CIENCIA 3(3), 247-254, 1995
Maracaibo, Venezuela

Direct determination of resorcinol in pharmaceuticals by using derivative spectrometry

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Recibido: 04-05-95 Aceptado: 12-12-95

Abstract

A direct UV derivative spectrometric method is proposed to determine resorcinol in several types of pharmaceutical preparations, eliminating the matrix interferences on the absorbance measurements. Samples and standards were dissolved in NaOH (0.01 M), and the five first derivative absorption spectra were recorded in the range 200-400 nm. Analytical features of the determination of resorcinol at different wavelengths in different derivative orders were established. Results showed that for some real samples, such as hydroalcoholic solutions, the use of derivatives is unnecesary, because direct absorbance measurements can provide accurate results. However, for the determination of resorcinol in ointments or suspensions, use of zero order spectra did not provide accurate results, but appropriate wavelength and derivative orders were identified which makes possible the background correction, therefore samples can be analyzed directly without any previous separation step, with accuracy relative errors of the order of 4.5%.

Key words: Derivative UV spectrometry; direct analysis of pharmaceuticals; resorcinol determination

Determinación directa de resorcinol en fármacos usando espectrometría de derivadas

Resumen

Se propone el uso del método directo de espectrometría de derivadas en UV para determinar resorcinol en varios tipos de preparados farmaceúticos, que hace posible la eliminación de las interferencias de la matriz en las medidas de absorbancia.Las muestras y los patrones se disolvieron en NaOH 0,01 M, y se registraron los cinco primeros espectros derivados de absorción en el intervalo de 200-400 nm, estableciendose las características analíticas para la determinación de resorcinol a diferentes longitudes de onda en diferentes órdenes de derivación. Los resultados muestran que para algunas muestras reales, como disoluciones hidroalcohólicas, el uso de derivadas es innecesario, ya que la medida directa de absorbancia puede proporcionar resultados exactos. Sin embargo, para la determinación de resorcinol en pomadas o suspensiones el uso de espectros de absorción no proporciona resultados correctos y en cambio la selección de la longitud de onda y el orden de derivación

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adecuados permite la corrección de las interferencias de modo que las muestras pueden analizarse directamente sin ningún paso previo de separación, con unos errores relativos del orden del 4,5%.

Palabras claves: Análisis directo de fármacos; determinación de resorcinol; Espectrometría de derivadas UV.

Introduction

Derivative spectrometry is a simple modification of the spectrophotometric methods, based on the mathematical treatment of spectra which provides a background correction and permits the direct determination of a compound in the presence of the matrix for different types of samples (1), or an easy resolution of mixtures (2) .

It has been shown to be a useful methodology for the analysis of pharmaceutical preparations (3).The determination of active ingredients of these preparations usually needs a sample clean-up due to the presence of other components, specially excipients, which can cause interferences in the absorbance measurements. Derivative spectrometry has been used in the determination of many active ingredients in pharmaceuticals, such as: tranquillizers (4), antibiotics (5-7), vitamins (8), antihypertensives (9-11), etc. and it has been also used to eliminate the effect of biological matrices in drug analysis (12-14).

Resorcinol (15) is a keratolytic agent mainly employed in ointments or lotions for the treatment of acne and in hair lotions for removing dandruff or as an oral antiseptic. The large variety of preparations in which resorcinol can be present introduces a serious drawback in establishing a simple methodology for the control analysis of pharmaceuticals by UV spectrometry.

In this paper, a direct UV derivative spectrometric method is developed to determine resorcinol in pharmaceutical preparations that eliminates matrix interferences.

Materials and Methods

Apparatus

A Hewlett Packard 8452 diode array spectrophotometer, equipped with a Vectra ES/12 computer and 1 cm quartz measurement cell, was employed to obtain the absorbance spectra. The system can mathematically generate different order derivative spectra from the zero order collected data.

Reagents

Aqueous standard solutions containing resorcinol (4, 6, 8, 10 and 12 µg/mL) in sodium hydroxide (0.01 M) were prepared from a stock solution (100 µg/mL in NaOH 0.01 M), obtained from the analytical grade reagent (Aldrich. Germany).

