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DETERMINATION OF PHENOBARBITONE IN TWO AND THREE COMPONENTS FORMULATIONS BY FIRST AND SECOND DERIVATIVE ULTRAVIOLET SPECTROPHOTOMETRY

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ABSTRACT

Phenobarbitone has been determined in a ternary mixture with oxyphenonium bromide and meprobamate (mixture A) and in binary mixtures with paracetamol (mixture B) or acetylsalicylic acid (mixture C) using derivative spectrophotometry applying zero-crossing technique of measurement. The combining active ingredients have also been deterimend. The procedures were proved using laboratory prepared mixtures and their utility in assay of pharmaceutical dosage forms were also presented.

INTRODUCTION

In medical practice, phenobarbitone is prescribed for any of the following reasons : to overcome insomnia, to reduce high blood pressure, to treat mental disorders and to sedate patients both before and after surgery [1]. Several methods have been reported for the determination of phenobarbitone in multicomponent drug preparations. The most recent methods include titrimetric [2], chromatographic [3-8], potentiometric [9] and spectrophotometric ones [10-18].

EXPERIMENTAL

Apparatus:

A Shimadzu recording spectrophotometer U.V. 260.

Materials :

Phenobarbitone, oxyphenonium bromide, meprobamate, acetylsalicylic acid and paracetamol (Aldrich Co. USA), Regulase tablets, Nile Co. Egypt, labeled to contain 2.5 mg oxyphenonium bromide, 200 mg meprobamate and 15 mg phenobarbitone per tablet; Sedamol paediatric suppositories, Misr Co., Egypt, labeled to contain 0.2 g paracetamol and 0.016 g phenobarbitone per 1 g suppository and Vegaskine infantile suppositories, Alex. Co. Egypt, labeled to contain 150 mg acetylsalicylic acid and 10 mg phenobarbitone per each suppository.

Stock and Working Solutions :

Aqueous stock solutions were prepared, containing 60 mg% phenobarbitone, 50 mg% oxyphenonium bromide, 380 mg% meprobamate, 50 mg% acetylsalicylic acid or 100 mg% paracetamol.

Working solutions containing the ranges stated in table 1 and laboratory prepared mixtures in the ratios related in table 1 were prepared by pipetting suitable aliquots stock solutions into 50 ml volumetric flasks and completing the volumes with distilled water.

Procedures :

1- For mixture A :

a) For laboratory prepared mixtures:

Phenobarbitone was determined by ^1D at 247 nm and ^2D at 214 & 252 nm. Oxyphenonium bromide was determined by ^1D at 234 nm.

b) For regulase tablets :

Remove almost completely the coating of twenty tablets by cotton wool moistened with water. Dry the tablets at room temperature for one hour or until constant weight. An accurately weighed portion of the finely powdered tablets (equivalent to 5 mg oxyphenonium bromide, 30 mg phenobarbitone and 400 mg meprobamate) was dissolved in 70 ml all distilled water, filtered if necessary, and completed to 100 ml with all distilled water. Working solutions containing the ranges stated in table 1 were pipetted into 50 ml volumetric flasks and completed to volume with all distilled water and completed as under 1-a.

2- For mixture B :

a) For a laboratory prepared mixture :

Phenobarbitone was determined by ^2D at 213 & 253 nm. Paracetamol was determined by ^1D at

214 & 302 and ^{2}D at 247 & 316 nm.

b) For sedamol pediatric suppositories :

Five suppositories were accurately weighed and cut into small pieces. The suppository mass was transferred into a porcelain dish and melted on a hot water bath until complete homogenity. An amount of the suppository mass equivalent to 8 mg phenobarbitone and 100 mg paracetamol was dissolved in 70 ml boiling water. The solution was cooled and filtered into a 100 ml volumetric flask. The residue was washed twice with 10 ml portions of boiling distilled water and the washings were collected into the same flask, cooled and completed to 100 ml with distilled water and continued as under 2-1.

