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Short Communication

Interference of mandelic acid with the determination of homatropine hydrobromide by second-order derivative spectroscopy

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Introduction

There have been numerous reports of the use of derivative spectroscopy for the analysis of pharmaceutical dosage forms. A variety of eye preparations containing tropane alkaloids (hyoscine, atropine, homatropine) have been determined using this technique [1, 2]. The use of the zero-order spectra for the determination of the drug content of such eye preparations is difficult due to the relatively weak absorbances of the drug and the strong absorbances of the preservatives. The derivative technique enables the determination of the active drug in the presence of preservatives.

During recent studies into the hydrolysis of homatropine hydrobromide, the UV spectra of homatropine and its degradation products were investigated. The hydrolysis of homatropine hydrobromide (1) results in the formation of mandelic acid (2) and tropine (3) (see Fig. 1). The zero-order UV spectrum of tropine is virtually nonexistent yet the spectrum of mandelic acid shows similarities with the spectrum of the parent compound. This observation suggested that the reported second-order derivative spectroscopic method for the determination of homatropine hydrobromide [2] may suffer from interference due to mandelic acid.

The zero-order and derivative spectra of homatropine hydrobromide, mandelic acid, tropine along with mixtures of these compounds have been investigated.

Materials and Methods

Apparatus

A Phillips PU 8720 UV/vis Scanning Spectrophotometer was used to record all spectra. Zero-, second- and third-order spectra (between 240 and 290 nm) were determined using a scan rate of 50 nm min^{-1} and no smoothing was applied. Spectra were determined using 1 cm quartz cuvettes (Starna Ltd).

Reagents

Homatropine hydrobromide (The Sigma Chemical Company Ltd), mandelic acid (Aldrich) and tropine (Fluka) were used as received. Homatropine Eye Drops BP (2% w/v) containing 0.025% benzalkonium chloride were obtained from Schering–Plough UK.

Procedures

Individual solutions of homatropine hydrobromide, mandelic acid and tropine as well as mixtures of these compounds were prepared in 0.01 M HCl as described in the text. The various spectra were determined using the conditions specified above.

The content of homatropine hydrobromide in various prepared solutions and in the eye drops sample was determined by reference to a calibration curve constructed using standard solutions of homatropine hydrobromide in the range 50–250 mg l^{-1} in 0.01 M HCl. The amplitude of peak at 252 nm (to the long wavelength satellite) in the second-order

