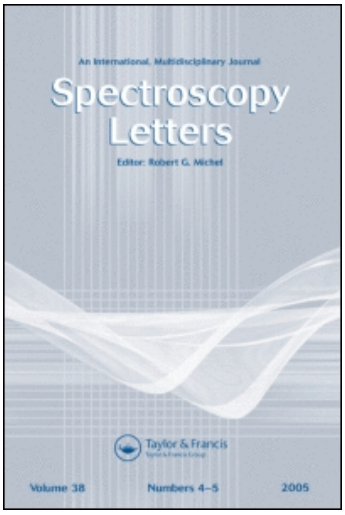

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Derivative Spectrophotometric Determination of Some Tranquilizer - Antidepressant Mixtures

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DERIVATIVE SPECTROPHOTOMETRIC DETERMINATION OF SOME TRANQUILIZER - ANTIDEPRESSANT MIXTURES

(**Keywords**; derivative spectrophotometry, perphenazine, amitriptyline, chlordiazepoxide, trifluoperazine, isopropamide).

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ABSTRACT

A method is presented for the determination of three tranquilizer-antipressant mixtures namely perphenazine amitriptyline, chlordiazepoxide-amitriptyline and trifluoperazine-isopropamide. The method depend on the application of first and second derivative spectrophotometric methods to resolve the interferance due to spectral overlapping. The method was applied to the determination of these compounds in synthetic mixtures and in pharmaceutical preparations. The coefficient of variation was less than 2%.

INTRODUCTION

The direct spectrophotometric analysis of drugs in multicomponent dosage forms is often complicated by interferances due to spectral overlapping of active ingred-

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* Correspondence.

ients and from formulation matrix. Recently, it has been shown that the application of derivative technique[1-3] to spectrophotometry is very useful in resolving spectral overlap and in cancelling irrelevant absorption from the formulation matrix. Application of derivative spectrophotometry for the analysis of two component mixture or multicomponent mixture utilized several technique through(i) the application of zero crossing technique for example determination of procaine hydrochloride and benzocaine in the presence of 4-amniobenzoic acid[4], and for the determination of strychnine and brucine in Nux vomica liquid extract[5]. (ii) solving two or three simultaneous equations to determine two component[6] or three component mixture[7]. (iii) application of differential-derivative spectrophotometry to determine oxazepan or phenobarbitone in presence of dipyridamole[8] and to determine ethinyloestradiol in presence of norethisterone[9].

This paper reports a simple, rapid and accurate method for the direct determination of three mixtures namely perphenazine-amitriptyline (Mixture I), chlordiazepoxide-amitriptyline (Mixture II), and trifluoperazine-isopropamide (Mixture III).

EXPERIMENTAL

Materials

Amitriptyline hydrochloride and chlordiazepoxide have been supplied by Roche Co., perphenazine by Schering Crop.,

isopropamide and trifluoperazine hydrochloride by Kahira Co., Egypt. Limbitrol Capsule, Roche Co., Contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline hydrochloride. Stelabide tablets, Kahira Co., contains 5 mg isopropamide and 1 mg trifluoperazine. All other reagents and solvents were of analytical grade.

Apparatus

The Perkin-Elmer Model 550 S UV-VIS spectrophotometer and Hitachi Model 561 recorder were used. The first and second derivative curve ($D_1 = dA/(d\lambda)$, $D_2 = d^2A/(d\lambda^2)$ of the UV spectra of reference and sample solutions were recorded in 1 cm quartz cell over the range of 350 to 220 nm. Suitable settings are : Scan speed 120 nm/min; chart speed 60 mm/min; ordinate maxima and minima $\pm$ 0.2 (Mixture I and II) and $\pm$ 0.04 (Mixture III); response time 10 sec.; spectral slit width 2 nm.

Standard Solutions

Weigh accurately 100 mg of the reference drug sample. Dissolve in 100 ml 0.1 N HCl (for the components of mixture I and II), or in methanol for trifluoperazine, or in 0.1 N NaOH for isopropamide (the components of mixture III). Prepare at least five serial dilutions within the concentration range and using the appropriate solvent stated in Table 1 for each component.

