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Derivative-ratio spectrophotometric method for the determination of ternary mixture of aspirin, paracetamol and salicylic acid

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Abstract

A derivative spectrophotometric method was developed for the assay of a ternary mixture of aspirin (ASP), paracetamol (PAR) and salicylic acid (SAL). The method is based on the use of the first and second derivatives of the ratio spectra and measurement at zero-crossing wavelengths. The ratio spectra were obtained by dividing the absorption spectrum of the mixture by that of one of the components. The concentration of the other components are then determined from their respective calibration curves treated similarly. The described method was applied for the determination of these combinations in synthetic mixtures and dosage forms. The results obtained were accurate and precise.

Keywords: Derivative ratio; Spectrophotometry; Zero-crossing; Absorption spectrum; Calibration curves; Synthetic mixtures; Dosage forms

1. Introduction

The resolution of complex multicomponent systems without separation of the constituting analytes is rather a difficult task. The resolution of binary mixtures of compounds with overlapped spectra by derivative technique is frequently made on the basis of zero-crossing measurements [1–3], or compensation technique [4,5].

However, in certain cases, the derivative technique cannot cope with the level of the interference especially when the spectra are strongly overlapped or in case of ternary mixtures.

A spectrophotometric method for resolving binary mixtures has been reported [6]. The method is based on the use of the first derivative of the ratio of the spectrum. This method has been extended to determine ternary mixtures by simultaneous use of the zero-crossing technique and Salinas method [7–9].

Aspirin (ASP) and paracetamol (PAR) are formulated as tablets in the ratio of 300:200. This combination is widely used for fever, and mild to moderate pain in case of headaches, rheumatic pain, muscular aches, toothache, period pain and sore throat.

However, ASP determination is quite a major problem since during preparation it may contain its main degradation product salicylic acid (SAL). So during the assay of ASP the presence of SAL must be considered. It is noteworthy here to mention that the literature reveals one method for determination of this mixture [10]. Therefore, the aim of this work is to develop a spectrophotometric method for determination of this ternary mixture.

2. Experimental

2.1. Apparatus

The spectrophotometric measurements were carried out on a Jasco V-530 double beam UV–vis spectrophotometer and an Epson LQ-300 printer. The absorption spectra were measured using 1 cm quartz cells.

For the derivative ratio method, the absorption spectra were recorded on the same spectrophotometer, with 1 cm quartz cells and supported with Jasco Spectra Manager software for GULLIVER Ver. 1.53, and an hp LaserJet 1015 printer.

2.2. Materials and Reagents

All materials and reagents were of analytical reagent grade.

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Table 1
Assay parameters and effect of the divisor concentration on the determination of ASP, PAR, and SAL

Drug	Conc. (mg/ml)	Method	Divisor		λ (nm)	Linear regression			Standard deviation of		
			Name	Conc. (mg/ml)		Intercept (*a*)	Slope (*b*)	Corr. Coeff. (*r*)	Slope (Sb)	Intercept (Sa)	$t = a/Sa^*$
ASP	0.07–0.16	^{1}DD	SAL	0.05	240	0.0152	0.291	0.9992	5.264×10^{-3}	0.0603	0.252
				0.075		0.0211	0.313	0.9991	5.841×10^{-3}	0.0669	0.316
				0.1		0.0281	0.312	0.9992	5.693×10^{-3}	0.0652	0.431
PAR	0.05–0.12	^{2}DD	SAL	0.05	241.6	0.0034	0.0256	0.9993	4.346×10^{-4}	0.00367	0.935
				0.075		0.0053	0.0259	0.9996	3.206×10^{-4}	0.00271	1.941
				0.1		0.007	0.0259	0.9992	4.449×10^{-4}	0.00376	1.876
SAL	0.05–0.15	^{1}DD	PAR	0.09	230.6	0.0132	0.257	0.9993	5.392×10^{-3}	0.0572	0.232
				0.1		0.0168	0.259	0.9999	2.211×10^{-3}	0.0235	0.718
				0.12		0.0211	0.257	0.9996	4.367×10^{-3}	0.0463	0.456

* Theoretical t values = 2.45 for 95% confidence levels.

