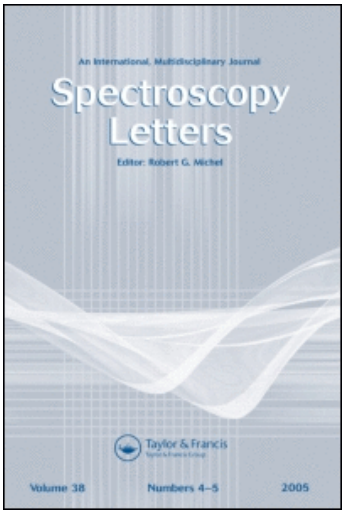

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U.V. and U.V. Derivative Spectrophotometric Determination of Two-Component Mixtures

Hesham Salem[a]; Magda El-Maamli[a]; Mohamed El-Sadek[a]; Afaf Aboul Kheir[a]
[a] Pharmaceutical Chemistry Department, Faculty of Pharmacy, Zagazig University, Zagazig, Egypt

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U.V. AND U.V. DERIVATIVE SPECTROPHOTOMETRIC DETERMINATION OF TWO- COMPONENT MIXTURES.

Hesham Salem; Magda El-Maamli; Mohamed El-Sadek and Asaf Aboul Kheir.

Pharmaceutical Chemistry Department, Faculty of Pharmacy, Zagazig University, Zagazig, Egypt.

In this paper, two-component mixtures (spironolactone with hydrochlorothiazide, captopril with hydrochlorothiazide, and spironolactone with furosemide) were assayed by U.V. (A), first derivative ($dA/d\lambda$) and second derivative ($d^2A/d\lambda^2$) spectrophotometric methods, applying "Zero-Crossing" technique of measurement.

The methods were proved using laboratory prepared mixtures. The utility of the methods in assay of dosage forms is also presented.

INTRODUCTION

The pharmacological action of hydrochlorothiazide, spironolactone, captopril and furosemide have been recommended as diuretic as well as hypotensive [1].

For hydrochlorothiazide assay; colorimetric [2], chromatographic [3], complexometric [4] and spectrophotometric [5] methods are reported.

For spironolactone determination; fluorimetric [6], colorimetric [7], and spectrophotometric [8] techniques are recommended.

For captopril assay; colorimetric [9], chromatographic [10], and spectrophotometric [11] techniques are reported.

For furosemide determination; colorimetric [12], chromatographic [13], titrimetric [14], and spectrophotometric [12] techniques are reported.

However, derivative spectrophotometry have been recommended for two-component mixtures [15-20].

In this paper, derivative spectrophotometry has been recommended for assay of two component mixtures of the above mentioned drugs.

EXPERIMENTAL

Apparatus:

A Shiamadzu recording spectrophotometer U.V. 260 with 1 cm quartz cuvettes. Suitable settings were; scan speed 40 nm min^{-1} chart speed 60 mm min^{-1} and slit width 2 nm.

Materials:

Sprionolactone (Kahira Co; Egypt), hydrochlorothiazide (Kahira Co; Egypt), captopril (Squibb Co; Egypt), furosemide (Memphis Co; Egypt), Aldactazide tablets (Kahira Co; Egypt) labeled to contain 25 mg spironolactone and 25mg hydrochlorothiazide per tablet, Capozide tablets (Squibb Co; Egypt) labeled to contain 50 mg captopril and 25 mg hydrochlorothiazide, Fructone capsules (Memphis Co; Egypt) labeled to contain 20 mg furosemide and 50 mg spironolactone per capsule & ethanol (Nasr Co; Egypt).

Stock and Working Solution:

Alcoholic stock solutions of spironolactone (100 mg%), captopril (100 mg%), hydrochlorothiazide (100 mg%) and furosemide (40 mg%) were prepared.

Working solutions were prepared by pipetting separately 1.0-6.0 ml aliquots of each stock solution into 25 ml.volumetric flasks and completing to volume with ethanol. In case of captopril 2.0-12.0 ml aliquots were applied.

Procedure:

A. For single authentic components and mixtures of them:

Determinations at different wavelengths were carried out using ethanol as a blank applying conditions in table 1.

