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Simultaneous determination of salicylic acid and acetylsalicylic acid in aspirin delayed-release tablet formulations by second-derivative UV spectrophotometry

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Abstract

A rapid, simple assay procedure was developed for simultaneous analysis of aspirin (ASA) and salicylic acid (SA) in aspirin delayed-release tablet formulation by 'zero crossing' second-derivative UV spectrophotometry. The zero-order absorption spectra and second derivative spectra of ASA and SA were recorded in diluting solution acetonitrile–formic acid (99:1). The accuracy of the method was demonstrated by the determination of ASA and SA in five tablets formulations (each 20 tablets of the same batch) by the described method and by high performance liquid chromatographic method, and the results were in good agreement. © 1998 Elsevier Science B.V. All rights reserved.

Keywords: Salicylic acid; Aspirin; Determination; Second-derivative UV spectrophotometry

1. Introduction

The official aspirin product monographs, USP 23, Polish Pharmacopoeia V, British Pharmacopoeia require the determination of impurity of the free salicylic acid in aspirin products [1–3]. The limit for free salicylic acid in 'Aspirin Extended-Release Tablets' and 'Aspirin Delayed-Release Tablets' is 3% and in 'Aspirin Effervescent Tablets for Oral Solutions' is 8% [1].

Various methods have been reported for the determination of aspirin and salicylic acid [1–7]. Polish Pharmacopoeia recommends determination of salicylic acid impurities based on its color complex formation with ferric ion [3], and USP 23 procedure involve HPLC analysis of the free salicylic acid.

The simultaneous determination of both drugs is not possible by direct UV spectrophotometry because of the spectral overlap of the main maxima.

In this paper a simple procedure is presented for the simultaneous determination of salicylic acid and aspirin by 'zero crossing' second-derivative UV spectrophotometry.

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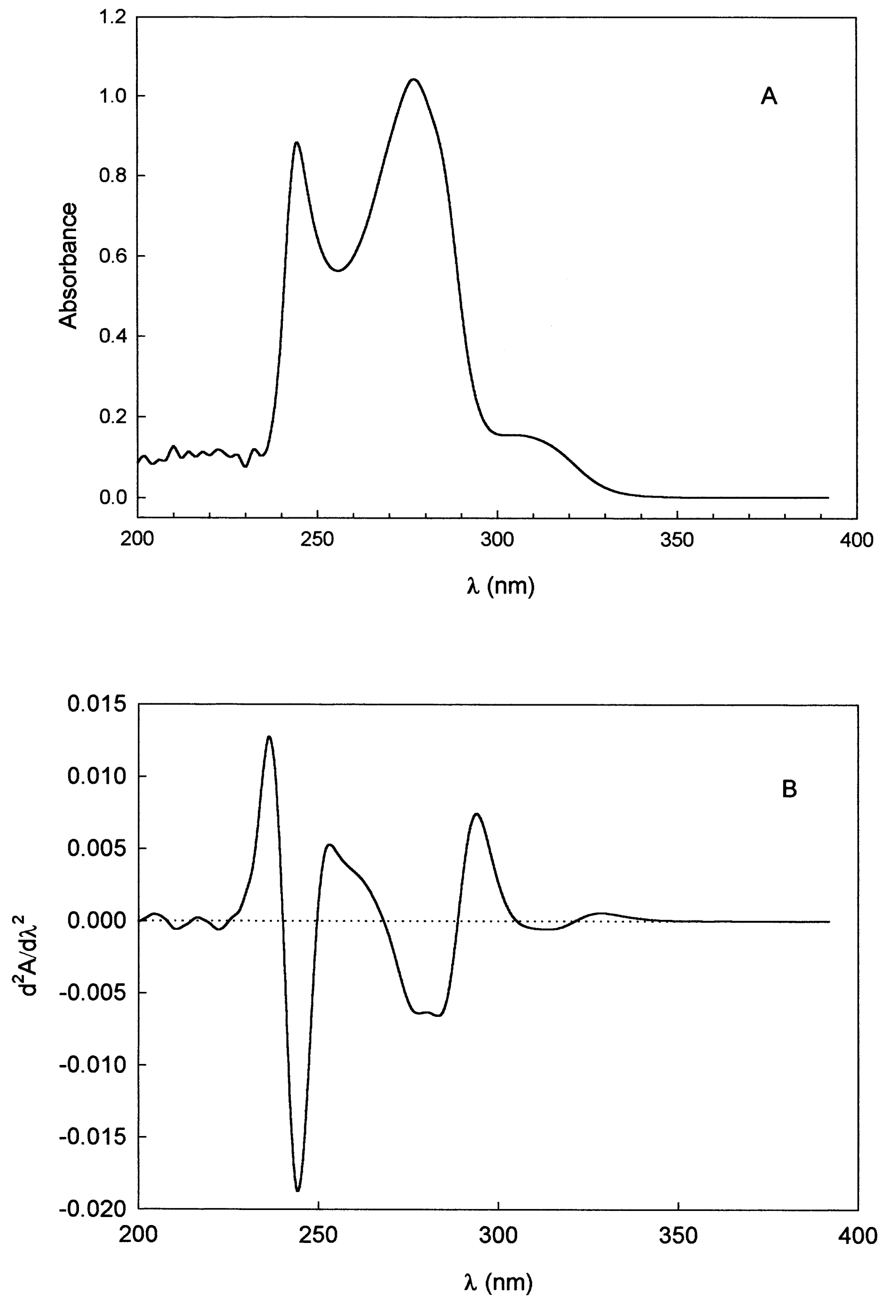