Three pharmaceutical preparations were analyzed as test samples, this is, ACNOMEL® (Smith Kline & French S. A.) , an ointment used for skin problems, ACNISDIN® (Lab. Isdin S. A.), an actiacne suspension, and DONNER® (Lab. C. Domenech Garcia), a mouth antiseptic hydroalcoholic solution, containing 2.0% w/w, 2.0% (w/v) and 1.3% (w/v) of resorcinol respectively. In these formulations a relative error of 10% of the content is permitted.

Samples were dissolved in sodium hydroxide (0.01 M) and appropiate dilutions, containing 6 µg/mL resorcinol, were directly analyzed by the proposed method. Some samples resulted in suspensions rather than real solutions, but the use of derivative spectra perfectly corrects for the possible interferences due to the suspended materials and, because of that, a previous filtration of samples can be avoided.

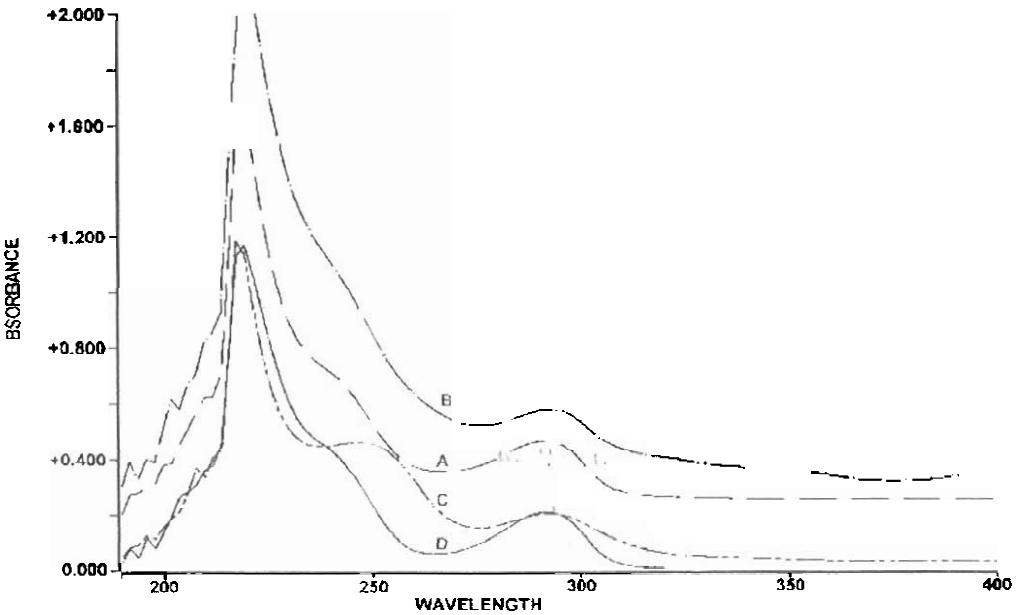

Figure 1. Absorption spectra of pharmaceutical samples and an aqueous standard solution each containing 6 µg/mL of resorcinol.
A Ointment sample (ACNOMEL®)
B Suspension sample (ACNISDIN®)
C Mouthwash solution sample (DONNER®)
D Standard.

General procedure

Absorbance spectra of samples and standards were recorded in the wavelength range 200 to 400 nm. Derivative spectra were obtained by mathematical differentiation to generate the first to the fifth derivative spectra. Wavelengths at which the derivative spectra of both samples and standards, at the same resorcinol concentration level, provided the same signal, were selected for each derivative order. The concentration of resorcinol in the pharmaceuticals was determined, at the selected wavelengths, using calibration data obtained from aqueous standard solutions containing resorcinol.

Results and Discussion

Figure 1 shows the absorption spectra of different sample solutions and an aqueous standard, each containing 6 µg/mL of resorcinol.

The DONNER® sample solution has an absorbance spectrum similar to that of the corresponding standard and thus it can be directly analyzed. However, ACNOMEL® and ACNISDIN® samples have a strong background absorption, due to some components which mask the resorcinol spectrum and to the presence of undissolved particles which provides a certain turbidity.