Table (1): Optimum parameters for calibration curves construction

First Mixture Spironolactone & Hydrochlorothiazide								Second Mixture Captopril & Hgdrochlorothiazide								Third Mixture Spironolactone & Furosemide							
Components	Measurements	λ nm	Concentration range mg %	Regression analysis			C.V.%	Components	Measurements	λ nm	Concentration range mg %	Regression analysis			C.V.%	Components	Measurements	λ nm	Concentration range mg %	Regression analysis			C.V.%
				B	K	R						B	K	R						B	K	R	
Spironolactone	^1D	220	4-24	0.0051	160.8511	0.9999	1.10	Captopril	^1D	221	8-48	0.9051	90.7081	0.9899	0.58	Spironolactone	^1D	224	4-24	-0.0080	11.8151	0.9989	0.81
	^2D	211	4-24	-0.0805	99.8511	0.9989	1.51		^2D	227	8-48	-0.0145	59.3815	0.9999	0.60		^1D	247	4-24	0.0093	23.5108	0.9999	0.86
	^2D	227	4-24	0.1050	107.9511	0.9990	0.35										^2D	210	4-24	-0.0516	104.5005	0.9996	0.83
	^2D	259	4-24	1.0561	89.0896	0.9997	1.40										^2D	235	4-24	1.0030	100.9158	0.9979	0.71
																	^2D	262	4-24	-0.0350	97.1500	0.9990	0.85
Hydrochlor-	U.V.	276	4-24	0.0851	53.8510	0.9999	0.64	Hydrochloro-	U.V.	271	4-24	0.9801	4.8951	0.9996	0.65								
othiazide	U.V	316	4-24	-0.0059	60.9110	0.9969	0.61	thiazide.	U.V.	315	4-24	0.0561	12.8319	0.9989	0.80	Furosemide	U.V.	276	1.6-9.6	0.0891	3.7871	0.9999	0.64
	^1D	278	4-24	-0.1009	9.5932	0.9991	1.32		^1D	258	4-24	1.5301	100.5671	0.9999	0.94		U.V.	330	1.6-9.6	-.1002	9.7660	0.9999	0.76
	^1D	332	4-24	0.0814	7.0859	0.9999	1.40		^1D	278	4-24	0.0851	160.1508	0.9899	0.56		^1D	235	1.6-9.6	0.0159	29.3411	0.9989	0.76
	^2D	281	4-24	0.9310	170.4703	0.9984	1.25		^1D	332	4-24	0.9851	140.3811	0.9999	1.06		^1D	280	1.6-9.6	0.0351	77.7018	0.9999	0.20
									^2D	270	4-24	0.0501	69.5871	0.9969	0.71		^2D	275	1.6-9.6	1.0400	101.3127	0.9969	1.00
									^2D	281	4-24	1.2083	105.0511	0.9997	0.97		^2D	285	1.6-9.6	-1.006	611.1988	0.9999	1.11

B. For assay of dosage forms (tablets & capsules):

Conditions in table 1 were applied after extraction with ethanol [21].

RESULTS & DISCUSSION

I. For first mixture (spironolactone with hydrochlorothiazide):

Spironolactone has maxima at the wavelengths (^{1}D) λ = 220 nm and (^{2}D) λ = 211, 227 & 259 nm (Figure 1), at which hydrochlorothiazide does not interfere. For comparison the measurements at these wavelengths together with the $A_{max.}$ method [28] were applied. Statistical analysis of the results (table 2) showed that most of the suggested measurements are equally precise and accurate to the $A_{max.}$ method.

Hydrochlorothiazide has maxima at the wavelengths (U.V.)λ = 276 & 316nm, (^{1}D)λ = 278 & 332 nm and (^{2}D)λ= 281 nm (Figure 1), at which spironolactone does not interfere. For comparison the measurements at these wavelengths together with the $A_{max.}$ method [23] were applied. Statistical analysis of the results (table 3) showed that all the suggested measurements are equally precise and accurate to the $A_{max.}$ method.

In order to prove the validity and the applicability of the proposed methods, six dilutions of a laboratory prepared mixture of spironolactone with hydrochlorothizide (1:1) were analyzed applying the proposed methods. In comparison with the modified Vierordt's method [24] statistical analysis of the results (table 6) showed that most of the suggested measurements are equally precise and accurate to the modified Vierordt's method.

Aldactazide tablets, were assayed for both spironolactone and hydrochlorothazide using the proposed methods. In comparison with the modified Vierordt's method statistical analysis of the results obtained (table 6) revealed that most of the suggested measurements are equally precise and accurate to the modified Vierordt's method.

II. For second mixture (captopril with hydrochlorothiazide):

Captopril has maxima at the wavelengths (^{1}D)λ= 221 nm and (^{2}D) λ = 227 nm (Figure 2), at which hydrochlorothiazide does not interfere. For

