Journal of Pharmaceutical & Biomedical Analysis
Vol. 7, No. 5, pp. 571–576, 1989
Printed in Great Britain

0731–7085/89 $3.00 + 0.00

Determination of sulphacetamide, sulphadimidine or sulphathiourea in the presence of their degradation products using first derivative spectrophotometry

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Abstract: A method is presented for the determination of sulphacetamide sodium, sulphadimidine and sulphathiourea in the presence of their acid-induced degradation products using first derivative spectrophotometry. By measuring the absolute value of the first derivative curves at the zero contribution of the corresponding degradation products, the concentration of the intact drug can be calculated directly without interference of the degradation product. The validity of the method was confirmed using synthetic mixtures of the intact drugs with their degradation products.

Keywords: *Sulphacetamide sodium; sulphadimidine; sulphathiourea; derivative spectrophotometry; stability-indicating assay.*

Introduction

Derivative UV spectrophotometry [1] has been successfully applied to the determination of certain drugs in the presence of their degradation products. These include the determination of: procaine in the presence of 4-aminobenzoic acid [2]; some 1,4-benzodiazepines in the presence of their acid-induced degradation products [3]; thiamine and pyridoxine in aged pharmaceutical preparations [4]; and some cephalosporins in the presence of their degradation products [5].

On the other hand, derivative spectrophotometry has been used for the determination of degradation products in the presence of intact drugs, such as the determination of salicylic acid in aspirin [6] and sulphoxide in degraded chlorpromazine [7].

This paper describes an application of first derivative (D_1) spectrophotometry to permit a simple, rapid and accurate method for determining sulphacetamide sodium (**I**), sulphadimidine (**II**) or sulphathiourea (**III**) in the presence of their corresponding degradation products.

Experimental

Instrument

A Shiamadzu recording spectrophotometer UV 260 was used with 1-cm quartz

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cuvettes. Suitable settings were: scan speed 40 nm min^{-1}, chart speed 60 nm min^{-1}, and slit width 2 nm.

Materials

Analytical standard grades of **I**, **II** and **III**, (Nasr Co. and Alex. Co. Egypt) were used. Sulphadimidine tablets (El Nasr Co.) were labelled to contain 0.5 g of **II** in each tablet. Bendonal tablets (Alex. Co.) were labelled to contain 0.5 g of **III** in each tablet. Ocusol eye drops (Alex. Co.) were labelled to contain 1 g of **I** in each 10 ml. Other reagents used were of analytical grade. Solutions of sulphonamides were protected from light during assay.

Calibration graphs

Standard solutions were prepared containing 20 mg of **I**, **II** or **III**/250 ml of 0.1 M HCl. For each drug, 2–15 ml of this solution was transferred by pipette into 50-ml separate flasks and diluted to volume with 0.1 M HCl. The first derivative (D_1) of the UV spectra was measured against 0.1 M HCl at 287, 290 and 245 nm for **I**, **II** and **III**, respectively (Figs 1–3).

Preparation of acid-induced degradation products [8]

One gram **I**, **II** or **III** (authentic powder) was weighed accurately and transferred into a 100-ml flask; 50 ml of 2 M HCl was added and the solution was refluxed for 6 h then cooled. 2 ml of the solution was transferred by pipette into a 250-ml volumetric flask, neutralized with 2 M NaOH (2 ml) and diluted to volume with 0.1 M HCl. The D_1 values were measured as mentioned under calibration graphs.

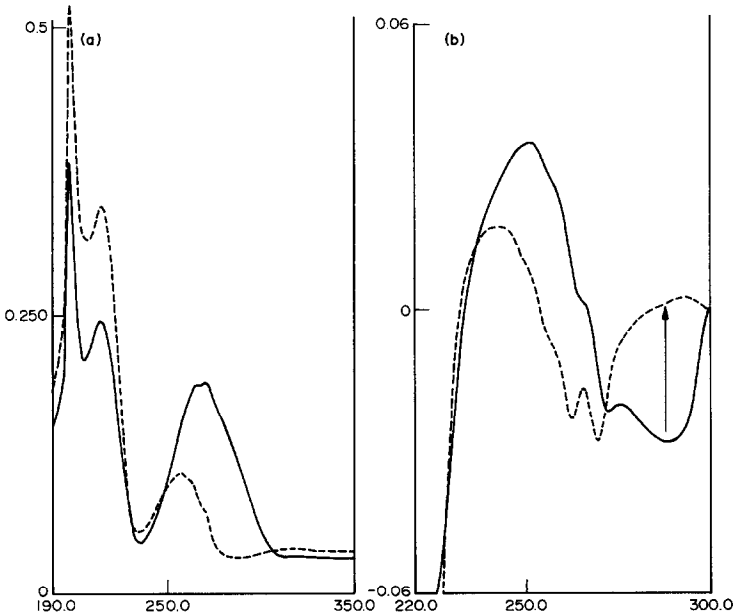

Figure 1
Zero-order (a) and first derivative (b) spectra of 0.8 mg/100 ml of **I** (——) and 0.94 mg/100 ml of its degradation (---) in 0.1 M HCl.