The direct determination of resorcinol in DONNER® at 292 nm provides a concentration value of 1.23 ± 0.02 with an associated accuracy error of 5.4% as compared with the reported value. However, concentration values of 13.3 ± 0.3 and 5.4 ± 0.4 were obtained at 292 nm for the analysis of ACNOMEL® and ACNISDIN®, respectively, which correspond to accuracy errors of

Table 1
Determination of resorcinol in pharmaceutical samples. Sample A is an ointment (ACNOMEL®) and sample B is a suspension (ACNISDIN®), both pharmaceuticals contain 2.0% resorcinol

Sample	Derivat. order	Wavelength (nm)	Calibration curve[1]	Regresion coef.	Conc. found (%)	Coef. of variation (%)[2]	Relative error (%)[3]
	1	302	$-2.2.10^{-5}-2.68.10^{-3}.C$	-09999	1.88	1.1	-6.0
	3	236	$-9.14.10^{-5}-8.66.10^{-5}.C$	-0.996	2.09	2.4	+4.5
A	3	272	$4.2.10^{-8}-3.98.10^{-6}.C$	-0.9994	1.97	2.5	-2.0
	4	242	$5.17.10^{-6}+1.57.10^{-5}.C$	0.9994	1.99	3.5	-0.5
	4	266	$-6.8.10^{-8}+2.44.10^{-6}.C$	0.99990	1.87	3.2	-6.0
	5	272	$1.1.10^{-8}-4.99.10-7.C$	-0.99996	1.87	3.2	-6.0
	3	236	$-9.14.10^{-5}-8.66.10^{-5}.C$	-0.996	2.09	2.4	+4.5
B	4	266	$-6.8.10^{-8}+2.44.10^{-6}.C$	0.99990	1.74	2.3	+13.0
	5	272	$1.1.10^{-8}-4.99.10-7.C$	-0.99996	1.67	1.2	+16.5
	5	292	$-2.26.10^{-8}+1.18.10^{-6}.C$	+0.99995	1.67	3.0	+16.5

Derivat.: derivative Coef.: coefficient Conc.: concentration Sample A: ACNOMEL® Sample B: ACNISDIN®

1 Calibration curve obtained for derivative peak height values as a function of resorcinol concentrations.

2 Coefficient of variation for three independent analysis of same sample.

3 Relative errors established from the comparison between results found by derivative spectrometry and those reported by the producer.

565% and 170% respectively. As a result, different derivative order measurements have been assayed in order to solve the aforementioned matrix interferences.

The first to the fith derivative spectra were obtained for a series of standard solutions and for the ointment and suspension samples.

Figures 2 and 3 show the derivative spectra for ACNOMEL® and ACNISDIN® samples and for a standard solution with the same concentration as that of the dispersed samples.

Absorption wavelengths for which both samples and standards provided the same height and shape were selected for each derivative order. In each case, the degree of interference in the determination of resorcinol arising from the pharmaceutical matrices was determined in order to establish the most appropiate conditions for the direct analysis of the drug. Table 1 shows the optimum results obtained for the determination of resorcinol in ACNOMEL® and ACNISDIN®.

As can be seen for the analysis of ACNOMEL® , there are several wavelengths at several derivative orders with which accurate results can be generated. However, for the analysis of ACNISDIN®, the minimum at 236 nm, obtained in the third order derivative spectrum, seems to be the only useful one with which to obtain accurate results.

Table 1 shows the calibration curve and regresion coefficients obtained for the analysis of each type of sample considered