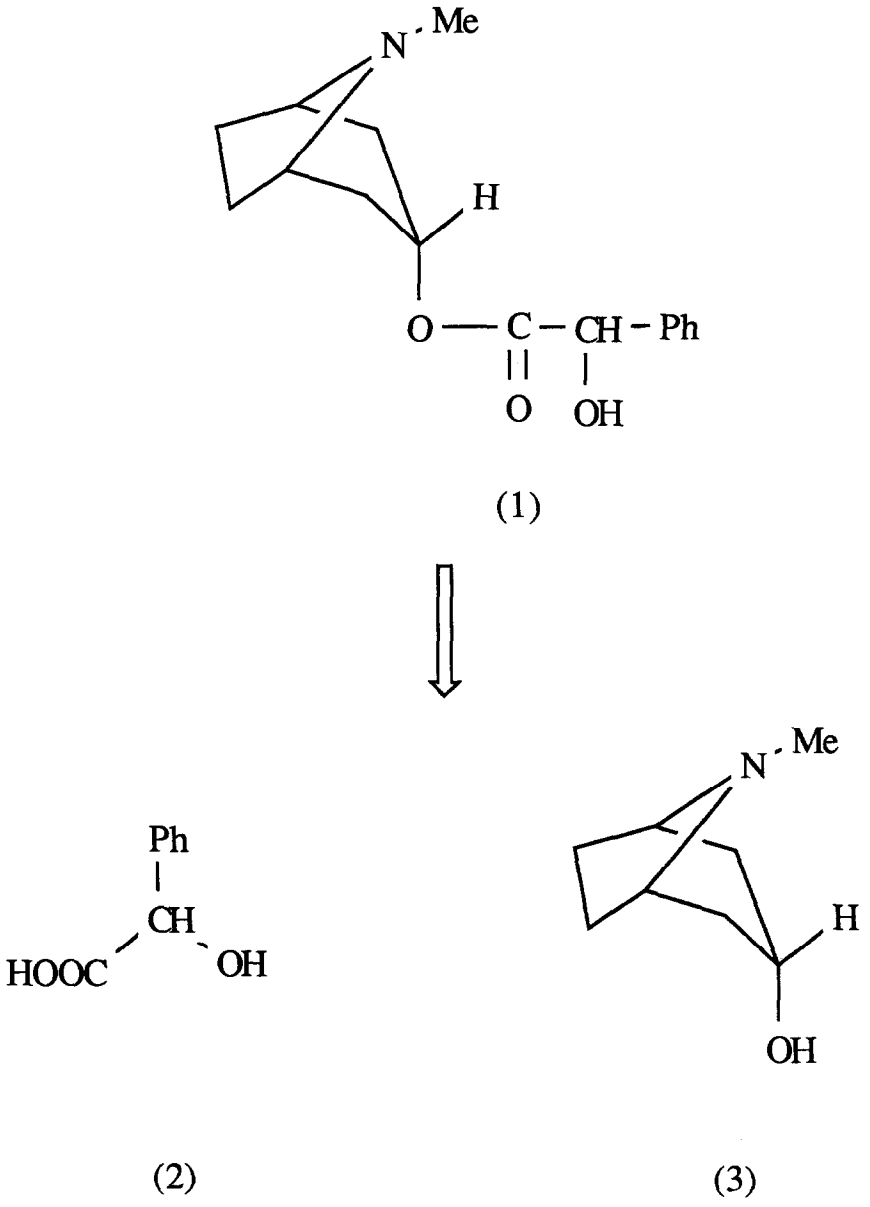

Figure 1
The hydrolysis of homatropine hydrobromide.

spectra was used in the construction of the calibration curve.

Results and Discussion

The zero-order spectra of equimolar solutions of homatropine hydrobromide, mandelic acid and tropine in 0.01 M HCl between 240 and 290 nm are shown in Fig. 2. As expected the spectrum of tropine is virtually nonexistent in this region of the UV spectrum. The spectra of the equimolar solutions of homatropine hydrobromide and mandelic acid can be seen to be almost identical. Figure 3 represents the second-order derivative spectra of equimolar solutions of homatropine hydrobromide, mandelic acid and tropine. Once again the close similarity of the spectra of homatropine hydrobromide and mandelic acid is obvious.

Given these similarities in the derivative spectra it seemed likely that mandelic acid (a known degradation product of homatropine hydrobromide) might interfere with the determination of homatropine hydrobromide by derivative spectra as described by Leung and Wong [2]. To investigate this possibility the method described by Leung and Wong [2] was