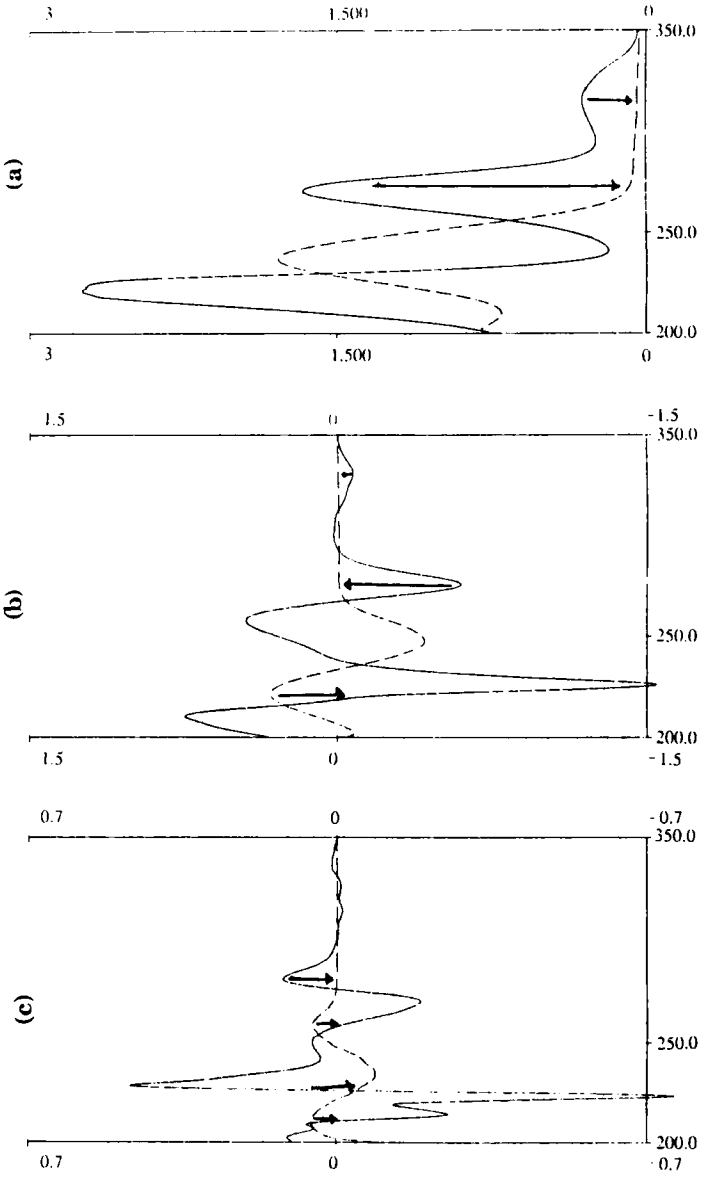

Figure (1): U.V. determination of hydrochlorothiazide at 276 & 316 nm, ^{1}D determination of hydrochlorothiazide at 278 & 332 nm and of spironolactone at 220 nm and ^{2}D determination of hydrochlorothiazide at 281 nm and of spironolactone at 211, 227 & 259 nm. Hydrochlorothiazide 16 mg% (—) and spironolactone 16 mg %(----).

Table (2):Statistical analysis of the results obtained for assay of spironolactone using first and second derivative spectrophotometric measurements using (Zero - Crossing) technique compared with the $A_{max.}$ method

	For spironolactone in the first mixture					For spironolactone in the third mixture				
Taken mg%	$A_{max.}$ method	^1D (λ = 220 nm)	^2D(λ = 211 nm)	^2D(λ = 227 nm)	^2D(λ = 259 nm)	^1D (λ = 224 nm)	^1D (λ =247 nm)	^2D (λ =210 nm)	^2D (λ =235 nm)	^2D(λ = 262 nm)
	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %
4	98.4	99.1	99.1	99.9	100.5	100.8	99.9	97.4	100.6	99.2
8	100.6	100.3	97.7	100.2	98.2	100.0	99.2	98.9	99.2	100.5
12	99.8	100.2	98.0	100.7	100.3	99.0	101.7	98.0	100.9	100.0
16	101.5	98.5	98.9	100.0	99.1	100.3	100.2	99.0	100.6	101.8
20	100.0	100.8	100.6	99.8	101.7	101.4	100.8	98.5	99.7	100.2
24	100.3	101.5	101.4	100.5	98.2	100.2	100.0	97.0	99.5	100.1
Mean recovery ($\bar{x}$)	100.1	100.1	99.3	100.2	99.7	100.3	100.3	98.1	100.1	100.3
± S.D.	10.2	1.10	1.50	0.35	1.40	0.81	0.86	0.81	0.71	0.85
N	6	6	6	6	6	6	6	6	6	6
V	1.04	1.21	2.25	0.12	1.96	0.66	0.74	0.66	0.50	0.72
t		0.00 (3.58)	1.31 (3.58)	0.16 (3.58)	0.53 (3.58)	0.38 (3.58)	0.37 (3.58)	3.76 (3.58)	0.00 (3.58)	0.37 (3.58)
F		1.16 (4.28)	2.16 (4.28)	8.67 (4.28)	1.88 (4.28)	1.58 (4.28)	1.41 (4.28)	1.58 (4.28)	2.08 (4.28)	1.44 (4.28)

Table (3): Statistical analysis of the results obtained for assay of hydrochlorothiazide using U.V., first and second derivative *spectrophotometric measurements using (Zero - Crossing) technique compared with the* $A_{max.}$ *method*

