Journal of Medicinal and Chemical Sciences 6 (2023) 1112-1119

Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Original Article

Simple Spectrophotometric Method for Determination of Drug Lisinopril in Pure Form and Pharmaceutical Formulations

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ARTICLE INFO

Article history

Receive: 2022-10-13
Received in revised: 2022-10-22
Accepted: 2022-10-24
Manuscript ID: JMCS-2210-1822
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Nadereh Shirvani
Editor who approved publication:
Dr. Khosro Khajeh,

DOI:10.26655/JMCHEMSCI.2023.5.16

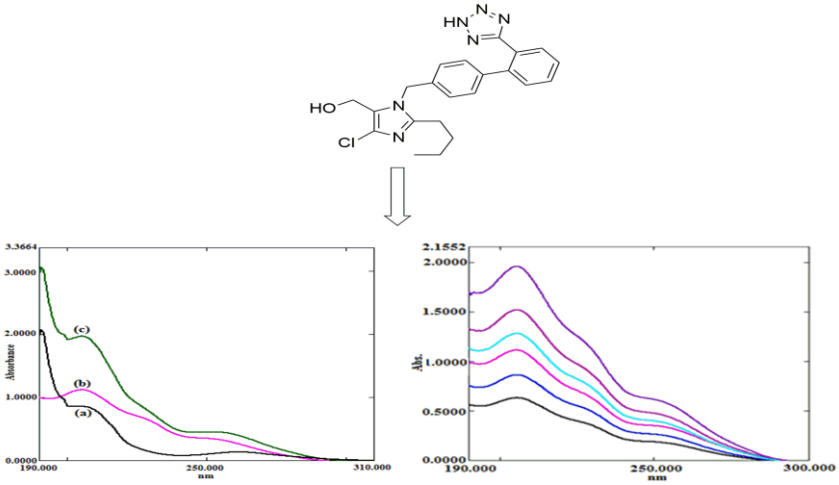
KEYWORDS

Medicine
Method
Determination
Pure
Pharmaceutical

ABSTRACT

A simple, sensitive method for simultaneous quantifying of lisinopril in the presence of losartan in its pure form and pharmaceutical formulations in tablet form by using UV-Vis spectrophotometric. This method depends on the first spectrum derivative utilization zero intersection, the summit to foundation line, and the summit of area measurement. A Linearity was used for a range of drugs, lisinopril concentrations 2-16 µg/mL and losartan concentrations 2-14 µg/mL in the mixture. The correlation coefficients of lisinopril in the presence of losartan (8 µg/mL) using peak to baseline 0.9980, 0.99674, and peak area 0.99944 but the correlation coefficients of losartan in the presence of lisinopril 6 µg/mL utilization peak to baseline 0.9997, 0.9984, 0.9994 and peak area 0.9972, 0.9952. The limits of detection (LOD) of 0.0125 µg/mL for lisinopril and losartan were measured by this method. Determination of precision and accuracy by measuring Relative Standard Deviation (RSD %) whose value is less than 4 % and Recovery% (Rec. %) of acceptable value. The method showed success in the direct estimation of each of the two drugs, lisinopril and losartan, in the presence of the other in pure form and pharmaceutical formulations in tablet form.

GRAPHICAL ABSTRACT



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Introduction

Lisinopril 1-[6-Amino-2-(1-carboxy-3-phenyl-propylamino)-hexanoyl]-pyrrolidine-2 carboxylic acid. Lisinopril has a molecular formula of $C_{21}H_{31}N_3O_5$ and a molecular weight equal to 441.52 g/mol [1]. *Lisinopril* is an angiotensin-converting enzyme ACE inhibitor indicated for the treatment of hypertension and heart failure. It is probably utilized alone as primary treatment, in conjunction with other categories of hypertension agents, or as an adjuvant therapy in managing heart failure in patients who do not respond adequately to diuretics and digitalis. ACE inhibitors discount the production of angiotensin II, a plus bradykinin level, and slash sympathetic nervous system activity. They pose a special feature in treating patient with diabetes, slowing the development and progression of diabetic glomerulopathy. It is only available in the market as oral tablets despite its low systems bioavailability of 25 % varying from 6- 60 % next oral management due to intersubject variability, figure (1: a) structure of lisinopril [2-4]. Losartan ([2- butyl-5- chloro-3- [[4-[2-(2*H*-tetrazole-5- yl) phenyl] phenyl] methyl] imidazol-4-yl] methanol) figure (1: b) is non-peptide medicine with gradual and long-lasting antihypertensive effect, which exerts its action via specific blockage of angiotensin II receptors (Figure 1) [5]. Losartan potassium is produced in different trade products: Cozaar, Lortaan, Neo-Lotan (Merck & Co.); Losaprex (Sigma-Tau); Oscaar (Riesel); Lavestra (Hungary); Lorista (Bulgaria, Romania); Losartan-Kalium TAD (Germany); Losartan Krka (Denmark, Greece, Italy, France); Lozitar (Pinewood Laboratories Ltd.) [6].

