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A new method for the assay of lisinopril using molybdophosphoric acid

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Abstract A new UV-Vis molecular absorbance spectrometric method was developed for the assay of lisinopril using molybdophosphoric acid in hydrochloric acid medium. The reaction product showed a maximum absorbance at 369 nm. The optimum conditions of the reaction were established. The developed method was validated. The method showed a good linearity in the range of 8.0 - 32 µg/mL (correlation coefficient r = 0.9995). The detection limit (LD) was 2.33 µg/mL and the quantification limit (LQ) was 7.79 µg/mL. The precision and the accuracy were determined, (RSD = 1.64%); mean recovery was 100.59% in the 98.51-102.39% concentration range.

Keywords: lisinopril, molybdophosphoric acid, spectrometric method, validation.

1. Introduction

Lisinopril is a drug of the angiotensin converting enzyme (ACE) inhibitor class that is primarily used in treatment of hypertension, congestive heart failure, heart attacks and also in preventing renal and retinal complications of diabetes. Historically, lisinopril was the third ACE inhibitor, after captopril and enalapril, and was introduced into therapy in the early 1990s. Lisinopril has a number of properties that distinguish it from other ACE inhibitors: it is hydrophilic, has long half-life and tissue penetration and is not metabolized by the liver [1].

This paper presents a UV-Vis molecular absorbance spectrometric method for the assay of lisinopril using the molybdophosphoric acid in hydrochloric acid medium [2, 3]. The developed method was validated using the following criteria: linearity, detection and quantification limit, precision, accuracy and robustness [4-7].

2. Experimental

2.1.Reagents and apparatus

- lisinopril (100.03% pure reference substance, produced by Lupin, India)
- aqueous solutions of hydrochloric acid: 0.1 M – 1.0 M, of molybdophosphoric acid (PMA): 0.1% - 3.0% and of sodium lauryl sulphate: 0.01%;
- stock solution (1 mg/mL): 100 mg lisinopril was dissolved in water in a 100 mL volumetric flask;
- working solutions containing from 2 to 40 µg/mL lisinopril were obtained by diluting the stock solution with water.
- analytical balance (Kern 770);
- UV-Vis Spectrophotometer (Hewlett Packard 8453).

Except lisinopril, all other reagents were purchased from Merck.

2.2. Principle of the method

Lisinopril forms with PMA in hydrochloric acid medium an insoluble compound which can be spectrometrically determined from the suspension at 369 nm.

In order to establish the optimum wavelength for the detection, 2 mL of the 10 µg/mL working solution were mixed with 1 mL 0.2 M hydrochloric acid and 1% PMA solution and then 1 mL 0.01% sodium lauryl sulphate were added, in order to

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prevent the precipitation. The UV-Vis absorption spectrum was recorded using 1 cm cell, after 20 minutes.

In order to establish the optimum working conditions, two solutions of 8 µg/mL and 32 µg/mL were used, while the parameters of the method were changed. We established the optimum concentration of the hydrochloric acid solution and of the necessary PMA solution and we determined the stability of the reaction product.

2.3. Procedure

1 mL 0.2 M hydrochloric acid and 1 mL of 1% molybdophosphoric acid solution were added to 2 mL lisinopril solution and 1 mL of 0.01% lauril sodium sulphate. The absorbance was measured at 369 nm versus a blank solution prepared in similar conditions.

3. Results and Discussions

From the analysis of the absorption spectra (**Fig. 1**), we observed a maximum of absorbance for the reaction product at 369 nm. This value was used for all the determinations.

