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SPECTROPHOTOMETRIC DETERMINATION OF AMLODIPINE BESILATE, BISOPROLOL HEMIFUMARATE AND SOTALOL HCL THROUGH OXIDATION REDUCTION REACTION

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ABSTRACT

Two simple sensitive and accurate methods have been developed for the determination of amlodipine besilate, bisoprolol hemifumarate and sotalol HCl through oxidation-reduction reaction. The first method involves the oxidation of the drugs with cerium(IV) sulphate in acidic medium and subsequent measurement of the decrease in reagent absorbance at 318 nm in the concentration ranges of 0.2-1.4, 0.25-2.75 and 0.5-4 μg ml^{-1} of amlodipine besilate, bisoprolol hemifumarate and sotalol HCl, respectively. The second method is based on the oxidation of the selected drugs with known excess cerium(IV) sulphate in acidic medium followed by determination of the unreacted cerium(IV) by measuring the decrease in absorbance of chromotrope 2R(C2R) at λmax 508 nm in the concentration ranges of 1.25-4.5, 0.75-3.25 and 0.5-3 μg ml^{-1} of amlodipine besilate, bisoprolol hemifumarate and sotalol HCl, respectively. The proposed methods were successfully applied for the analysis of the investigated drugs pharmaceutical dosage forms. Results obtained by the proposed methods were compared with those obtained by the reference methods and no significant differences were found.

INTRODUCTION

Amlodipine besilate is 3-Ethyl 5-methyl (4RS)-2-[(2-aminoethoxy) methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate benzenesulphonate [1]. It is a dihydropyridine calcium-channel blocker. It is used in the management of hypertension and angina pectoris [2]. Spectrophotometric methods were reported for amlodipine determination in bulk drug and in pharmaceutical preparation [3-13]. Spectrofluorimetric methods were reported for its determination [7,9,14]. Other methods of analysis including HPLC [15,16], LC-MS/MS [17], RP-HPLC [18], HP-TLC [19], GC [20] and voltammetric methods were used [21].

Bisoprolol Hemifumarate is 1-[4-[[2-(1-methylethoxy) ethoxy] methyl] phenoxy]-3-[(1-methylethyl) amino2-Propanol fumarate (2:1). It is a highly selective α1-receptor blocking agent used for the treatment of hypertension and angina pectoris [2]. Spectrophotometric methods were reported for Bisoprolol determination in pharmaceutical preparation [22-25]. Several methods were used including spectroflourimetric [26], HPLC [27], RP-HPLC [28], LC [29], GC-MS [30], HP-TLC [31], capillary electrophoresis [32], potentiometric [33] and voltammetric [34] methods.

Sotalol hydrochloride is N-[4-[(1RS)-1-hydroxy-2-[(1-methylethyl) amino] ethyl] phenyl]methanesulphonamide hydrochloride [1]. It is a non-cardioselective beta blocker with class II and III antiarrhythmic properties [2]. Several methods were used for sotalol HCl determination in pure and pharmaceutical dosage forms.

These methods include spectrophotometric [35-40], spectroflourimetric [41,42], HPLC [38,40,43], RP-HPLC [44], LC [45],capillary zone electrophoresis [46] and NMR spectroscopic methods [47].

was diluted with the same solvent then further dilution with distilled water to obtain working standard solution of concentration 50μg ml^{-1}.

Cerium Cerium(IV) as an oxidising agent has been used successfully for the determination of many drugs such as diclofenac sodium [48], phenolic ß-lactam antibiotics [49], risedronate sodium, alendronate sodium, etidronate disodium [50], nizatidine [51], ambroxol HCl and orciprenaline sulphate [52]. In the present work, two accurate, easy and sensitive spectrophotometric procedures were developed for the analysis of the cited drugs in bulk form and pharmaceutical preparations through oxidation with Cerium (IV) and with cerium (IV)-chromotrope 2R.

EXPERIMENTAL

Instrumentation

A Shimadzu recording spectrophotometer UV 1800 equipped with 10 mm matched quartz cells was employed for all absorbance measurements.

Marerials and reagents

All reagents were of analytical grade and distilled water was used. Amlodipine besilate (Amyria, Egypt), Bisoprolol hemifumarate (Amoun Pharm, Egypt), Sotalol HCl (Amoun Pharm, Egypt), Cerium (IV) sulphate (Merck, England), 0.1 %, 0.04% w/v and 5×10^{-4} M solutions in 2M sulphuric acid, Chromotrope 2R: 2-(Phenylazo) chromotropic acid disodium salt, (Aldrich), 0.03% w/v prepared solution in distilled water were used.

Standard drug solutions

1. 0.1 mg ml^{-1} solution of amlodipine besilate in least amount of methanol was diluted with distilled water to obtain working standard solution of concentration 20 μg ml^{-1} and 50 μg ml^{-1}.
2. 0.1 mg ml^{-1} solution of bisoprolol hemifumarate and sotalol HCl in distilled water

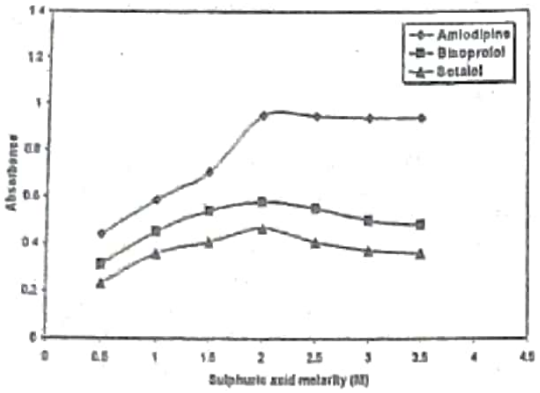

Fig. (2): Effect of sulphuric acid molarity on the reaction of cerium(IV) sulphate with:
- 1.4 μg ml^{-1} amlodipine besilate.
- 1.5 μg ml^{-1} bisoprolol hemifumarate.
- 1.5 μg ml^{-1} sotalol HCl.