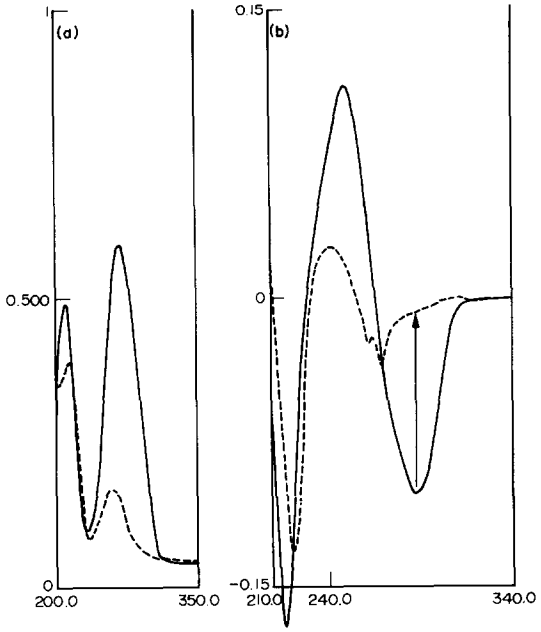

Figure 2
Zero-order (a) and first derivative (b) spectra of 0.3 mg/100 ml of **II** (——) and of 0.8 mg/100 ml of its degradation product (---) in 0.1 M HCl.

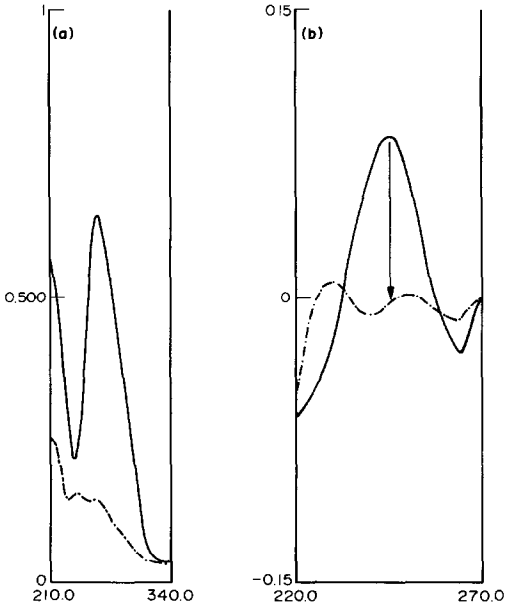

Figure 3
Zero-order (a) and first derivative (b) spectra of 0.8 mg/100 ml of **III** (——) and of 0.32 mg/100 ml of its degradation product (---) in 0.1 M HCl.

Preparation of tablets and drops

Sulphadimidine and Bendonal tablets. An accurately weighed amount of the powdered tablets, equivalent to about 20 mg of the drug, was dissolved in 0.1 M HCl. This solution was filtered and diluted to volume with 0.1 M HCl in a 250-ml volumetric flask. The procedure was then continued as described under calibration graphs.

Ocusol eye drops. 10 ml of Ocusol eye drops equivalent to 1 g of **I** was diluted to volume in a 100-ml volumetric flask with 0.1 M HCl. The procedure was then continued as described under calibration graphs.

Results and Discussion

Figures 1–3 show that the absorption curves of either **I**, **II** or **III** in 0.1 M HCl overlapped considerably with those of the corresponding degradation products [8]. The figures also show that **I** possesses a maximum D_1 value at 287 nm, whereas that of the degradation product at the same wavelength is approximately equal to zero; on the other hand, **II** and **III** appear to have maximum D_1 values at 290 and 245 nm, respectively, whereas their degradation products have D_1 values equal to zero at the same wavelengths. Therefore, the absolute value of the first derivative of the zero-order sum curves of the intact drug and its degradation product at the appropriate wavelength can be used to determine each of the intact drugs.

The plots of the D_1 values at 287 nm for **I**, 290 nm for **II** and 245 nm for **III** against concentration C, showed a linear relationship within the range of 0.32–2.4 mg/100 ml. The three linear equations were found to be:

$$C = 0.0910 + 26.274\ D_1 \quad (r = 0.9869), \text{ for } \mathbf{I}$$

$$C = -0.1101 - 10.193\ D_1 \quad (r = 0.9945), \text{ for } \mathbf{II}$$

and

$$C = -0.0325 + 5.863\ D_1 \quad (r = 0.9994), \text{ for } \mathbf{III}$$

where $D_1 = (dA/d\lambda)$, and C is concentration in mg/100 ml.