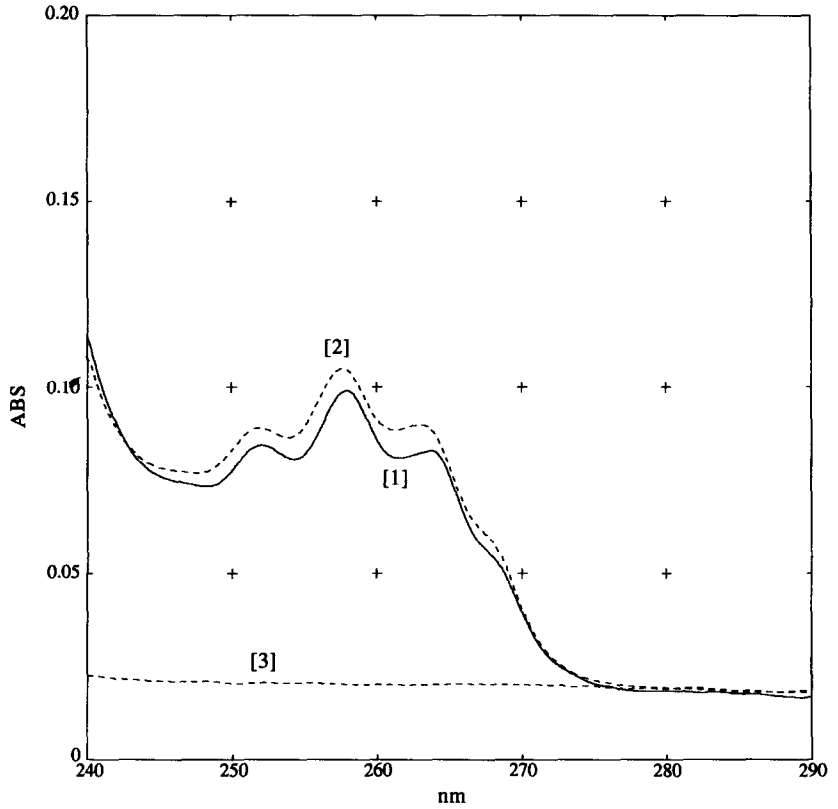

Figure 2
The zero-order spectra of homatropine hydrobromide [1] (150.0 mg l^{-1}), mandelic acid [2] (64.0 mg l^{-1}) and tropine [3] (59.4 mg l^{-1}) in 0.01 M HCl.

investigated. Standard solutions of homatropine hydrobromide in 0.01 M HCl in the concentration range 50–250 mg l^{-1} were prepared. The second-order spectra were measured in the range 240–290 nm. A calibration graph was constructed using the amplitude of the peak at 252 nm (to the long wavelength satellite) vs concentration. The regression equation for the calibration graph is shown below [equation (1)]

$$y = 0.066859\,x - 0.17865 \qquad r^2 = 0.9993 \qquad (1)$$

where y = peak amplitude (252 nm) and x = concentration of homatropine hydrobromide (mg l^{-1}).

Determination of two solutions containing 151 and 204 mg l^{-1} gave values of 145 and 199 mg l^{-1}, respectively. A solution of homatropine hydrobromide eye drops (2% w/v) was investigated. The sample was diluted to a concentration of 200 mg l^{-1} with 0.01 M HCl and the second-order derivative spectra recorded. Determination of three samples of this solution gave values of 206, 211 and 205 mg l^{-1}. From these measurements it would appear that the method gives satisfactory results for the determination of homatropine hydrobromide.