2. Effect of ceric(IV) sulphate concentration

Maximum decrease in absorbance was obtained using 1.5 ml 0.1% w/v ceric (IV) sulphate. Concentrations higher than 0.14% and volumes higher than 2.5 ml 0.1% of the reagent leads to higher unacceptable absorbance values and the shape of absorbance spectra changed due to the increase of blank absorbance. Figs. (3,4)

3. Effect of temperature and heating time

Heating for 30, 15 and 25 min in a boiling water bath was optimum for amlodipine besilate, bisoprolol hemifumarate and sotalol HCl. Figs(5,6).

4. Effect of diluting solvent

Water, ethanol, methanol, acetone and 2M H_2SO_4 were tried. Water was optimum solvent for the three drugs.

5. Stoichiometric relationship

By applying Job's method of continuous variation[53] the ratio of ceric (IV) sulphate to the studied the drugs was (4 : 1). Fig. (7)

Method (b): Spectrophotometric procedure using ceric sulphate and chromotrope 2R

It involves two stages: the first one is the oxidation of the selected drugs with known excess Ce^{+4} in acidic medium under the effect of heating as explained previously, and the second one involves the determination of the unreacted oxidant by measuring the decrease in absorbance of C2R at the suitable λmax 508 nm. Fig. (8).

The decrease in color intensity is attributed to the oxidation of the dye to its degradable products, results in the formation of formic acid as the main oxidation product.

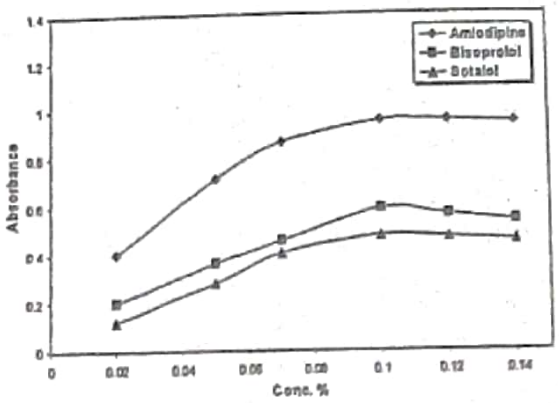

Fig. (3): Effect of cerium(IV) sulphate concentration on the reaction with:
- 1.4 μg ml^{-1} amlodipine besilate.
- 1.5 μg ml^{-1} bisoprolol hemifumarate.
- 1.5 μg ml^{-1} sotalol HCl.

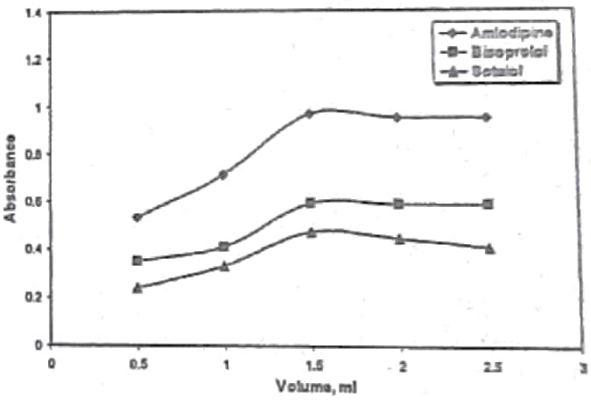

Fig. (4): Effect of volume of 0.1% w/v cerium(IV) sulphate on the reaction with:
- 1.4 μg ml-1 amlodipine besilate.
- 1.5 μg ml-1 bisoprolol hemifumarate.
- 1.5 μg ml-1 sotalol HCl.

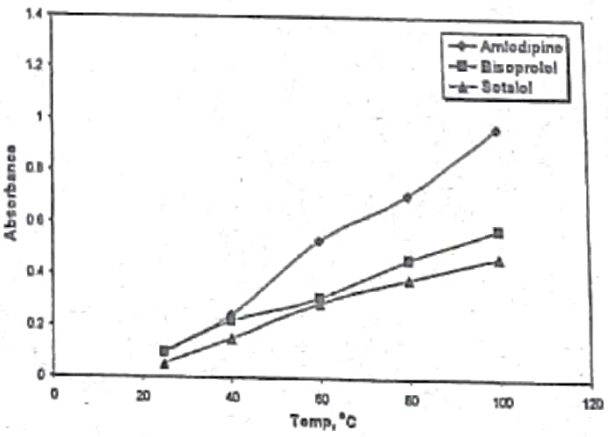

Fig. (5): Effect of heating temperature on the reaction of cerium(IV) sulphate with:
- 1.4 μg ml^{-1} amlodipine besilate.
- 1.5 μg ml^{-1} bisoprolol hemifumarate.
- 1.5 μg ml^{-1} sotalol HCl.

