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DETERMINATION OF LOSARTAN AND HYDROCHLOROTHIAZIDE IN A COMBINED PHARMACEUTICAL UV DERIVATIVE SPECTROPHOTOMETRIC METHODS

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ABSTRACT

A new spectrophotometric methods for determination Losartan (LOS) and Hydrochlorothiazide (HCTZ) depends on 1st and 2nd derivative spectrum of the two drugs by using (Water:methanol:ethanol 60:20:20) as a solvent. Many techniques were proportionated with concentration (peak to base line, peak to peak and peak area). The linearity of the methods ranged between (5-50µg.ml-1). The results were precise and accurate throw RSD% were between (0.229-0.994%) and (0.228-0.995%), Rec% values between (98.23-102.64 %) and (97.91-102.50%) while the LOD between (0.0510-0.2310 µg.ml-1) and (0.055-0.316 µg.ml-1) and LOQ between (0.17-0.77µg.ml-1) and (0.183-1.130 µg.ml-1) of (LOS) and of (HCTZ) respectively. These methods were successfully Applied to determination of (LOS) and (HCTZ) in the pharmaceutical preparations.

Keywords: Spectrophotometric, determination, Losartan and Hydrochlorothiazide, First and second order derivative of spectrum.

1. Introduction

Losartan (LOS) is an angiotensin II receptor antagonist and chemically it is 2-n-butyl-4-chloro-5-hydroxymethyl-1-[2'-(1H-tetrazol-5-yl) (biphenyl-4-yl) methyl] imidazole, a strong antihypertensive agent Fig.1. Losartan was developed by DuPont-Merck laboratories as a potent non-peptide angiotensin II receptor (type AT1) antagonist for hypertension treatment [1]. is a Loop Diuretics used as an antihypertensive by reducing symtomatic oedema. This reduces the volume of the blood, decreasing blood return to the heart and thus cardiac output and, by other mechanisms, is believed to lower peripheral vascular resistance. Literature survey reveals the availability of several methods for estimation of both Losartan [2-7]. However, several methods have been described for the determination of losartan drug substance in tablet of losartan drug substance in tablet Various methods developed are HPLC, [8-11]spectrophotometric, [12-14] capillary electrophoresis (CE), [15] voltamatric, [16] capillary zone electrophoresis HPTLC and liquid chromatography electrospray ionization tandem mass spectrometry.

Hydrochlorothiazide (HCT), 6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulphonamide 1,1-dioxide, is a popular diuretic drug of the thiazide classFig.2. The diuretic action of HCT reduces plasma volume, with consequent increase in urinary loss, plasma renin activity, aldosterone secretion and decrease in serum [17]. There are several methods for the determination hydrochlorothiazide in tablet dosage forms by using spectrophotometric [18- 20], fluorodensistometric [21], gas and liquid chromatographic [22- 24], LCM SMS [25] polarographic techniques [26]. The aim of this study is to develop spectral methods based on the first and second derivative

as a pure substance. In pharmaceutical preparations using the peak to baseline height, peak to peak height, in addition to the area of the peak.

