A New Spectrometric Method for Quantitative Determination through Molecular Absorption of Lisinopril

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A simple and accurate spectrometric method was developed for the quantitative determination of lisinopril. The method was based on the precipitation reaction with phosphotungstic acid in acidic medium. Optimum working conditions were established and the new method was validated. The maximum absorbance of the precipitate was measured at 335nm. The method presented a good linearity in the concentration range 9-33μg/mL and regression coefficient 0.9995. The RSD for the precision of the method was 0.42, the RSD for the intermediate precision was 1.11, and the recovery values were ranged between 99.15-100.97%. The proposed method for the determination of lisinopril was simple, rapid and cost effective compared with other techniques.

Keywords: spectrophotometric method, validation, lisinopril, phosphotungstic acid.

Lisinopril is an angiotensin converting enzyme inhibitor drug used in the treatment of hypertension, congestive heart failure, heart attacks and also in preventing renal and retinal complications of diabetes [1]. It is a derivative that belongs to nitrogen heterocycle compounds with the following chemical name [(S)-1-[N2-(1-carboxy-3-phenylpropyl)-L-lysyl]-L-proline dihydrate] [1-4].

This new spectrofotometric method for the quantitative determination of lisinopril through molecular absorption uses phosphotungstic acid in acidic medium [5-7]. The developed method was validated using the following criteria: linearity, detection and quantification limits, precision, accuracy and robustness [8-10].

Experimental part

The reagents and apparatus used were: lisinopril as 100.03% pure reference substance (Lupin, India), phosphotungstic acid (Merck), hydrochloric acid (Merck), sodium lauryl sulphate (Merck), Kern 770 analytical balance, Hewlett Packard 8453UV-Vis Spectrophotometer.

Lisinopril forms with phosphotungstic acid in acidic medium an insoluble compound which can be spectrometrically measured at 335nm.

In order to establish the optimum wavelength for the detection, a 24 μg/mL Lisinopril sample was analyzed. 2mL of the 60μg/mL lisinopril solution was mixed with 1mL of 2% phosphotungstic acid solution and 1mL of 0.5M hydrochloric acid solution and 1mL of 0.01% sodium lauryl sulphate solution. The UV-Vis absorption spectrum was recorded using 1cm quartz cell, after 15 min.

In order to establish the optimum acidity of the medium, it was first established that hydrochloric acid was the best option and then seven different concentration levels (0.2M, 0.3M, 0.4M, 0.5M, 0.6M, 0.7M, 0.8M) of reagent were used, while the parameters of the method were maintained unchanged.

In order to establish the optimum concentration of phosphotungstic acid, five solutions of reagent (0.50, 1.00, 1.50, 2.00, 2.50 and 3.00%) were used, while the parameters of the method were maintained unchanged.

In order to establish the optimum concentration of the sodium lauryl sulphate, six solutions of reagent (0.0050, 0.0075, 0.0100, 0.0200, 0.0300 and 0.0400%) were used, while the parameters of the method were maintained unchanged.

In order to assess the optimum time for measuring the absorbance values at 335nm, 2 samples containing 9μg/mL and 33μg/mL of lisinopril were used. Their absorbance was measured every 5 min for 60 min at 335nm, against a blank prepared in the same conditions in a 1cm cell.

Results and discussions

From the analysis of the absorption spectra (fig. 1), was observed a maximum of absorbance for the reaction product at 335nm. That wave length was used for all the determinations.

The reaction in between lisinopril and phosphotungstic acid occurs in acidic medium. The best concentration of hydrochloric acid solution was established at 0.5M, because when using that solution the maximum absorbance measured at 335nm had the greatest value (table 1). The optimum concentration of phosphotungstic acid solution was established based on the experimental data from table 2.

To stabilize the suspension it was necessary to add a surfactant. We have undertaken a study for choosing the best surfactant of the following: glycerin, sodium lauryl sulfate, methyl cellulose, carboxymethyl cellulose. The best results were obtained when sodium lauryl sulfate was used. The optimum concentration of sodium lauryl sulfate was established based on the experimental data from table 3.