TABLE 1.

Optimum Parameters and Regression Data for the Assay of Different Components Existing in Mixtures.

Mixture components	Method*	Concentration range mg/100 ml	λnm	Ordinate	Solvent	Regression data			
						a	b	r	CV%
Perphenazine	D_1	1-9	314	±0.2	0.1N HCl	-0.7625	10.3125	0.9998	0.79
Amitriptyline HCl	D_1	1-1.8	243	±0.2	0.1N HCl	2.275	62.125	0.9998	0.46
Chlordiazepoxide	D_1	0.8-1.4	320	±0.2	0.1N HCl	-1.85	29.75	0.9995	0.65
Amitriptyline HCl	D_2	0.4-1.6	252	±0.2	0.1N HCl	-0.125	30.06	0.9999	0.64
Trifluoperazine	D_2	0.25-1.25	248-264	±0.04	methanol	0.225	132.3	0.9999	0.38
Isopropamide	D_2	2-8	232	-0.05	0.1N NaOH	3.125	10.4652	0.9995	1.92

* Peak height measurements (except for trifluoperazine peak trough is used).
** a = intercept, b = slope, r = correlation coefficient, CV% = coefficient of variation.

Sample preparation

Peraphenazine-amitriptyline tablets :

Mix 250 mg of the tablet filler (lactose 90, starch 7, talc 2.7 and magnesium stearate 0.3 parts) with a mixture of perphenazine-amitriptyline composed from a ratio of 4 : 10 to 4 : 50 in mg. Extract with (4 x 20 ml) 0.1 N HCl by decantation through filter paper into 100-ml volumetric flask. Complete to volume with 0.1 N HCl and mix. Prepare different concentrations in the range stated in Table 1.

Chlordiazepoxide-amitriptyline hydrochloride Capsules :

a) For chlordiazepoxide : transfer an accurate weight of the mixed contents of 20 capsules (equivalent to 25 mg chlordiazepoxide) into a 50 ml conical flask. Extract with methanol (3 x 25 ml) by decantation through filter paper into a 100 ml volumetric falsk. Complete to volume with methanol, and mix. Prepare different concentrations in the range stated in Table 1.

b) For amitriptyline hydrochloride : transfer an accurate weight of the mixed contents of 20 capsules (equivalent to 50 mg of amitriptyline hydrochloride) into a 100 ml conical flask using 0.1 N HCl. Warm at 30° ± 2°C. Decant through filter paper into a 250 ml volumetric falsk. Complete to volume with 0.1 N HCl, and mix. Prepare different conentrations in the range stated in Table 1.

Trifluoperazine-isopropamide tablets: Mix and finely powder 20 tablets.

a) For trifluoperazine : transfer an accurate weight equivalent to 3 mg of trifluoperazine into a 50 ml conical flask. Extract with methanol (3 x 25 ml) by decantation through filter paper into a 100 ml volumetric flask. Mix and complete to volume with methanol. Prepare different concentration in the range stated in Table 1.

b) For isopropamide : transfer an accurate weight equivalent to 100 mg isopropamide to a 100 ml separatory funnel containing 20 ml 0.05 M HCl. Render alkaline (to litmus paper) with 0.1 M NaOH solution. Extract the coexisting drug with 2 x 10 ml chloroform. Reject the chloroformic extract. Transfer quantitatively the aqueous phase to 100 ml volumetric flask. Completing to volume with 0.1 N NaOH solution. Take an aliquot of 0.5-2.5 ml into 25 ml volumetric flask, completing to volume with 0.1 N NaOH.

Spectrophotometric measurements :

Record the D_1 and D_2 curve of the standard and sample solutions in a duplicate (without refilling the cells) against solvent blank. Measure the D_1 and D_2 value in mm of the derivative curve at the chosen wavelength (Table 1).