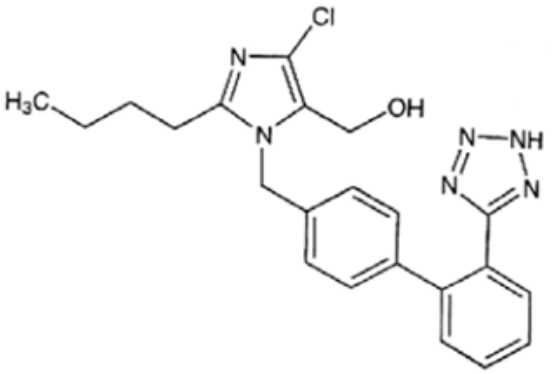

Fig. 1: Chemical structure of Losartan

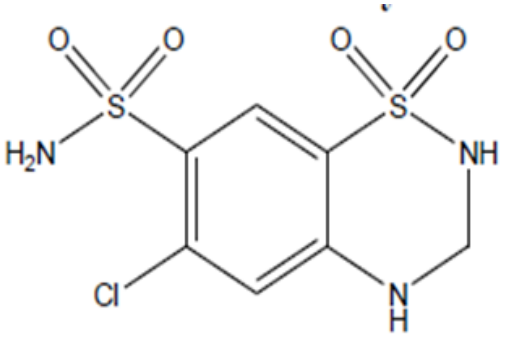

Figure. 2: Chemical structure of Hydrochlorothiazide

2. Materials and Methods

Losartan (LOS) and Hydrochlorothiazide (HCTZ) were kindly supplied by Grem-spiny and Hetero Pharmaceuticals, India. Marketed sample of LOS and HCTZ

(Angizaar-H ,MİCRO) in their combined tablet dosage form. Each tablet contained 50mg of LOS,12.5mg of HCTZ. ForUV work distilled water was prepared in the laboratory. Methanol nad ethnol used was of UV and were purchased from Baker Chemicals.

A double-beam SHIMADZU UV-Visible- Lc-20AB instrument has been used in the analysis of these two drugs. The measurements has been made within wavelength range of (109-400 nm), package width of (2.0nm) and medium scanning speed by using quartz cells.

2.1.Methods

A range of concentrations (5-50 µg/ml) of Losartan and hydrochlorothiazide has been prepared. A scan of the wavelengths between (190-400 nm) was performed for zero-scale spectrometry. As it showed compliance with the law of Per - Lambert and then the first and second derivatives of the zero spectrum were recorded and the calibration curves were constructed depending on D1 at wavelength (231,276 nm) for (peak to base line) and(231+276 nm) for (peak to to peak) and wavelength (267-312nm) for (area peak).D2 at wavelength(240,262,287nm) for (peak to base line) and wavelength (240-262,262-287nm)for(peak to peak) and wavelength(228-248,248-276,276-310) for (area peak).While, determine reckon on D1 at wavelength (231.75,254.52,280,24,330 nm) for (peak to base line) and wavelength (231.75-254.52,254.52-280.24,280.24+330 nm) for(peak to peak) and wavelength (218-246,246-268,268-300,300-358 nm) for (area peak).D2 at wavelength (221,242,268,288nm) for (peak to base line) and wavelength (221-242,242-268,268+288nm) for (peak to peak) and wavelength (210-231,231-256,256-278,278_304nm) for (area peak) losartan and hydrochlorothiazide respectively As inTable 1.

2.2.Standard Stock Solutions 1000µg/ml

0.1g and (99) purity of losartan and hydrochlorothiazide that obtained from Grem-spiny andHetero company has been dissolved individually in an amount of (water:methnol:ethnol 60:20:20) and then the 100ml volumetric flask was filled to the mark by adding solvent. Dilute solutions were prepared with concentrations of (5-50 µg/ml) using the solvent.

2.3.Analysis of Tablet Formulation

Twenty pill of MİCRO were milled and a mean weight of pill contains 0.05 g of Losartan and 0.0125g of hydrochlorothiazide was dissolved in 100 ml of the solvent and placed in the ultrasound bath. It was then filtered with a 0.42 Whatman paper to give concentrations of 500 µg/ml and 125 µg/ml respectively.

2.4.Absorption Spectra

The absorbance spectra of the medicinal drugs, which show the absorbance spectrometry of the zero derivative of the Losartan, hydrochlorothiazide and mixture, were recorded at a concentration of (20:15:20-10 µg/ml) respectively, showing the highest absorption at (250,263, 267 nm) respectively, as shown in the Fig.3.