3- For mixture C :

a) For a laboratory prepared mixture :

Phenobarbitone was determined by ^{2}D at 213 & 234 nm. Acetylsalicylic acid was determined by U.V. at 301 nm, ^{1}D at 238, 284 & 323 nm and ^{2}D at 300 & 340 nm.

b) For Vegaskine infantile suppositories :

Five suppositories were accurately weighed and the procedure was completed as under 2b using an amount of the suppository mass equivalent to 7 mg phenobarbitone and 100 mg acetylsalicylic acid. Then the procedure was continued as under 3-a.

RESULTS and DISCUSSION

For phenobarbitone :

Phenobarbitone has absorbances at ^{1}D 247 nm (Fig. 1b), ^{1}D 214 & 252 nm (Fig. 1c) for mixture A, ^{2}D 213 & 253 nm (Fig. 2c) for mixture B and ^{2}D 213 & 234 nm (Fig. 3c) for mixture C.

At the above mentioned wavelengths, oxyphenonium bromide and meprobamate in mixture A, paracetamol in mixture B and acetylsalicylic acid in mixture C, have negligible or almost no interferences. Thus at these wavelengths phenobarbitone can be determined. For comparison, the official method [19] was applied for the determination of the intact drug. Statistical analysis of the results (Table 2) showed that all the suggested procedures are as precise and accurate as the official one [19].

For oxyphenonium bromide :

As it appears from Fig. 1b, oxyphenonium bromide has absorbance at 1D 234 nm for mixture A. At this wavelength, phenobarbitone and meprobamate have no absorbance and oxyphenonium bromide can be determined without overlapping or interferences. For comparison, the official method[19] was applied for the determination of the intact drug and statistical analysis of the results (Table 2) showed that the suggested procedure is as precise and accurate as the official one [19].

For paracetamol :

As it appears from Figs. 2b & c, paracetamol has absorbances at ^{1}D 214 & 302 nm and ^{2}D 247 & 316 nm for mixture B. At the above mentioned wavelengths, phenobarbitone has negligible or almost no interferences. Thus at these wavelengths, paracetamol can be determined in presence of phenobarbitone. For comparison, the official method[19] was applied for determination of the intact drug and statistical analysis of the results (Table 2) showed that all the suggested procedures are as precise and accurate as the official one[19].

For acetylsalicylic acid :

As it appears from Figs. 3a, b & c, acetylsalicylic acid has absorbances at U.V. 301 nm, ^{1}D 238, 284 & 323 nm and ^{2}D 300 & 340 nm for mixture C. At the above mentioned wavelengths, phenobarbitone has no interferences and acetylsalicylic acid can be determined in presence of it. Statistical analysis of the results obtained, compared with the official method [19] (Table 2) showed that all the suggested procedures are as precise and accurateas the official one.

For laboratory prepared mixtures :

To prove the validity and the applicability of the proposed methods, six dilutions of the laboratory prepared mixture A were analyzed for phenobarbitone and oxyphenonium bromide and stastistically compared with the modified Vierordt's method [20] (Table 3). The results obtained for phenobarbitone, showed that most of the suggested procedures are as precise and accurate as that of the modified Vierordt's method [20]. However, the results obtained for oxyphenonium bromide showed less accuracy and reproducibility.

Six dilutions of laboratory prepared mixtures B & C were analyzed for their components. The

