HPLC and cyano-bonded in the normal phase
- The detectors are selected based on the nature of the analyte. If the analyte has chromophores it is detected by UV-detectors. Fluorescence detectors are used in the case of trace analysis and in preparative HPLC refractive index detectors are used. The HPLC method development often follows the series of steps summarized Figure No 1.

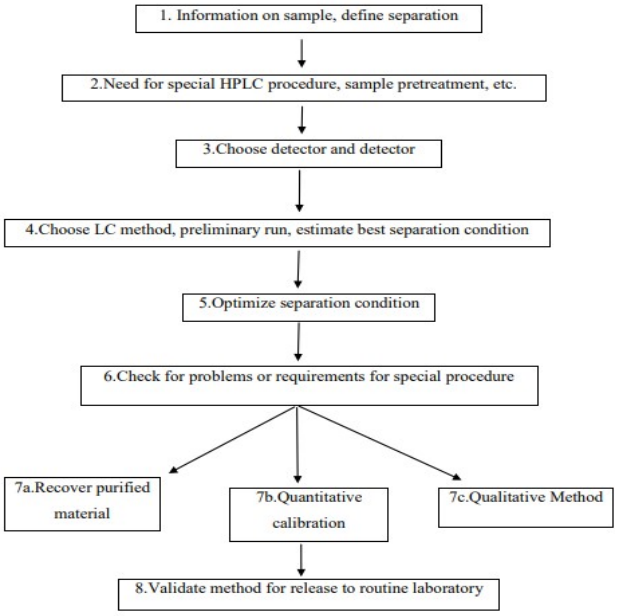

Figure 1. Steps Involved in HPLC Method Development

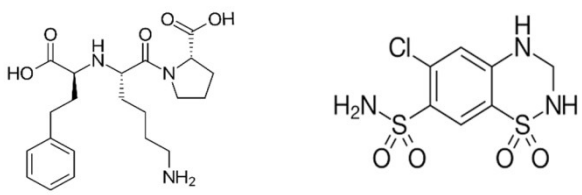

Figure 2. Lisinopril and Hydrochlorothiazide

MATERIALS AND INSTRUMENTS

Procurement of drug sample

Table 1. Details of drug sample

Name of Drug	Quantity	Drug Supplier
Lisinopril	5 gm	PharmaTech solutions, Nashik
Hydrochlorothiazide	5 gm	PharmaTech solutions, Nashik

Reagents and chemicals

All the chemicals used are of HPLC and AR grade. Chemicals used are as follows

Table 2. Reagents and Chemicals

Sr.No	REAGENTS	GRADE	MANUFACTURES
1	Water	HPLC	Merck specialities private limited, Mumbai
2	Acetonitrile	HPLC	Merck specialities private limited, Mumbai
3	Methanol	HPLC	Merck specialities private limied, Mumbai
4	Potassium dihydrogen phosphate	AR	Labogens
5	o-phosphoric Acid	AR	Sigma Aldrich

Instruments

- **FTIR**
  Make: Bruker
  Software: OPUS7.5
  Attachments: Transmitter, ECO-ATR
- **UV Spectrophotometer**
  Specifications of double beam UV-Visible spectrophotometer
  Make: Shimadzu
  Model: UV 1800
  Software: UV Probe 2.51
  Path length: 10 mm
  Slit width: Variable
- **HPLC**
  Specification of Analytical Technologies
  Make: Analytical Technologies
  Detector: UV-3000 – M
  Software: WorkStation
  Pump: Binary Pump
  Column: Cosmosil C18 (250mm x 4.6ID, Particle size: 5 micron)
- **Analytical balance**
  Make: Shimadzu
  Model: AY-220
- **Ultrasonicator**
  Make: Bio-Technics India
  Model: ICO 900/2000

Experimental Work

- **Identification of drug:**
  Organoleptic properties of drug: The sample of Lisinopril and Hydrochlorothiazide was checked for organoleptic properties such as color and odor.
- **Solubility analysis**
  Solubility of Lisinopril and Hydrochlorothiazide was checked by dissolving it in number of solvents. It was found that Lisinopril and Hydrochlorothiazide was soluble in water, Ethanol, Methanol, Isopropyl Alcohol, Phosphate buffer pH 4.5.
- **Fourier Transform Infra-Red Spectroscopy (FTIR)**
  The IR study of pure drug was carried out by using Fourier transform infrared spectrophotometer (BRUKER). Infrared absorption spectrum of Lisinopril and Hydrochlorothiazide was recorded and interpreted over the wave number 4000 to 600 cm^{-1} using Fourier Transform spectrophotometer (Bruker, ECO- ATR).
- **High performance Liquid Chromatographic Method**
  Optimization of Detection Wavelength: The sensitivity of HPLC method that uses UV detection depends upon proper selection of detection wavelength. An ideal wavelength is one that gives good response for the drugs that are to be detected. For good response, optimization of wavelength was done at different wavelengths by UV detector. In the present study, drug solutions of 20 µg/ml of Lisinopril and 25 µg/ml Hydrochlorothiazide were prepared in methanol. After observing UV spectra of the drug, wavelength by Overlain spectra was found at 291 nm and selected for further study[10, 11].