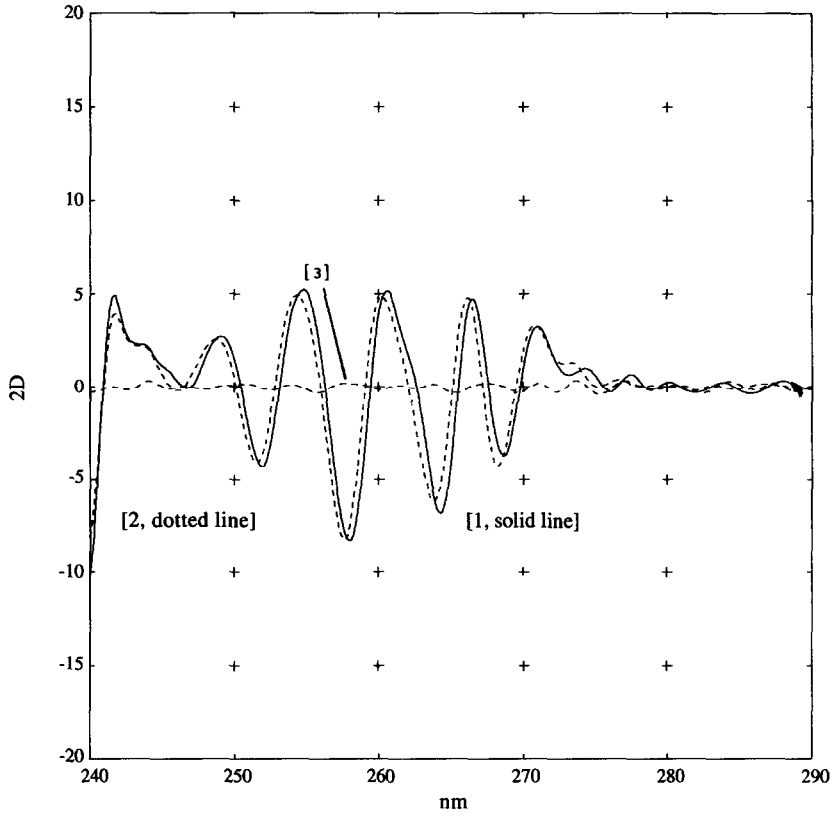

Figure 3
The second-order derivative spectra of homatropine hydrobromide [1] (150.0 mg l^{-1}), mandelic acid [2] (64.0 mg l^{-1}) and tropine [3] (59.4 mg l^{-1}) in 0.01 M HCl.

A mixture containing homatropine hydrobromide (150 mg l^{-1}), mandelic acid (21.4 mg l^{-1}) and tropine (19.8 mg l^{-1}) in 0.01 M HCl was prepared. This sample is equivalent to a solution of homatropine hydrobromide (200 mg l^{-1}) which had degraded by 25%. Figure 4 shows the second-order derivative spectra of this mixture and a solution of homatropine hydrobromide (200 mg l^{-1}) and, as can clearly be seen, the two spectra are virtually superimposable. This would indicate that, if this second-order derivative method for the determination of homatropine hydrobromide in formulated products is used in isolation, false results may be obtained. This observation would also seem to apply to the derivative methods indicated for the determination of atropine and hyoscine [1, 2] where hydrolysis would result in the formation of tropic acid. If these methods are used in conjunction with suitable control procedures to determine the level of degradation (e.g. the TLC methods for related substances in homatropine hydrobromide and homatropine hydrobromide eye drops detailed in the British Pharmacopoeia 1993 [3, 4]) then the technique would appear capable of providing reliable results.

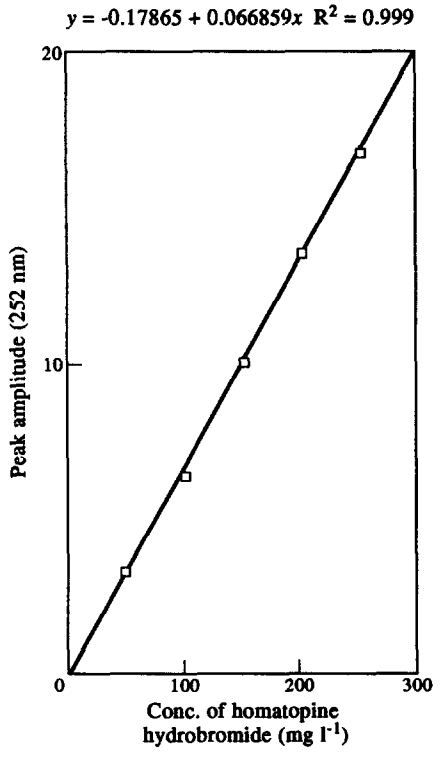

Figure 4
The second-order derivative spectra of homatropine hydrobromide [1] (200.0 mg l^{-1}) and a mixture [2] containing homatropine hydrobromide (150.0 mg l^{-1}), mandelic acid (21.4 mg l^{-1}) and tropine (19.8 mg l^{-1}) in 0.01 M HCl.

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