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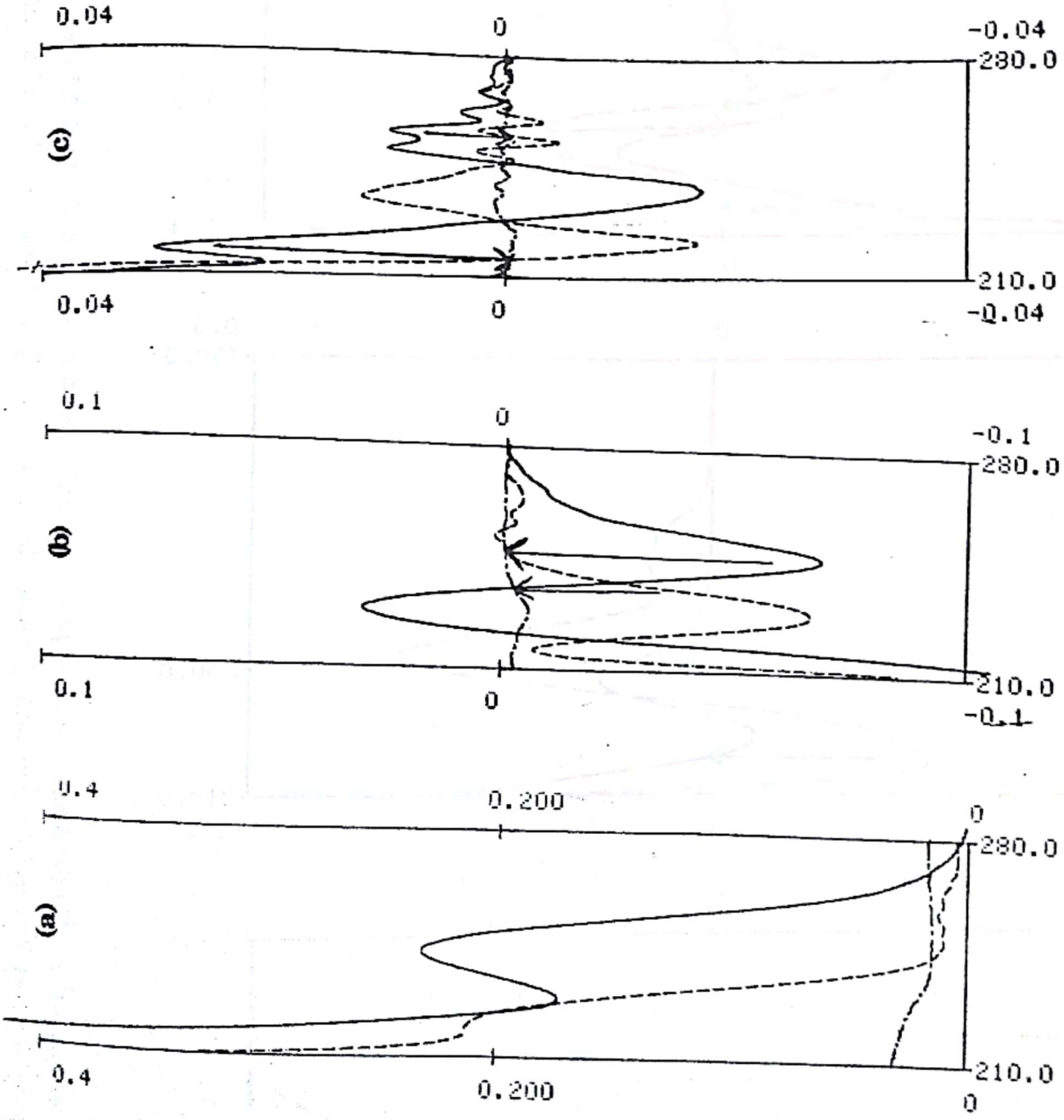

Figure (1): U.V. absorption (a), ^{1}D determination of phenobarbitone at 247 nm and of oxyphenonium bromide at 234 nm (b) and ^{2}D determination of phenobarbitone at 214 & 252 nm (c). Phenobarbitone 6 mg% (——), oxyphenonium bromide 1 mg% (——) and meprobamate 240 mg % (– – –).