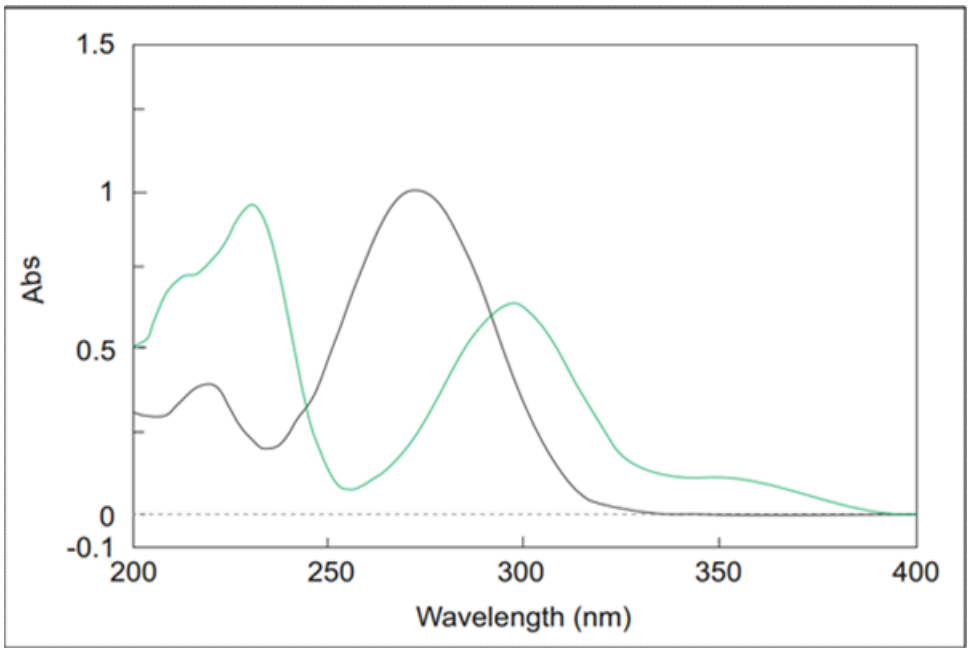

Figure 3. Overlain UV Spectra of Lisinopril and Hydrochlorothiazide Showing Isosbestic point at 291 nm (Isosbestic Point)