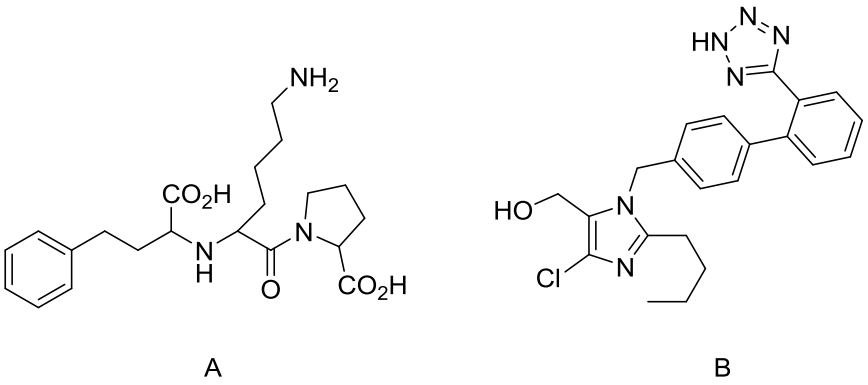


Figure 1: a) structure of lisinopril and b) structure of losartan

Several methods have been developed for the estimation of lisinopril using HPLC methods [7-9], UV-Vis [10-18], Chromatographic [19], LC-MS/MS [20], Potentiometriy [21, 22], Voltammetric [23], Spectrofluorometric [24, 25], FT-IR [26, 27], X-Ray [28] and Polarographic [29]. This research aims to use a sensitive and accurate spectrophotometric method using the derivative to estimate lisinopril in its pure form and the pharmaceutical formulations in the presence of the drug losartan, which is close to it in the spectrum; it is not possible to use other more accurate and sensitive methods for its estimation.

Materials and Methods

All solutions used were dissolved in distilled water. Pure lisinopril, losartan, fructose-glucose – lactose, and sucrose were commercially obtained from Samarra company in Iraq S D I. The tablets of lisinopril contained 5 mg lisinopril from two American companies, Bristol and Accord. The tablets of losartan contained 50 mg losartan from Micro Company in India, also a pioneer company in Iraq.

Standard preparation

The standard solution for both lisinopril and losartan was prepared with solution 0.01 g in distilled water, then transferred to a volumetric flask of 100 mL, also completed the volume to the mark with distilled water. From this standard

solution of drugs, lisinopril and losartan were prepared with concentrations ranging from 2-16 µg/mL to 2-14 µg/mL.

Sample preparation

Ten tablets of both drugs were taken, crushed and mixed. Then the weight was taken equal to the rate of one tablet; after that, it was dissolved in distilled water and transferred to a volumetric flask of 100 mL, and a volume was completed to the mark with distilled water. A solution was filtered to get 100 µg/mL for both.

Apparatus

UV-Vis double beam spectrophotometer model 1800 Shimadzu made in Japan was used. Absorbance for samples together blank was registered by utilization cell 1 mL made of quartz. Each model's wavelength range was measured at 190-1100 nm.

Procedures

Absorbance was measured for standard solutions 2-16 µg/mL and 2-14 µg/mL from lisinopril and losartan, respectively, by using zero rank method utilization scanning of UV-Vis from 190-300 nm to get the maximum wavelength for each of the lisinopril and losartan. A solution from many mixtures for each medicine was made of the standard 100 µg/mL solution. The first step was made of the mixture via transferring volumes different from lisinopril 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, and 0.8 mL to eight calibrated flasks volumes 5 mL containing volumes of constant from losartan 0.3 mL. The second step was made of the mixture via transferring the same sizes of volumes from lisinopril in eight calibrated flasks, volumes 5 mL with the same size contained constant from losartan 0.7 mL. the third step was made of the mixture via transferring volumes different from losartan 0.1, 0.2, 0.3, 0.4, 0.5, and 0.7 mL to six volumetric flasks size 5 mL containing constant from lisinopril 0.1 mL. The fourth step was made of the mixtures via transferring volumes of the same from losartan into six volumetric flasks size 5 mL containing a constant volume from lisinopril 0.6 mL. Each mixture was used to dilute them with distilled water and measure the first derivative of the spectrum.