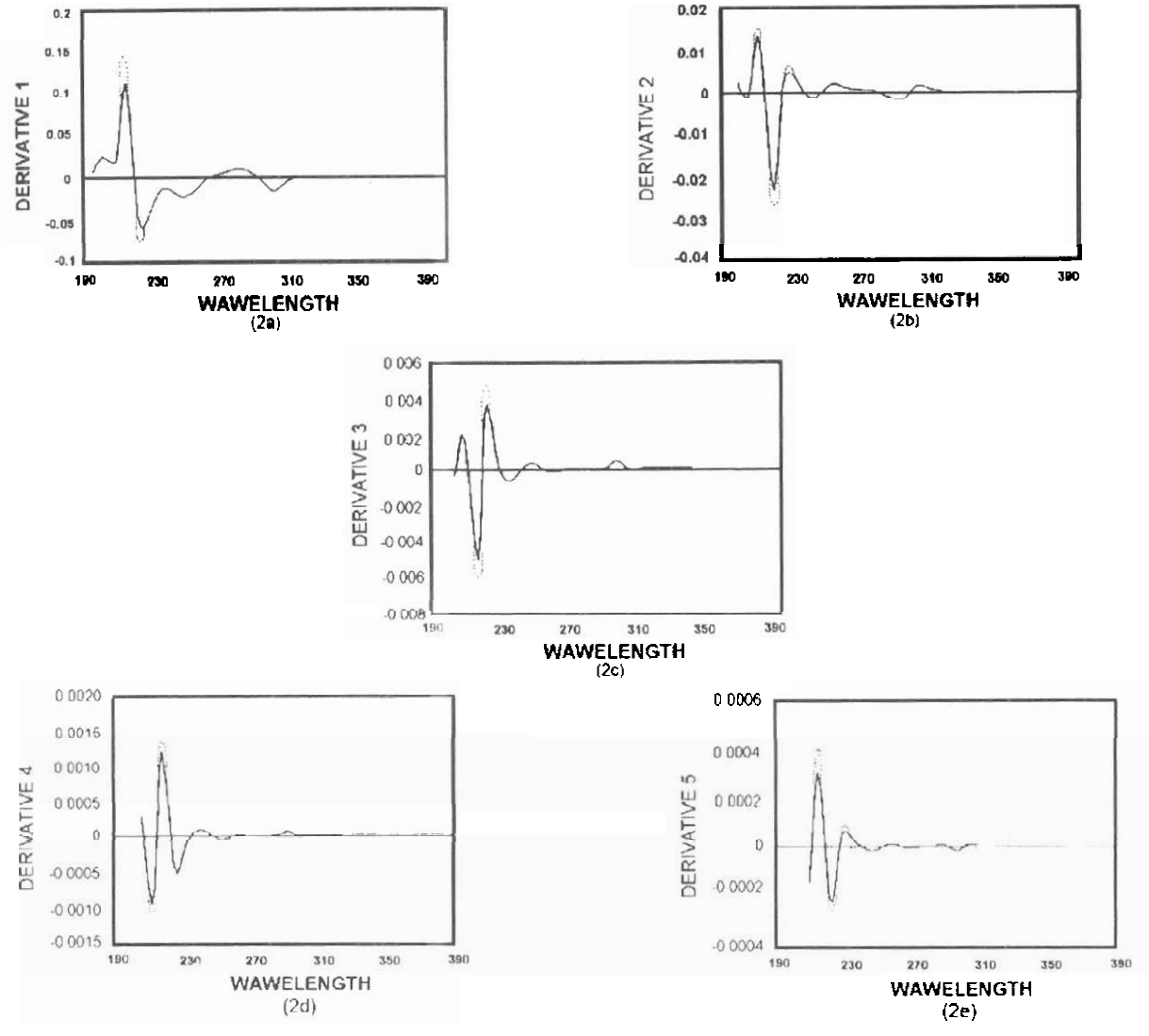

Figure 2. Derivative spectra of an ointment sample (A) and an aqueous standard solution (D) each containing 6 µg/mL of resorcinol.
Ointment sample (ACNOMEL®)
Standard.
2.a.) First derivative order spectra
2.b.) Second derivative order spectra
2.c.) Third derivative order spectra
2.d.) Fourth derivative order spectra
2.e.) Fifth derivative order spectra