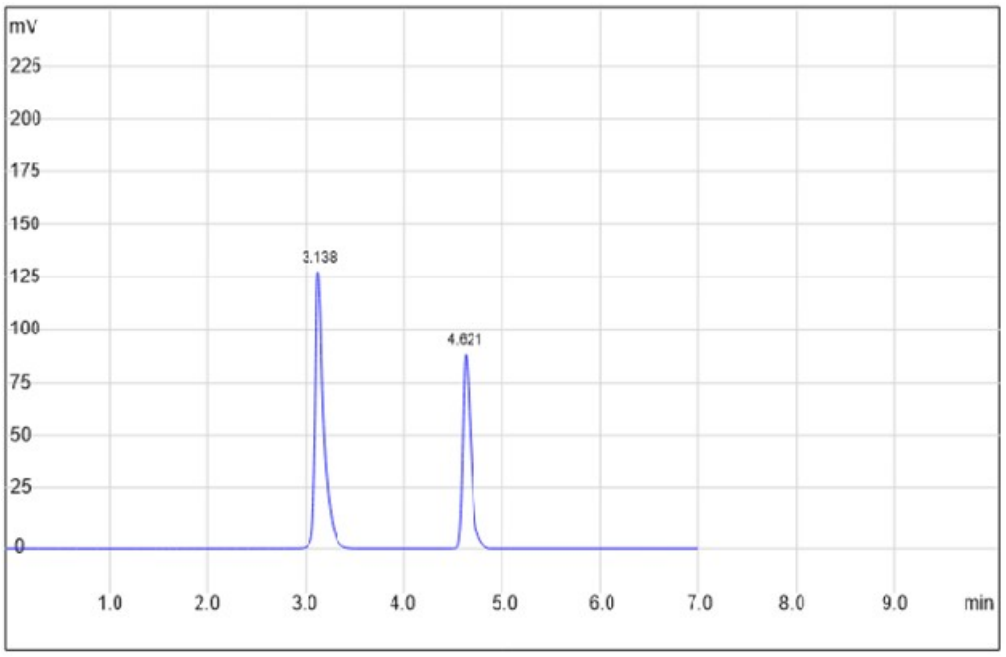

Figure 4. Chromatogram of Lisinopril and Hydrochlorothiazide

- **Selection of Chromatographic Conditions**
  The selection of HPLC method depends upon the nature of the sample, its molecular weight and solubility. RP-HPLC method was selected for the initial separations because of its simplicity and suitability. The chromatographic variables such as mobile phase ratio and flow rate were studied. The condition that gave the best resolution, symmetry and selectivity was selected.
- **Optimization of Chromatographic Parameters**
  Optimizations in HPLC is the process of finding a set of conditions that sufficiently enable the quantification of the analyte with acceptable accuracy, precision, sensitivity, specificity, cost, ease and speed.
- **Preparation of standard stock solutions**
  Accurately Weighed and transferred 20 mg of Lisinopril and 25 mg of Hydrochlorothiazide working Standards into a 1000ml clean dry volumetric flask, add 3/4th volume of diluent, sonicated for 5 minutes and make up to the final volume with diluents and the final concentration of Lisinopril is 20 µg/ml and 25 µg/ml is of Hydrochlorothiazide. The working standard solutions of these drugs were obtained by appropriate dilution of the respective stock solution with mobile phase.
- **Optimization of Mobile Phase Strength**
  Based on drug solubility, stability and suitability of drug in different solvents, various mobile phases and compositions were tried to get a good resolution and sharp peak. For selection of mobile phase, various mobile phase compositions containing Methanol, Water and Phosphate buffer in different ratios were tried by gradient programming. Each mobile phase was filtered through 0.45 µm membrane filter and degassed by sonication for 20 min. From the various mobile phases tried, mobile phase containing methanol, water and Phosphate buffer pH 4.5 in isocratic program was selected, since it gave sharp peaks with symmetry within limits and significant retention times for drugs.
- **Preparation of Mobile Phase A (pH 4.5 Phosphate buffer):**
  Dissolve 6.80 g of potassium dihydrogen phosphate R in water and dilute to 1000.0 ml with the same solvent. Adjust the pH 4.5 with o-phosphoric Acid. Mobile phase was filtered through 0.45µm membrane filter and degassed by sonication for 20 min.

- **Preparation of Diluent:** Dilute with methanol upto mark.
- **Selection of mobile phase**
  Standard solutions of Lisinopril (20µg/ml) and Hydrochlorothiazide (25µg/ml) were injected into the RP-HPLC system and run in different solvent systems. Different mobile phase's systems like Phosphate buffer and methanol were initially tried in the isocratic mode in order to determine the best conditions.
- **Solubility Study**
  Solubility of Lisinopril and Hydrochlorothiazide was observed by dissolving them in different solvents and the observed resultsare given in the Table no 7.
- **Stability Study**
  After observation it was found that there was node gradation of sample with solvent Phosphate buffer, water and Methanol.

Table 3. Chromatographic Condition for Lisinopril and Hydrochlorothiazide

Mobile phase	Phosphate buffer: Methanol (85:15) adjust pH 4.5 with orthophosphoric acid
Selection of column	Cosmosil C18 (250mm x 4.6mm ID, Particle size: 5 µm)
Flow rate	0.8 ml/min
Column temperature	Room Temperature
Detection wavelength	291 nm
Conclusion	Retention time is as expected and Peaks are showing resolution and sharpness, hence selected

Optimized Chromatographic Conditions

Table 4. Optimized Chromatographic conditions for Lisinopril and Hydrochlorothiazide

Mobile phase	Phosphate buffer: Methanol (85:15) adjust pH 4.5 with orthophosphoric acid
Selection of column	Cosmosil C18 (250mm x 4.6mm ID, Particle size: 5 µm)
Injection volume	20 µl
Flow rate	0.8 ml/min
Column temperature	Room Temperature
Detection wavelength	291 nm
Run Time	7.0 minutes
Retention time	Lisinopril (3.1 min) and Hydrochlorothiazide (4.6 min)

RESULTS AND DISCUSSION

Identification of drug

Organolepticproperties of drug

Table 5. Organolepticproperties of drugs

Sr. No.	Organoleptic Property	Lisinopril	Hydrochlorothiazide
1	Colour	White to Off-white powder	Whitepowder
2	Odor	Odourless	Odourless

Melting point of drug

Table 6. Melting point of drug

Sr. No.	Name of drug	M.P. (˚C)
1	Lisinopril	158-161 ^{o}C
2.	Hydrochlorothiazide	266-269 ^{o}C

Table 7. Solubility Study

Sr. No	Solvents	Solubility	
		Lisinopril	Hydrochlorothiazide
1	Water	Soluble	Slightly Soluble
2	Methanol	Freelysoluble	Freelysoluble
3	Phosphate Buffer pH 4.5	Freelysoluble	Freelysoluble
4	ACN	Soluble	Soluble

