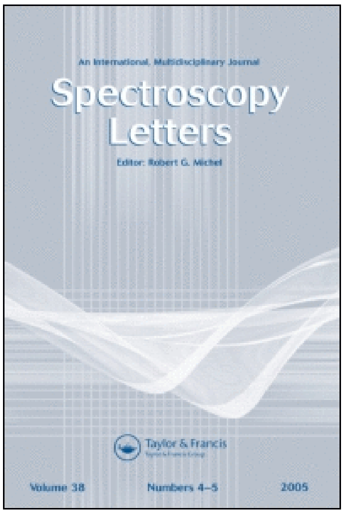

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Application of Third Derivative UV Spectrophotometry to the Simultaneous Determination of N-Methyl-5,6-Benzoquinoline Methyl Sulfate and Thonzylamine Hydrochloride, In Multi Component Collyrium

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APPLICATION OF THIRD DERIVATIVE UV SPECTROPHOTOMETRY TO THE SIMULTANEOUS DETERMINATION OF N-METHYL-5,6-BENZOQUINOLINE METHYL SULFATE AND THONZYLAMINE HYDROCHLORIDE, IN MULTI COMPONENT COLLYRIUM.

Key words: N-methyl-5,6-benzoquinoline methyl sulfate; thonzylamine hydrochloride; UV derivative.

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ABSTRACT

A simple and fast analytical method for the determination of the title compounds (BZQ and TZL) by derivative UV spectrophotometry, in ethanol, is described.

The procedure was defined by regression analysis for a high number of standard solutions.

Linear relationships were obtained between mixture composition and absorbance maximum ^{0}D at 370 nm, or amplitude of minimum at ^{1}D 380 nm or peak trough ^{3}D 288,296 amplitude, for BZQ quantitation, and peak trough ^{3}D 257,264 amplitude by utilising binomial equation deriving from MLRA, for TZL quantitation.

The method, yielding accurate and precise results, was satisfactorily applied to laboratory mixtures and to a commercial formulation.

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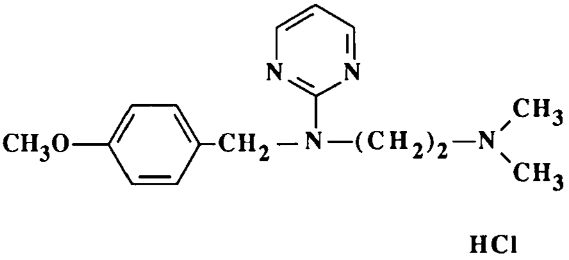
INTRODUCTION

Thonzylamine HCl, N,N dimethyl - N'- (p-methoxy benzyl) -N'-(2 pyrimidil) ethylen diamine hydrochloride (**I**), an antihystaminic agent , and N-methyl-5,6- benzoquinoline methyl sulfate (**II**), are formulated in association in collyrium which activity is to prevent the inflammatory phenomena on the conjunctiva , cornea and pupil tissues caused for short wavelenght radiations. Several procedures has been reported for the determination of Thonzylamine HCl including UV spectrophotometric (1), fluorimetric (2,3) and ^{13}C NMR methods(4), while anything about evaluation of N-methyl 5-6, benzoquonoline methyl sulfate is described. The present paper describes a quantitative method for the simultaneous determination of the two drugs in eye drops, by UV spectrophotometry. Zero order, first and third UV derivative was applied to the determination of BZQ, and third derivative to TZL determination.



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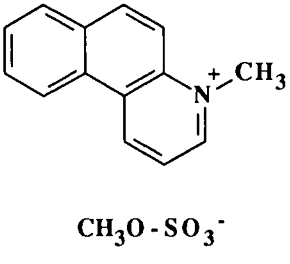

II

EXPERIMENTAL

Apparatus and conditions:

Spectrophotometric measurements were recorded in 10 mm silica quartz cell, at 26-28 °C, using a Perkin Elmer 320 UV-visible spectrophotometer. Spectral bandwidth was 1 nm, the scan rate 1 nm sec^{-1} and the response (time constant) 1 sec.