Aspirin, paracetamol, and salicylic acid were purchased from Fluka Chemie GmbH, Switzerland.

2.3. Preparation of standard solutions

Stock solutions containing 1 mg/ml ASP, 1 mg/ml PAR, and 0.5 mg/ml SAL were prepared in ethanol. Further dilutions were done using ethanol as described under construction of calibration graphs.

2.4. Construction of calibration graphs

Into three sets of 10 ml volumetric flasks, different aliquots of the standard solutions of ASP, PAR, and SAL, within the concentration range in Table 1, was transferred. The solutions were then completed to the volume with ethanol. The absorption spectrum of each solution was recorded and stored.

2.5. Spectrophotometric measurements

The absorbance of the standard solutions were recorded within the wavelength range 200–300 nm and stored.

3. Results and Discussion

3.1. Assay conditions

This mixture contains PAR, ASP, and SAL. The absorption spectra of the three components are strongly overlapped that no zero-crossing point is present to determine any component in presence of the other two (Fig. 1). Moreover, the application of the first and second derivative zero-crossing techniques failed to resolve it (Figs. 2 and 3). On the other hand, this spectral overlapping was sufficiently enough to demonstrate the resolving power of the proposed method.

In this respect, different solutions of ASP, PAR, and SAL were prepared in the concentration ranges stated in Table 1. The absorption spectra of these concentrations were recorded and stored.

For the determination of ASP, the stored absorption spectra of standard solutions of ASP, PAR, and SAL and a solution of their mixture were divided (amplitude by amplitude at the appropriate wavelengths) by the absorption spectrum of a standard solution of 0.05 mg/ml SAL, then the first derivative of the obtained ratio spectra (^{1}DD) were calculated with $\Delta\lambda = 1$ nm (Fig. 4). From this figure, ASP can be determined in this mixture by measuring the amplitude at 240 nm where there is no contribution from PAR (zero-crossing point of PAR).

On the other hand, for the determination of PAR, an analogous procedure was followed, where the ratio spectra were obtained

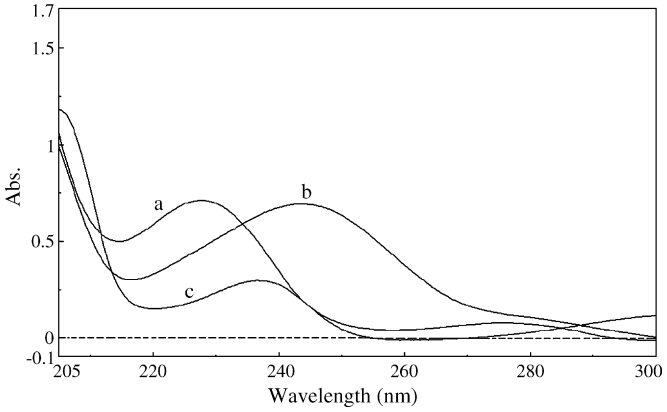

Fig. 1. Absorption spectra of (a) 0.15 mg/ml ASP, (b) 0.1 mg/ml PAR, and (c) 0.05 mg/ml SAL.

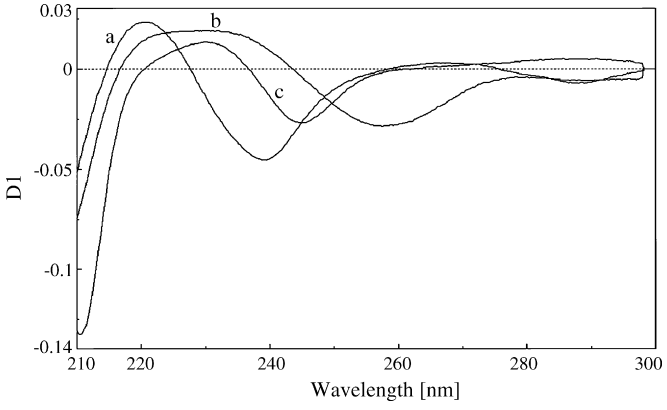

Fig. 2. First derivative spectra of (a) 0.15 mg/ml ASP, (b) 0.1 mg/ml PAR, and (c) 0.05 mg/ml SAL.