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Derivative UV-spectroscopic determination of salbutamol sulphate in the presence of gelatin

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Summary

Gelatin has been found to interfere in the accurate estimation of salbutamol sulphate by visible UV spectroscopy. UV-spectrophotometric determinations by zero-, second- and fourth-orders were carried out for aqueous solutions containing a fixed concentration of salbutamol sulphate (20 μg/ml) and varying concentrations of gelatin (1–8 μg/ml; 10–80 μg/ml). Results of observations show that as the order of the derivative is increased, the spectral interference by gelatin is decreased significantly.

Introduction

The quality control of drugs and excipients before and after formulation often involves the use of visible-UV spectrophotometry for qualitative and, more probably, quantitative analysis. Unless the drug components are separated selectively from the formulation matrix, their spectra can be subject to serious interference by those formulation components which also absorb in the same parts of the spectra (Thomas et al., 1977; Fell, 1978; Fasanmade and Fell, 1985). Spectral overlap and non-specific, irrelevant absorption adversely affect the interpretation of data for even the simplest single-component drug systems, leading to variable intercepts on the absorbance axis and systematic errors in the graphs of absorbance versus concentration (Shiga et al., 1971; O'Haver and Green, 1975a; Shibata, 1976). For this reason, the precise determination of λ_{max} of a broad peak or resolution of a multi-component mixture where peak overlap is present, can be difficult.

The measurement techniques that are very sensitive often lack the inherent selectivity to allow straightforward application to the kind of highly complex materials for which the analytical chemist is often called upon to develop analytical methods. Prior separation procedures involving extraction, chromatography and others are often useful and indeed essential. But there are applications in which, for reasons of speed and simplicity, a more direct approach will be desirable. Thus, there has always been interest in the techniques that can improve the selectivity of measurement methods themselves. Among the most conceptually simple

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of these methods is derivative spectroscopy (Hammand and Price, 1953; Morrison, 1953; Giese and French, 1955; Collier and Singleton, 1956; Martin, 1957, 1959; O'Haver and Green, 1975b).

Gelatin, a heterogeneous product, is a very commonly employed pharmaceutical excipient for many of the classical dosage forms, as well as for some of the novel delivery devices. Gelatin microspheres have been prepared containing drugs like 5-fluorouracil and salbutamol sulphate. It has been observed that gelatin causes significant interference in the in vitro estimation of the drugs when analyzed by direct, non-isolating techniques

TABLE 1

UV absorbance (^0D) of solutions containing salbutamol sulphate (20 μg/ml) and gelatin (1–8 μg/ml)

Concentration of gelatin (μg/ml)	Zero order	
	Absorbance ± S.D.	Percent error
1.0	0.5322 ± 0.0200	0.69
2.0	0.5356 ± 0.0360	1.33
3.0	0.5455 ± 0.0150	3.20
4.0	0.5633 ± 0.0100	6.60
5.0	0.5699 ± 0.0600	7.25
6.0	0.5799 ± 0.0100	9.71
7.0	0.5852 ± 0.0400	10.71
8.0	0.6010 ± 0.0206	13.70