Results and Discussion

The absorption spectrum at λ_{max} values of pure lisinopril, losartan, and a mixture of each drug were located at 204, 205, and 205.2 nm, as shown in Figure 2. The spectrum for absorption using blank was registered before the measurement of samples; Table 1 shows the first derivative of pure lisinopril and pure losartan.

First derivative style. Zero-order absorption cannot estimate lisinopril and losartan at the same time in a mixture of solutions. So, the derived spectrum from the first-order method was successfully utilized to display perfect spectra for individuals and a mixture of drugs in Figure 3.

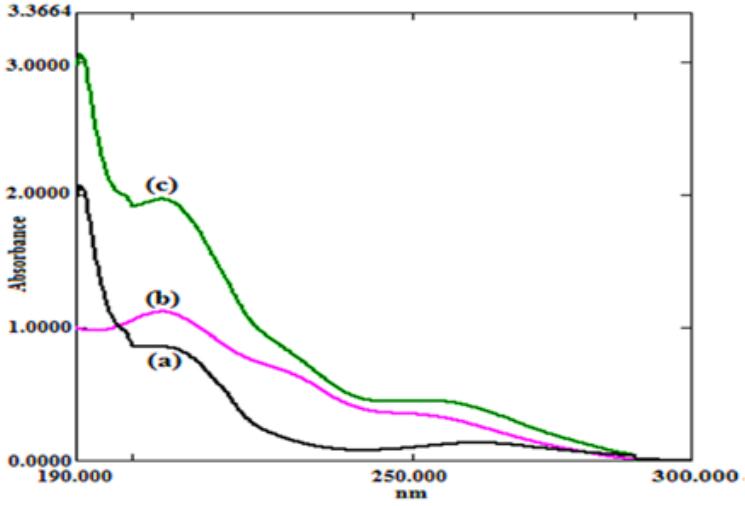


Figure 2: Zero order a) pure lisinopril 16 µg/mL b) pure losartan 6 µg/mL c) mixture of both drugs

Table 1: Statistical analysis of the first derivative for the determination of pure lisinopril and pure losartan

Slope	Correlation coefficient	Regression equation	λ (nm)	Mode of Calculation	Compound
Lisinopril	-0.0024	0.99809	Y=-0.0024x+0.0132	197.8	Peak to baseline
	-0.0024	0.9981	Y=-0.0017x+0.0044	215.2	Peak to baseline
	0.0009	0.9994	Y=0.0009x+0.0007	213.4-216.8	Peak area
	-	-	-	200.8	Zero cross
Losartan	0.0018	0.9957	Y= 0.0018x+0.0079	199.6	Peak to baseline
	-0.0012	0.9983	Y=-0.0012x+0.0051	224.6	Peak to baseline
	-0.9990	0.9990	Y=-0.0003x-0.0008	247.8	Peak to baseline
	0.0129	0.9953	Y= 0.0129x+0.064	139.4-205.4	Peak area
	0.0253	0.9981	Y=0.0253x+0.1098	233.4-262.8	Peak area
	-	-	-	205.4	Zero cross

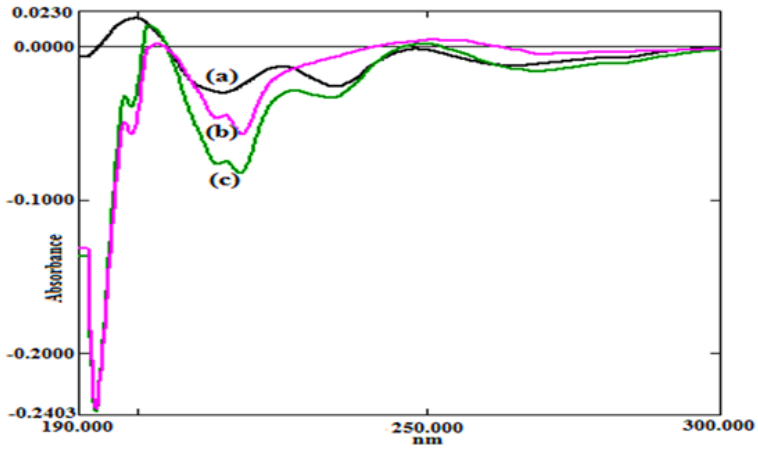


Figure 3: Derived spectrum first order for a) losartan 6 µg/mL, b) lisinopril 16 µg/mL also c) mix of each drug