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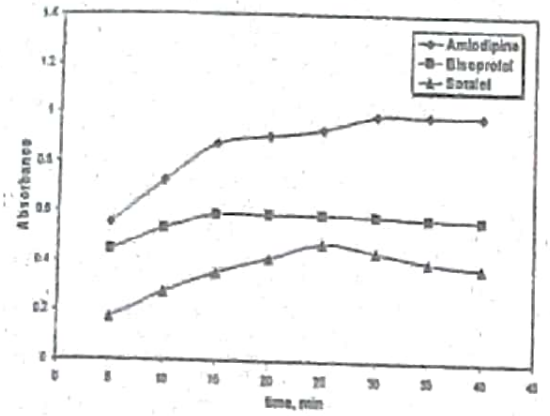

Fig (6): Effect of heating time on the reaction of cerium(IV) sulphate with:
- 1.4 µg ml^{-1} amlodipine besilate.
- 1.5 µg ml^{-1} bisoprolol hemifumarate.
- 1.5 µg ml^{-1} sotalol HCl.

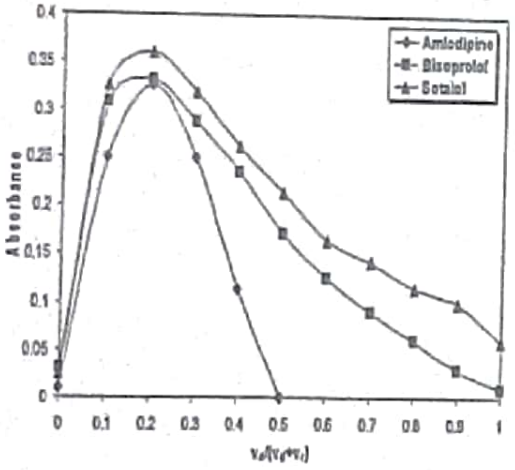

Fig. (7): Continuous variation plot of the reaction between:
(a) 5×10^{-4} M amlodipine besilte and 5×10^{-4} M cerium(IV) sulphate in 2M H_2SO_4.
(b) 5×10^{-4} M bisoprolol hemifumarate and 5×10^{-4} M cerium(IV) sulphate in 2M H_2SO_4
(c) 5×10^{-4} M sotalol HCl and 5×10^{-4} M cerium(IV) sulphate in 2M H_2SO_4.

Investigation of assay parameters

1. Effect of sulphuric acid concentration

Using different sulphuric acid concentrations ranging from 0.1 to 3.5M solutions, the optimum concentration that gave maximum decrease in absorbance and maximum fluorescence intensity was 2M solution. Fig. (9)

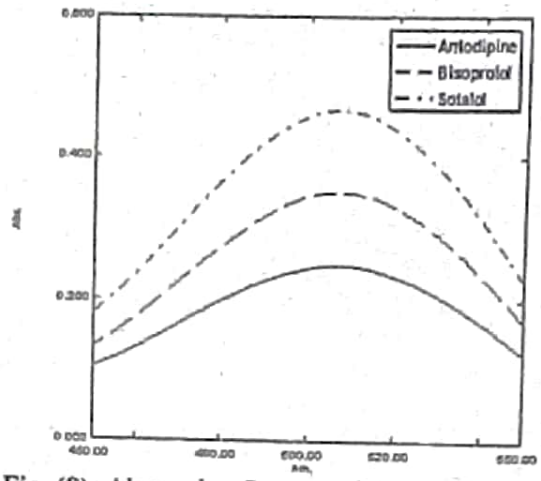

Fig. (8): Absorption Spectra of the reaction products of Cerium(IV) sulphate and C2R with:
- 2 µg ml-1 amlodipine besilate
- 2 µg ml-1 bisoprolol hemifumarate.
- 2 µg ml-1 sotalol HCl

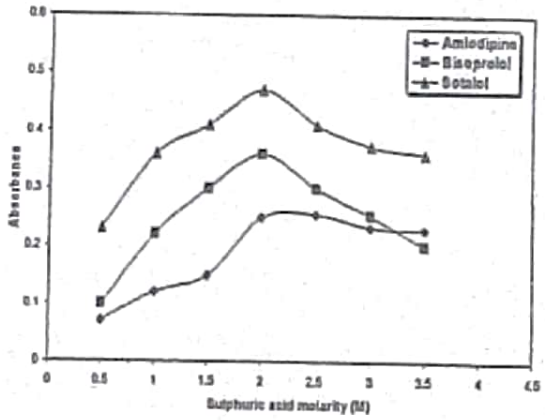

Fig. (9): Effect of sulphuric acid normality on the reaction of cerium(IV) sulphate and C2R with:
- 2 µg ml^{-1} amlodipine besilate
- 2 µg ml^{-1} bisoprolol hemifumarate.
- 2 µg ml^{-1} sotalol HCl

2. Effect of ceric (IV) sulphate concentration

Maximum increase in absorbance was obtained using 3 ml 0.04% w/v ceric (IV) sulphate for amlodipine besilate and bisoprolol hemifumarate, while 2 ml 0.04% w/v was the best for sotalol HCl. Figs. (10,11)

3. Effect of temperature and heating time:

Heating for 15, 20 and 25 min in a boiling water bath was optimum for amlodipine besilate, bisoprolol hemifumarate and sotalol HCl, respectively. Figs. (12, 13)