Fig. 1. Zero order absorption spectra (A) and second-derivative spectra (B) of salicylic acid (5 μg ml^{-1}) in the presence of acetylsalicylic acid (150 μg ml^{-1}).

To determine the validity of the method, five tablet formulations (each 20 tablets of the same batch) were analyzed by this spectrophotometric method and by high performance liquid chromatographic method described in USP 23 [1].

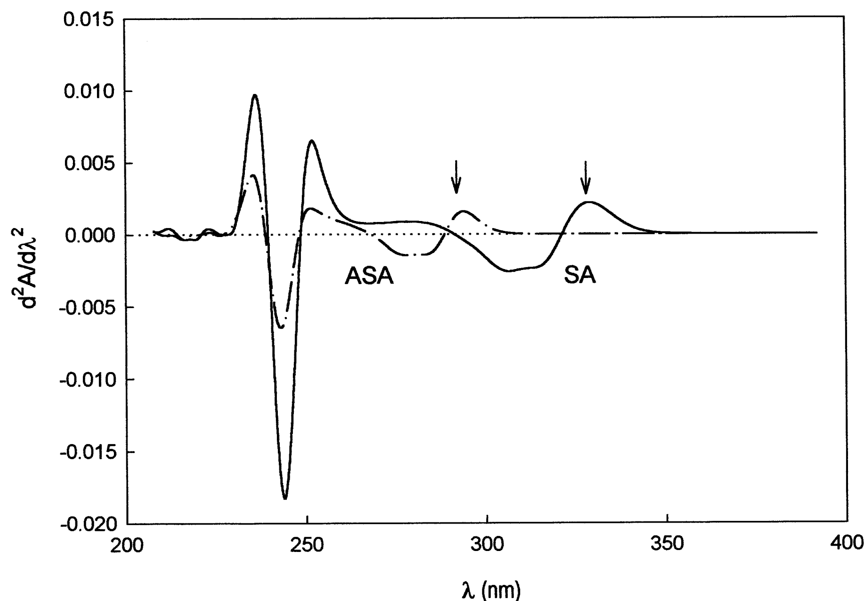

Fig. 2. Second derivative spectra of salicylic acid (SA) (20 μg ml^{-1}) and acetylsalicylic acid (ASA) (30 μg ml^{-1})

Table 1
Regression analysis of results of assay by second-derivative UV spectroscopy

Drug	λ (nm)	r^2	Intercept	Slope
SA in the presence of ASA (150 μg ml^{-1})	328	0.999	6.011×10^{-5}	4.814×10^{-5}
ASA in the presence of SA (4.5 μg ml^{-1})	292	0.999	2.0108×10^{-5}	1.0454×10^{-4}

2. Experimental

2.1. Materials

Acetronitrile and methanol were from J.T. Baker and sodium 1-heptanosulfonate was purchased from Sigma, all HPLC grade reagents. Glacial acetic acid (J.T. Baker), formic acid A.C.S. reagent (Aldrich) were analytical grade and were used as received. Analytically pure standards of acetylsalicylic acid (ASA) and salicylic acid (SA) (Fluka) was used. Water was three times redistilled from quartz apparatus.

2.2. UV analysis

A Hewlett Packard 8452A diode array spectrophotometer with 1 cm quartz cells was used, and spectra were determined from 200 to 400 nm. The zero-order absorption spectra and second-derivative spectra of ASA and SA (in diluting solution acetonitrile–formic acid 99:1) [1] were recorded between 200–400 nm, and stored in the memory of the spectrophotometer. The absolute values of the derivative were measured at 292 nm for determination of ASA and 328 nm for the analysis of SA.