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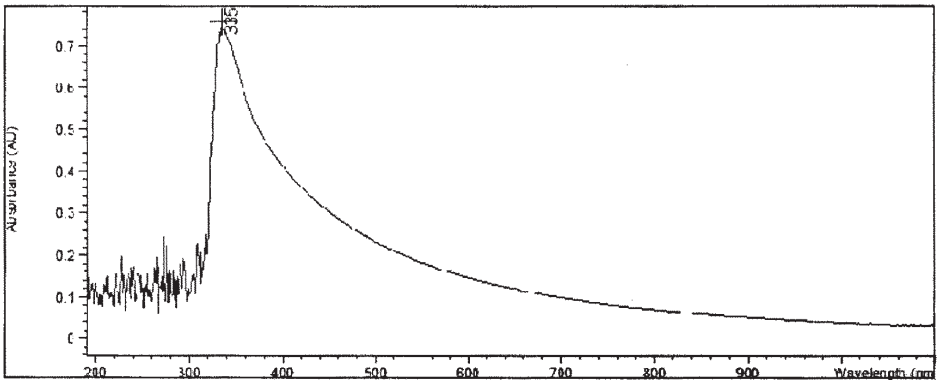

Fig. 1. The spectrum of the reaction product obtained for 10μg/mL lisinopril

Table 1
OPTIMUM CONCENTRATION OF HYDROCHLORIC ACID

Hydrochloric acid (mol/L)	Lisinopril	
	9.0μg/mL	33.0μg/mL
	Absorbance (335nm)	
0.2	0.05423	0.64528
0.3	0.09655	0.77582
0.4	0.15286	0.90155
0.5	0.17325	1.04980
0.6	0.15263	1.00990
0.7	0.14254	0.98122
0.8	0.13241	0.88311

Table 2
OPTIMUM CONCENTRATION OF PHOSPHOTUNGSTIC ACID

Phosphotungstic acid (%)	Lisinopril	
	9.0μg/mL	33.0μg/mL
	Absorbance (335nm)	
0.5	0.01965	0.28510
1.0	0.04356	0.58221
1.5	0.09252	0.79853
2.0	0.17256	1.05489
2.5	0.16642	0.99211
3.0	0.14265	0.91630

After studying the stability of the samples it was established that the chemical reaction between lisinopril and phosphotungstic acid was final after 15 min (table 4). Also, it was proved that the absorbance remains almost the same for at least another 15 min, time sufficient enough for the analysis to be performed.

Optimum procedure: 2mL of lisinopril working solutions were mixed with 1mL of 0.5M hydrochloric acid solution, 1mL of 0.2% phosphotungstic acid solution and 1mL 0.01% sodium lauryl sulphate solution. The final lisinopril concentration of the samples were in the 9-33μg/mL range. The absorbance was measured after 15 min at 335nm versus a blank solution prepared in similar conditions.

Table 3
OPTIMUM CONCENTRATION OF SODIUM LAURYL SULFATE

Sodium lauryl sulfate (%)	Lisinopril	
	9.0μg/mL	33.0μg/mL
	Absorbance (335nm)	
0.005	0.03781	0.65293
0.075	0.08945	0.89136
0.010	0.16956	1.05325
0.020	0.16715	1.00994
0.030	0.15262	0.99362
0.040	0.12565	0.89235

Table 4
STABILITY STUDY

Time (minutes)	Lisinopril	
	9.0μg/mL	33.0μg/mL
	Absorbance (335 nm)	
5	0.09026	0.76824
10	0.14236	0.89562
15	0.16331	1.0542
20	0.16242	1.0512
25	0.16542	1.0492
30	0.15821	1.0504
40	0.14742	1.0221
50	0.12655	0.99522
60	0.11502	0.89412

Linearity was studied in the 3-36μg/mL concentration range (fig. 2). The obtained data were statistically evaluated (table 5) and the calibration curve was obtained (fig. 3).

According to the experimental data, the developed method for lisinopril determination was linear in 9-33μg/mL concentration range. When we compared this concentration range with that of other published methods [11-14] we found that it was very similar, but this new method has the following advantage: it does not involve rare or complex reagents. It is simple and easy to perform.