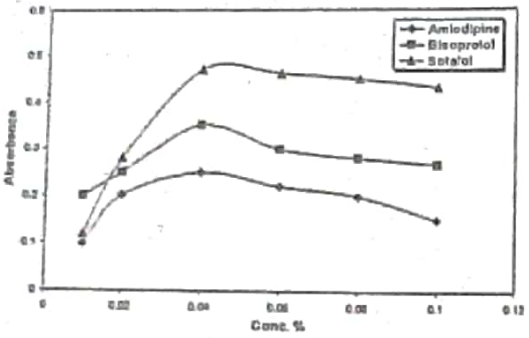

Fig. (10): Effect of cerium(IV) sulphate concentration on its reaction with C2R and:
- 2 μg ml^{-1} amlodipine besilate
- 2 μg ml^{-1} bisoprolol hemifumarate.
- 2 μg ml^{-1} sotalol HCl

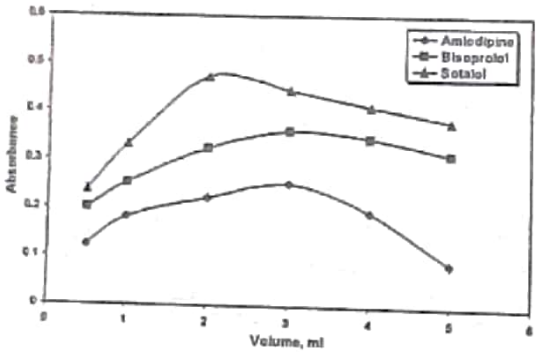

Fig. (11): Effect of volume of cerium(IV) sulphate (0.04%w/v) on its reaction with C2R and:
- 2 μg ml^{-1} amlodipine besilate
- 2 μg ml^{-1} bisoprolol hemifumarate.
- 2 μg ml^{-1} sotalol HCl

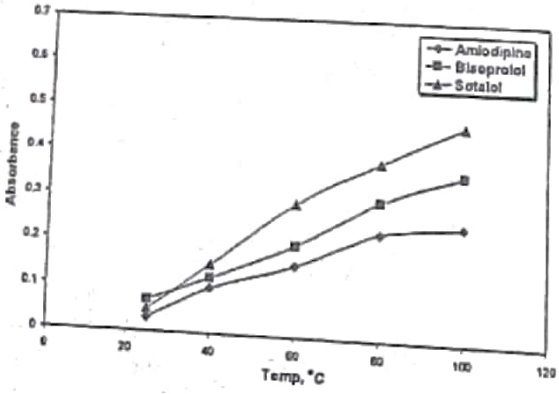

Fig. (12): Effect of heating temperature on the reaction of cerium(IV) sulphate and C2R with:
- 2 μg ml^{-1} amlodipine besilate
- 2 μg ml^{-1} bisoprolol hemifumarate.
- 2 μg ml^{-1} sotalol HCl

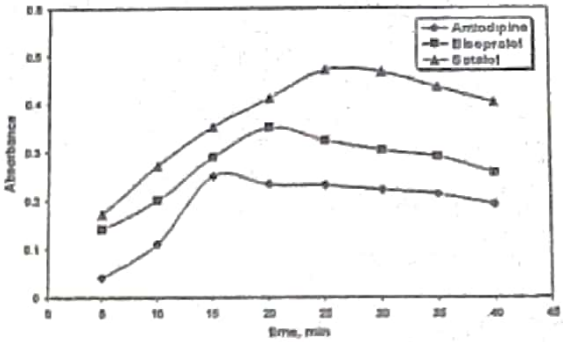

Fig. (13): Effect of heating time on the reaction of cerium(IV) sulphate and C2R with:
- 2 μg ml^{-1} amlodipine besilate
- 2 μg ml^{-1} bisoprolol hemifumarate.
- 2 μg ml^{-1} sotalol HCl

4. Effect of chromotrope 2R (C2R) concentration

Maximum increase in the absorbance was achieved by using 1.5 ml of 0.03% w/v of C2R for amlodipine besilate and bisoprolol hemifumarate, while 1 ml 0.03% w/v was the best for sotalol HCl. Figs. (14,15)

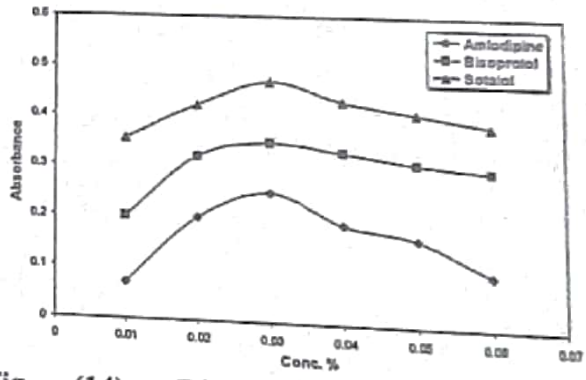

Fig. (14): Effect of chromotrope 2R concentration on its reaction with cerium(IV) sulphate and:
- 2 μg ml^{-1} amlodipine besilate
- 2 μg ml^{-1} bisoprolol hemifumarate.
- 2 μg ml^{-1} sotalol HCl

5. Effect of diluting solvent

Water, ethanol, methanol, acetone and 2M H_2SO_4 were tried. Water was optimum solvent for the three drugs.

Quantification, accuracy and precision

Linear correlation was found between the decrease in absorbance and concentration of the studied drugs. Beer's law range, molar absorbtivity, correlation coeffiecient, intercept and slope of the calibration curve were calculated.

