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Notes

Simultaneous determination of polythiazide and prazosin in tablets by second-order derivative UV spectroscopy

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Summary

A second-derivative spectroscopic method for the simultaneous determination of polythiazide and prazosin in tablets was developed. Solutions of these tablets in 0.2 N methanolic hydrochloric acid were analyzed by measurement of the amplitudes of the positive peak at 356 nm with respect to the negative peak at 346 nm ($^2D_{346,356}$) for prazosin, and the amplitude of the positive peak at 236 nm with respect to the baseline ($^2D_{236}$) for polythiazide. Confirmation of the technique was established using HPLC. The use of derivative spectroscopy in this manner provides a specific, rapid and accurate determination of the binary mixture in the tested concentration range of 1–10 μg/ml for polythiazide and 1–20 μg/ml prazosin.

Polythiazide (Fig. 1) is well-known diuretic and antihypertensive agent (Scriabinė et al., 1961; Pratesi, 1962; Spiekerman et al., 1963). Prazosin (Fig. 1), a quinazoline derivative, is also antihypertensive (Stokes, 1984). Tablets of this drug combination produce a more pronounced antihypertensive response than occurs after either prazosin or polythiazide alone in equivalent doses (Davey, 1981).

Several analytical methods have been described for assaying polythiazide: these include spectrophotometry (Sastry et al., 1988), liquid chromatographic determination (Schoeneshoefer et al., 1987), HPLC (Bachman, 1986; Smith et al., 1987), thin-layer chromatography (Agarwal and Nwaiwu, 1986) and determination by iodometric titrations (Shukla et al., 1984). Also, spectrophotometric and fluorometric assay (Mohammed and Aboul-Enein, 1985), HPLC method (Daldrup et al., 1981; Jane et al., 1985; Bachman, 1986; Sidhu et al., 1987), thin-layer chromatography (Daldrup et al., 1981) and coulometric methods (Nikolic and Velasevic, 1988) have been described for prazosin determination. Only the HPLC method (Bachman, 1986) has been described for their simultaneous quantification in two-component mixtures. In the present article, the second-order derivative (^2D) spectrophotometric method is described for the simultaneous determination of polythiazide and prazosin in tablets.

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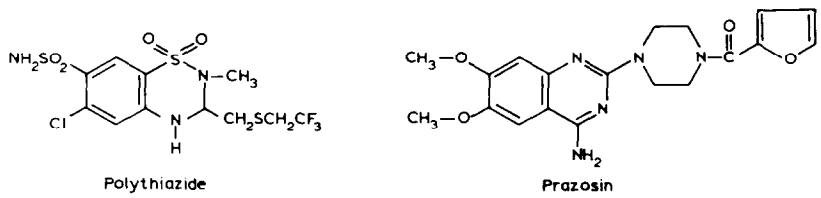

Fig. 1. Chemical structure of polythiazide and prazosin.

Derivative spectrophotometry has found extensive application in drug mixture analysis. Transformation of a spectrum to its second-order derivative often yields a more highly characteristic profile than the zero-order spectrum. The derivative method tends to emphasize subtle spectral features by presenting them in a new and visually more accessible way, moreover, the signal-to-noise ratio is degraded by approximately a factor of two in each successive derivative order due to the ability of the method to eliminate matrix interference and to enhance resolution (Clarke, 1986).

Polythiazide and prazosin (Pfizer Co.) were used without further purification. All other reagents are analytical grade. 0.2 N methanolic hydrochloric acid stock solutions of polythiazide (0.5 mg/ml) and prazosin (1.0 mg/ml) were prepared. A series of working standards (1–10 μg/ml polythiazide and 1–20 μg/ml prazosin) were obtained by appropriate dilution with 0.2 N methanolic hydrochloric acid. Polythiazide-prazosin binary mixtures were also prepared so that the concentration ratio between the analyte and the potentially interfering components could span the range from 50 to 200% of their ratio in the tablets.

A Hewlett Packard Model 8452A Diode Array UV-visible spectrophotometer equipped with derivative module and 1 cm quartz cells was used. The zero- and second-order derivative spectra were recorded in the wavelength range 190–350 nm.

Drug analysis using the second-order derivative method was validated using HPLC. The liquid chromatographic system consisted of a model LKB 2152 controller, LKB 2150 pump, LKB 2151 variable-wavelength UV detector, LKB 2220 recording integrator, LKB 2210 2-channel recorder, LKB Ultrapac LiChrosorb RP18 column (25 cm × 4.6 mm i.d.) and Rheodyne 7125 sample injector with a 20 μl loop. The chromatographic conditions for the simultaneous determination of polythiazide and prazosin in tablets were similar to those employed by Bachman (1986). Diltiazem was employed as internal standard. Retention times were: prazosin, 4.38 min; polythiazide, 6.21 min; diltiazem, 9.78 min. The results of the HPLC analysis on polythiazide prazosin tablets are presented in Table 1.