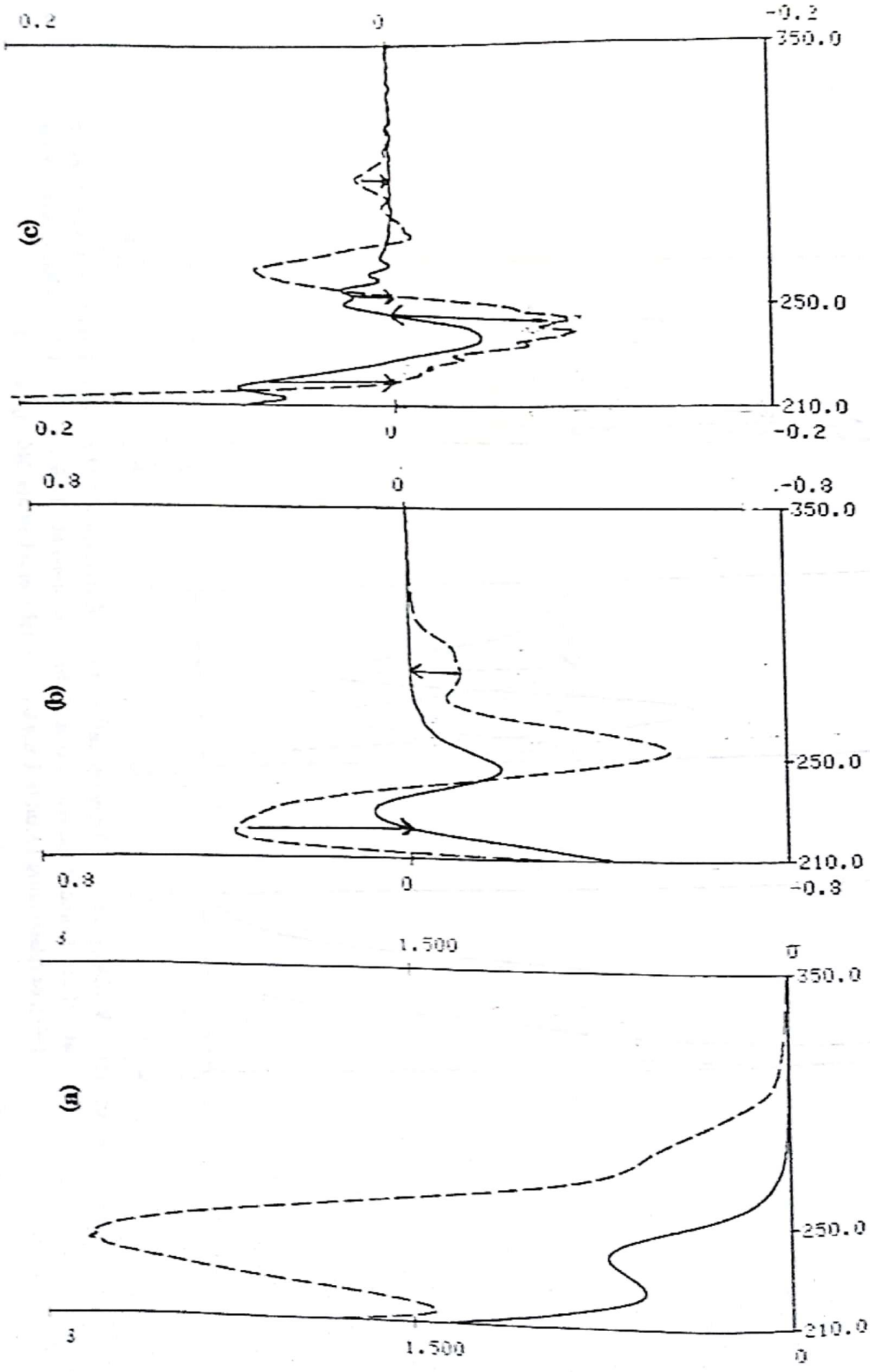

Figure (2): U.V. absorption (a), ^{1}D determination of paracetamol at 214 & 302 nm (b) and ^{2}D determination of phenobarbitone at 213 & 253 nm and of paracetamol at 247 & 316 nm (c). Phenobarbitone 1 mg % (——) and paracetamol 80 mg% (----).