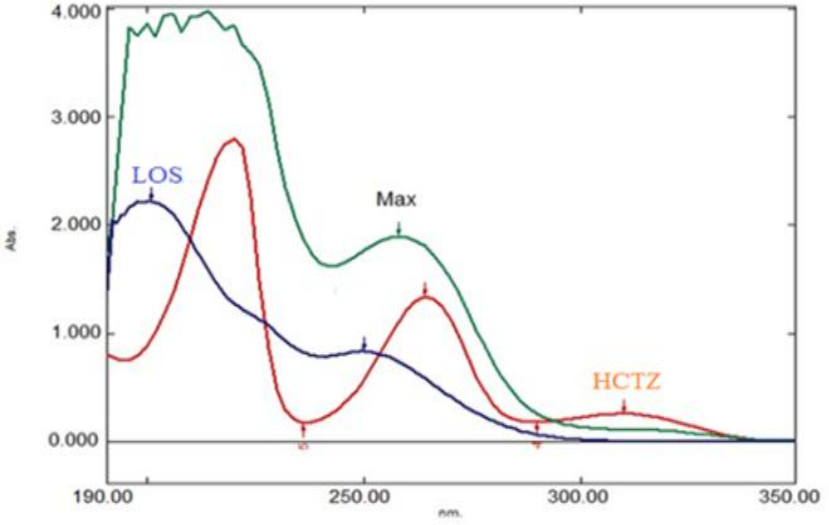

Fig.3: (A) Absorbance spectra for LOS 20 µg / mL (B) Absorbance spectra for HCTZ 15 µg / mL (C) Absorbance spectra for LOS 20 µg / mL and HCTZ 10 µg / mL

While the Figs 4.-7show the absorption spectra of the first and second derivatives of Losartan and hydrochlorothiazide the range of concentrations (5-50 µg/ml) respectively