	For hydrochlorothiazide in the first mixture						For hydrochlorothiazide in the second mixture						
Taken mg%	$A_{max.}$ method	U.V.(λ= 276 nm)	U.V. (λ = 316 nm)	^{1}D(λ = 278 nm)	^{1}D(λ = 332 nm)	^{2}D(λ =281 nm)	U.V (λ = 271 nm)	U.V. (λ = 315 nm)	^{1}D (λ = 258 nm)	^{1}D(λ = 278 nm)	^{2}D (λ = 332 nm)	^{2}D (λ = 270 nm)	^{2}D (λ = 281 nm)
	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %
4	100.0	100.9	100.8	97.8	100.5	99.5	100.0	100.0	98.8	100.8	99.8	99.0	100.8
8	101.5	100.3	100.2	98.4	98.2	98.2	99.5	99.8	100.5	100.2	1003	99.8	100.1
12	100.7	101.3	100.5	100.0	100.3	100.7	101.1	100.9	100.8	100.1	99.7	100.5	99.7
16	100.3	100.9	101.0	99.1	99.1	101.4	100.4	101.5	100.7	101.5	101.5	98.7	100.3
20	99.8	99.6	100.0	101.2	101.7	100.3	100.9	99.3	98.9	100.6	100.0	99.9	100.8
24	98.3	100.0	99.3	100.6	98.2	101.5	99.7	100.5	100.6	100.0	98.2	100.3	98.2
Mean recovery (X̄)	100.1	100.5	100.3	99.5	99.7	100.3	100.3	100.3	100.1	100.5	99.9	99.7	100.0
± S.D.	1.07	0.64	0.61	1.31	1.40	1.25	0.65	0.80	0.94	0.56	1.06	0.71	0.97
N	6	6	6	6	6	6	6	6	6	6	6	6	6
V	1.14	0.41	0.37	1.72	1.96	1.56	0.42	0.64	0.88	0.31	1.12	0.50	0.94
t		0.79 (3.58)	0.44 (3.58)	0.87 (3.58)	0.56 (3.58)	0.30 (3.58)	0.39 (3.58)	0.37 (3.58)	0.00 (3.58)	0.81 (3.58)	0.33 (3.58)	0.76 (3.58)	0.17 (3.58)
F		2.78 (4.28)	3.08 (4.28)	1.51 (4.28)	1.72 (4.28)	1.37 (4.28)	2.71 (4.28)	1.78 (4.28)	1.30 (4.28)	3.68 (4.28)	1.02 (4.28)	2.28 (4.28)	1.21 (4.28)

