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COMPUTERIZED DERIVATIVE SPECTROPHOTOMETRIC ASSAY OF TWO COMPONENT MIXTURE USING LEAST SQUARES METHOD

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ABSTRACT

Two computerized spectrophotometric methods; the derivatve (D-) method and the derivative under least squares approach (D-LS) method; have been described for the assay of two component mixture. That mixture has been solved for chlorpheniramine maleate (CP) and phenylephrine hydrochloride (PE) existing in a ratio range of 1/0.8 to 1/2. Being more versatile and fast, the proposed methods supersede the Vierordt's method in dealing with the assay of two component mixture since the latter is subjective to many limitations.

INTRODUCTION

Lately, derivative spectrophotometry has been used for the solution of different pharmaceutical problems [1-3]. Examples are the drug assays in single component [4-6] or multicomponent [7-9] dosage forms as well as the drug determination in the presence of its degradation products [10,11].

Hitherto, the application of such technique in solution of problems dealing with multicomponent analysis or spectral interferences [12] is still limited.

The high spectral resolution of derivative spectrophotometry could solve the problems involved in the two component mixture analysis, when use of Vierordt's method is invalid due to the limitations provided by Glenn[13].

In the two component analysis by derivative spectrophotometry (D-method) two equations are required to be solved.

$$(D_o)_1 = C_1 \alpha_{11} + C_2 \alpha_{21} \quad \ldots\ldots\ldots\ldots \quad (1)$$
$$(D_o)_2 = C_1 \alpha_{12} + C_2 \alpha_{22} \quad \ldots\ldots\ldots\ldots \quad (2)$$

where $(D_o)_1$ and $(D_o)_2$ are the derivative values of the mixture (containing first component in concentration C_1 and second component in concentration C_2) at λ_1 and λ_2, respectively. Subscript o denotes derivative order (first, second, third,..... etc). α_{11} and α_{12} are the $(D_o)^{1\%}_{1\,cm}$, of first component 1 at λ_1 and λ_2, respectively. α_{21} and α_{22} are the $(D_o)^{1\%}_{1\,cm}$ of second component 2 at λ_1 and λ_2, respectively.

In order to improve the results precision of the analyte concentration the derivative spectrophotometry may be utilized under least squares approach[14-17], hereafter termed D-LS. In such instance the number of source equations, m, must exceed the number of mixture components. The error, e, expectable for the corresponding equation at any of the jth wavelength may be accumulated as

$$\sum_{j=1}^{m} e_j^2 = \sum_{j=1}^{m} \left[(D_o)_j - (C_1 \alpha_{1j} + C_2 \alpha_{2j})\right]^2 \ldots\ldots \quad (3)$$

Minimizing such error by partial differentiation with respect to C_1 and C_2 and equating to zero, we get a number of equations equal to the components' number. The resulting equations could be arranged in this form

$$\begin{bmatrix} \sum_{j=1}^{m} (D_o)_j \cdot \alpha_{1j} \\ \sum_{j=1}^{m} (D_o)_j \cdot \alpha_{2j} \end{bmatrix} = \begin{bmatrix} \sum_{j=1}^{m} \alpha_{1j}^2 & \sum_{j=1}^{m} \alpha_{2j}\alpha_{1j} \\ \sum_{j=1}^{m} \alpha_{1j}\alpha_{2j} & \sum_{j=1}^{m} \alpha_{2j}^2 \end{bmatrix} \begin{bmatrix} C_1 \\ C_2 \end{bmatrix} \quad \ldots\ldots\ldots(4)$$

The above matrix could be solved[18] for C_1 and C_2.

In this article a generalized BASIC computer program has been designed for the solution of two component mixture. That mixture has been solved for chlorpheniramine maleate (CP) and phenylephrine hydrochloride (PE) in commercial syrup using the proposed D and D-LS methods.

EXPERIMENTAL

Apparatus.

A Shimadzu Model UV-120-02 ultraviolet/visible spectrophotometer with 1-cm quartz cuvettes, an Olivetti M24 personal computer, 128 K byte, and an Epson HI-80 plotter were used.

Materials.

- Phenylephrine hydrochloride, Alexandria Co. for Pharmaceutical and Chemical Industries, Egypt.
- Chlorpheniramine maleate, Misr Co. for Pharmaceutical Industries, Egypt.
- All other reagents and solvent were of analytical grade.

Pharmaceutical preparation.

SINE-UP syrup (Pharco Pharmaceuticals, Egypt,labelled to contain 50 mg of chlorpheniramine maleate and 100 mg of phenylephrine hydrochloride per 100 ml syrup.

Standard solutions.

A 100 mg aliquot of the reference drug sample was accurately weighed and dissolved in 100.0 ml 0.1 N hydrochloric acid.
Five serial dilutions in same solvent were prepared within the concentration ranges of 2-4 mg per 100 ml for chlorpheniramine maleate and 5-10 mg per 100 ml for phenylephrine hydrochloride.