RESULTS AND DISCUSSION

Figure 1(a) shows that the amitriptyline absorption maximum at 240 nm is overlapped by the perphenazine absor-

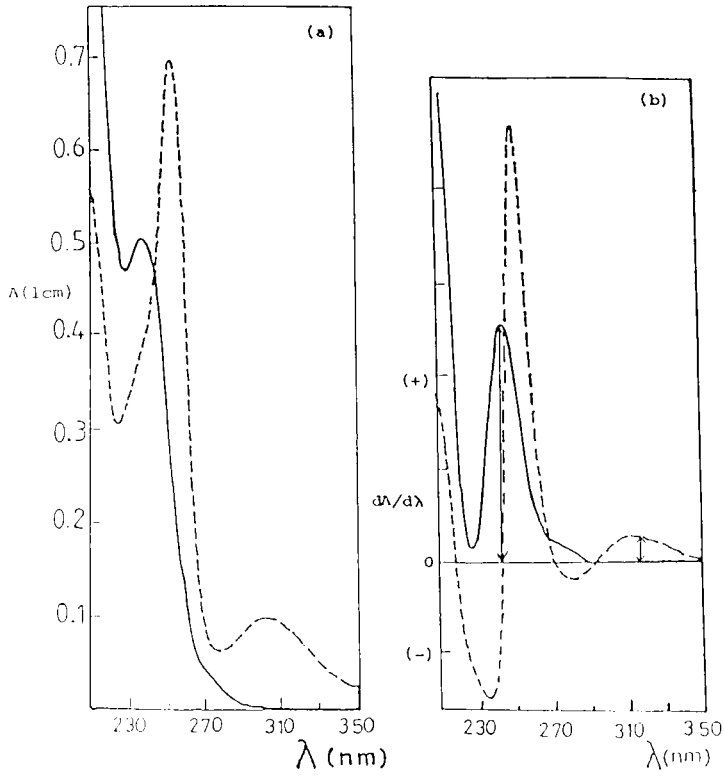

FIG 1. a) Absorption spectra, and (b) D_1 spectra of 1.0 mg/100 ml amitriptyline hydrochloride (——) and 1.0 mg/100 ml perphenazine (...) in 0.1 N HCl.

ption spectrum (Mixture I). Meanwhile, in the corresponding D_1 curves (Fig.1b), the amitriptyline maximum is located at zero crossing point of the coexisting compound. At longer wavelength perphenazine exhibits absorbance value or D_1 value, where amitriptyline shows nil interference. Figure (2a) shows that the chlordiazepoxide absorption maximum overlaps that of amitriptyline(Mixture II). In their D_1