FTIR spectrum of Lisinopril

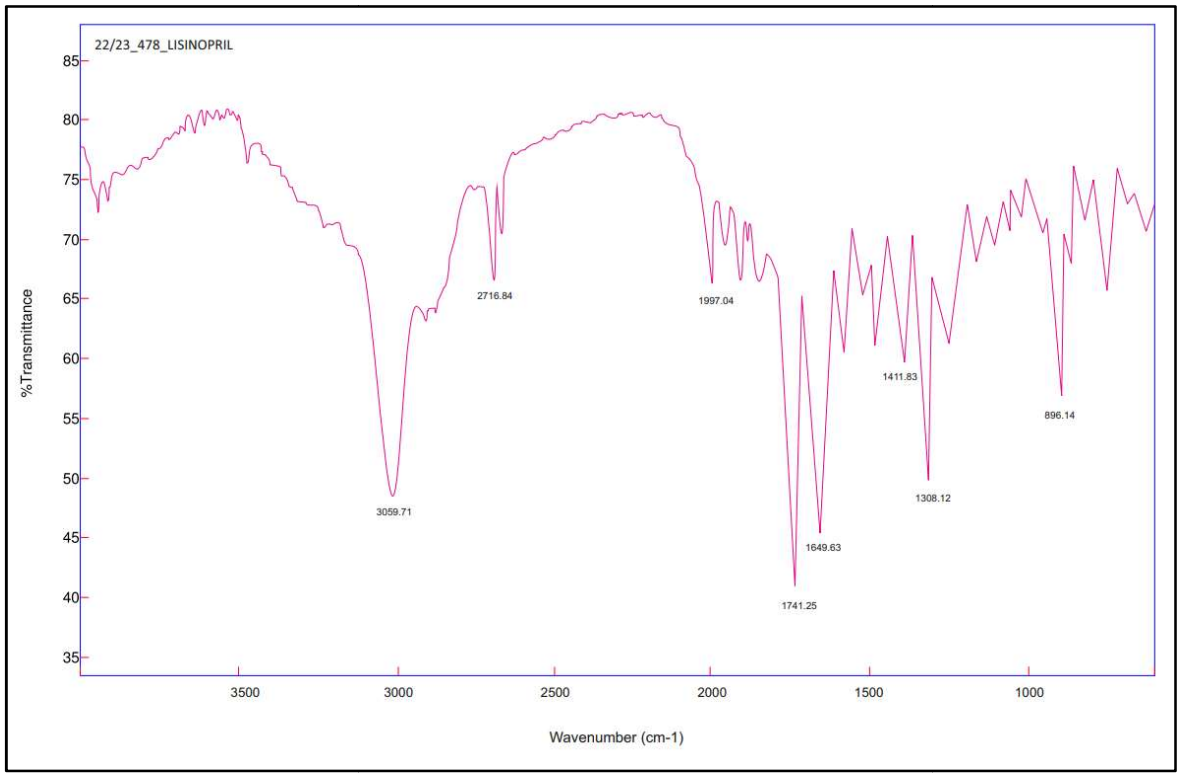

Fig. 8. IR Spectrum of Lisinopril

Table 13. Interpretation of FTIR Spectrum of Lisinopril

Figure 5. FTIR spectrum of Lisinopril

Sr. No.	Functional group	Standardrange (cm-1)	Observedrange (cm-1)
1	O-H Stretching	3200-3000	3059.71
2	C-N Stretch	2850-2600	2716.84
3	C-H stretch	1980-1700	1741.25
4	C-C stretch	1350-1100	1308.12