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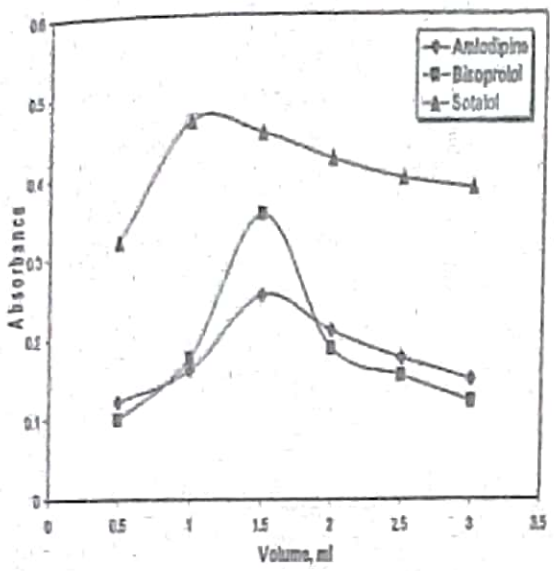

Fig. (15): Effect of volume of chromotrope 2R (0.03%w/v) on its reaction with cerium(IV) sulphate and:
- 2 μg ml^{-1} amlodipine besilate
- 2 μg ml^{-1} bisoprolol hemifumarate.
- 2 μg ml^{-1} sotalol HCl

Also relative standard deviation, analytical standard error, detection and quantification limits were calculated and listed in tables (1,2).

The proposed methods were used for determination of the selected drugs in their pharmaceutical preparations by standard addition technique, Tables (3,4). Results obtained were compared with the reference methods [11,24,38] by student's t-test and variance ratio F-test, Table (5). The calculated values did not exceed the theoretical ones.

Accuracy and precision

Accuracy and precision were carried out by six determinations at four different concentrations of the three drugs in the same day (intra-day), and in six different days (inter-day). Percentage relative standard deviation (R.S.D. %) as precision and percentage relative error (Er %) as accuracy of the suggested method were calculated.

The percentage relative error calculated using the following equation:

Er% = [(found − added) / added] × 100

The results of accuracy and precision show that the proposed methods have good repeatability and reproducibility able (6)

Table (1): Spectral data for determination of amlodipine besilate, bisoprolol hemifumarate and sotalol HCl using cerium (IV) sulphate and cerium(IV) sulphate-chromotrope 2R.

Parameters	Cerium(IV) sulphate method			Cerium(IV) sulphate + C2R method		
	Amlodipine besilate	Bisoprolol hemifumarate	Sotalol HCl	Amlodipine besilate	Bisoprolol hemifumarate	Sotalol HCl
Linearity range (μg ml^{-1})	0.2-1.4	0.25-2.75	0.5-4	1.25-4.5	0.75-3.25	0.5-3
Apparent molar absorptivity* ($mol^{-1}cm^{-1}$)	4.08×10^{5}	1.62×10^{5}	9.14×10^{4}	6.92×10^{4}	6.60×10^{4}	7.62×10^{4}
Sandell's sensitivity (mg ml^{-1} per 0001A)	7.19×10^{-3}	4.24×10^{-3}	2.96×10^{-3}	1.22×10^{-2}	1.72×10^{-2}	2.47×10^{-2}
Limit of detection (μg ml^{-1})	0.059	0.072	0.114	0.483	0.218	0.145
Limit of quantification(μg ml^{-1})	0.197	0.240	0.381	1.197	0.726	0.484
Regression equation**:						
Slope (b)	0.6400	0.3075	0.2213	0.0275	-0.0197	0.0897
Intercept (a)	0.0749	0.1287	0.1172	0.1117	0.184	0.1891
Correlation coefficient (r)	0.9999	0.9999	0.9999	0.9998	0.9998	0.9999

*Calculated on the basis of the molecular weight of the drug.
** A=a + bc

Table (2): Determination of amlodipine besilate, bisoprolol hemifumarate and sotalol HCl using cerium (IV) sulphate and cerium (IV) sulphate-chromotrope 2R.

Statistics	Cerium(IV) sulphate method						Cerium(IV) sulphate + C2R method					
	Amlodipine besilate		Bisoprolol hemifumarate		Sotalol HCl		Amlodipine besilate		Bisoprolol hemifumarate		Sotalol HCl	
	Taken µg ml^{-1}	Recovery* %	Taken µg ml^{-1}	Recovery* %	Taken µg ml^{-1}	Recovery* %	Taken µg ml^{-1}	Recovery* %	Taken µg ml^{-1}	Recovery* %	Taken µg ml^{-1}	Recovery* %
	0.2	101.64	0.25	99.12	0.5	99.23	1.25	101.34	0.75	99.06	0.5	99.74
	0.6	99.24	0.5	98.27	0.75	98.08	1.75	99.50	1.00	98.75	1.0	99.05
	0.9	99.84	0.75	100.59	1.25	100.42	2.25	100.07	1.25	100.74	1.5	100.23
	1.1	99.45	1.00	99.48	1.75	100.39	2.75	99.13	2.00	100.46	2.0	100.56
	1.2	101.18	1.25	100.89	2.00	100.27	3.00	100.72	2.50	101.24	2.5	100.54
	1.3	99.89	1.50	98.80	3.00	100.73	3.25	99.86	3.00	99.04	3.0	99.47
	1.4	99.90	1.75	100.64	3.50	99.77	3.5	99.37	3.25	99.95		
			2.25	100.08	4.00	99.61	4.5	100.37				
			2.50	100.07								
			2.75	99.35								
Mean±S.D.	100.16±0.897		99.73±0.863		99.82±0.856		100.04±0.743		99.89±0.965		99.93±0.613	
N	7		10		8		8		7		6	
S.D.	0.897		0.863		0.856		0.743		0.965		0.613	
R.S.D.	0.896		0.866		0.858		0.742		0.966		0.613	
V	0.805		0.746		0.733		0.551		0..931		0.376	
S.E.	0.339		0.273		0.303		0.263		0.36		0.250	

* Average of three experiment

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Table (3): Application of standard addition technique for determination of amlodipine besilate, bisoprolol hemifumarate and sotalol HCl in their pharmaceutical formulations using ceric(IV) sulphate.