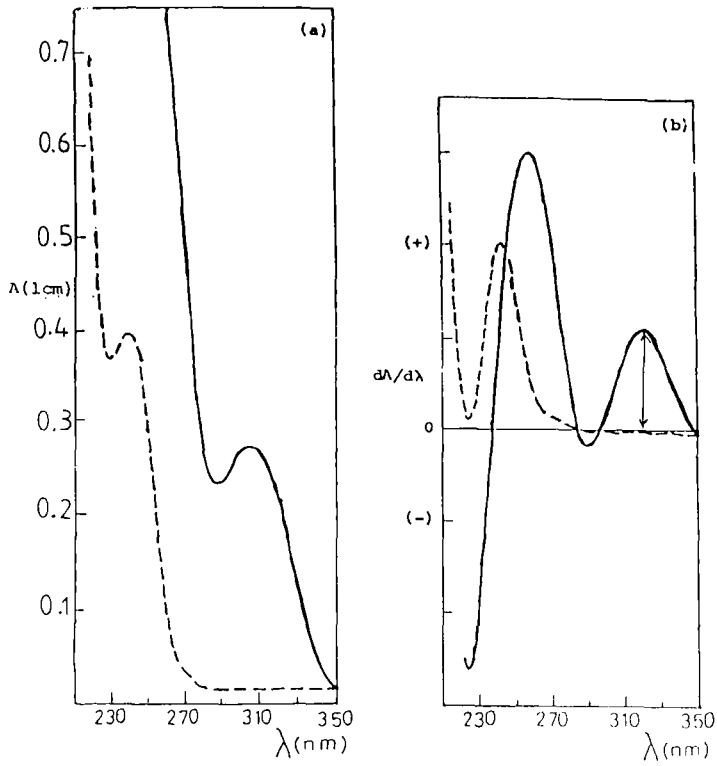

FIG 2. (a) Absorption spectra, (b) D_1 and (c) D_2 spectra of 1.0 mg/100 ml chlordiazepoxide (——) and 1.0 mg/100 ml amitriptyline hydrochloride (...) in 0.1 N HCl.

spectra (Fig.2b), the maximum of the latter is obscured by the ascending slope of the former, while at the amitriptyline D_2 maximum (Fig.2c), chlordiazepoxide exhibits zero D_2 value.

In zero-order spectrum isopropamide absorption maximum is superimposable by trifluoperazine (Mixture III) (Fig.3a).

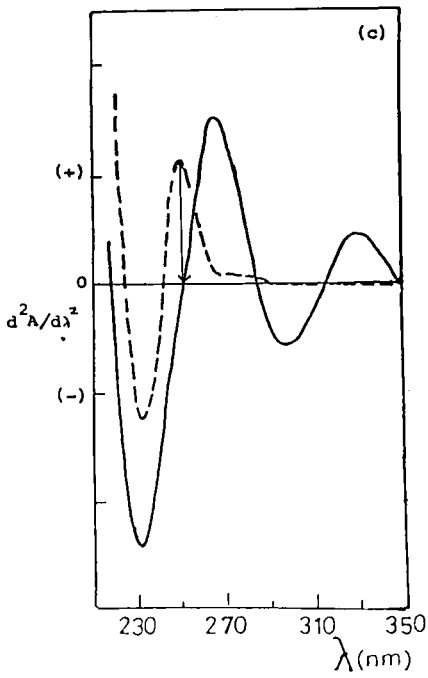

Fig 2c.

The appropriate D_2 value of isopropamide occurs at zero crossing of the coexisting component at 232 nm (Fig.3c). On the other hand peak-trough measurements of the D_2 spectrum of trifluoperazine could be made at 248-264 nm where isopropamide exhibits zero value (Fig.3c). The optimum parameters of the assay of these drugs are presented in Table 1.

Under the described experimental conditions, the graphs obtained by plotting D_1 and D_2 values versus concentration in the range stated in Table 1 show linear relationships. Regression analysis using the method of least

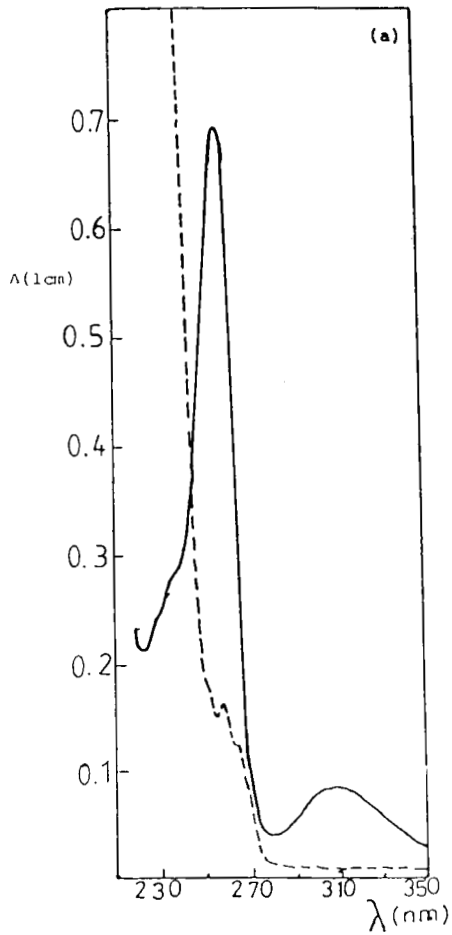

FIG 3. (a) Absorption spectra, (b) D_1 and (c) D_2 spectra of 1.0 mg/100 ml trifluoperazine and 20.0 mg/100 ml isopropamide in methanol.