FTIR spectrum of Hydrochlorothiazide

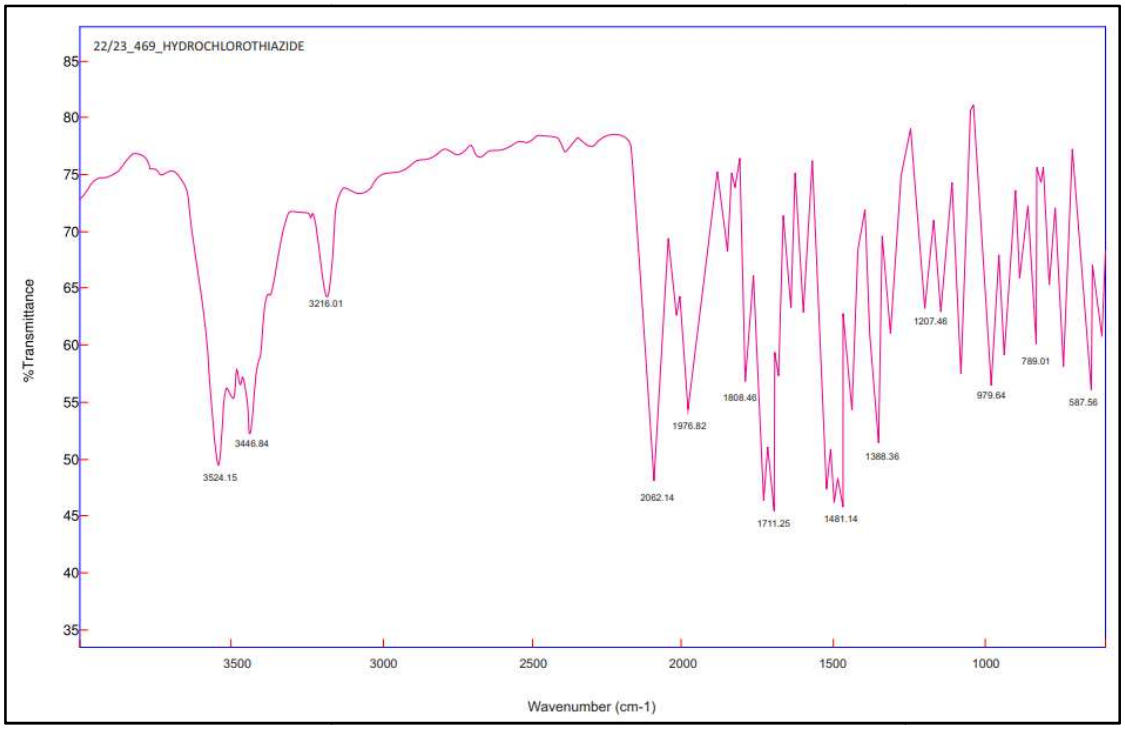

Figure 6. FTIR spectrum of Hydrochlorothiazide

Sr. No	Functional group	Standardrange (cm-1)	Observedrange (cm-1)
1	N-H Stretching	3580-3450	3524.15
2	S=O stretch	2200-1850	2062.14
3	C=O Stretch	1980-1700	1711.25
4	C-H stretch	1450-1300	1388.36

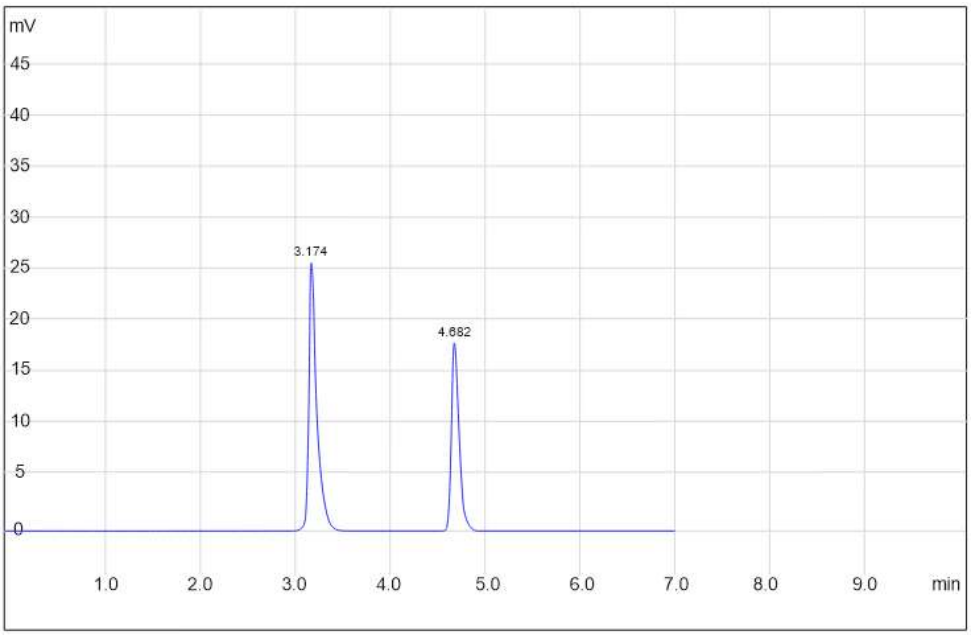

Figure 7. Optimized chromatogram of Lisinopril and Hydrochlorothiazide

Table 8. Data of calibrationcurve of Lisinopril and Hydrochlorothiazide by HPLC method

Sr. No.	Lisinopril		Hydrochlorothiazide	
	Concentration (µg/ml)	Area	Concentration (µg/ml)	Area
1	4	546487	5	436850
2	8	1137958	10	889546
3	12	1630548	15	1292045
4	16	2206569	20	1715480
5	20	2710498	25	2108246