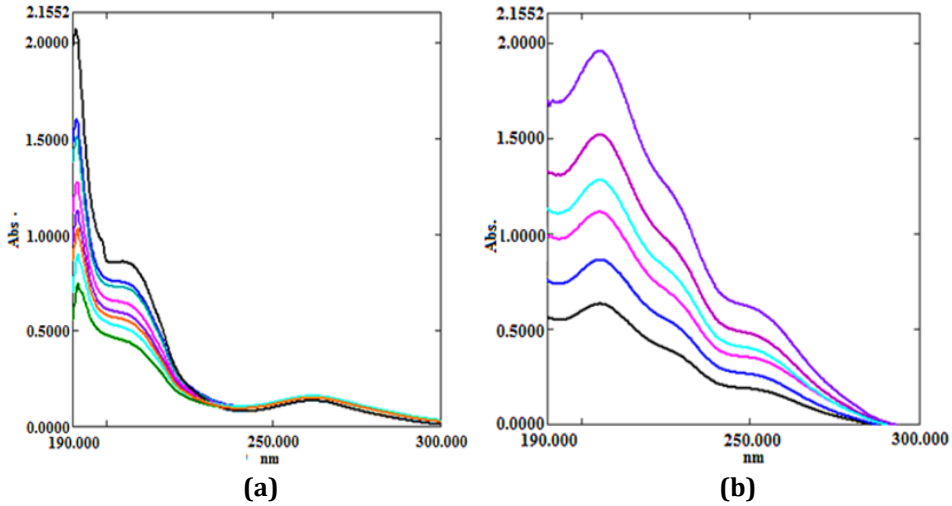


Figure 4: Spectra of a) lisinopril (2-16 µg/mL) and b) losartan (2-14 µg/mL) using method the zero-order

Table 2: Estimation lisinopril 2-16 µg/mL with losartan 8 µg/mL utilizing derived spectrum first method

correlation coefficient	regression of equation	λ (nm)	Method of analysis
-	-	200.8	Zero-cross
0.9980	Y= -0.0024x-0.0132	197.8	Peak to baseline
0.99674	Y= -0.0017x-0.0044	215.2	Peak to baseline
0.99944	Y= 0.0009x-0.0007	213.5-216.8	Peak area

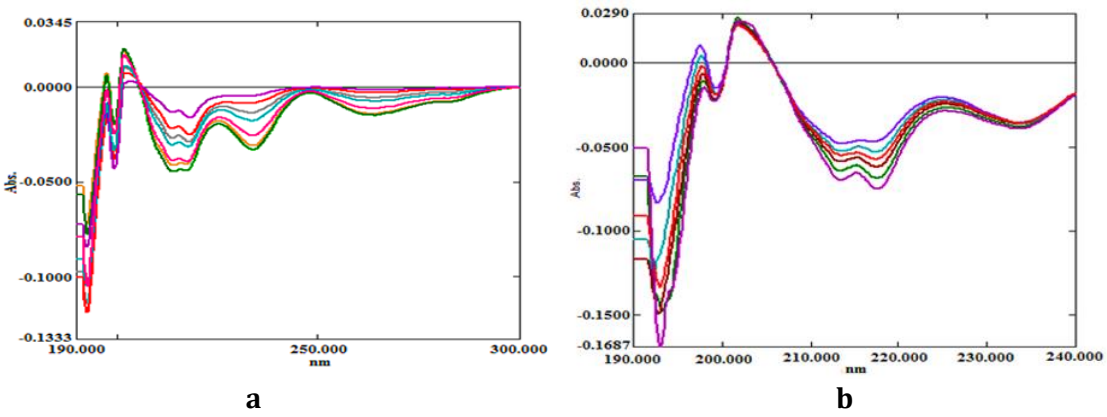
Table 3: Estimation Losartan 2-14 µg/mL with lisinopril (6 µg/mL) utilizing method derived spectrum first

Method of analysis	λ (nm)	regression of equation	correlation coefficient
Zero-cross	205.4	-	-
Peak to baseline	200.2	Y= -0.0021x-0.0329	0.9997
Peak to baseline	224.6	Y= -0.0028x-0.012	0.9984
Peak to baseline	247.8	Y= - 0.0003x-9E05	0.9994
Peak area	218. -231.8	Y= 0.0096x+0.0481	0.9972
Peak area	240.4-259	Y= 0.0115x+0.0048	0.9952

Plots of calibration to find values of the derivative spectra were utilized in sundry forms of graphical, especially zero intersection (zero-cross), summit to foundation line, and summit area. Each drug of lisinopril and losartan in this analysis was measured in the individual mixed solution of both drugs Figure 4. Tables 2 and 3 display the analytical parameters for the estimation of each drug via the derived spectrum first method.