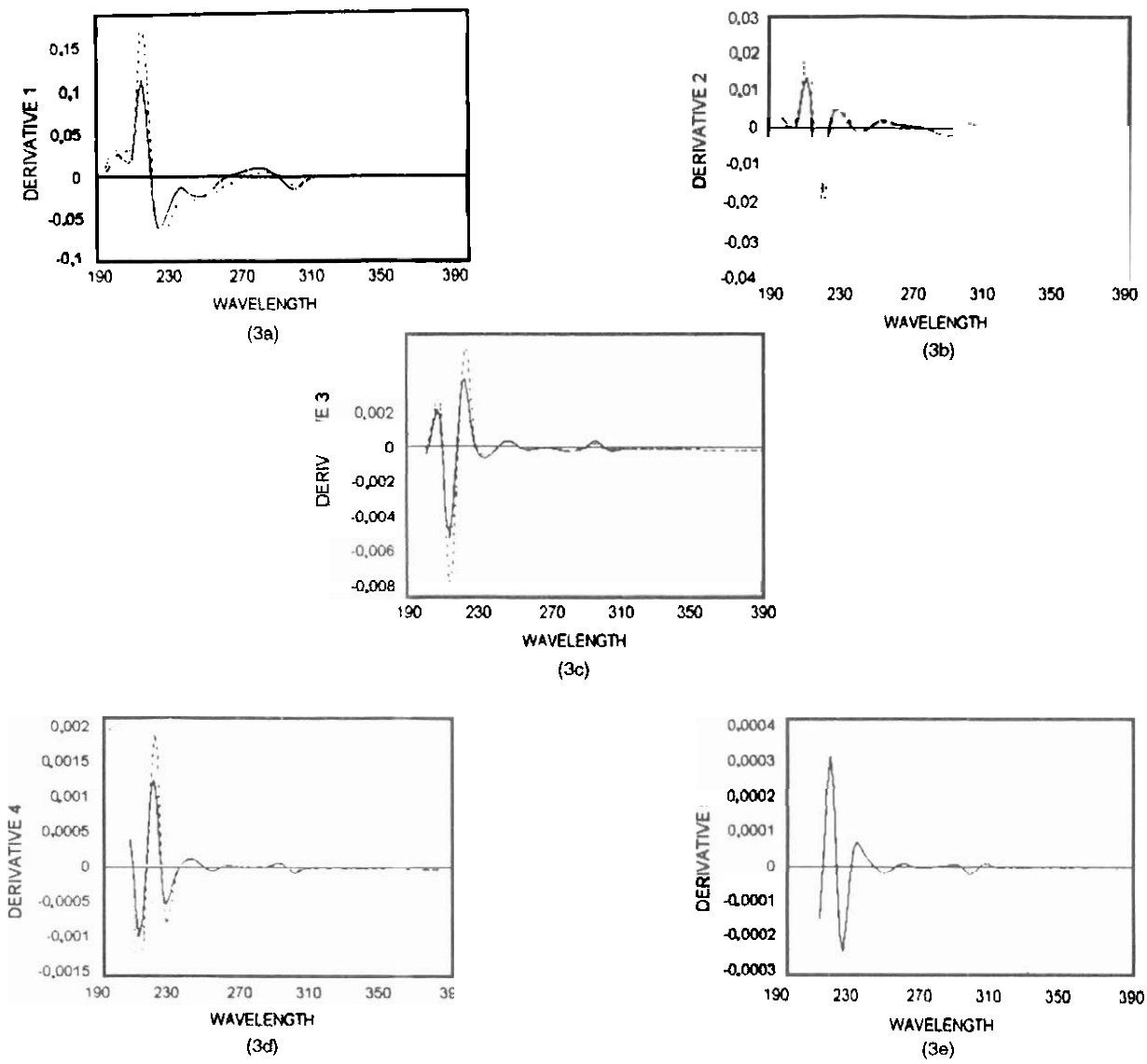

Figure 3. Derivative spectra of a suspension sample (B) and an aqueous standard solution (D) each containing 6 µg/mL of resorcinol.
Suspension sample (ACNISDIN®)
Standard.
3.a.) First derivative order spectra
3.b.) Second derivative order spectra
3.c.) Third derivative order spectra
3.d.) Fourth derivative order spectra
3.e.) Fifth derivative order spectra

as well as data concerning the coefficient of variation for three independent analysis of each sample, and the relative error obtained by comparison with the reported value.

The peaks at 242 nm in the fourth derivative spectra and 272 nm in the third one gave the lowest relative errors in the determination of resorcinol in ACNOMEL® (-0.5 and -2.0% respectively) with coefficients of variation of 3.5 and 2.5%, respectively.

The peak at 236 nm in the third derivative gave the lowest relative error in the determination of resorcinol in the ACNISDIN® sample suspension (+4.5%) with a coefficient of variation for this sample of 2.4%.

A statistical test (16) has been used to study the agreement of the means using the peak at 242 nm in the fourth derivative spectra for ACNOMEL® and the peak at 236 nm in the third derivative for ACNISDIN®

The difference between the mean obtained by the derivative spectrophotometric determination and the value given by the manufacturers is not statistically significant at the 5% level (probability = 95%) in all the cases because it is less than the confidence limit of the mean.

We wish emphasize that only one paper about the determination of resorcinol using derivative spectrophotometry has been found in a computerized revision by the Analytical Abstracts (17) and, in this paper, samples (except mouth-wash preparations) not were directly analyzed, they were previously extracted with HCl (0.1 M) and the extract was filtered.

Conclusion

The use of UV derivative spectra permits the direct determination of resorcinol in pharmaceuticals without requiring any previous separation step, thereby avoiding the matrix effects observed when using the zero order absorption spectra.

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