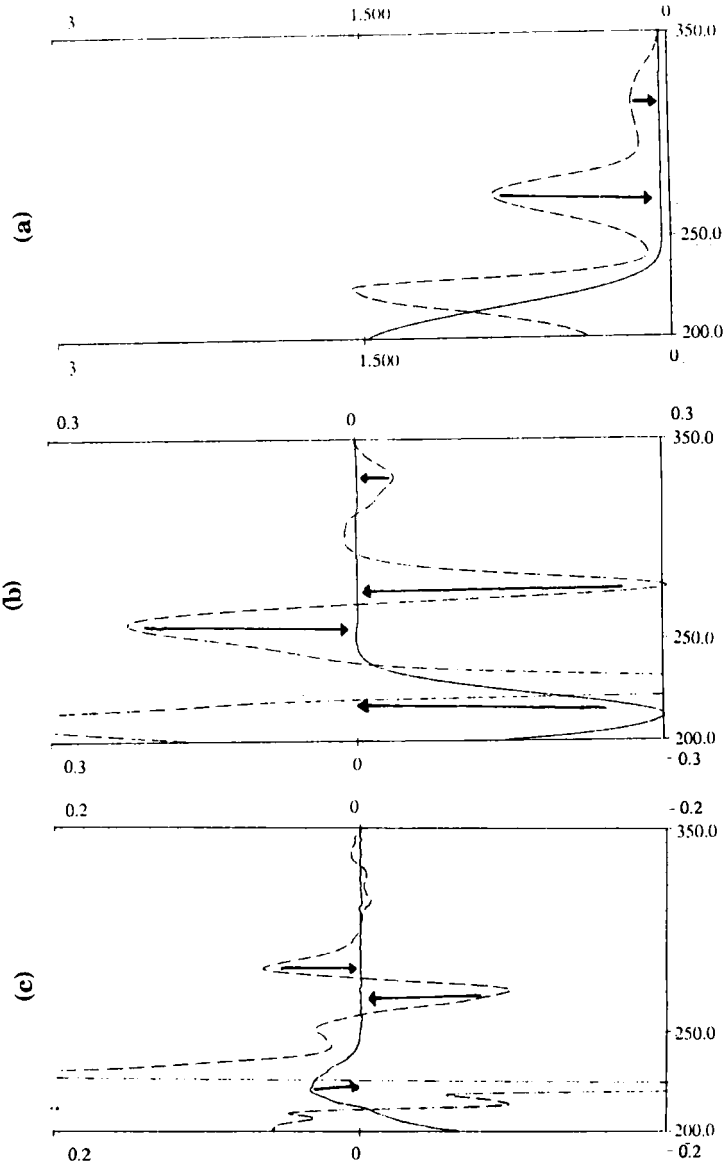

Figure (2): U.V. determination of hydrochlorothiazde at 271 & 315 nm, ^{1}D determination of captopril at 221 nm and of hydrochlorothiazide at 258, 278 & 332 nm and ^{2}D determination of captopril at 227 nm and of hydrochlorothiazide at 270 & 281 nm. Captopril 16 mg% (——) and hydrochlorothiazide 8 mg% (----).

comparison the measurements at these wavelengths together with the $A_{max.}$ method [25] were applied. Statistical analysis of the results (table 4) showed that all the suggested measurements are equally precise and accurate to the $A_{max.}$ method.

Hydrochlorothiazide has maxima at the wavelengths (U.V.) λ = 271 & 315 nm, (^{1}D) λ = 258, 278 & 332 nm and (^{2}D) λ = 270 & 281 nm (Figure 2), at which captopril does not interfere. For comparison, the measurements at these wavelengths together with the $A_{max.}$ method [23] were applied. Statistical analysis of the results (table 7) showed that all the suggested measurements are equally precise and accurate to the $A_{max.}$ method.

In order to prove the validity and the applicability of the proposed methods, six dilution of a laboratory prepared mixture of captopril and hydrochlorothiazide (2:1) were analyzed applying the proposed methods. In comparison with the modified Vierordt's method [24] statistical analysis of the results (table 7) showed that most of the suggested measurements are equally precise and accurate to the modified Vierordt's method.

Capozide tablets, were assayed for both captopril and hydrochlorothiazide using the proposed methods. In comparison with the modified Vierordt's method statistical analysis of the results obtained (table 7) revealed that the suggested measurements are equally precise and accurate to the modified Vierordt's method.

III. For third mixture (spironolactone with furosemide):

Spironolactone has maxima at the wavelengths (^{1}D)λ = 224 & 247 nm and (^{2}D) λ= 210, 235 & 262 nm (Figure 3), at which furosemide does not interfere. For comparison the measurements at these wavelengths together with the $A_{max.}$ method [22] were applied. Statistical analysis of the results (table 2) showed that most of the suggested measurements are equally precise and accurate to the A_{max}.method.

Furosemide has maxima at the wavelengths (U.V.) λ = 276 & 330 nm, (^{1}D)λ = 235 & 280 nm and (^{2}D) λ =275 & 285 nm (Figure 3), at which

Table (4): Statistical analysis of the results obtained for assay of captopril using first and second derivative spectrophotometric measurements compared with the $A_{max.}$ method.

Taken mg%	$A_{max.}$ method	$^1D(\lambda = 221$ nm)	$^2D(\lambda = 227$ nm)
	Recovery %	Recovery %	Recovery %
8	100.6	99.6	98 5
16	98.5	100.7	100.6
24	100.0	99.6	101.3
32	99.6	101.1	100.4
40	100.4	99.8	101.3
48	101.1	98.5	100.8
Mean recovery ($\bar{x}$)	100.0	99.9	100.5
± S.D.	0.91	0.58	0.60
N	6	6	6
V	0.83	0.34	0.36
t		0.22 (3.58)	1.12 (3.58)
F		2.44 (4.28)	2.31 (4.28)