$\Delta\lambda$ (first derivative bandwidth) 2 nm; (third derivative bandwidth) 6nm.

Recorder scales: 20 nm cm^{-1} for x-axis; as most suitable, for y-axis. All amplitude measurements (expressed as mm) were referred to ± 1,00 scale.

Reagent and chemicals

Drugs were kindly supplied by Bruschettini s.r.l., via Isonzo 6, Genova (Italy).

Pharmaceutical speciality "Ascotodin" collyrium, manufactured by Bruschettini s.r.l. Composition in 100 mL: BZQ 0.300 g; TZL 0.100 g; p-methyl 0.0313 g; p-propyl 0.0157 g.

Ethanol 95°, diethyl ether, were analytical grade (C. Erba).

Standard solutions

Standard solutions in ethanol were prepared with BZQ concentration ranged from 3.00 to 30.00 mcg mL^{-1}.

Corresponding mixture solutions were prepared with TZL concentration ranged from 0.75 to 13.5 mcg mL^{-1}.

In all cases BZQ/TZL ratio from 1.5 to 7 were performed. Spectrophotometric analysis were measured against ethanol as a blank.

Sample solutions

-Laboratory mixtures in water were prepared with BZQ and TZL concentrations in the range 150 - 300 and 50 - 100 mg·100 mL^{-1} respectively. Dilute 1.0 mL aliquot to 100 mL with ethanol 95° in a volumetric flask.

These solutions were utilized to establish the validity of the analytical method for determination of both substances.

-Eye drops (without parabens)

Transfer 5.0 mL of collyrium to a separating funnel and add 10 mL of water. Extract with four successive 10 mL portions

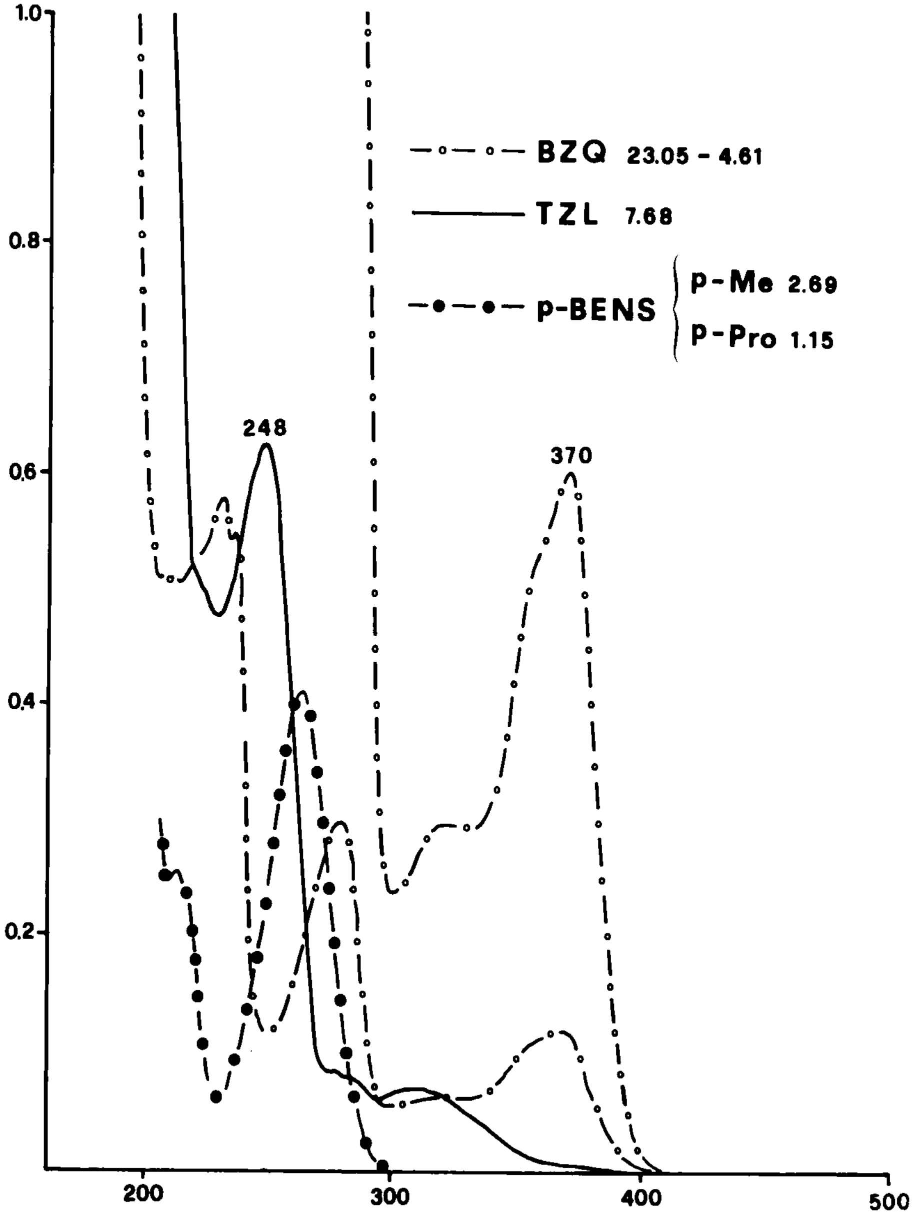
1.0
0.8
0.6
0.4
0.2
200
300
400
500
248
370
BZQ 23.05 - 4.61
TZL 7.68
p-BENS
p-Me 2.69
p-Pro 1.15