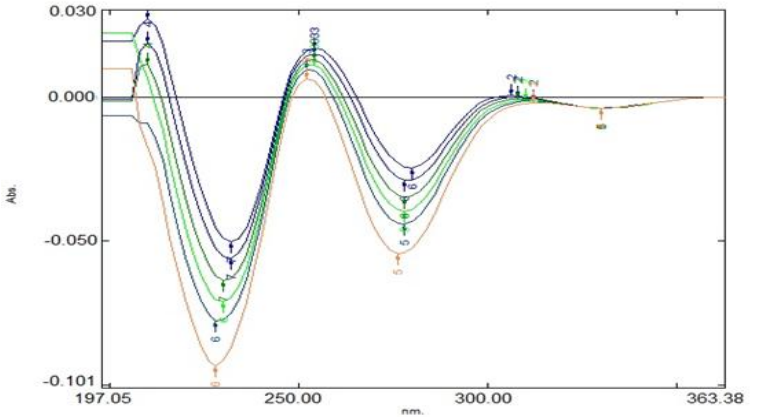

Fig. 4: First derivative spectrum for LOS

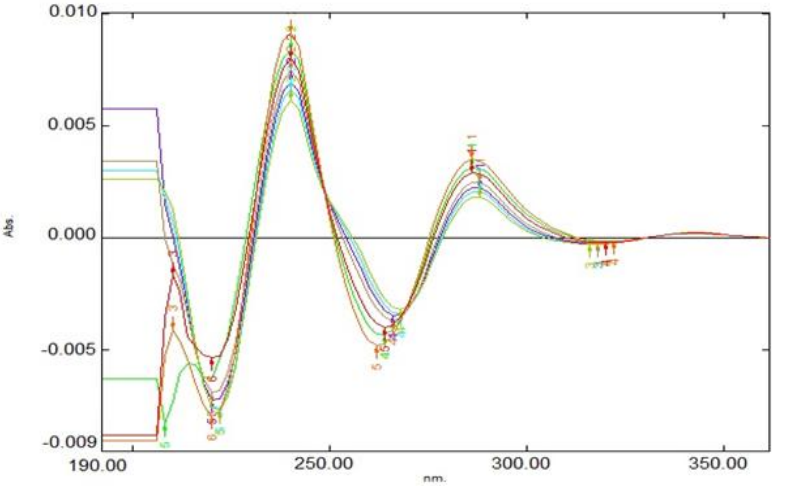

Fig. 5: Ssecond derivative spectrum for LOS

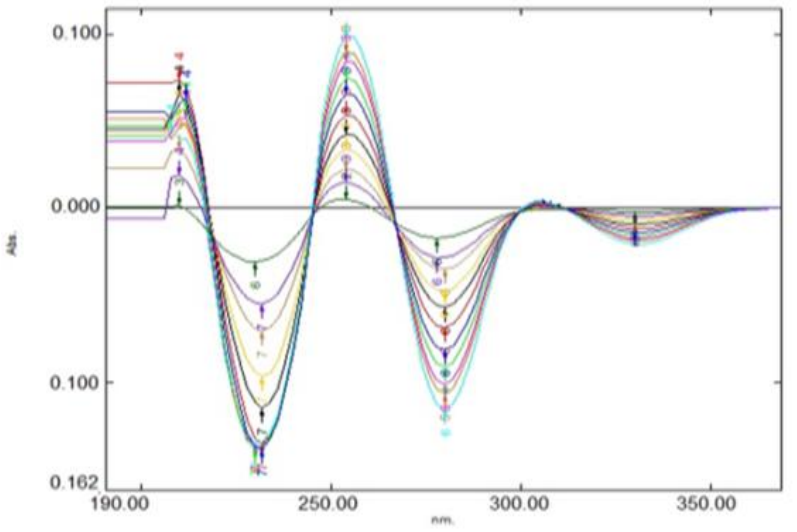

Fig.6: First derivative spectrum for HCTZ

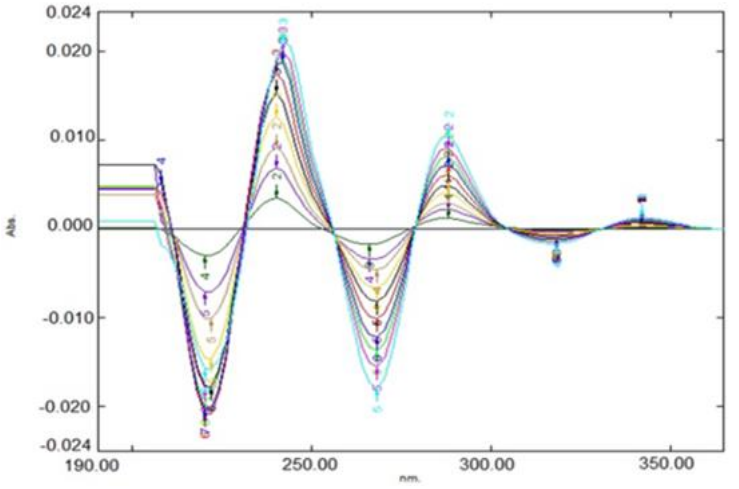

Fig.7: Second derivative spectrum for HCTZ

3.Calibration Curves

3.1.Limit of Detection (LOD) and Limit of Quantitation (LOQ)

The calibration curves has been constructed peak high to base line, peak to peak and peak area of the first and second derivatives. The linearity of the methods ranged between (5-50µg.ml^{-1}). the LOD between (0.0510-0.2310 µg.ml-1) and (0.055-0.316 µg.ml-1) and LOQ between (0.17-0.77µg.ml-1) and (0.183-1.130 µg.ml-1) of (LOS) and of (HCTZ) respectively as shown in table1.

4.Accuracy and Precision

In order to evaluate the results of the methods used in the estimation of these two drugs, the accuracy and compatibility have been calculated for them. The linearity of the methods ranged between (5-50µg.ml-1). The results were precise and accurate throw RSD% were between (0.229-0.994%) and (0.228-0.995%), Rec% values between (98.23-102.64 %) and (97.91-102.50%) of losartan and hydrochlorothiazide respectively as shown in table2.

5.Application Method

The results of the suggested methods for estimating the two drugs were used in pharmaceutical preparations. Table 3 shows the results of a variety of different pharmaceutical

both drugs Losartan and Hydrochlorothiazide respectively as shown in table3.