In order to confirm the validity and applicability of the proposed method, five synthetic mixtures of **I**, **II** or **III**, each with its degradation products, were prepared and analysed using the proposed method. The concentrations of the intact drugs in these mixtures were in the range 0.32–2.4 mg/100 ml in presence of 0.32 mg/100 ml of the corresponding degradation products. The mean percentage recoveries were 99.6 ± 0.53, 100.8 ± 0.63 and 101.0 ± 0.77 for **I**, **II** and **III**, respectively (Table 1).

For comparison, the A_{max} method was applied to the determination of the intact drugs in the above mixtures and the results were unacceptably high owing to the contribution of the degradation product (Table 1). The error decreased with an increase in the concentration of the intact drug, relative to that of the degradation product.

The modified Vierordt's [9] method was applied to the determination of **I** (λ_1 = 238 nm, λ_2 = 270 nm), **II** (λ_1 = 240 nm, λ_2 = 262 nm) and **III** (λ_1 = 230 nm, λ_2 = 272 nm) in the same mixtures, and the mean percentage recoveries were 100.2 ± 1.3, 100.8 ± 0.79 and 99.8 ± 0.8, respectively (Table 1). However, the presence of a constant or linear irrelevant absorption, as may originate from differences between batches of the sample and the reference, will certainly lead to erroneous results in the

Table 1
Determination of **I**, **II** and **III** by different methods

	Recovery (%)*		
	Proposed method	Vierordt's method	A_{max} method†
I			
Authentic powder mixtures‡	100.1 ± 0.87	—	—
	99.6 ± 0.53	100.2 ± 1.3	110.6 ± 9.4
Ocusol eye drops (Alex. Co.)§	96.6 ± 0.30	99.4 ± 0.73	99.7 ± 0.6
II			
Authentic powder mixtures‡	100.7 ± 0.45	—	—
	100.8 ± 0.63	100.8 ± 0.79	109.9 ± 6.2
Sulphadimidine tablets (Nasr. Co.)§	100.2 ± 0.72	100.2 ± 0.92	98.9 ± 1.1
III			
Authentic powder mixtures‡	100.2 ± 0.51	—	—
	101.0 ± 0.77	99.8 ± 0.8	110.5 ± 3.9
Bendonal tablets (Alex. Co.)§	99.1 ± 0.37	100.1 ± 0.45	99.0 ± 1.0

*Mean of five determinations ±SD.
†Wavelengths were 270, 272 and 260 nm for **I**, **II** and **III**, respectively.
‡Mixture of authentic powder (within the range of 0.32–2.4 mg/100 ml) and it's corresponding degradation product (0.32 mg/100 ml).
§Pharmaceutical preparation (without degradation product).

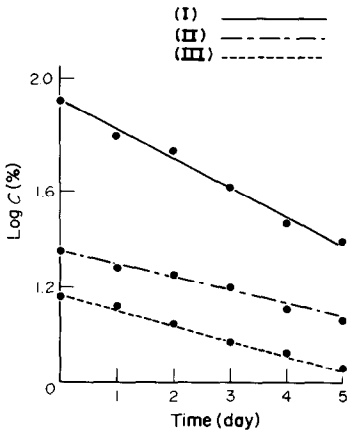

Figure 4
Stability study of **I**–**III**.

modified Vierordt's method. On the other hand, the results obtained using the derivative technique will not be affected by the presence of irrelevant absorption.

Commercial tablets of **II** and **III** and commercial eye drops of **I** were assayed using the proposed and A_{max} methods. Both procedures gave concordant results (Table 1).

Stability study on the degradation of I, II and III

Solutions containing 1 g/100 ml of each drug in 2 M HCl were prepared and kept in the dark at room temperature. Aliquots equivalent to 20 mg of the drug were neutralized with 2 M NaOH and diluted with 0.1 N HCl to 250 ml at zero time and every day over a period of 6 days. The D_1 values for each aliquot were measured at the specified wavelengths and the concentration of the intact drugs were calculated using the linear regression equation previously mentioned. The plots of log C% against time gave

straight lines indicating that the proposed method, based on measuring the D_1 values at the appropriate wavelengths, is specific for the intact drug and is independent of degradation products (Fig. 4).

With the wide availability of spectrophotometers equipped with derivative capabilities the application of the proposed method as a stability-indicating assay could be attractive.

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[Received for review 6 October 1987; revised manuscript received 14 January 1988]