Sample preparation.

A 5.0 ml aliquot of the syrup was transferred to a dry 250-ml separatory funnel and 20.0 ml 0.1 N hydrochloric acid was added. The solution was shaken for 10 minutes with 100 ml ether (previously saturated with 0.1 N hydrochloric acid). A 5.0 ml portion of the aqueous acidic layer was diluted to 25.0 ml with 0.1 N hydrochloric acid.

Spectrophotometric measurements.

Absorbances were measured in the range of 300 to 250 nm at 2 nm intervals against a solvent blank. Each absorbance measurement was the mean of two readings, each involving a prior re-setting of the wavelength scale. Absorbances were fed into the computer and the first derivative

values, $D_1 (= \frac{dA}{d\lambda})$, were then calculated using the proposed computer program.

RESULTS AND DISCUSSION

The absorption and first-derivative (D_1) curves of chlorpheniramine maleate (CP) and phenylephrine hydrochloride (PE) in 0.1 N hydrochloric acid are presented in Fig. 1. The absorption maximum of PE is obscured by the ascending slope of CP. In the vicinity of 270 to 264 nm, the PE spectrum is descending while that of CP is ascending resulting in a prominant D_1 maximum of PE at 263 nm which is separable from the optimum wavelength selected for CP at 273 nm.

To quantify the mixture for its two components, absorbances were measured over the range 300 to 250 nm at 2 nm intervals with subsequent calculation of the first-derivative values, $D_1 (= \frac{dA}{d\lambda})$. The concentration of both components were computed applying (i) Vierordt's method (using two absorbance coefficients) where the coefficients at λ_1 = 264 nm and λ_2 = 274 nm for CP are 201.67 and 137.00, respectively and for PE are 59.40 and 88.40, respectively, (ii) D method (using two D_1 coefficients) where the coefficients at λ_1 = 273 nm and λ_2 = 263 nm for CP are -9.833 and 1.333, respectively and for PE are 0.200 and 4.500, respectively, and (iii) D-LS method using twelve D_1 coefficients over the wavelength range 253 to 297 nm at 4 nm intervals.