Compound	Order of derivative	Mode of calculation	λ .max (nm)	Regression equation	R^2	LOD	LOQ	Linearity	Slope
LOS	First	Peak to base line	231	y = -0.0011x - 0.046	0.9996	0.0760	0.2530	5-50 µg.ml^{-1}	-0.0011
		Peak to base line	276	y = -0.0011x - 0.0184	0.9996	0.0960	0.3200		-0.0011
		Peak to Peak	231+276	y = 0.0022x + 0.0645	0.9998	0.0510	0.1700		0.0022
		Peak area	215-245	y = -0.0286x -	0.9994	0.1210	0.4030		-

				0.5905					0.0286
		Peak area	267-312	y = -0.0287x - 0.4983	0.9997	0.1410	0.4700		-0.0287
	Second	Peak to base line	240	y = 9E-05x + 0.0061	0.9994	0.2310	0.7700	5-50µg.ml^{-1}	9E-05
		Peak to base line	262	y = -3E-05x - 0.0032	0.9995	0.0780	0.2600		-3E-05
		Peak to base line	287	y = 0.0001x + 0.0017	0.9992	0.0930	0.3100		0.0001
		Peak to Peak	240+262	y = 0.0001x + 0.0093	0.9992	0.0660	0.2200		0.0001
		Peak to Peak	262+287	y = 0.0001x + 0.0049	0.9993	0.0790	0.2630		0.0001
		Peak area	228-248	y = 0.0005x + 0.0808	0.9998	0.0560	0.1860		0.0005
		Peak area	248-276	y = -0.0012x - 0.0572	0.9997	0.1410	0.4700		0.0012 -
		Peak area	276-310	y = 0.0002x + 0.0484	0.9996	0.076	0.253		0.0002
HCTZ	First	Peak to base line	231.75	Y=-0.0032x-0.0004	0.9996	0.0990	0.3300	5-50 µg.ml^{-1}	-0.0032
		Peak to base line	254.52	Y=-0.0022x-0.0014	0.9996	0.1780	0.5930		-0.0022
		Peak to base line	280.24	Y=-0.0024x-0.0021	0.9998	0.0870	0.2900		-0.0002
		Peak to base line	330	Y=-0.0004x-0.0015	0.9997	0.3010	1.0030		-0.0004
		Peak to Peak	231+254.52	Y=0.0054x+0.0018	0.9998	0.0950	0.3160		0.0054
		Peak to Peak	254.52+280.24	Y=0.0046x+0.0034	0.9999	0.2860	0.9530		0.0046
		Peak to Peak	280.24+330	Y=0.0028x+0.0036	0.9999	0.0790	0.2630		0.0028
		Peak area	218-246	Y=-0.0439x-0.3773	0.9999	0.3160	1.0530		0.0439
		Peak area	246-268	Y=0.0251x+0.0251	0.9998	0.0740	0.2460		0.0251
		Peak area	268-300	Y=-0.0278x-0.296	0.9996	0.3130	1.0400		0.0278
		Peak area	311-358	Y=-0.0084x-0.0332	0.9994	0.0940	0.3130		-0.0084

	Second	Peak to base line	221	Y=-0.0004x+0.0002	0.9997	0.0550	0.1830	5-50µg.ml^{-1}	0.0004
		Peak to base line	242	Y=0.0005x+0.0009	0.9996	0.1210	0.4030		0.0005
		Peak to base line	268	Y=-0.0003x-0.0001	0.9998	0.1780	0.5930		-0.0003
		Peak to base line	288	Y=0.0002x+0.0002	0.9999	0.1840	0.6130		0.0002
		Peak to Peak	221+248	Y=0.0009x+0.0007	0.9998	0.0550	0.1830		0.0009
		Peak to Peak	242+268	Y=0.0008x+0.001	0.9998	0.2010	0.670		0.0008
		Peak to Peak	268+288	Y=0.0005x+0.0003	0.9999	0.0810	0.2700		0.0005
		Peak area	210-231	Y=-0.0028x-0.0314	0.9995	0.0860	0.2860		-0.0028
		Peak area	231-256	Y=0.0057x+0.0456	0.9998	0.0640	0.213		0.0057
		Peak area	256-278	Y=-0.0037x-0.0151	0.9994	0.3390	1.130		0.0037
		Peak area	278-304	Y=0.0058x-0.0432	0.9997	0.0980	0.326		0.0058