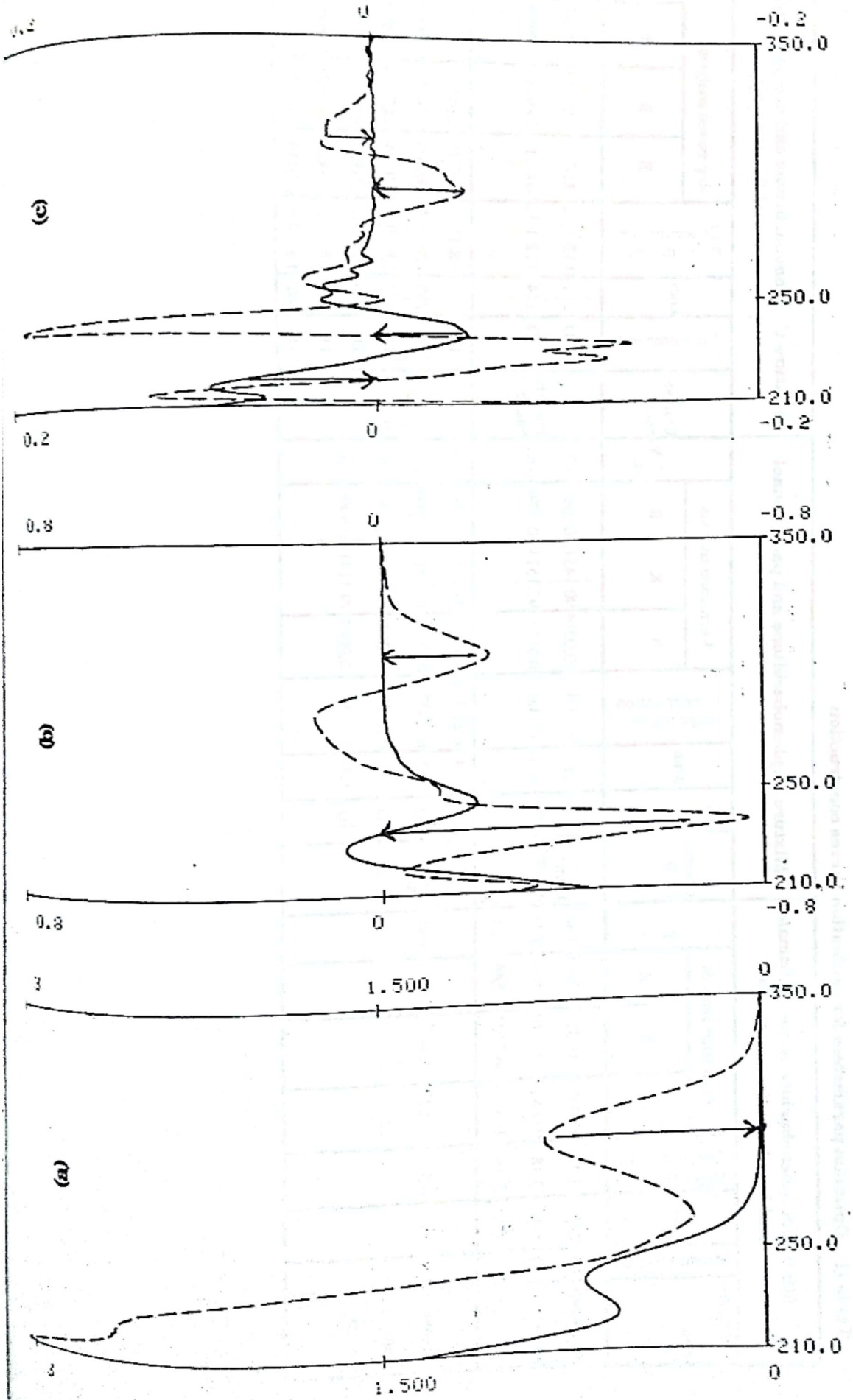

Figure (3): U.V. determination of acetylsalicylic acid at 301 nm (a), ^{1}D determination of acetylsalicylic acid at 238, 284 & 323 nm (b) and ^{2}D determination of phenobarbitone at 213 & 234 nm and of acetylsalicylic acid at 300 & 340 nm (c). Phenobarbitone 1 mg % (——) and acetylsalicylic acid 15 mg % (- - - - - - -).