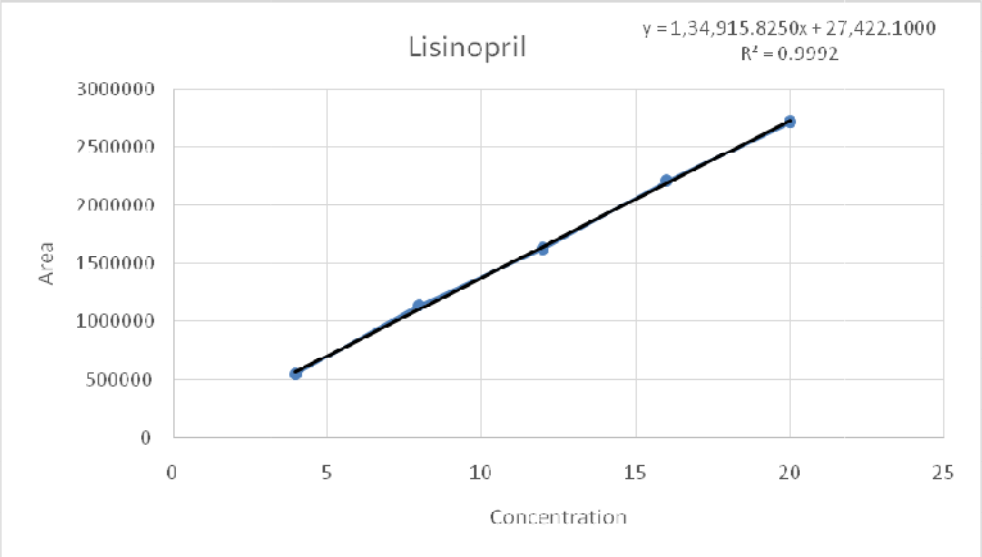

Figure 8. Calibrationcurve for Lisinopril

- **Development of simultaneous HPLC method for Lisinopril and Hydrochlorothiazide.**

High-performance liquid chromatographic method was developed and validated for determination of Lisinopril and Hydrochlorothiazide in bulk and dosage form. Mobile phase consists of Phosphate buffer: Methanol (85:15) adjusts pH 4.5 with orthophosphoric acid. Chromatogram obtained was shows the maximum wavelength where the drug shows maximum response was 291 nm and is shown in Figure No 7.

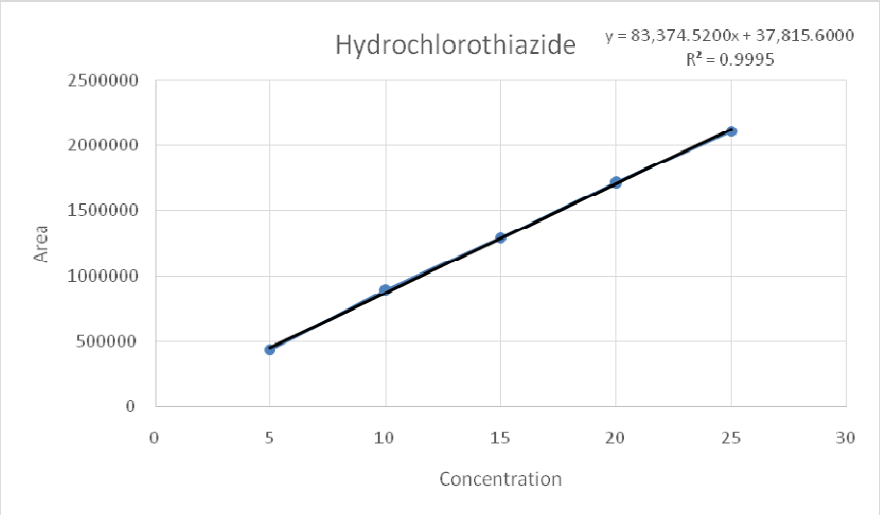

Figure 9. Calibrationcurve for Hydrochlorothiazide

Table 9. Optical characteristics for Lisinopril and Hydrochlorothiazide

Sr.No	Parameters	Lisinopril	Hydrochlorothiazide
1	λmax(nm)	291	291
2	Beer's lawlimit (µg/ml)	9-45	3-60
3	Regression equation[y]	y = 1,34,915.8250x + 27,422.1000	y = 83,374.5200x + 37,815.6000
4	Slope[m]	1,34,915.825	83,374.520
5	Intercept [c]	27,422.100	37,815.6000
6	Correlation coefficient [r^2]	0.9992	0.9995
7	Limitof detection (LOD)(µg/ml)	0.05	0.10
8	Limitof quantitation (LOQ) (µg/ml)	0.16	0.30

Table 10. Data for recovery study of Lisinopril by HPLC method

Level of addition	Standard added (µg/ml)	conc. (µg/ml)	Total conc. (µg/ml)	Area obtained*	Std Area	Drug recovered (µg/ml)	%Recovery
	4	8	12	1625641		11.96	99.70
50%	4	8	12	1632012	1630548	12.01	100.09
	4	8	12	1642504		12.09	100.73
	8	8	16	2171464		15.75	98.41
100%	8	8	16	2212474	2206569	16.04	100.27
	8	8	16	2198316		15.94	99.63
	12	8	**20**	2705646		19.96	99.82
150%	12	8	**20**	2719265	2710498	20.06	100.32
	12	8	**20**	2721963		20.08	100.42