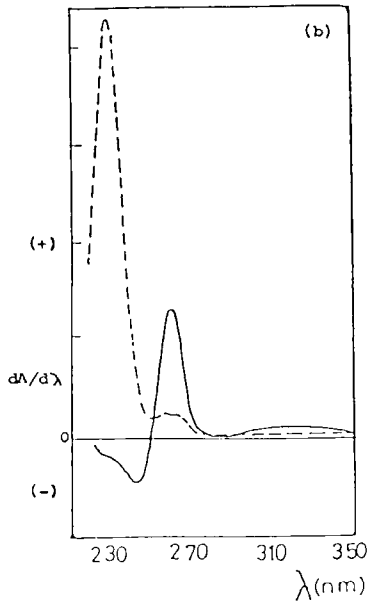

Fig 3b.

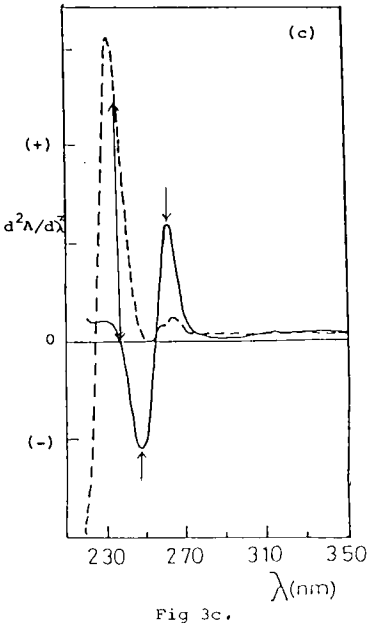

Fig 3c.

squares was made for the slope (b), intercept (a) and correlation coefficient (r) values presented in Table 1. The method precision has been assessed through calculation of the coefficient of variation for replicate determination, values of which were less than 2% (Table 1). This finding indicates the high precesion of the proposed method.

The laboratory made mixtures prepared in different proportions as well as the different dosage forms of the three mixtures have been assayed for both components using D_1 and/or D_2 measurements. The results obtained are presented in Table 2.

TABLE 2.

Assay Results for the Determination of Different Components Existing in Mixtures.

Sample	Recovery*,%	(Mean + CV%)
Mixture I	Perphenazine	Amitriptyline HCl
Method	D_1 (314 nm)	D_1 (243 nm)
Synthetic Mixtures**	98.7 + 0.5	100.5 + 1.5
Prepared tablets	99.4 ∓ 1.2	102.1 ∓ 1.8
Mixture II	Chlordiazepoxide	Amitriptyline HCl
Method	D_1 (320 nm)	D_2 (252 nm)
Synthetic Mixtures***	98.9 + 0.4	99.9 + 1.6
Capsules	101.8 ∓ 0.8	102.5 ∓ 1.2
Mixture III	Trifluoperazine	Isopropamide
Method	D_2 (248-264 nm)	D_2 (232 nm)
Synthetic Mixtures****	100.7 + 0.3	101.5 + 1.6
Tablets	98.0 ∓ 1.0	103.2 ∓ 0.6

* 5 separate determinations

** prepared in concentration range 4 mg/100 ml for perphenazine and 0.6-1.92 mg/100 ml for amitriptyline.

*** prepared in concentration range 0.4 mg/100 ml for chlordiazepoxide and 0.4-1.6 mg/100 ml for amitriptyline.

**** prepared in concentration range 1 mg/100 ml for trifluorperazine and 3-7 mg/100 ml for isopropamide.

The proposed method is rapid, simple and direct as it estimates each drug independent of the other. It is also accurate and reproducible (Table 2). Therefore, this method could be applied for routine assays of these drug mixtures.

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