FIGURE 1

of ether. Dilute 0.5 mL of aqueous solution to 100 mL with ethanol 95° in a volumetric flask. (BZQ 15 mcg·mL^{-1}, TZL 5 mcg·mL^{-1} approssimately).

Parabens evaluation

Wash the combined extracts with 5 mL of water. The organic extract was dried over sodium sulfate, filtrated through cotton and concentrated to dryness under N_2. The residue, dissolved in 10.0 mL of ethanol, was used for quantitative determination of parabens by TLC densitometry, according to F. Mecarelli (5).

RESULTS AND DISCUSSION

Figure 1 shows the UV absorption spectra of BZQ, TZL and methyl and propyl parabens in usual ratio. The concentrations of all the components correspond to collyrium composition (values reported are mcg mL^{-1}).It is evident that the TZL absorption, in the 230-300 nm region, is overlapped by strong band of BZQ and is influenced by absorption of p-bens, while evaluation of BZQ is easy execute by utilizing only absorbance maximum at 370 nm.

The best results are obtained by utilizing absorbance maximum at $^0D_{370}$ nm, or amplitude minimum at $^1D_{380}$ nm or peak trough $^3D_{288,296}$ amplitude for BZQ quantitation.

TZL quantitation was carried out by multiple linear regression analysis (MLRA), using peak trough $^3D_{257,264}$ amplitude (FIG.2), over solutions without p-bens, because of the relative low contribute of BZQ at this wavelenght, as evident by comparison of absorption spectra of the TZL and of the diluted BZQ.

Following regression equations were defined between a high number of standard solutions, having sure concentrations, and the spectral signals previously mentioned.