	Amlodipine besilate (Norvasc tablets)			Bisoprolol hemifumarate (Concor tablets)			Sotalol HCl (Betacor tablets)		
	Taken	Added	Recovery*	Taken	Added	Recovery*	Taken	Added	Recovery*
	$\mu g\ ml^{-1}$		%	$\mu g\ ml^{-1}$		%	$\mu g\ ml^{-1}$		%
	0.2	--	102.42	0.25	--	100.42	0.50	--	98.33
		0.2	100.86		0.75	99.72		0.50	101.04
		0.3	100.57		1.00	100.78		0.75	99.89
		0.3	101.99		1.25	99.07		2.00	99.59
		0.7	99.13		1.50	99.01		2.50	100.46
		1.1	100.58		1.75	101.20		2.75	101.52
		1.2	99.88		2.25	100.36		3.00	98.78
								3.25	99.66
Mean±S.D.	100.50±0.962			100.03±0.904			100.14±0.935		
N	6			6			7		
V	0.925			0.817			0.874		
S.D.	0.962			0.904			0.935		
S.E.	0.392			0.369			0.382		

* Mean of three different experiments

Table (4): Application of standard addition technique for determination of amlodipine besilate, bisoprolol hemifumarate and sotalol HCl in their pharmaceutical formulations using ceric(IV) sulphate and chromotrope 2R.

	Amlodipine besilate (Norvasc tablets)			Bisoprolol hemifumarate (Concor tablets)			Sotalol HCl (Betacor tablets)		
	Taken	Added	Recovery*	Taken	Added	Recovery*	Taken	Added	Recovery*
	μg ml^{-1}		%	μg ml^{-1}		%	μg ml^{-1}		%
	1.25	--	99.91	0.75	--	101.23	0.50	--	98.68
		1.25	98.48		0.75	99.78		0.50	100.79
		1.50	100.57		1.00	100.38		0.75	100.33
		1.75	98.48		1.25	101.61		1.00	98.52
		2.00	100.04		1.50	100.25		1.25	100.39
		2.25	99.67		1.75	99.29		1.5	100.93
		2.50	99.37		2.00	99.10		1.75	99.21
Mean±S.D.	99.44±0.842			100.07±0.909			100.03±0.957		
N	6			6			6		
V	0.709			0.825			0.917		
S.D.	0.842			0.909			0.957		
S.E.	0.344			0.371			0.391		

* Mean of three different experiments

Table (5): Statistical data for determination of amlodipine besilate, bisoprolol hemifumarate and sotalol HCl using ceric (IV) sulphate and ceric(IV) sulphate - Chromotrope 2R .

Drug		ceric(IV) sulphate method	Ceric(IV) sulphate+ C2R method	Reference or reported method
Amlodipine besilate	Mean ±S.D	100.16±0.897	100.00±0.717	100.06±0.844[11]
	N	7	8	7
	Variance	0.805	0.514	0.713
	Student-t-test	0.215 (2.179)*	0.613 (2.262)*	
	F-test	1.129 (4.280)*	1.301 (4.740)*	
Bisoprolol hemifumatate	Mean ±S.D	99.73±0.863	100.04±0.744	100.24±0.782[24]
	N	10	8	6
	Variance	0.746	0.554	0.612
	Student-t-test	1.182 (2.145)*	0.022 (2.262)*	
	F-test	1.219 (4.780)*	3.166 (4.740)*	
Sotalol HCl	Mean ±S.D	99.81±0.856	99.85±0.537	100.11±0.930[38]
	N	8	8	8
	Variance	0.733	0.288	0.865
	Student-t-test	0.671 (2.145)*	0.559 (2.262)*	
	F-test	1.180 (3.790)*	1.309 (4.740)*	

*Theoretical values of t and F at p = 0.05

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Table (6): The intra-day and inter-day accuracy and precision data for amlodipine besilate, bisoprolol hemifumarate and sotalol HCl obtained using cerium(IV) sulphate and cerium(IV) sulphate-chromotrope 2R.

