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Short Communication

Use of isosbestic points of derivative absorption curves: the dissolution rate determination of Aspirin

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Introduction

Derivative spectrophotometry is a technique which has proved to be very useful in solving particular analytical problems [1–5].

Derivative spectrophotometry possesses different advantages including precise determination of λ_{max}, quantitative determination in presence of turbidity, enhancement of minor spectral features found on a broad background and quantitative separation of overlapping absorption peaks. It has been successfully used for the analysis of pharmaceutical dosage forms and for the determination of several drugs alone or in mixtures [3–8]. Derivative ratios have been used to evaluate the efficiency and validity of the derivative technique in elimination of interference prior to its application in spectrophotometric analysis [8, 9]. It has been reported that ratios of first derivative maxima and compensated derivative curves could be used to reveal the presence and the shape of interference with the possibility of its elimination. Compensated derivative curves have been used for two-component mixture analysis [10].

An isosbestic point is the wavelength at which the two absorbing species in equilibrium have the same absorbance value. At this wavelength the absorbance depends on the total molar concentration of the two absorbing species. Isosbestic points of derivative spectra can be used for the quantitative determination of the total amount of two absorbing species in equilibrium. In comparison with the isosbestic point of the conventional absorption spectra, it has the same advantages of derivative curves in providing better resolution, high sensitivity and elimination of matrix interference including turbidity.

The USP method [11] for dissolution rate determination of Aspirin tablets in acetate buffer pH 4.5, is performed using the isosbestic point of conventional absorption curves. The present work deals with the use of isosbestic points of derivative curves for the determination of the dissolution rate of Aspirin. For isosbestic point determination Aspirin was kept at 60°C in 0.1 N hydrochloric acid and measured at 1 h intervals. The isosbestic points of Aspirin and its degradation product, salicylic acid, were identified for first (D_1) and second (D_2) derivative techniques. These points have been involved in the dissolution rate study.

Experimental

Instruments

Conventional and derivative UV spectra were measured using a Perkin–Elmer (Model 550 S) UV–vis spectrophotometer. Derivative spectra were recorded in 1-cm quartz cells over the range 300–200 nm at a scan speed of 120 nm min^{-1}, chart speed of 240 mm min^{-1}, response time 10 s and ordinate maximum and

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minimum of ±0.1 for first derivative curves (D_1) and ±0.01 for second derivative curves (D_2).

Dissolution rate studies were run using a six-station dissolution tester with sampling device and diskette (Model QC 72 R 24-6A, Hanson Research, Northridge, CA, USA).

Materials and reagents

Pure samples of Aspirin and salicylic acid were kindly provided by Pharco (Egypt). All reagents were of analytical grade. Stock solution of Aspirin was prepared to contain 0.5 mg ml^{-1} of Aspirin in ethanol.

Isosbestic point determination

Accurately weighed 25 mg of Aspirin were dissolved in 5 ml of ethanol and diluted to 50 ml with 0.1 N hydrochloric acid. The solution was left in a water bath at 60°C. A 0.5 ml volume was diluted at 1 h intervals to 50 ml with 0.1 N hydrochloric acid. The first and second derivative spectra were recorded against 0.1 N hydrochloric acid.

Preparation of calibration graph

Accurately measured 0.2–0.6 ml portions of standard Aspirin solution were transferred into 50 ml volumetric flasks and diluted to volume with 0.1 N hydrochloric acid. The D_1 and D_2 spectra were recorded and the derivative values were measured at the isosbestic points (232.5 nm for D_1 and 236 nm for D_2).

Dissolution rate investigation

The dissolution medium consisted of 900 ml 0.1 N hydrochloric acid solution stirred at 75 rpm and maintained at 37 ± 0.5°C. At the appropriate intervals, 5-ml aliquots were withdrawn and assayed, after suitable dilution, at the isosbestic points using first and second derivative measurements.