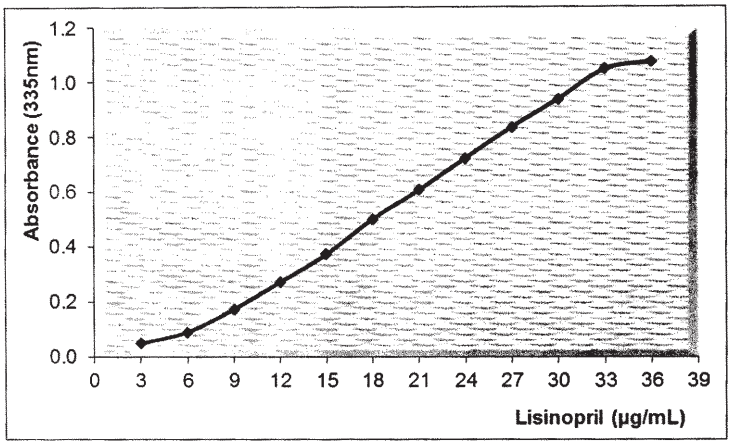

Fig. 2. Study of method linearity

Lisinopril (μg/mL)	Absorbance (335nm)				
	Ist Serie	IInd Serie	IIIrd Serie	IVth Serie	Average
3	0.06369	0.06025	0.06936	0.00594	0.04981
6	0.08506	0.08562	0.10535	0.08845	0.09112
9	0.15969	0.16969	0.19468	0.17456	0.17465
12	0.26235	0.27123	0.28459	0.27002	0.27204
15	0.36139	0.35139	0.40375	0.37452	0.37276
18	0.49511	0.48751	0.51833	0.50426	0.50130
21	0.59697	0.60697	0.62430	0.60254	0.60769
24	0.73912	0.72912	0.71146	0.71458	0.72357
27	0.81787	0.85787	0.83282	0.83450	0.83576
30	0.93735	0.93535	0.94347	0.93451	0.93767
33	1.04610	1.05020	1.05430	1.03650	1.04677
36	1.01260	1.05420	1.10620	1.12510	1.07452
Correlation and regression coefficients r = 0.9997, r^2 = 0.9994; Standard error = 0.0275; Intercept = -0.1658; Slope = 0.0368					

Table 5
STUDY OF METHOD LINEARITY

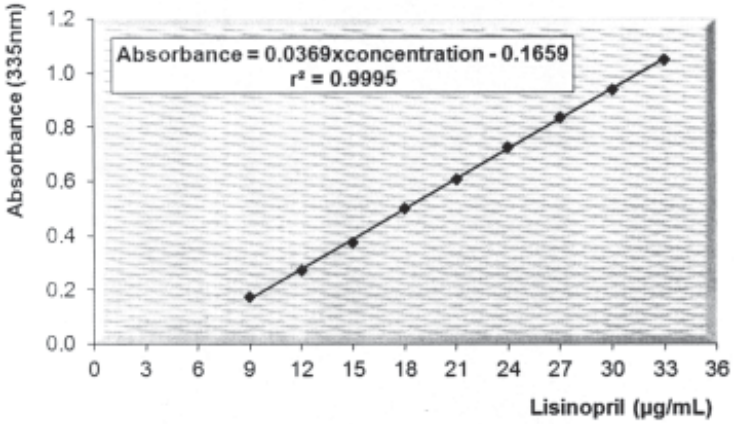

Fig. 3. Calibration curve

Lisinopril (μg/mL)	Precision		Intermediate precision		Accuracy	
	Found (μg/mL)	RSD (%)	Found (μg/mL)	RSD (%)	Absorbance	Recovery (%)
18	18.0999	0.94	0.49627	1.26	0.48217	100.07
	18.0223		0.51248		0.47956	99.74
	17.7754		0.49998		0.48917	100.96
21	21.0465	0.75	0.60982	0.86	0.60872	99.61
	20.9645		0.61025		0.61356	100.13
	21.2739		0.59854		0.59652	98.27
24	24.1629	0.91	0.72831	0.71	0.73215	98.96
	24.1865		0.71985		0.72971	98.73
	23.7944		0.71596		0.73654	99.38
					Mean	99.54

Table 6
STUDY OF THE PRECISION AND ACCURACY OF THE METHOD

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

LD = 3 x Standard error/Slope = 2.24 μg/mL

LQ = 10 x Standard error/Slope = 7.47μg/mL

Precision: three samples of 18, 21 and 24μg/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 concentrations of the samples were calculated using the calibration curve equation (table 4). We observed that for each set of data and for both sets together the relative standard deviation was lower than 2% (at most RSD = 0.67%) [4]. That proved that the proposed method was precise.