		Cerium(IV) sulphate method					Cerium(IV) sulphate + C2R method				
		Taken µg/ml	Found µg/ml	Recovery %	RSD%	Er %	Taken µg/ml	Found µg/ml	Recovery %	RSD%	Er %
Amlodipine besilate	Intra-day	0.2	0.204	101.90	1.047	1.90	3	3.017	100.57	1.106	0.57
		0.6	0.595	99.16	0.889	-0.84	3.5	3.486	99.59	0.925	-0.41
		0.9	0.897	99.64	0.618	-0.36	4.5	4.528	100.63	0.899	0.63
		1.1	1.091	99.19	0.704	-0.81					
	Inter-day	0.2	0.203	101.25	1.064	1.25	3	3.024	100.82	1.194	0.82
		0.6	0.592	98.68	0.687	-1.32	3.5	3.478	99.37	1.174	-0.63
		0.9	0.892	99.15	0.655	-0.85	4.5	4.520	100.43	0.992	0.43
		1.1	1.088	98.90	0.509	-1.09					
Bisoprolol hemifumarate	Intra-day	0.25	0.248	99.12	1.172	-0.88	2.5	2.532	101.28	1.225	1.28
		0.50	0.490	97.95	0.695	-2.05	3	2.987	99.55	0.713	-0.45
		0.75	0.759	101.17	0.750	1.17	3.25	3.249	99.98	0.673	-0.02
		1.00	0.990	99.05	0.645	-0.95					
	Inter-day	0.25	0.247	98.91	0.989	-1.09	2.5	2.533	101.31	1.039	1.31
		0.50	0.488	97.63	0.842	02.37	3	2.990	99.67	0.987	-0.33
		0.75	0.758	101.03	0.767	1.03	3.25	3.347	99.92	0.931	-0.08
		1.00	0.986	98.56	0.605	-1.44					
4Sotalol HCl	Intra-day	0.5	0.495	98.93	1.248	-1.07	2	2.014	100.69	1.218	0.69
		0.75	0.736	98.08	1.288	-1.91	2.5	2.506	100.22	1.115	0.22
		1.25	1.253	100.24	1.180	0.24	3	2.983	99.44	1.543	-0.56
		1.75	1.755	100.31	0.841	0.31					
	Inter-day	0.5	0.492	98.48	1.581	-1.52	2	2.016	100.78	1.373	0.77
		0.75	0.737	98.29	1.141	-1.71	2.5	2.513	100.54	1.337	0.54
		1.25	1.252	100.18	1.133	0.18	3	2.993	99.78	1.174	-0.22
		1.75	1.753	100.18	0.838	0.18					

REFERENCES

1. The British Pharmacopoeia, Volumes II and III, Her Majesty's Stationery Office, London, UK, (2008).
2. Sweetman S. C., "Martindale-The Complete Drug Reference", 35th ed., The Pharmaceutical Press, London, (2007).
3. Sridhar K., Sastry C. S. P., Reddy, M. N., Sankar, D. G., Srinivas, K. R., **Analytical Lett.**, 30(1), 121, (1997).
4. Golcu A., Yucesoy C., Serin S., **Sci. Pharm.**, 68(3), 235, (2000).
5. Rahman N., Azmi S. N. H., **Anal. Sci.**, 16(12), 1353, (2000).
6. Rahman N., Azmi S. N. H., Farmaco, 56(10), 731, (2001).
7. Gazy A. A. K., **Bull. Fac. Pharm. (Cairo Univ.)**, 41(2), 245, (2003).
8. Rahman N., Nasrul H. M., **J. Pharmaceut. Biomed. Anal.**, 31(2), 381-392, 2003
9. Haggag R. S., Belal S. F. Shaalan R.A., **Mansoura J. Pharm. Sci.**, 25(1), 22, (2009).
10. Shama S. A., Amin A. S., Mabrouk E. M. Omara H. A., **Arabian J. Chem.**, 2(1), 95, (2009).
11. Dhabale P. N., Burade K. B., Hosmani A. H., Gonjari I. D., Rakesh S. U. Patil P. R., **Arch Pharm. Sci. Res.**,1(2) 158, (2009).
12. Almani F., Rind F. M. A., Memon A. H., Mughal U. R., Laghari M. G. H., Memon N., Maheshwari M. L., Khuhawar M. Y., **Asian J. Chem.**, 22(2), 1205, (2010).
13. Jain N., Jain R., Jain A., Pandey S. P. Jain, D. K., **EJAC.**, 5(3), 212, (2010).
14. Abdel-Wadood H. M., Mohamed N. A. Mahmoud A. M., **Spectrochim. Acta.**, Part A: Molecular and Biomolecular Spectroscopy, 70A(3), 564, (2008).
15. Patki R. V., Tamhankar C. P., Tipnis H. P ., **Indian Drugs**, 31(12), 560, (1994).
16. Dong Y., Qian X., Sun J., **Zhongguo Yaopin Biaozhun**, 11(3), 213, (2010).
17. Gu H., Miao J., Zhang S., Liu Y., Liu G., Lu C., Yu C., **Zhongguo Xinyao Yu Linchuang Zazhi**, 26(10), 737, (2007).
18. Avadhanulu A. B., Srinivas J. S., Anjaneyulu Y., **Indian Drugs**, 33(1), 36, (1996).
19. Pandya K. K., Satia M., GandhiT. P., Modi I. A., Modi R. I., Chakravarthy B. K., **J. Chrom. B Biomed. Sci. Appl.**, 667(2), 315, (1995).
20. Scharpf F., Riedel K. D., Laufen H., Leitold M., **J. Chrom. B Biomed. Sci. Appl.**, 655(2), 225, (1994).
21. Gazy A. A. K., **Talanta**, 62(3), 575, (2004).
22. Salem H., **J. Pharmaceut. Biomed. Anal.**, 29(3), 527, (2002).
23. Vadia N. H., Sahu R., Patel V. B., **Indian Pharmacist**, 6(59), 81, (2007).
24. Tuljarani G., Sankar D. G., Kadgapathi P., Suthakaran R., Satyanarayana B., **Int. J. Chem. Sci.**, 8(4), 2253, (2010).
25. Yang X. M., Wang C. B., **Fenxi Shiyanshi**, 20(3), 54, (2001).
26. Hefnawy M. M, Sultan M. A., Al-Shehri M. M., **J. Liq. Chromatogr. R. T.**, 29 (17-20), 2901, (2006).
27. Yu B., Shu M., Yao J., Zeng R., **Huaxi Yaoxue Zazhi**, 20(6), 550, (2005).
28. Caudron E., Laurent S., Billaud E. M., Prognon P., **J. Chromatogr. B: Anal. Technol. Biomed. Life Sci**, 801 (2), 339, (2004).
29. Paik M. J., Lee J. W., Kim K. R., **Anal. Chim. Acta**, 601 (2), 230, (2007).
30. Kakde R. B., Kotak V. H., Kale D. L., **Asian J. Res. Chem.**, 1(2), 70, (2008).
31. Awadallah B., Schmidt P. C., Holzgrabe U., Wahl M. A., **Electrophoresis**, 24 (15), 2627, (2003).
32. Hassan S. S. M., Abou-Sekkina M. M., El-Ries M. A., Wassel A. A., **J. Pharmaceut. Biomed. Anal.**, 32 (1), 175, (2003).
33. Rajendra N., Goyal R. N., Tyagi A., Bachheti N., Bishnoi S., **Electrochim. Acta**, 53 (6), 2802, (2008).
34. Sultan S. M., Bukhari A. M., Perzanowski H., **J. Pharmaceut. Biomed. Anal.**, 8(7), 569, (1990).
35. Banerjee S. K., Mashru R., **Indian J. pharm. Sci.**, 53(6), 243, (1991).
36. Erram S. V., Tipnis H. P., **IndianDrugs**, 31(1), 16, (1994).
37. Wang W., Zhao G., Cheng X., Jiang, W., **Shandong Yike Daxue Xuebao**, 39(3), 215, (2001).
38. Amin A. S., Ragab G. H., Saleh H., **J. Pharmaceut. Biomed. Anal.**, 30(4), 1347, (2002).