Results and Discussion

Figure 1 presents (a) the zero order, (b) first order D_1, and (c) second order D_2, derivative spectra of equimolar concentration of Aspirin and salicylic acid in 0.1 N hydrochloric acid. The zero order absorption curves show two isosbestic points at 276 and 232 nm. The derivative spectra show one isosbestic point at 232.5 nm for D_1 and 236 nm for D_2 curves.

Aspirin undergoes hydrolytic reaction to give an equimolar amount of salicylic acid. Hydrochloric acid (0.1 N) at 60°C was selected

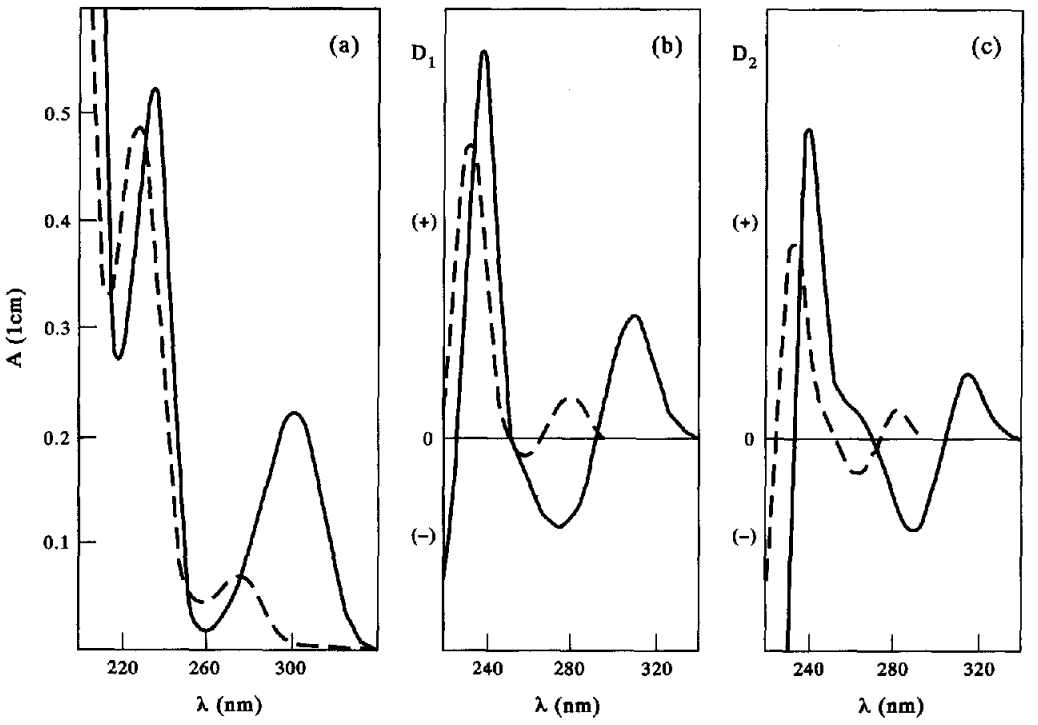

Figure 1
(a) Zero order spectra, (b) first derivative spectra and (c) second derivative spectra of 1 mg % Aspirin (---) and 0.8 mg % salicylic acid (———) in 0.1 N hydrochloric acid.

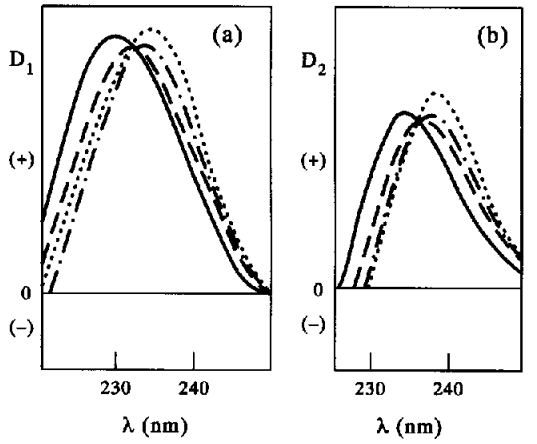

Figure 2
(a) First derivative spectra and (b) second derivative spectra of Aspirin degradation process, in 0.1 N hydrochloric acid. ———, Zero time; – – –, after 2 h; ····, after 3 h; and – · – · –, after 5 h.