Table (1) : Optimum parameters for calibration curves construction

Mixture A (phenobarbitone, meprobamate and oxyphenonium bromide)								Mixture B (phenobarbitone and paracetamol								Mixture C (phenobarbitone and acetylsalicylic acid)							
Components	Measurements	λnm	Concentration range mg %.	Regression analysis			C.V. %	Components	Measurements	λnm	Concentration range mg %.	Regression analysis			C.V. %	Components	Measurements	λnm	Concentration range mg %.	Regression analysis			
				B	K	R						B	K	R						B	K	R	C.V. %
Phenobarbitone	^1D	247	3-18	-0.0019	7.0132	0.9999	0.48	Phenobrbitone	^2D	213	0.5-3.0	-0.0014	90.1451	0.9997	0.79		^2D	213	0.12-1.32	-0.0015	105.014	0.9997	0.48
	^2D	214	3-18	0.0081	79.7810	0.9999	0.73		^2D	253	0.5-3.0	0.0152	97.1513	0.9998	0.65	Phenobrbitone	^2D	234	0.12-1.32	0.0031	90.9145	0.9999	0.71
	^2D	252	3-18	-0.0214	66.7104	0.9999	0.65																
Oxypheno-nium bromide	^1D	234	0.5-3	0.93/2	7.9945	0.9348	0.64	Paracetamol	^1D	214	6.25-37.5	-0.0107	9.0145	0.9997	0.32	Paracetamol	U.V.	301	1.8-19.8	0.0030	2.1437	0.9999	0.21
									^1D	302	6.25-37.5	0.0031	12.3314	0.9999	0.51		^1D	238	1.8-19.8	-0.0017	5.1476	0.9999	0.31
									^2D	247	6.25-37.5	0.0051	101.1012	0.9989	0.55		^1D	284	1.8-19.8	0.0134	14.7514	0.9997	0.52
									^2D	316	6.25-37.5	-0.0001	79.1141	0.9999	0.61		^1D	323	1.8-19.8	-0.0011	9.2381	0.9999	0.44
																	^2D	300	1.8-19.8	-0.0015	74.7185	0.9996	0.34
																	^2D	340	1.8-19.8	0.0139	29.1453	0.9989	0.41

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Table (2): Statistical analysis of the results obtained for assay of the authentic drugs compared with the official methods.

Method	Phenobarbitone							Oxyphenonium bromide	Paracetamol				Acetylsalicylic acid					
Official / Mean*	99.8± 0.65							100.3±0.32	100.5±0.91				100.7±0.27					
Suggested	^{1}D 247	^{2}D 214	^{2}D 252	^{2}D 213	^{2}D 253	^{2}D 213	^{2}D 234	^{1}D 234	^{1}D 214	^{1}D 302	^{2}D 247	^{2}D 316	U.V. 301	^{1}D 238	^{1}D 284	^{1}D 323	^{2}D 300	^{2}D 340
Mean*	100.3±0.75	100.1±0.66	99.9±0.95	99.7±0.57	99.8±0.90	100.0±0.58	100.1±0.60	100.1±0.41	100.7±0.89	100.0±0.99	100.1±1.01	99.9±0.95	100.2±0.19	100.3±0.20	100.5±0.28	100.9±0.4	100.5±0.30	100.4±0.33
t**	0.53	0.71	0.73	0.80	0.59	0.66	0.71	0.49	0.66	0.38	0.29	0.51	0.41	0.51	0.51	0.47	0.29	0.37
F**	1.2	1.0	1.5	1.1	1.4	1.1	1.1	1.3	1.0	1.1	1.1	1.0	1.4	1.4	1.0	1.3	1.1	1.2

* Mean of six determinations ± S.D.
** P = 0.05, t (2.23), F (5.05)

Table (3): Statistical analysis of the results obtained for assay of the laboratory prepared mixtures and pharmaceutical dosage forms of the investigated drugs compared with the modified Vierordt's method.