The results obtained from the analysis of lisinopril 2-16 µg/mL with losartan drug 8 µg/mL also analysis of losartan 2-14 µg/mL with lisinopril 6 µg/mL utilizing method-derived spectrum, Figure 5 displays the results.

A simple statistical analysis was utilized to investigate the developed method's precision and accuracy. Each medicine using a different concentration was measured five times utilizing the method-derived spectrum first. The analysis method showed that it was suitable for the simultaneous estimation of lisinopril and losartan in models, as shown in Table 4.



a **b**

Figure 5: derived spectrum first for each medicine in mix a) lisinopril 2-16 µg/mL with losartan 8 µg/mL also b) losartan 2-12 µg/mL with lisinopril 6 µg/mL

Table 4: Precision and accuracy for estimation of lisinopril and also losartan in mixture utilizing derived, first for n=5

Medicine	Summit to baseline	λ (nm)	Con. µg/mL		RSD %	Rec.%
			Taken	Found		
Lisinopril	Summit to baseline	215.2	4	3.947	1.544	98.675
			8	8.077	0.980	100.962
	Peak area	213.4-216.8	4	4.061	1.390	101.525
			8	8.168	2.085	102.100
Losartan	Peak to baseline	224.6	2	1.957	2.813	97.650
			10	9.957	0.582	99.570
	Peak area	240.4-259	2	2.087	3.957	104.350
			10	10.06	0.551	100.600

1000 µg/mL stock solution from the nested is made in a volumetric flask size 5 mL. Volume 0.5 ml from both nested added to solution containing 6 µg/mL of lisinopril. Volume 0.5 mL of both nested was also added to the solution of the sample containing 12 µg/mL losartan. There was no significant variation in nested according to the suggested method; Table 5 displays the results.

The limit of Detection (LOD) was calculated using the theoretically (slope method)

LOD =3S_B / slope

S_B = σ_{n-1} standard deviation of blank for n=13, LOD for each drug lisinopril and losartan equal 0.0125 (µg/mL).

Analytical applications of the derived spectrum method utilized in this research to estimate these two drugs, lisinopril and losartan in tablet form, successfully analyzed the content of these compounds in tablet form. Each taken also found from sample concentration the comparison was made to show whether there was an effect on the origin of the sample. Table 6 displays the results. The suggested method can also estimate two drugs in pharmaceutical formulations in the form of tablets manufactured by other companies.

Table 5: nested effect on estimation of lisinopril also losartan

Medicine	Nested	Con. µg/mL		Rec.%
		taken	Found	
Lisinopril	Glucose	6	6.000	100.000
	Sucrose		6.090	101.500
	Starch		5.998	99.966
Losartan	Glucose	12	12.010	100.083
	Sucrose		12.002	100.016
	Starch		11.999	99.991

Table 6: derived spectrum first estimation of lisinopril also losartan in tablets

Type of medicine	Mode of calculation	λ (nm)	taken µg/mL	found µg/mL	Rec.%	RSD%
Lisinopril Bristol, UK (5 mg)	Peak to baseline	215.2	8	8	100.000	1.25
Lisinopril Accord, UK (5 mg)	Peak to baseline	215.2	8	8.2	102.500	3.856
Losartan Pioneer, Iraq (50 mg)	Peak area	240.4-259	10	9.8	98.000	3.061
Losartan Micro, India (50 mg)	Peak area	240.4-259	10	10.2	102.000	0.980

Conclusion

In this study, the derivative method was used to estimate these two drugs, lisinopril and losartan, in the pure form and the form of tablets. The method proved its success in estimating each of the two drugs in the presence of the other. Other reagents were used to convert it to another picture for its estimation. The derivative method is a good spectroscopic method for estimating any compound singly or in a mixture for future use.

Acknowledgments

After completing the writing of the research, we would like to extend our thanks and appreciation to everyone who contributed to the completion of this research, even if it was a word of encouragement.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

The author declared that they have no conflict of interest.

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HOW TO CITE THIS ARTICLE
Elham N. Mezaal, Maha A. Mohammed, kawther Ahmed Sadiq. Simple spectrophotometric method for determination of drug lisinopril in pure form and pharmaceutical formulations. *J. Med. Chem. Sci.*, 2023, 6(5) 1112-1119
https://doi.org/10.26655/JMCHEMSCI.2023.5.16
URL: http://www.jmchemsci.com/article_159646.html