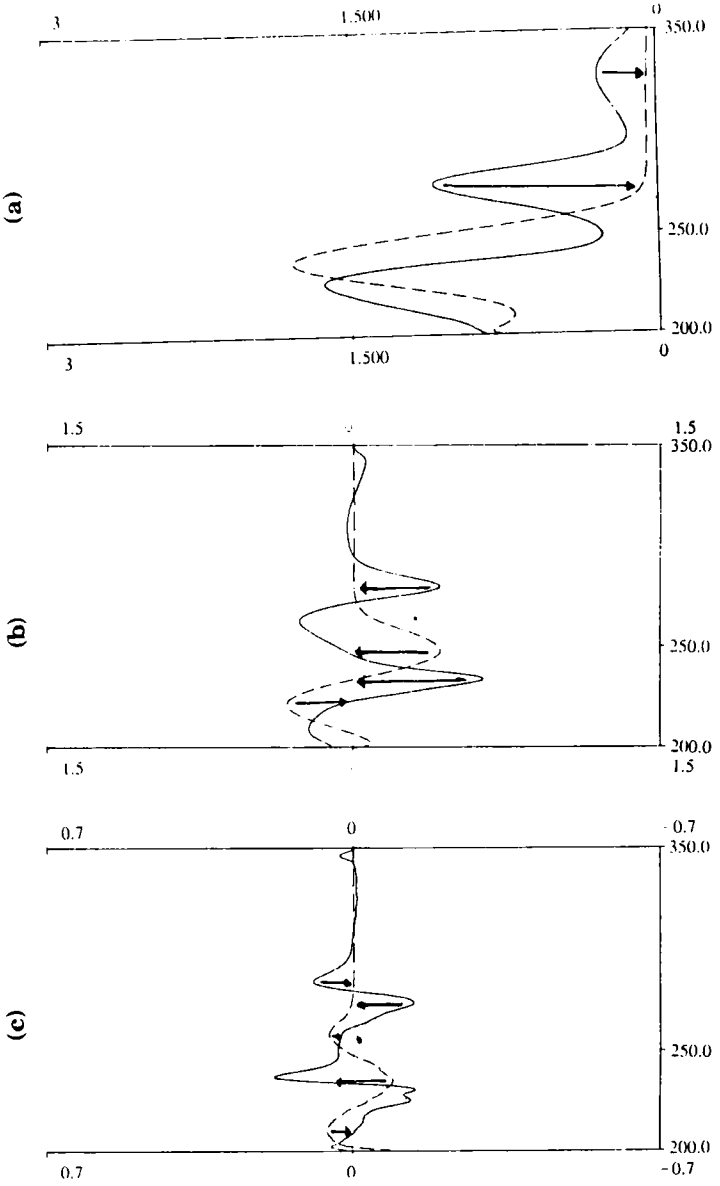

Figure (3): U.V. determination of furosemide at 276 & 330 nm, ^{1}D determination of furosemide at 235 & 280 nm and of spironolactone at 224 & 247 nm and ^{2}D determination of furosemide at 275 & 285 nm and of spironolactone at 210, 235 & 262 nm. Furosemide 6.4 mg% (——) and spironolactone 16 mg% (----).

Table (5): Statistical analysis of the results obtained for assay of furosemide using U.V., first and second derivative spectrophotometric measurements compared with the $A_{max.}$ method.

Taken mg%	$A_{max.}$ method	U.V. (λ = 276 nm)	U.V. (λ = 330 nm)	^1D(λ = 235 nm)	^1D(λ = 280 nm)	^2D(λ = 275 nm)	^2D (λ = 285 nm)
	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %	Recovery %
1.6	100.6	100.9	101.0	99.6	100.2	99.6	101.0
3.2	98.1	100.3	100.2	99.7	100.3	100.0	100.8
4.8	101.5	101.3	100.5	100.4	100.5	101.5	98.0
6.4	100.0	100.9	100.0	99.6	100.0	100.3	100.5
8.0	101.2	99.6	99.4	98.7	100.6	98.6	99.5
9.6	99.0	100.0	98.9	100.9	100.4	100.9	100.1
Mean recovery (x̄)	100.0	100.5	100.0	99.8	100.3	100.2	100.0
± S.D.	1.31	0.64	0.76	0.76	0.20	1.01	1.11
N	6	6	6	6	6	6	6
V	1.72	0.41	0.58	0.58	0.04	1.02	1.23
t		0.84 (3.58)	0.00 (3.58)	0.32 (3.58)	0.55 (3.58)	0.30 (3.58)	0.00 (3.58)
F		4.20 (4.28)	2.97 (4.28)	2.97 (4.28)	43.00(4.28)	1.69 (4.28)	1.40 (4.28)

Table (6):Assay results of spironolactone and hydrochlorothiazide in a laboratory prepared mixture and in Aldactazide tablets.

Sample		For spironolactone					For hydrochlorothiazide					
		Modified Vierordt's method	^1D (λ = 220 nm)	^2D (λ = 211 nm)	^2D (λ = 227 nm)	^2D (λ = 259 nm)	Modified Vierordt's method	U.V. (λ = 276 nm)	U.V. (λ = 316 nm)	^1D(λ = 278 nm)	^1D(λ = 332 nm)	^2D(λ = 281 nm)
Laboratory prepared mixture	% Recovery ± S.D.	100.8±0.51	100.1±0.74	98.0±0.55	100.5±0.45	100.2±0.60	99.6±1.05	100.1±0.99	100.4±0.49	99.6±1.03	100.3±0.89	100.2±1.25
	N	6	6	6	6	6	6	6	6	6	6	6
	V	0.26	0.55	0.30	0.20	0.36	1.10	0.98	0.24	1.06	0.79	1.56
	t		1.89 (3.58)	9.14 (3.58)	1.08 (3.58)	1.85 (3.58)		0.85 (3.58)	0.63 (3.58)	0.00 (3.58)	1.25 (3.58)	0.50 (3.58)
	F		2.12 (4.28)	1.15 (4.28)	1.30 (4.28)	1.38 (4.28)		1.12 (4.28)	4.58 (4.28)	1.04 (4.28)	1.39 (4.28)	1.42 (4.28)
Tablets (Aldactazide)	% Recovery ± S.D.	100.0±1.05	100.4±0.98	100.3±1.00	99.8±0.89	101.0±1.05	99.7±0.45	100.4±0.35	100.0±0.39	100.1±0.41	99.8±0.55	101.9±0.69
	N	6	6	6	6	6	6	6	6	6	6	6
	V	1.10	0.96	1.00	0.79	1.10	0.20	0.12	0.15	0.17	0.30	0.48
	t		0.69 (3.58)	0.51 (3.58)	0.36 (3.58)	1.73 (3.58)		3.02 (3.58)	1.24 (3.58)	1.61 (3.58)	0.35 (3.58)	7.77 (3.58)
	F		1.14 (4.28)	1.10 (4.28)	0.72 (4.28)	1.00 (4.28)		1.67 (4.28)	1.33(4.28)	1.18 (4.28)	1.50 (4.28)	2.40 (4.28)