Laboratory prepared mixtures and dosage forms		Phenobarbitone								Oxyphenonium bromide		Paracetamol					Acetylsalicylic acid						
		Mod. Viero.	^{1}D 247	^{2}D 214	^{2}D 252	^{2}D 213	^{2}D 253	^{2}D 213	^{2}D 234	Mod. Viero.	^{1}D 234	Mod. Viero.	^{1}D 214	^{1}D 302	^{2}D 247	^{2}D 316	Mod. Viero.	U.V. 301	^{1}D 238	^{1}D 284	^{2}D 323	^{2}D 300	^{2}D 340
Mixt. (A) 1:1:1	$\bar{x}$	99.8± 0.71	99.1± 0.70	99.5± 0.69	100.0± 0.73					100.3± 0.28	100.2± 0.25												
	t		0.61	0.22	0.19						0.24												
	F		1.0	1.0	1.0						1.1												
Mixt. (A) 1:6:80	$\bar{x}$	100.2± 0.73	99.5± 0.71	99.7± 0.68	100.3± 0.71					99.1± 0.23	92.0± 0.91												
	t		0.71	0.35	0.29						2.9												
	F		1.0	1.1	1.0						4.0												
Regulase tablets	$\bar{x}$	99.5± 0.63	99.9± 0.69	99.0 0.70	99.7± 0.60					97.1± 0.19	91.9± 0.60												
	t		0.57	0.59	0.55						3.4												
	F		1.1	1.1	1.0						3.2												
Mixt. B	$\bar{x}$	100.7± 0.55				100.5± 0.51	100.4± 0.57					100.0± 0.14	99.8± 0.13	100.2± 0.15	100.4± 0.17	100.1± 0.10							
	t					0.60	0.63						0.12	0.19	0.15	0.21							
	F					1.1	1.0						1.1	1.1	1.2	1.4							
Sedamol Ped. Supp.	$\bar{x}$	99.0± 0.29				99.2± 0.33	98.7± 0.28					100.1± 0.49	100.0± 0.51	100.3± 0.50	100.7± 0.49	100.5± 0.53							
	t					0.48	0.44						0.33	0.31	0.37	0.38							
	F					1.1	1.0						1.0	1.0	1.0	1.1							
Mixt. C	$\bar{x}$	99.7± 0.50						100.0± 0.55	99.9± 0.56								100.5± 0.33	100.0± 0.35	100.3± 0.37	100.5± 0.37	100.8± 0.30	100.4± 0.33	100.7± 0.34
	t							0.11	0.14									0.61	0.61	0.00	0.51	0.55	0.49
	F							1.1	1.1									1.1	1.1	1.2	1.1	1.0	1.0
Vegaskine inf. supp.	$\bar{x}$	100.5± 0.33						100.4± 0.35	100.6± 0.30								99.7± 0.50	100.0± 0.53	100.3 0.44	99.6± 0.47	99.6± 0.44	99.7± 0.49	99.8 0.54
	t							0.23	0.31									0.35	0.41	0.34	0.40	0.39	0.29
	F							1.1	1.1									1.1	1.1	1.1	1.1	1.0	1.1

* Mean of six determinations ± S.D.

** P = 0.05, t (2.23), F (5.05)

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results obtained revealed a high degree of accuracy and reproducibility compared to the modified Vierordt's method [20].

For pharmaceutical dosage forms :

Regulase tablets (for phenobarbitone and oxyphenonium bromide), Sedamol pediatric suppositories (for phenobarbitone and paracetamol) and Vegaskine children's suppositories (for phenobarbitone and acetylsalicylic acid) were assayed using the proposed methods. Statistical analysis of the results obtained, compared with the modified Vierordt's method (Table 3) revealed that most of the suggested measurements are as precise and accurate as the modified Vierordt's method except that of oxyphenonium bromide.

As a general conclusion, the proposed procedures are rapid, simple and direct, as they estimate each drug independent of the other, as well as accurate and reproducible. They could be applied for routine assays of these drug mixtures.

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تقدير مركب الفينوباربيتون فى مخاليط ثنائية وثلاثية باستخدام طريقتى المشتق التفاضلية الاولى والثانية لمنحنى الامتصاص الضوئى

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** قسم الكيمياء – كلية البنات – الرياض – السعودية

فى هذا البحث تم تعيين الفينوباربيتون فى وجود كلا من المبروباميت والاوكسيفينونيم بروميد (المخلوط الاول) ، وتم تعيينه فى وجود الباراسيتامول (المخلوط الثانى) وكذلك تم تعيينه فى وجود حمض الاسيتيل ساليسليك (المخلوط الثالث) باستخدام طريقتى المشتق التفاضلية الاولى والثانية لمنحنى الامتصاص الطيفضوئى فى المنطقة فوق البنفسجية . ولقد أمكن تعيينه بدون تداخل طيفضوئى مع المركبات الاخرى . ولقد طبقت الطرق المقترحة علي المستحضرات الصيدلية (أقراص الرجيوليز – لبوس سيدامول للأطفال – لبوس فيجاسكين للأطفال) وبمقارنة الطرق المقترحة بالطريقة الدستورية أعطت نتائج متماثلة في الدقة والتكرار.