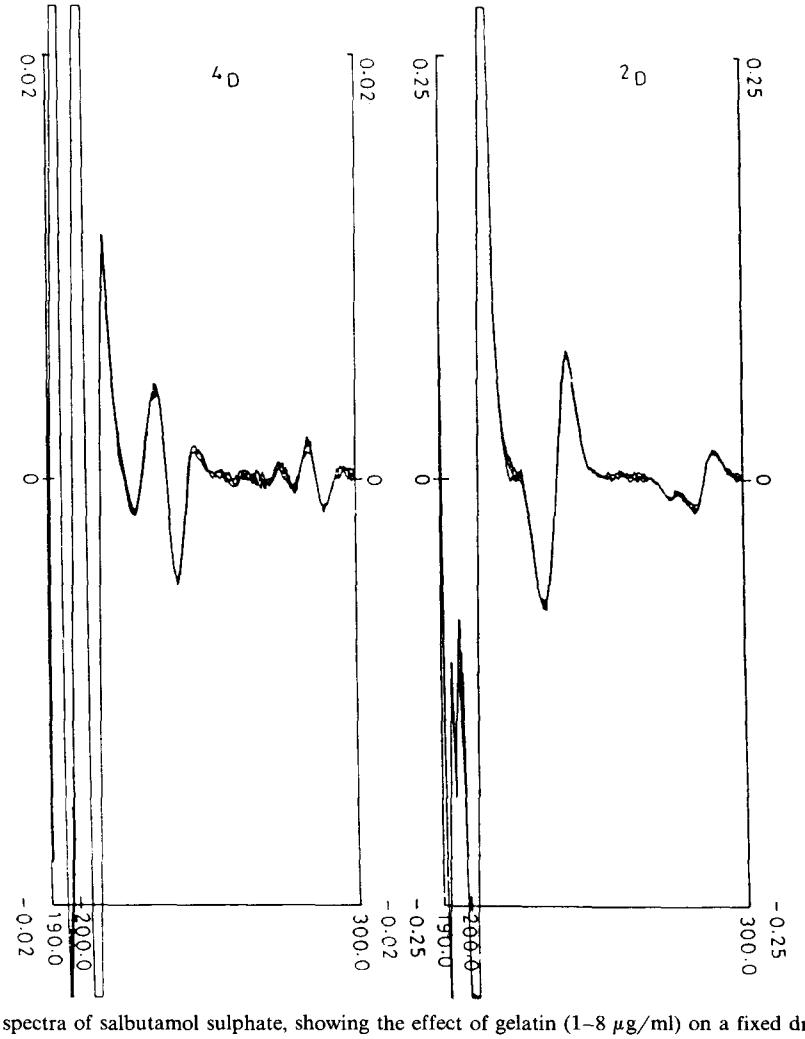

Fig. 1. UV-derivative spectra of salbutamol sulphate, showing the effect of gelatin (1–8 μg/ml) on a fixed drug concentration of 20 μg/ml.

like visible and UV spectroscopy. In the present study, the derivative UV-spectroscopic technique has been used to analyze salbutamol sulphate in the presence of gelatin.

Experimental

Materials and equipment

Salbutamol sulphate (Ranbaxy Laboratories, India) and gelatin, type-B (Associated Capsules Ltd, India) were used.

A Shimadzu UV-260 double-beam spectrophotometer was used for the analysis.

Procedure

Aqueous solutions of salbutamol sulphate were prepared, each containing a fixed amount of the drug (20 μg/ml) and varying concentrations of gelatin, from 1, 2, up to 8 μg/ml and, 10, 20, up to 80 μg/ml. Zero-order (^{0}D), second-order (^{2}D) and fourth-order (^{4}D) UV absorption spectra were recorded for each solution against distilled water as blank. The absorbance was noted at 224.2 nm for ^{0}D. The amplitude of the peak lying between 236 and 227 nm for ^{2}D, and that between 236 and 228 nm for ^{4}D, were measured. Results of six determinations are shown. The order of the derivative (0, 2, 4) has been numerically indicated at the appropriate places by designation as a superor subscript.

Results and Discussion

UV spectra of solutions having a fixed quantity of salbutamol sulphate and varying quantities of gelatin should merge with each other as a perfect overlap if there is no interference from the latter. Table 1 shows the UV absorbance (^{0}D) spectra of solutions containing 20 μg/ml of salbutamol sulphate and 1–8 μg/ml of gelatin. Keeping a ceiling of 1.0 for percentage error, only 1.0 μg/ml of gelatin can be present in solution for an accurate estimation of 20 μg/ml of salbutamol sulphate. The correlation coefficient, r^0, equals 0.9915 and the regression equation is given as $y_0 = 0.01x + 0.519$, where x is the concentration of gelatin (μg/ml) in solution and y_0 is its corresponding absorbance.

By derivatization of the above discussed ^{0}D absorbance into ^{2}D and ^{4}D, the spectra obtained (Fig. 1) show overlap of the bands due to different gelatin solutions. Relevant statistical data cannot be calculated as there is no correlation in the amplitude with respect to concentration of gelatin. Percentage errors for ^{2}D and ^{4}D were 0.02 and 0.75, respectively.

TABLE 2

UV absorbance (^{0}D) / amplitude (^{2}D, ^{4}D) of solutions containing salbutamol sulphate (20 μg / ml) and gelatin (10–80 μg / ml)