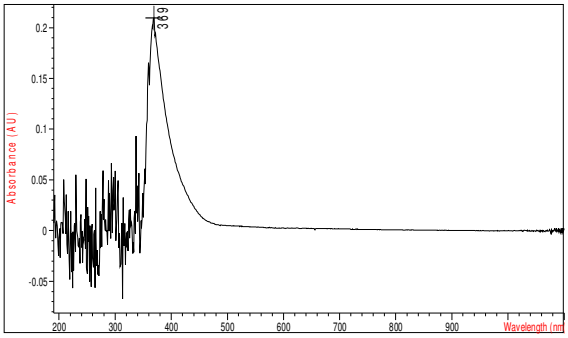

Fig. 1. The spectrum of the reaction product obtained for 20 µg/mL lisinopril

The best concentration of the hydrochloric acid was established at 0.2 M, because when using this solution the maximum absorbance measured at 369 nm had the greatest value (as seen in **Table 1**). The same criterion was used when optimum concentration of molybdophosphoric acid was set to 1% (**Table 2**). After studying the stability of the samples it was established that the chemical reaction between lisinopril and molybdophosphoric acid was final 20 minutes after the last reagent was added. Also, the results shown in **Table 3** proved that the absorbance remains almost the same for at least another 20 minutes, time sufficient enough for the analysis to be performed.

Table 1. Study of media acidity

HCl mol/L	Lisinopril (369 nm)	
	8 µg/mL	32 µg/mL
0.1	0.01965	0.29441
0.2	**0.06743**	**0.99145**
0.3	0.06021	0.97125
0.4	0.05742	0.90426
0.5	0.05096	0.75522

Table 2. Study of reagent concentration

Molybdophosphoric acid %	Lisinopril (369 nm)	
	8 µg/mL	32 µg/mL
0.1	0.01965	0.2851
0.5	0.02856	0.68221
1	**0.06752**	**0.99853**
2	0.06741	0.98963
3	0.06642	0.98211

Table 3. Stability study

Time (minutes)	Lisinopril (369 nm)	
	8 µg/mL	32 µg/mL
5	0.01965	0.36854
10	0.05221	0.59562
15	0.06521	0.85422
20	**0.06642**	**0.99429**
25	0.06637	0.99422
30	0.06634	0.99341
40	0.06589	0.99317
50	0.06555	0.99322
60	0.06502	0.98702

3.1. Linearity

Linearity was studied in the 2 - 40 µg/mL concentration range (**Fig. 2**). The obtained data were statistically evaluated (**Table 4**) and the calibration curve was obtained (**Fig. 3**).

Table 4. Study of the linearity of the method

Lisinopril (μg/mL)	Absorbance (369 nm)				
	Ist Series	IInd Series	IIIrd Series	IVth Series	Average
2	0.01199	0.01325	0.01348	0.01237	0.01277
4	0.05103	0.01335	0.04596	0.04258	0.03823
8	0.06696	0.06672	0.06907	0.06132	0.06602
12	0.22289	0.22251	0.20025	0.20291	0.21214
16	0.38779	0.38281	0.37350	0.36929	0.37835
20	0.55873	0.57047	0.58727	0.54170	0.56454
24	0.73901	0.74634	0.74559	0.73601	0.74174
28	0.90498	0.90912	0.94829	0.90673	0.91728
32	1.10170	1.10910	1.08880	1.10554	1.10129
36	1.16540	1.16240	1.15970	1.17210	1.16490
40	1.18520	1.18690	1.18221	1.18253	1.18421
Correlation and regression coefficients r = 0.9995, r^2 = 0.9990; Standard error = 0.0339; Intercept = – 0.3025; Slope = 0.04356					

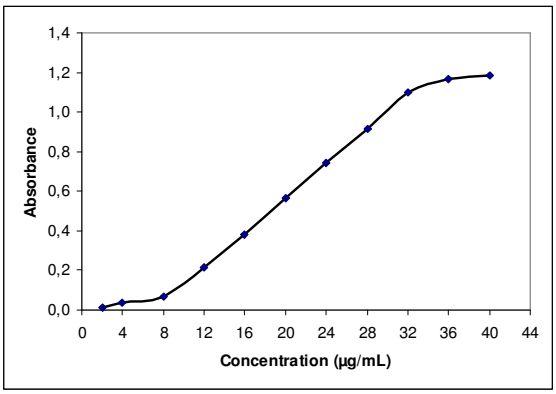

Fig. 2. Study of method linearity

According to the experimental data, the developed method for lisinopril determination was linear in 8 – 32 μg/mL concentration range.