Table (7): Assay results of captopril and hydrochlorothiazide in a laboratory prepared mixture and in Capozide tablets.

Sample		For captopril			For hydrochlorothiazide							
		Modified Vierordt's method	^1D (λ = 224 nm)	^2D (λ = 227 nm)	Modified Vierordt's method	U.V (λ = 271 nm)	U.V (λ = 315 nm)	^1D (λ = 258 nm)	^1D (λ = 278 nm)	^1D (λ = 332 nm)	^2D(λ = 270 nm)	^2D(λ = 281 nm)
Laboratory prepared mixture	% Recovery ± S.D.	99.6±0.85	100.1±2.15	99.8±0.90	100.0±2.10	100.0±1.80	99.8±2.05	100.3±1.59	100.0±2.00	100.6±2.30	99.8±0.19	100.4±1.99
	N	6	6	6	6	6	6	6	6	6	6	6
	V	0.72	4.62	0.81	4.41	3.24	4.20	2.53	4.00	5.29	0.04	3.96
	t											
	F		0.53 (3.58)	0.40 (3.58)		0.09 (3.58)	0.25 (3.58)	0.28 (3.58)	00.0 (3.58)	0.47 (3.58)	0.51 (3.58)	0.34 (3.58)
			6.42 (4.28)	1.13 (4.28)		1.36 (4.28)	1.05 (4.28)	1.74 (4.28)	1.10 (4.28)	1.20 (4.28)	11.03 (4.28)	1.11 (4.28)
Tablets (Capozide)	% Recovery ± S.D.	100.2±0.57	100.1±0.61	100.3±0.49	101.6±0.85	100.8±1.00	100.9±0.95	101.0±0.80	98.1±0.75	100.7±0.66	100.9±0.79	100.6±0.85
	N	6	6	6	6	6	6	6	6	6	6	6
	V	0.32	0.37	0.24	0.72	1.00	0.90	0.64	0.56	0.44	0.62	0.72
	t		0.29	0.33 (3.58)		1.49 (3.58)	1.35 (3.58)	1.69 (3.58)	7.57 (3.58)	2.05 (3.58)	1.48 (3.58)	1.78 (3.58)
	F		1.16	1.33 (4.28)		1.39 (4.28)	1.25 (4.28)	1.13 (4.28)	1.29 (4.28)	1.64 (4.28)	1.16 (4.28)	1.00 (4.28)

Table (8): Assay results of spironolactone and furosemide in a laboratory prepared mixture and in Fructone capsules.

Sample		For spironolactone						For furosemide						
		Modified Vierordt's method	^{1}D (λ = 224 nm)	^{1}D (λ = 247 nm)	^{2}D (λ = 210 nm)	^{2}D (λ = 235 nm)	^{2}D (λ = 262 nm)	Modified Vierordt's method	U.V. (λ=276 nm)	U.V. (λ= 330 nm)	^{1}D (λ = 235 nm)	^{1}D (λ = 280 nm)	^{2}D(λ = 275 nm)	^{2}D(λ = 285 nm)
Laboratory prepared mixture	% Recovery ± S.D.	100.0±1.05	99.8±0.95	100.2±1.00	100.1±0.89	99.9±1.03	102.2±0.99	99.8±0.69	100.1±2.01	100.0±0.67	100.5±0.71	100.3±0.76	100.7±0.49	100.1±0.56
	N	6	6	6	6	6	6	6	6	6	6	6	6	6
	V	1.10	0.90	1.00	0.79	1.06	0.98	0.48	4.04	0.45	0.50	0.58	0.24	0.31
	t		0.35 (3.58)	0.34 (3.58)	0.18 (3.58)	0.16 (3.58)	3.73 (3.58)		0.35 (3.58)	0.51 (3.58)	1.78 (3.58)	1.18 (3.58)	2.22 (3.58)	0.82 (3.58)
	F		1.20 (4.28)	1.10 (4.28)	1.39 (4.28)	1.04 (4.28)	1.12 (4.28)		8.40 (4.28)	1.07 (4.28)	1.04 (4.28)	1.21 (4.28)	2.00 (4.28)	1.55 (4.28)
Capsules (Fructone)	% Recovery ± S.D.	100.9±0.85	99.8±0.90	100.0±1.01	100.2±0.88	100.1±0.89	100.9±0.79	100.7±0.90	99.1±0.91	100.1±1.03	100.6±0.88	100.1±0.92	100.8±1.03	99.7±0.58
	N	6	6	6	6	6	6	6	6	6	6	6	6	6
	V	0.72	0.81	1.02	0.77	0.79	0.62	0.81	0.82	19.6	0.77	0.58	1.96	0.72
	t		1.37 (3.58)	1.67 (3.58)	1.04 (3.58)	1.59 (3.58)	0.00 (3.58)		3.08 (3.58)	1.08 (3.58)	0.19 (3.58)	1.14 (3.58)	0.18 (3.58)	1.99 (3.58)
	F		1.12 (4.28)	1.42 (4.28)	1.07 (4.28)	1.10 (4.28)	1.16 (4.28)		1.01 (4.28)	1.31 (4.28)	1.05 (4.28)	1.05 (4.28)	1.31 (4.28)	1.13 (4.28)