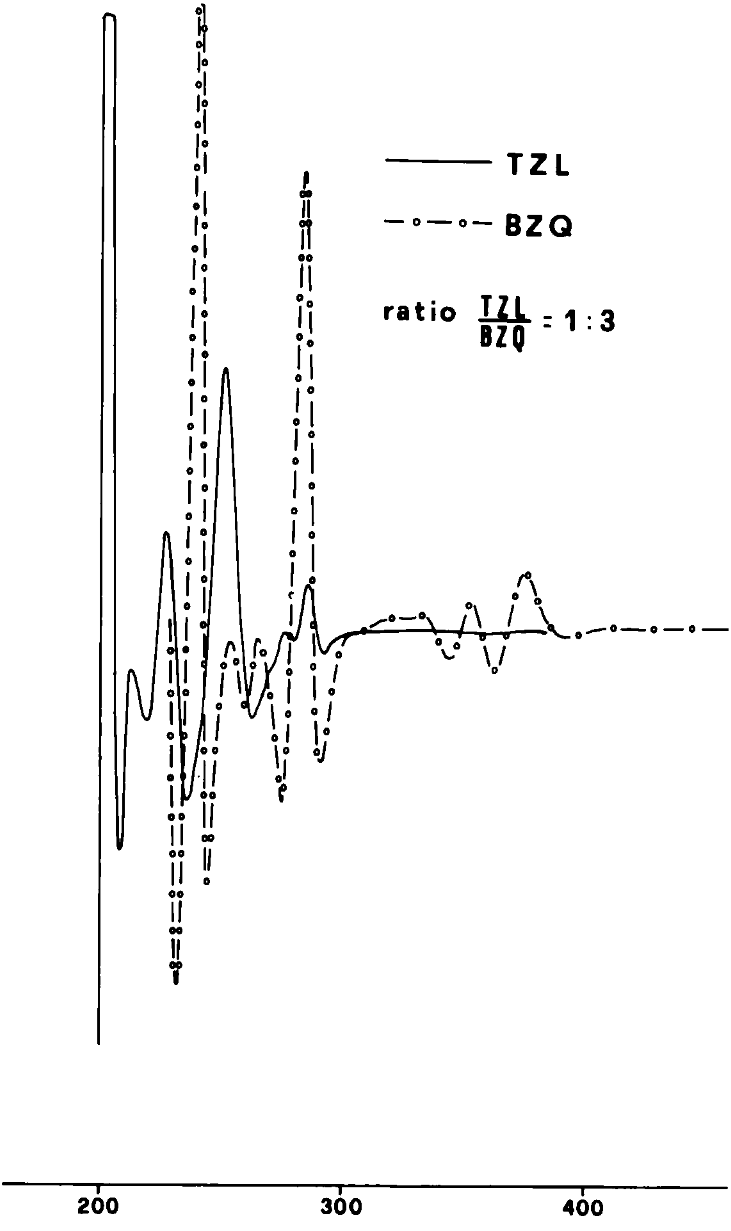

FIGURE 2a

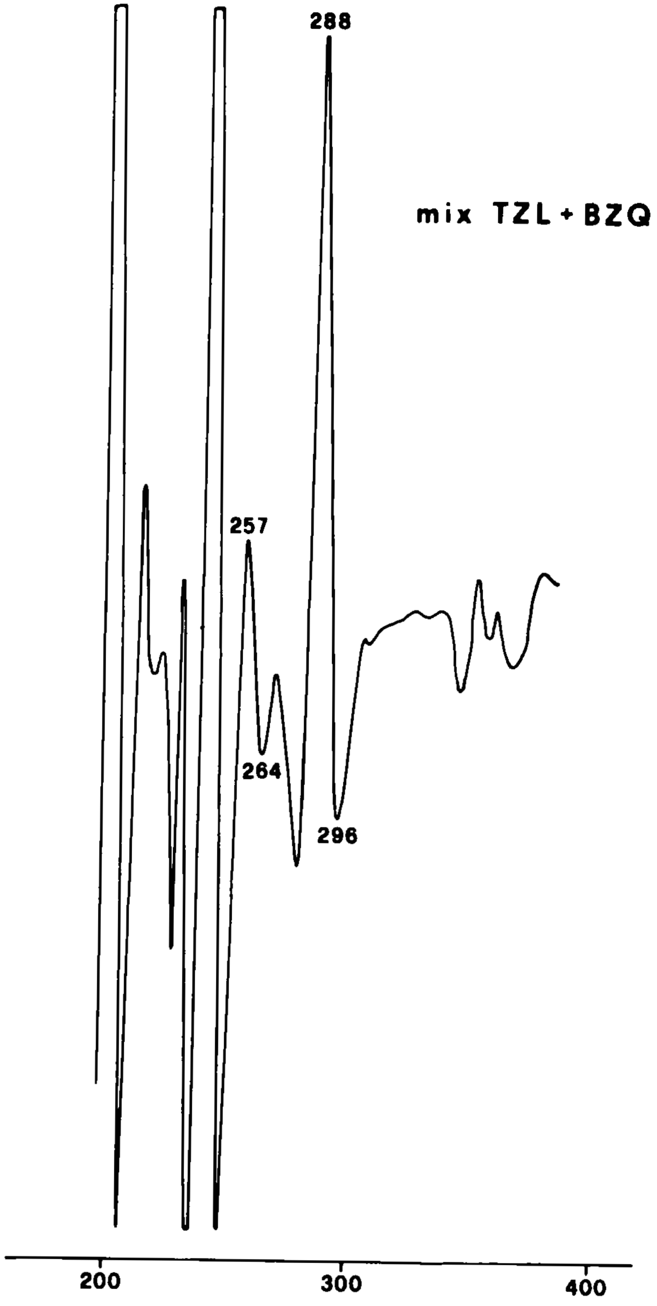

FIGURE 2b

BZQ determination.

The BZQ determination is performed by utilizing the equations:

$$Y = m X + n$$

Derivative order	Signal (X)	Slope	Intercept	r
0	370 (max)	39.520	-0.827	0.99986
1	380 (min)	1.633	-1.458	0.99988
3	288,296	0.084	-0.598	0.99998

where Y = BZQ (mcg mL-1). X = A% in zero order or mm amplitude on the scale ±1 for the others orders.

TZL determination

The TZL determination is performed by measuring the peak through amplitude (mm on the scale 1) between 257 and 264 nm in the third derivative spectrum and utilizing the contribution deriving from BZQ (mcg mL^{-1}) determined as previously described. The following multiple linear equation gives the TZL concentration:

$$Y = -0.2927\ (BZQ) + 0.1945\ X - 0.0289 \qquad r = 0.9989$$

where Y = TZL (mcg mL^{-1}); X = mm amplitude on the scale ±1.

VALIDATION

Accuracy: a recovery assay was carried out by applying the procedure on standard laboratory mixtures. Results obtained show that the method is very accurate for BZQ. Percent