On observing the superimposed second-order derivative spectra of polythiazide and prazosin (Fig. 2c), it is evident that not all peaks recorded would be useful in the quantitation of mixtures owing to some interference. The spectral analysis revealed that the derivative signal $^2D_{236}$ was specific for polythiazide and $^2D_{346,356}$ for prazosin; these amplitudes were selected because the respective signal magnitude of the interfering component was negligible at the chosen wavelength. Calculations were made from the calibration curve plotting the peak amplitude vs concentration (μg/ml). The 95% confidence limits for the calibration graphs were typically ± 0.01 μg/ml for polythiazide and ± 0.02 μg/ml for prazosin at the

TABLE 1

Analyses on four separate batches of polythiazide / prazosin tablets labelled to contain 0.5 mg polythiazide and 1 mg prazosin per tablet

Batch	Average recovery (%) CV ($n = 5$)			
	Polythiazide method [a]		Prazosin method [a]	
	A	B	A	B
1	102.4 (1.1) [b]	102.8 (0.9)	98.3 (1.5)	99.8 (1.4)
2	101.6 (1.0)	100.1 (1.3)	99.1 (0.9)	100.4 (1.5)
3	98.7 (1.5)	97.9 (0.7)	101.2 (1.2)	99.7 (1.0)
4	99.3 (1.6)	98.2 (1.2)	97.8 (0.8)	99.1 (0.9)

[a] A, second-order derivative method; B, HPLC method.
[b] ±S.D.

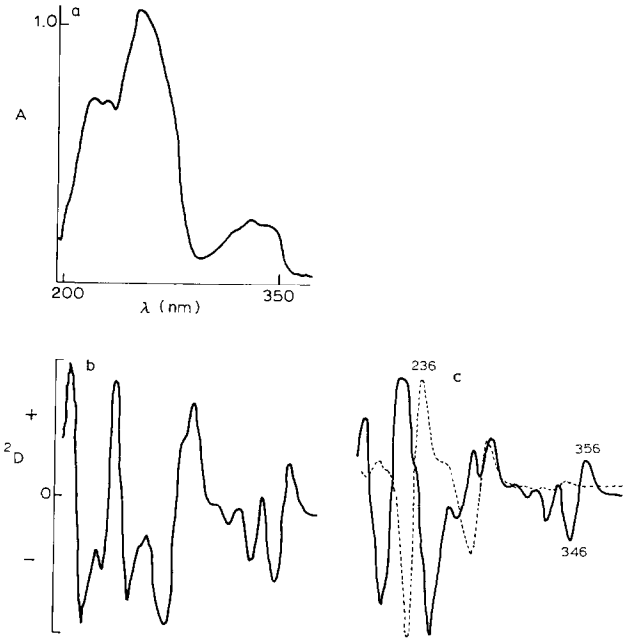

Fig. 2. Zero-order (a) and second-order (b) derivative UV spectra of a binary mixture of polythiazide (4 μg/ml) and prazosin (10 μg/ml) in methanolic HCl. (c) Second-order derivative of polythiazide (broken line) and prazosin (solid line) overlaid to show areas of spectral overlap.

central calibration concentration of 5.0 and 10.0 μg/ml, respectively. The zero- and second-order derivative spectra of a polythiazide-prazosin mixture (at the same respective concentration as in Fig. 2c) are presented in Fig. 2a and b; in particular $^2D_{236}$ for polythiazide and $^2D_{346,356}$ for prazosin are unchanged. Linear correlations were obtained between the respective derivative amplitude of the polythiazide-prazosin mixture and the corresponding component concentration over the range of 1–10 μg/ml for polythiazide and 1–20 μg/ml for prazosin. The least-square regression equations (for polythiazide) were:

$$y = 0.093x + 0.141 \qquad n = 8;\ r = 0.9995;$$

$$s = 0.104$$

and for prazosin:

$$y = 0.205x + 0.067 \qquad n = 8;\ r = 0.9997;$$

$$s = 0.175$$

where y is concentration in mg/ml and x is displacement ^2D. The concentration values of polythiazide and prazosin determined by second-order derivative spectroscopy were found to correlate well with values obtained by HPLC; for polythiazide ($r = 0.997$, slope = 0.994, intercept = 0.021, $n = 8$); for prazosin ($r = 0.998$, slope = 0.990, intercept = 0.082, $n = 8$).

Interaction studies for constant polythiazide or prazosin levels, but varying polythiazide or prazosin concentrations, showed that the selected derivative amplitude was independent of the presence of the other component; in fact, the recovery was in every instance close to quantitative.

One polythiazide/prazosin tablet was placed in a 100 ml volumetric flask and diluted to volume with 0.2 N methanolic hydrochloric acid. The second-order derivative spectrum was recorded against 0.2 N methanolic hydrochloric acid and displacements $^2D_{236}$ and $^2D_{346,356}$ were measured for polythiazide and prazosin, respectively.

The results of the analyses on polythiazide/prazosin tablets (ALKALOID, Skopje, Yugoslavia) are presented in Table 1. The relative standard deviations for both drugs were less than 2%.

We conclude that the described second-order derivative spectroscopic method does have the potential for application to quality control, since it permits rapid, precise, accurate and low-cost analyses of polythiazide/prazosin mixtures in tablets without extraction procedures, and is easily applied to routine usage.

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