Table 1: Results of meta - analysis of Losartan and Hydrochlorothiazide using the first and second derivatives

Compound	Order of derivative	Mode of analysis	λ .max (nm)	Drug conc. (µg.mL^{-1})		Rec%	*R.S.D%
				Taken	Found		
LOS	First	Peak to base line	231	24	24.6	102.5	0.583
				34	34.5	101.47	0.771
		Peak to peak	231-276	24	24.4	101.66	0.526
				34	33.9	99.70	0.337
		Peak area	215-245	24	24.2	100.83	0.604
				34	34.4	101.17	0.884
	Second	Peak to base line	240	24	24.5	101.47	0.294
				34	34.2	100.58	0.639
		Peak to peak	240-262	24	24.4	101.66	0.551
				34	34.6	101.76	0.228
		Peak area	228-248	24	24.1	100.41	0.393
				34	34.4	101.17	0.832
HCTZ	First	Peak to base line	231.75	24	23.7	98.75	0.478
				34	34.4	101.17	0.629
		Peak to	231.75-	24	24.4	101.66	0.982

		peak	254.52	34	34.2	100.88	0.749
		Peak area	246-268	24	23.6	98.33	0.738
				34	34.5	101.47	0.563
	Second	Peak to base line	242	24	24.4	101.66	0.933
				34	33.6	98.82	0.729
		Peak to peak	221-242	24	23.6	98.33	0.228
				34	34.4	101.17	0.682
		Peak area	231-256	24	23.8	99.16	0.604
				34	33.4	98.23	0.995

Table 2: Calculate the Accuracy and precision of Losartan and Hydrochlorothiazide meta-analysis results in the proposed work method

Sample	Order	Mode of analysis	λ(nm)	Drug.amount(mg)		Rec%	*R.S.D%
				Taken.d	Found		
Losartan (50mg)	First	Peak to base line	231	50	51.4	102.84	0.117
			267	50	50.9	101.91	0.664
		Peak to Peak	231-276	50	50	100	0.729
		Peak area	215-245	50	51.1	102.31	0.993
			267-312	50	50.7	101.45	0.629
	Second	Peak to base line	240	50	51.2	102.51	0.412
			262	50	49.49	98.99	0.582
			287	50	50.9	101.81	0.839
		Peak to Peak	240-262	50	50.7	101.41	0.936
			262-287	50	51.08	102.17	0.748
		Peak area	228-248	50	49.50	99.01	0.296
			248-276	50	51.33	102.66	0.473
			276-310	50	50.7	101.58	0.572

hydrochlorothiazide (12.5 mg)	First	Peak to base line	231.75	12.5	12.71	101.69	0.739
			254.52	12.5	12.52	100.16	0.117
		Peak to Peak	231.75-254.52	12.5	12.18	97.44	0.529
		Peak area	218-245	12.5	12.84	102.72	0.549
			245-267	12.5	12.93	103.44	0.337
	(Second)	Peak to base line	221	12.5	12.39	99.12	0.304
			242	12.5	12.5	100	0.782
			268	12.5	12.5	100	0.412
		Peak to Peak	221-242	12.5	12.70	101.63	0.473
			2242-268	12.5	12.59	100.72	0.739
		Peak area	210-231	12.5	12.56	100.55	0.839
			231-256	12.5	12.67	101.36	0.584
			256-278	12.5	12.60	100.81	0.774

Table 3: Estimation of Losartan and Hydrochlorothiazide in some pharmaceutical preparations according to the proposed methods

6.Conclusions

A range of simple, sensitive and rapid spectral methods were developed, based on spectrums of the first and second derivatives for estimating the Losartan and hydrochlorothiazide drugs. In their pure forms and their pharmaceutical preparations. These methods are suitable for quality control laboratories and routine work because they do not need to control the working conditions and do not need expensive detectors or solvents.

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