recoveries ($\bar{x} \pm ts/\sqrt{n}$, $\alpha = 0.05$) were 99.5 ± 0.8% (n = 5) for 0th derivative, 99.9 ± 0.7% (n = 5) for 1th derivative, 101.2 ± 0.6% (n = 5) for 3th derivative.

Percent recovery for TZL was 95.6 ± 4.5% (n = 5) for drops without parabens.

Precision: the precision (third derivative) of the procedure was determined by assaying a sample of laboratory mixture several times. The standard deviation determined was 0.24 mcg mL^{-1} for 28.5 mcg mL^{-1} of BZQ (relative standard deviation, 0.84%) showing that the procedure has good precision. Corresponding values for TZL were: standard deviation 0.73 mcg mL^{-1} for TZL = 9.33 mcg mL^{-1} (relative standard deviation, 7.8%).

REFERENCES

1) Serpil D., Hayriye A. : Istanbul Univ. Eczacilik Fak. Mecm. 1970; 6: 14-20.

2) Saburo N., Hirokazu T., Takako F. : Yakugakuzasshi 1972; 92: 411-16.

3) Wilson D., Wirz D.,Scheuk G. : Analytical chemistry 1973; 45:1447-55.

4) Chang C., Peck G.E.: ibidem 1976; 65: 1019-23.

5) Mecarelli F., Rocci I.: Il Farmaco Ed. Pr. 1972; 27: 243-52.

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