Table 11. Statistical validation of Lisinopril by HPLC method

*Average of three determination

Table 12. Data for recovery study of Hydrochlorothiazide by HPLC method

Level of addition	Standard added (µg/ml)	conc. (µg/ml)	Total conc. (µg/ml)	Area obtained*	Std Area	Drug recovered (µg/ml)	% Recovery
50%	5	10	15	1284645	1292045	14.91	99.43
	5	10	15	1271462		14.76	98.41
	5	10	15	1274044		14.79	98.61
100%	10	10	20	1710547	1715480	19.94	99.71
	10	10	20	1729882		20.17	100.84
	10	10	20	1739080		20.28	101.38
150%	15	10	25	2108477	2108246	25.00	100.01
	15	10	25	2090245		24.79	99.15
	15	10	25	2118507		25.12	100.49

- **Linearity**

Lisinopril was found to be linear in the concentration range of 4-20 µg/ml and Hydrochlorothiazide is in the range of 5-25 µg/ml. Results obtained are shown in Table 8 and calibration plotobtained was shown in Figure No 8 & 9for Lisinopril and Hydrochlorothiazide respectively.

- **Optical characteristics**

Optical characteristics and statistical data of linearity for Lisinopril and Hydrochlorothiazide by HPLC method aresummarized in Table No 9.

- **Accuracy**

Accuracy was studied by standard addition method and % recovery found was within acceptable limit. Results of recovery study are shown in Table no.17& 19 and statistical validation is shown in Table no. 10 & 11.

Table 13. Statistical validation of Hydrochlorothiazide by HPLC method

Level of addition	% Mean recovery*	SD	% RSD
50%	98.81	0.54	0.55
100%	100.64	0.85	0.84
150%	99.88	0.68	0.68

***Average of three determination**

Table 14. Data forintraday precision of Lisinoprilby HPLC method

Sr. No.	Conc. (µg/ml)	Area	Mean	SD	%RSD
1	4	550421			
2	4	549594	546999.00	5227.26	0.96
3	4	540982			
4	12	1626504			
5	12	1635971	1630993.67	9504.61	0.58
6	12	1630506			
7	20	2716546			
8	20	2710414	2710537.00	5948.45	0.22
9	20	2704651			

Table 15. Data forinterday precision of Lisinopril by HPLC method

Sr. No.	Conc. (µg/ml)	Area	Mean	SD	%RSD
1	4	540982	547429.67	5753.89	1.05
2	4	552042			
3	4	549265			
4	12	1631204	1633418.67	5756.89	0.35
5	12	1629098			
6	12	1639954			
7	20	2715104	2717589.00	2184.24	0.08
8	20	2718458			
9	20	2719205			

Precision Study for Hydrochlorothiazide

The % RSD found below 2, Hence results complies as per guidelines

Table 16. Data forintraday precision of Hydrochlorothiazide by HPLC method

Sr. No.	Conc. (µg/ml)	Area	Mean	SD	%RSD
1	5	436305			
2	5	439804	435977.67	4000.06	0.92
3	5	431824			
4	15	1298072			
5	15	1298508	1297576.67	2509.23	0.19
6	15	1296150			
7	25	2105478			
8	25	2110548	2107540.67	2663.74	0.13
9	25	2106596			

Table 17. Data forinterday precision of Hydrochlorothiazide by HPLC method

Sr. No.	Conc. (µg/ml)	Area	Mean	SD	%RSD
1	5	435555			
2	5	432924	432767.67	2868.70	0.66
3	5	429824			
4	15	1296046			
5	15	1306526	1300326.00	5497.49	0.42
6	15	1298406			
7	25	2106564			
8	25	2115649	2109592.67	5244.94	0.25
9	25	2106565			

- **Precision**
  Intraday and interday precision assures there peatability of test results. The % RSD found was below 2 for both Lisinopril and Hydrochlorothiazide. Result of intraday and interday precision was shown in Table no. 14 and Table no. 15 respectively for Lisinopril and Resul to fintraday and interday precision was shown in Table no.16and Table no. 17respectively for Hydrochlorothiazide.
- **Precision Study for Lisinopril**
  The % RSD found below 2, Hence results complies as per guidelines.
- **Robustness**
  Robustness was studied by different deliberate variations in the chromatographic conditions i.e. Change in flow rate and wavelength. From robustness study % RSD was found to be within limit of 2 % for the Lisinopril and Hydrochlorothiazide.