2.3. HPLC analysis

The liquid chromatograph consisted with pump LC 10 AS, UV detector SPD 10A and integrator Chromatopac C-R6A (all Shimadzu), injection valve 20 μl (Rheodyne). The analytical column was a Nucleosil C18, (Alltech, 5 μm, 250 × 4.6 mm). The mobile phase was prepared according to USP 23 ‘Aspirin delayed-release tablets’ monograph [1]. The mixture was filtered and deaerated. A flow rate of 1.5 ml was used.

Table 2
Comparison of the results of assay by second-derivative UV spectroscopy and by HPLC

Tablet formulation			
Salicyclic acid (mg per tablet)	UV	HPLC	%
ASA CH3/96	1.762	1.659	1.92
ASA CH5/96	1.516	1.469	1.82
ASA CH6/96	1.921	1.965	2.13
POL 05	0.481	0.468	0.08
BPI 1	0.256	0.231	0.06
O-acetylsalicyclic acid (mg per tablet)	UV	HPLC	Declared
ASA CH3/96	78.193	76.012	75.00
ASA CH5/96	75.560	75.203	75.00
ASA CH6/96	79.292	82.657	75.00
POL 05	525.155	522.143	500.00
BPI 1	325.455	323.732	325.00

2.4. Standard solutions

Stock solutions (0.6 mg ml^{-1}) of ASA and SA were prepared in diluting solution (acetonitrile and formic acid 99:1). It was prepared fresh daily.

Working standards: suitable aliquots of stock solution of ASA or SA was transferred into a 25 ml volumetric flask and filled to the volume with diluting solution.

For UV measurements of SA a calibration graph was prepared in the range 0.5–40 μg ml^{-1} and each solution containing ASA 150 μg ml^{-1}; for ASA assay it was 5–200 μg ml^{-1} and each solution containing SA 4.5 μg ml^{-1}. For the HPLC analysis a calibration graph for the measurements of SA was in the range of 0.5–40 μg ml^{-1}, but for ASA it was in the range 5–550 μg ml^{-1}.

2.5. Assay procedure for tablets

Assay procedure was based on the 'Assay preparation' described for 'Aspirin delayed-release tablets' monograph in the USP 23 [1]. A total of 20 tablets were weighed and finely powdered. An accurately weighed quantity of the powder, equivalent to about 100 mg of aspirin, was transferred to a 50 ml Erlenmeyer flask and 20 ml of diluting solution was added. A mixture was vigorously shaken for 10 min and a 10 ml of supernatant was centrifuged at 3500 rpm for 5 min. Then for HPLC analysis a 1 ml of clear supernatant was pipetted into a 10 ml volumetric flask, and for the UV measurements a 0.3 ml of the supernatant was transferred into a 10 ml volumetric flask and all were filled up to a volume with a diluting solution.

3. Results and discussion

All solutions of ASA and SA were prepared in diluting solution (acetonitrile and formic acid, 99:1), which is recommended for the same kind of determinations by USP 23.

The zero-order absorption spectra of both drugs (Fig. 1A) showed very strong spectral interferences and it could not be overcome by the use first-derivative spectrophotometry. In the second-derivative spectra (Fig. 1B) the interference was considerably reduced, and zero-crossing wavelengths at 292 and 328 nm were selected for ASA and SA respectively (Fig. 2).

Calibration was performed with the standards containing additionally the other compound in the range typically found in the aspirin delayed-release formulations.

Calibration graphs were constructed by plotting derivative absorbance (DA) values against concentrations (C). Good linear relationships were obtained over the ranges studied. The regression equations were the following $DA = 1.045 \times 10^{-4} \times C - 2.011 \times 10^{-5}$ for salicylic acid and $DA = 4.814 \times 10^{-5} \times C + 6.011 \times 10^{-5}$ for ASA (Table 1).

The precision of the system was determined by making six replicate scans of two solutions containing salicylic acid at concentrations 10 $\mu g\ ml^{-1}$ and ASA 25 $\mu g\ ml^{-1}$ and determining the relative standard deviation of the second derivative values. Mean second derivative value of 0.001061 with RSD of 1.56% was obtained for salicylic acid and mean 0.001191 with RSD of 1.36% was for acetylsalicylic acid.

The accuracy of the method was demonstrated by the simultaneous determination of ASA and SA in six tablets formulations (each 20 tablets of the same batch) and the results were compared with those by a high performance liquid chromatographic method described in USP 23. The results (Table 2) are in good agreement, at 95% confidence level there was no difference between them.

A simple UV method for the determination of impurities of salicylic acid in aspirin tablet formulations was developed. The proposed method can be recommended for the routine analysis and quality control of the drug investigated.

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