Table (9): Assay of Aldactazide tablets using the suggested first and second derivative spectrophotometric measurements applying the standard addition technique.

Taken mg%	Added mg%	For spironolactone		For hydrochlorothiazide	
		^1D (λ = 220 nm)	^2D (λ = 227 nm)	^1D (λ = 278 nm)	^2D (λ = 281 nm)
		Recovery %	Recovery %	Recovery %	Recovery %
	----	----	----	----	----
	4	99.8	100.5	100.0	99.7
	8	100.4	101.2	100.8	98.5
4	12	99.9	100.2	100.5	99.9
	16	100.0	100.9	100.8	100.4
	20	100.8	99.0	99.4	100.3
$\bar{X}$		100.2	100.4	100.3	99.8
± S.D.		0.41	0.85	0.60	0.76

Table (10): Assay of Capozide tablets using the suggested first and second derivative spectrophotometric measurements applying the standard addition technique.

		For captopril				For hydrochlorothiazide	
		^1D (λ = 221 nm)	^2D (λ = 227 nm)			^1D (λ = 278 nm)	^2D (λ = 281 nm)
Taken mg%	Added mg%	Recovery %	Recovery %	Taken mg%	Added mg%	Recovery %	Recovery %
	---	---	---		---	---	---
	8	100.5	99.7		4	99.6	97.9
	16	100.9	99.0		8	99.9	99.6
8	24	100.0	100.4	4	12	100.5	99.3
	32	100.3	100.6		16	100.8	100.1
	40	100.5	100.0		20	100.6	99.0
$\bar{X}$		100.4	99.9			100.3	99.2
± S.D.		0.33	0.63			0.51	0.82

Table (11): Assay of Fructone capsules using the suggested first and second derivative spectrophotometric measurements applying the standard addition technique.

		For spironolactone				For furosemide	
		^1D (λ = 247 nm)	^2D (λ = 262 nm)			^1D (λ = 235 nm)	^2D (λ = 285 nm)
Taken mg%	Added mg%	Recovery %	Recovery %	Taken mg%	Added mg%	Recovery %	Recovery %
	---	---	---		---	---	---
	4	100.8	99.8		1.6	98.9	100.8
	8	100.6	100.6	1.6	3.2	100.5	100.0
4	12	99.5	100.3		4.8	101.0	99.6
	16	100.3	100.0		6.4	100.3	100.7
	20	100.0	98.5		8.0	100.5	100.8
$\bar{X}$		100.2	99.8			100.2	100.4
± S.D.		0.51	0.81			0.79	0.55

spironolactone does not interfere. For comparison the measurements at these wavelengths together with the $A_{max.}$ method [26] were applied. Statistical analysis of the results (table 5) showed that most of the suggested measurements are equally precise and accurate to the $A_{max.}$ method.

In order to prove the validity and the applicability of the proposed methods, six dilutions of a laboratory prepared mixture of spironolactone with furosemide (2.5:1) were analyzed applying the proposed methods. In comparison with modified Vierordt's method [24] statistical analysis of the results (table 8) showed that most of the suggested measurements are equally precise and accurate to the modified Vierordt's method.

Fructone capsules, were assayed for both spironolactone with furosemide using the proposed methods. In comparsion with modified Vierordt's method statistical analysis of the results obtained (table 8) revealed that all the suggested measurements are equally precise and accurate to the modified Vierordt's method.

Moreover, accuracy of the suggested procedures was further checked by applying standard addition tectnique. The results obtained (tables 9, 10 & 11) revealed high degree of accuracy.

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