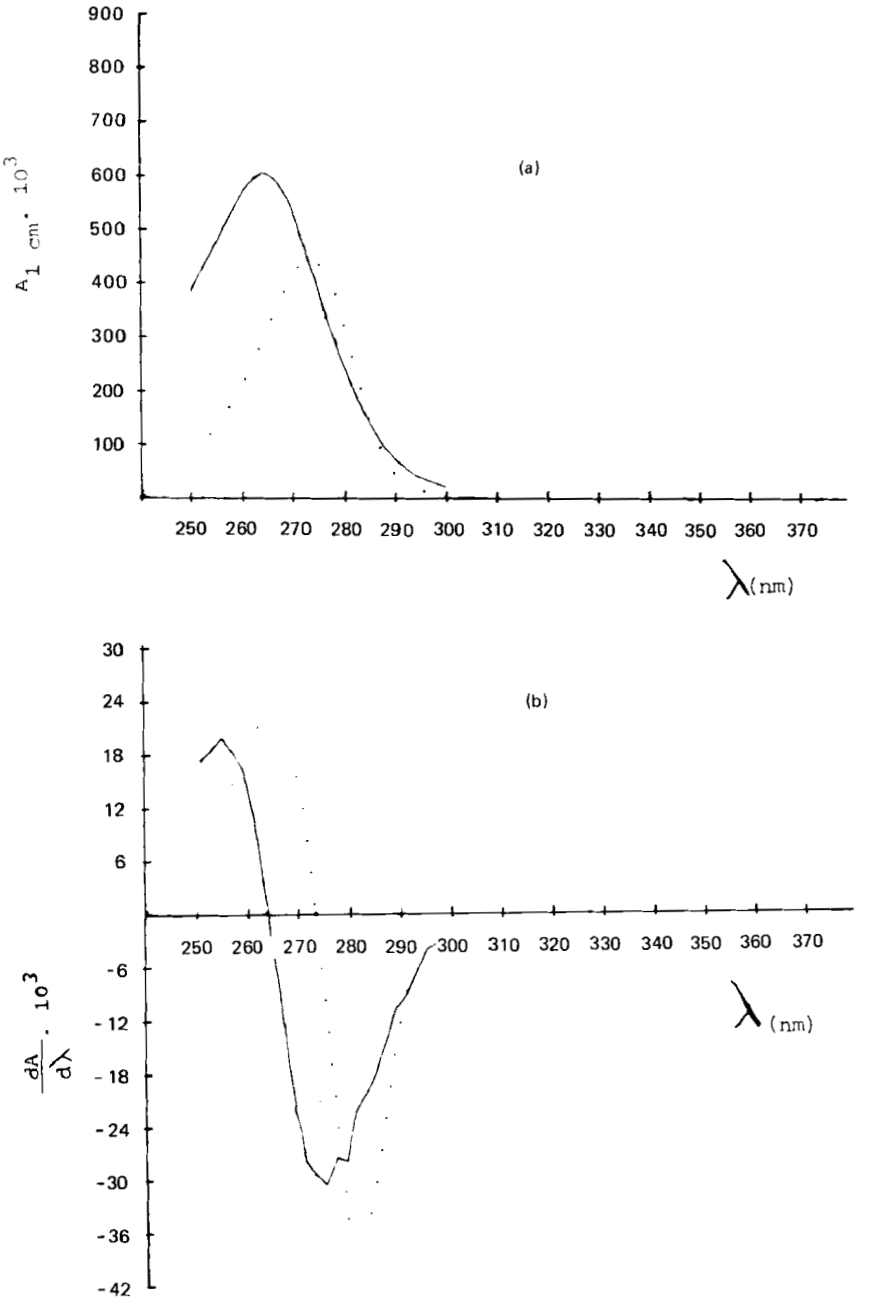

FIGURE 1

Absorption curves (a) and first-derivative curves (b) of 3 mg% w/v chlorpheniramine maleate (——) and 5 mg% w/v phenylephrine hydrochloride (---) in 0.1 N hydrochloric acid.

To assess the applicability and validity of the proposed methods, synthetic mixtures and commercial syrup have been assayed for both CP and PE components. Such assay has been performed with the assistance of computer program. The proposed program is designed to be general and to perform different tasks (Viz i-storage of data collected from spectrophotometer, ii-calculation of derivative values, iii-solution of n simultaneous equations for n components and iv-application of least squares method).

The assay results for CP and PE in synthetic mixtures and commercial syrup are presented in Table 1 . Six two-component mixtures (CP in PE) have been prepared in a ratio range of 1:0.8 to 1:2 (Table 1). The results of CP using the D and D-LS methods are comparable to those of Vierordt's method. Meanwhile using Vierordt's method PE exhibits negative systematic error. This is attributed most probably to the low absorptivity of PE compared with the coexisting component CP. With D and D-LS methods such error has been corrected and more accurate results (t-test) have been obtained.

In syrup assay, however, the presence of additives like preservatives, sweetening agents, stabilizers and coloring matters may exhibit serious interference during spectrophotometric measurement. To decrease such interference a simple clean-up procedure[19] has been adopted prior to syrup assay. Nevertheless the results of Vierordt's method are still suffering from negative

TABLE 1

Spectrophotometric determination of chlorpheniramine maleate (CP) and phenylephrine hydrochloride (PE) in synthetic mixtures and commercial syrup using different methods

	Mean % Recovery					
	CP			PE		
	Vierordt's method	D method	D-LS method	Vierordt's method	D method	D-LS method
	Synthetic Mixtures [a]					
Mean	100.93	101.64	101.49	97.42	100.27	99.07
± S.D	0.97	0.27	0.32	1.09	1.07	0.86
t-Value [b]		1.73	1.34		4.57	2.91
F-Value [b]		12.91	9.19		1.04	1.61
	Commercial Syrup					
Mean [c]	94.66	99.75	100.78	95.41	99.06	97.94
± S.D	1.83	1.16	0.79	1.25	1.04	0.41
t-Value [d]		6.22	8.12		5.94	5.09
F-Value [d]		2.49	5.37		1.44	9.3o

a - Six mixtures are prepared in which component conc. (mg %) are (2,2,2,2,2.5 & 2.5)CP and(2,2.5,3,4,4 & 2)PE .

b - t-and F-values are calculated with respect to vierordt's method. The corresponding theoretical values are 2.228 (α = 0.05) and 5.05 (5% level) respectively.

c - Mean for seven experiments .

d - t-and F-values are calculated with respect to Vierordt's method. The corresponding theoretical values are 2.179 (α = 0.05) and 4.28 (5% level), respectively.

systematic error for both CP and PE components. Again such error has been corrected using the proposed D and D-LS methods. In the presence of interferences (i.e. in syrup assay) the D-LS method offered more reproducible results (F-test) than Vierordt's method. Meanwhile D method gave results of equal reproducibility like Vierordt's method. Accordingly use of least squares approach amend the results reproducibility.

In conclusion, the use of the proposed D and D-LS methods in two-component mixture assay is considered superior compared with Vierordt's method since the utility of the latter is oftenly subjected to many limitations as outlined by Glenn[13]. The designed computer program make the use of the proposed methods more versatile, fast and render them of wide use specially in automated routine analysis. It should be emphasized that these computer-assisted spectrophotometric (D and D-LS) methods could be used in solving mixtures consisting of more than two components. Such proposal is currently under investigation in our laboratory and using other derivative orders.

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