ISSN 1110-5089

39. Santoro M. I. R. M., Tsubone C., Gomes F. P., Kedor-Hackmann E. R. M., García P. G., **Anal. Lett.**, 41(11), 2044, (2008).
40. Garrett E. R., Schnelle K., **J. Pharm. Sci.**, 60(6), 833, (1971).
41. Zhang H., Yang J., Du L., Li C., Wu H., **Anal. Methods**. 3(5), 1156, (2011).
42. Herrmann R., **J. Pharmaceut. Biomed. Anal.**,, 13(3) 329, (1995).
43. Baranowska I., Wilczek A., **Anal. Sci.**, 25(9), 769, (2009).
44. Rbeida O., Christiaens B. , Chiap P., Hubert P., Lubda D., Boos K. S., Crommen J., **J. Pharmaceut. Biomed. Anal.**, 32(4-5), 829, (2003).
45. Dogrukol-Ak D., Dal A. G., Tunçel M., **Chromatographia**., 66(1), 159, (2007).
46. Iorio M. A., Mazzeo-Farina A., Doldo A., **J. Pharmaceut. Biomed. Anal.**, 5(1), 1, (1987).
47. Kamath B. V., Shivram K., **Anal. Lett.**, 26(5), 903, (1993).
48. Salem H., Saleh G. A., **J. Pharmaceut. Biomed. Anal.**, 28(6), 1205, (2002).
49. Taha E. A., Youssef N. F., **Chem. Pharm. Bull.**, 51(12), 1444, (2003).
50. El-Yazbi F. A., Gazy A. A., Mahgoub H., El-Sayed M. A., Youssef R. M., **J. Pharmaceut. Biomed. Anal.**, 31(5), 1027, (2003).
51. Anis S. M., Hosny M. M., Abdellatef H. E., El-balkiny M. N., **Mansoura J. Pharm. Sci.**, 24 (2), 213, (2008).
52. Rose J.; Advanced Physio-Chemical Experiments, Pitman, London, 54, (1964).
53. Rizvi S. A. I., **Mikrochem. J.**, 18 (4), 398, (1973).

طرق طيفية لتعيين كل من الأملوديبين بيسيلات والبيزوبرولول هيمي فيومارات و السوتالول هيدروكلورايد عن طريق استخدام تفاعلات الأكسدة

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يتناول هذا البحث طريقتين جديدتين لتعيين مركبات الأملوديبين بيسيلات و البيزوبرولول هيمي فيومارات و السوتالول هيدروكلورايد عن طريق استخدام تفاعلات الأكسدة. تعتمد الطريقة الأولي علي إستخدام سلفات السيريوم لأكسدة هذه الأدوية ثم حساب تركيزات الأدوية عن طريق قياس الكمية المتبقية من سلفات السيريوم الذي يمكن قياسه عند ٣١٨ نانومتر وذلك عند تركيزات للأدوية تتراوح بين ٠,٢ - ٤ ميكروجرام/ مل. اما الطريقة الثانية فتشمل اكسدة الأدوية بزيادة من سلفات السيريوم الأدوية ثم حساب تركيزات الأدوية عن طريق قياس الكمية المتبقية من سلفات السيريوم التي تؤكسد الكروموتروب ٢ آر الذي يقاس عند ٥٠٨ نانومتر ووجد أن النقص في شدة امتصاصه متناسب مع تركيزات الأدوية التي تتراوح بين ٠,٧٥ - ٤,٥ ميكروجرام/ مل.

و في كلتا الحالتين تم تقدير ناتج التفاعل بطريقة طيفية, وقد حققت هذه الطريقة نتائج طيبة عند تطبيقها في صورتها النقية و في المستحضرات الصيدلية, و تمت مقارنة النتائج بالطرق المرجعية, وثبت نجاحها.