When we compared this concentration range with that of other published methods [8-10] we found that it was very similar, but this new method has the following advantages: it does not involve rare or complex reagents, nor does it involve the use of toxic solvents. It is simple and easy to perform.

The calibration curve equation was established:

Absorbance = 0.043 x Concentration – 0.302.

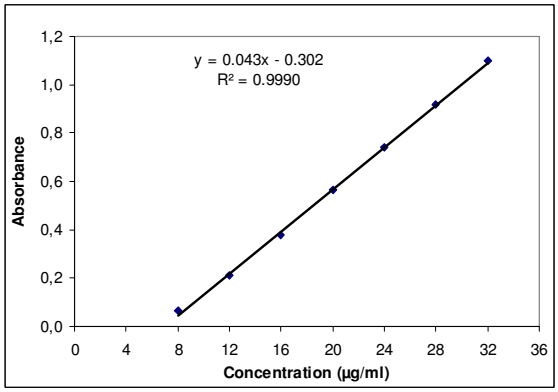

Fig. 3. Calibration curve

3.2. *Detection and quantification limits*

Detection and quantification limits were calculated using the following formulas [2,3]:

LD=3 x Standard error / Slope=2.3398 μg/mL

LQ=10 x Standard error / Slope=7.7995 μg/mL

Table 5. Study of the precision and of the accuracy of the method

Concentration (μg/mL)	Precision		Intermediate precision		Accuracy	
	Real concentration (μg/mL)	RSD %	Real concentration (μg/mL)	RSD %	Real concentration (μg/mL)	Recovery (%)
16	15.6801	1.56	15.7618	1.11	16.3822	102.39
	15.8130		16.0907		15.7618	98.51
	16.1589		15.8125		15.8718	99.20
20	19.6551	1.40	19.8016	1.84	19.9085	99.54
	19.9574		20.4447		20.2152	101.08
	20.2147		19.8092		20.4030	102.01
24	23.7856	1.66	24.3808	1.40	23.8877	99.53
	24.5851		23.7615		24.1939	100.81
	24.1258		24.3050		24.5465	102.28
					mean	100.59

3.3. Precision

For precision determination, three solutions of 16, 20 and 24 μg/mL lisinopril were used. Three assays were performed for each concentration. Two sets of assays were performed in different days in order to evaluate the *intermediary precision*.

The samples concentrations were calculated using the calibration curve equation (**Table 5**). We observed that for each set of data and for both sets together the relative standard deviation was lower than 2% (at most RSD = 1.66%) [4]. This fact proved that the proposed method was precise.

3.4. Accuracy

In order to establish the accuracy of the method, lisinopril solutions of 16, 20 and 24 μg/mL were analyzed. For each concentration, three determinations were performed [6].

The concentration of the samples was calculated from the experimental values of the absorbance, using the regression curve equation (Table 5). We observed that the recovery was 100.59% for the studied concentration range, the mean (minimum was 98.51% and maximum was 102.39%) and the relative standard deviation was under 2% (RSD = 1.42 %). These values prove that the proposed method was accurate.

3.5. Robustness

The evaluation of robustness was performed for system suitability to ensure the validity of analytical procedure. This was done by varying the instrument, analyst, and time of study. The analysis was performed on Shimadzu UV-Visible spectrophotometer, model-1700. Interday and intraday analysis was performed by changing the analyst.

Reproducibility of the results confirmed the robustness of the method.

4. Conclusions

A UV-VIS molecular absorbance spectrophotometric method was developed for the assay of lisinopril using molybdophosphoric acid in hydrochloric acid medium. The reaction product shows a maximum absorbance at 369 nm.

The analytical method was validated by establishing the linearity domain in the range of 8.0 – 32 μg/mL, with a correlation coefficient of r = 0.9995, the detection limit is 2.33 μg/mL, the quantification limit is 7.79 μg/mL lower than the lowest concentration from the linearity domain, method precision RSD% = 1.64% [4] and the accuracy evaluated by recovery is R = 100.59%.

In conclusion, the proposed method is simple, easy to perform, sensitive, linear, precise, accurate and robust.

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6. References

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