to accelerate the degradation process. Figure 2 shows the first (D_1) and second (D_2) derivative spectra of Aspirin degradation process. The obtained isosbestic points of Aspirin and its degradation product were found to be at 232.5 and 236 nm for D_1 and D_2, respectively, which are in agreement with the isosbestic points of Aspirin and salicylic acid (Fig. 1) obtained by using equimolar concentration.

Calibration graphs at the isosbestic points were constructed for Aspirin in 0.1 N hydrochloric acid. The D_1 and D_2 values measured at the selected isosbestic points were found to be linear over the concentration range 0.2–0.6 mg per 100 ml. The following linear regression equations have been derived using the method of least squares:

$$D_1 = -0.12 + 12.85\,C \qquad (r = 0.9997),$$
$$D_2 = -0.05 + 9.15\,C \qquad (r = 0.9997),$$

Where C is the concentration in mg per 100 ml.

The selected isosbestic points of the first and second derivative spectra of Aspirin and its degradation product were utilized for dissolution rate studies of Aspirin.

Figure 3 represents the dissolution rate profile for three different Aspirin brands in 0.1 N hydrochloric acid using D_1 (or D_2) isosbestic point at 232.5 nm (or 236 nm). The amount of the drug released within 30 min was 92.4% (D_1), 90.7% (D_2) for brand A and 95.7% (D_1), 89.1% (D_2) for brand B. On the other hand, the proportion of the drug released within 3 h in 0.1 N hydrochloric acid was

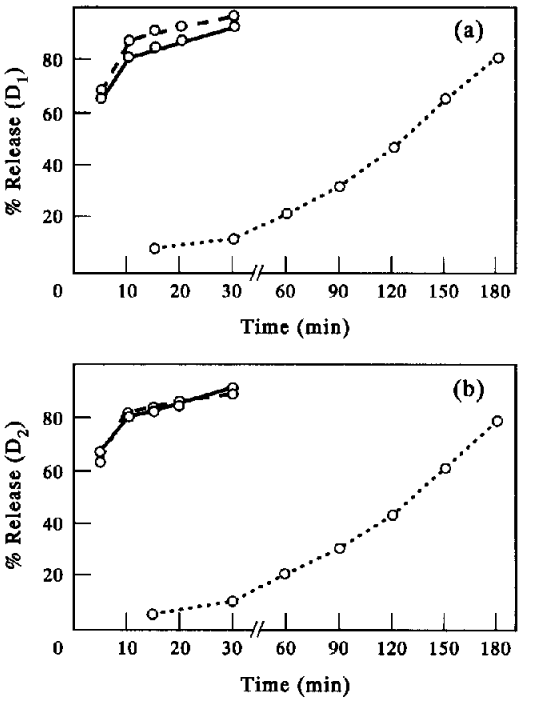

Figure 3
Dissolution rate profile for [A(–O–O–), B (--O-O--) and C (..O..O..)] Aspirin brands in 0.1 N hydrochloric acid using D_1 measurement at 232.5 nm (a) and D_2 measurement at 236 nm (b).

80.6% (D_1), 78.4% (D_2) for brand C (sustained release Aspirin tablets).

In conclusion, application of isosbestic points of derivative spectra in dissolution rate investigation can correct for the interference that may originate from excipients or due to the presence of another component in the formulation that possesses a zero derivative value at the used isosbestic point. The method might also find useful application in the dissolution rate determination of suppositories, where the resulting turbidity will be cancelled whenever isosbestic points of second derivative curves are used.

Use of isosbestic points of derivative curves and their advantage over the conventional method in pH determination will be the subject of a further publication [12].

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