Table 18. Results of LOD and LOQ values of Lisinopril and Hydrochlorothiazide

Drugs	LOD (µg/ml)	LOQ (µg/ml)
Lisinopril	0.05	0.16
Hydrochlorothiazide	0.10	0.30

Table 19. Data for Robustness study of Lisinopril and Hydrochlorothiazide

Sr.No	Parameter	Condition	Lisinopril				Hydrochlorothiazide			
			Area	Mean	SD	% RSD	Area	Mean	SD	%RSD
1	Change in Flow rate (ml/min)	0.7	1623505	1626394	12047	0.74	1290872	1292729	4691	0.36
2		0.8	1639624				1289250			
3		0.9	1616054				1298065			
1	Change in Wavelength (nm)	289	1635987	1637193	2943	0.18	1287154	1279585	8092	0.63
2		291	1640549				1271055			
3		293	1635045				1280546			

Table 20. Data for ruggedness study of Lisinopril and Hydrochlorothiazide

Sr.No	Analyst	Lisinopril				Hydrochlorothiazide			
		Area	Mean area*	SD	% RSD	Area	Mean area*	SD	% RSD
1	Analyst-I	1632605	1631368	1370	0.08	1298054	1298354	4097	0.32
		1629894				1294415			
		1631604				1302594			
2	Analyst-II	1629045	1632268	3111	0.19	1290544	1287283	6003	0.47
		1632504				1290950			
		1635255				1280354			

Table 21. Data for specificity study of Lisinopril and Hydrochlorothiazide

Drug	Drug conc. (µg/ml)	Excipients (µg/ml)	Total conc. (µg/ml)	Area	Mean	SD	%RSD
Lisinopril	4	8	12	556245	552777.67	3217.99	0.58
	4	8	12	549887			
	4	8	12	552201			
	8	8	16	1125054	1127454.67	3986.13	0.35
	8	8	16	1132056			
	8	8	16	1125254			
	12	8	20	1626054	1629765.00	3492.27	0.21
	12	8	20	1630254			
	12	8	20	1632987			
Hydrochlorothiazide	5	10	15	436598	431163.33	5264.65	1.22
	5	10	15	426087			
	5	10	15	430805			
	10	10	20	889254	887933.00	1167.21	0.13
	10	10	20	887504			
	10	10	20	887041			
	15	10	25	1289040	1290284.33	11692.27	0.91
	15	10	25	1279264			
	15	10	25	1302549			

Table 22. Data of % Assay of marketed formulation

Sr. NO.	Drug	Area of Sample	Area of Standard	Drug Recovered	% Assay
1	Lisinopril	1626508	1630548	19.95	99.75
2	Hydrochlorothiazide	1281098	1292045	39.66	99.15

Table 23. Datafor System suitability study

Sr. No.	Lisinopril			Hydrochlorothiazide		
	Retention Time (min)	Theoretical plates	Asymmetry Factor	Retention Time (min)	Theoretical plates	Asymmetry Factor
1	3.125	8846	1.08	4.61	9820	1.09
2	3.202	8716	1.09	4.598	8956	1.1
3	3.186	8955	1.08	4.633	9263	1.09
4	3.196	8845	1.08	4.684	9163	1.09
5	3.174	9026	1.08	4.615	9324	1.09
6	3.089	8756	1.09	4.587	9059	1.1
Mean			1.08			1.09
SD			0.01			0.01
%RSD			0.48			0.47

Hence it is robust and complies as per ICH guidelines. Results are shown in Table no. 19.

- **Ruggedness**
  Ruggedness was studied by different analysts. From robustness study % RSD was found to be within limit of 2 % for the Lisinopril and Hydrochlorothiazide. Hence it complies as per ICH guidelines. The results obtained are shown in Table no.20.
- **Specificity**
  Excipientsandimpuritieswerenotinteractingwiththestandarddrugs.Hencethe method is specific. Results of specificity are shown in Table no. 21.
- **% Assay of Marketed formulation**
  The % Assay of (Lipril-H) marketed formulation of Lupin Pharmaceutical was calculated and given in Table No. 22.
- **System Suitability**
  System suitability parameters were measured to verify the system, method and column performance. Standard solution of Lisinopril and Hydrochlorothiazide was injected in to the system for fivetimes and system suitability parameters were checked.

CONCLUSION

In the present research work, a successful attempt was made for determination of Lisinopril and Hydrochlorothiazide in Bulk and dosage form by high-performance liquid chromatography. The method was developed by experimentation, based on literature survey. The simplicity, rapidity, reproducibility and economy of the proposed method completely fulfill the objective of this research work.All the analyzed validation parameters showed acceptable data with satisfactory correlation co-efficient and lower % RSD as per the ICH guidelines. The developed method can be utilized by industry for quantitative simultaneous estimation of Hydrochlorothiazide and Lisinopril as bulk and in tablet dosage form.

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