Accuracy: in order to establish the accuracy of the method, lisinopril samples of 18, 21 and 24μg/mL were analyzed. For each concentration, three determinations were performed [5].

The concentration of the samples was calculated from the experimental values of the absorbance, using the regression curve equation (table 6). Was observed that the recovery was 99.54% for the studied concentration range, the mean (minimum was 98.27% and maximum was 100.96%) and the relative standard deviation was under 2% (RSD = 0.81%). These values prove that the proposed method was accurate.

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 a 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.

Conclusions

A spectrophotometric method was developed for the assay of lisinopril using phosphotungstic acid in acidic medium. The reaction product showed a maximum molecular absorbance peak at 335nm.

The analytical method was validated by establishing the linearity domain in the range of 9.0–33.0 μg/mL, with a correlation coefficient of r = 0.9997, the detection limit is 2.24μg/mL, the quantification limit is 7.47μg/mL lower than the lowest concentration from the linearity domain.

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

References

1. BUTNARIU, R., MANGALAGIU, I.I., Bioorgan. Med. Chem., **17**, 2009, p. 2823.
2. BALAN, A.M., FLOREA, O., MOLDOVEANU, C., ZBANCIOC, GH., IUREA, D., MANGALAGIU, I.I., Eur. J. Med. Chem., **44**, 2009, p. 2275.
3. BUTNARIU, R., CAPROSU, M., BEJAN, V., UNGUREANU, M., POIATA, A., TUCHILUS, C., FLORESCU, M., MANGALAGIU, I.I., J. Heterocyclic Chem., **44**, 2007, p. 1149.
4. MANDRESCU, M., SPAC, A.F., DORNEANU, V., Rev. Chim. (Bucharest), **60**, no. 2, 2009, p. 160.
5. VIERIU, M., BIBIRE, N., PESTE, G., DORNEANU, V., POTORAC, L., Rev. Chim. (Bucharest), **64**, no. 3, 2013, p. 298.
6. PANAINTE, A.D., BIBIRE, N., TANTARU, G., APOSTU, M., VIERIU, M., DORNEANU, V., Rev. Chim. (Bucharest), **65**, no. 8, 2014, p. 916.
7. GHERMAN, S., ZAVASTIN, D., SPAC, A., DORNEANU, V., Rev. Chim. (Bucharest), **64**, no. 11, 2013, p. 1224.
8. ROMAN. L., BOJITA, M., SANDULESCU, R., MUNTEAN, D.L., Validarea metodelor analitice, Ed. Medicala, Bucuresti, 2007, p. 201.
9. ICH Topic Q2B: Validation of Analytical Procedures (CPMP/ICH/281/95), The European Agency for the Evaluation of Medicinal Products.
10. BIBIRE, N., VIERIU, M., TANTARU, G., APOSTU, M., AGOROAEI, L., PANAINTE, A.D., ZNAGOVAN, A., VLASE, A., Rev. Chim.(Bucharest), **65**, no.7, 2014, p. 807.
11. ANDREI, C., MOISE, C., Mat. Plast., **40**, no. 1, 2003, p. 53.
12. PANA, A.M., RUSNAC, L.M., BANDUR, G., DELEANU, C., BALAN, M., SILION, M., Mat. Plast., **47**, no. 3, 2010, p. 299.
13. IONESCU, D., POPESCU, M., RIZEA, G.D., MIHELE, D., BULEARCA, G., IVOPOL, M., MIHALCEA, F., Rev. Chim. (Bucharest), **65**, no. 5, 2014, p. 507.
14. INCEU, M., MEGHESAN, A., SANDU, I., HOSU, A., CIMPOIU, C., Rev. Chim. (Bucharest), **66**, no. 3, 2015, p. 368.

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