Concentration of gelatin (μg/ml)	Zero order		Second order		Fourth order	
	Absorbance ± S.D.	% error	Amplitude ± S.D.	% error	Amplitude ± S.D.	% error
10.0	0.6073 ± 0.0278	14.89	4.4190 ± 0.1249	−00.67	3.450 ± 0.054	0.12
20.0	0.6685 ± 0.0224	26.47	4.4090 ± 0.0797	−00.90	3.445 ± 0.093	0.03
30.0	0.7111 ± 0.0264	34.53	4.2760 ± 0.0740	−03.89	3.434 ± 0.095	0.35
40.0	0.7506 ± 0.0113	42.01	4.0925 ± 0.1067	−08.01	3.442 ± 0.040	0.12
50.0	0.8124 ± 0.0062	53.70	3.9840 ± 0.1246	−10.45	3.461 ± 0.020	0.43
60.0	0.8288 ± 0.0215	56.80	3.9166 ± 0.0830	−11.97	3.430 ± 0.105	0.46
70.0	0.8799 ± 0.0129	66.47	3.8928 ± 0.0609	−12.50	3.461 ± 0.070	0.44
80.0	0.9229 ± 0.0204	74.60	3.8600 ± 0.0619	−13.24	3.456 ± 0.050	0.29
	$r^0 = 0.9956$		$r^2 = -0.9669$		$r^4 = 0.3200$	
	$b^0 = 0.0044$		$b^2 = -0.0091$		$b^4 = 0.0001$	
	$y_0 = 0.0044x + 0.5747$		$y_2 = -0.0091x + 3.6967$		$y_4 = 0.0001x + 3.4429$	

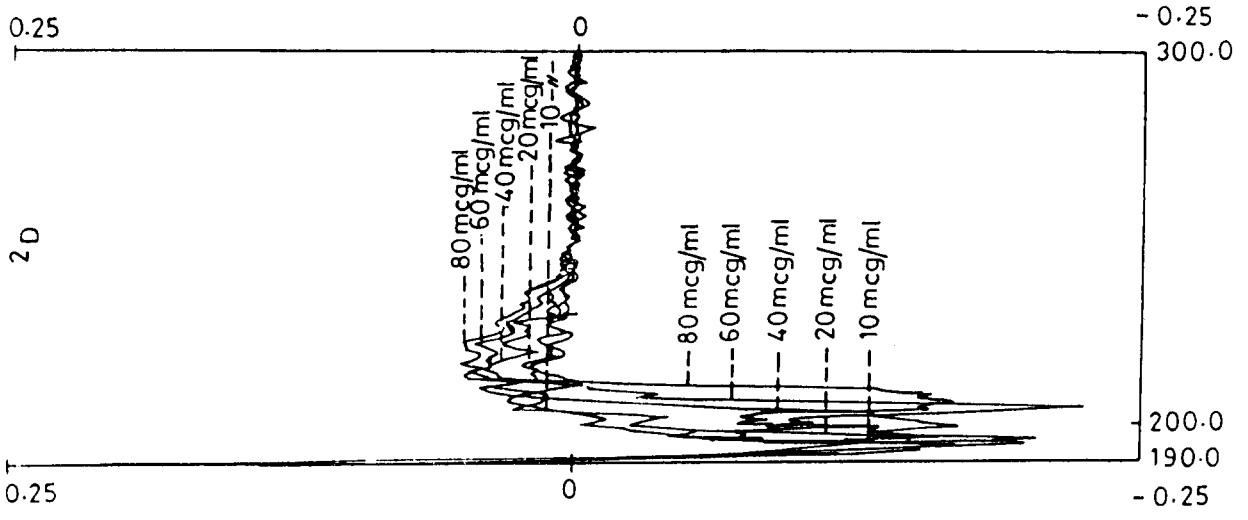

Fig. 2. UV-derivative (^{2}D) spectra of aqueous solutions of gelatin (10–80 μg/ml).

By increasing the concentration of gelatin (10–80 μg/ml) in solutions containing the same amount of salbutamol sulphate (20 μg/ml) a progressive increase in percentage error in ^{0}D was found (Table 2). Based upon amplitude measurements for ^{2}D, 20 μg/ml of the drug can be analyzed in the presence of as high as 20 μg/ml of gelatin. However, it should be noted from Table 2 that as the concentration of gelatin increases, the amplitude in the ^{2}D spectra progressively decreases. Hence, all the percentage error values have negative prefixes. This can be justified based on ^{2}D spectra of pure gelatin, as shown in Fig. 2. Gelatin shows a sharp dip between 190 and 210 nm and a concentration-dependent rise between 215 and 230 nm. Since the ^{2}D amplitude for salbutamol sulphate is measured as the difference in height between the trough at 227 nm and the crest at 236 nm, the trough at 227 nm due to the drug is progressively raised upwards with increasing levels of gelatin. Since, at around 236 nm, the gelatin bands become convergent and horizontal, the crest at that wavelength due to the drug is not affected by gelatin. Hence, the overall difference in amplitude between 227 and 236 nm progressively decreases with rising concentrations of gelatin.

The result obtained from the measurement of amplitude in ^{4}D spectra is very encouraging, as can be seen from Table 2. The percentage error is less than 1.0 for all concentrations of gelatin. This is also reflected in the low value for coefficient of correlation.

Conclusion

The UV-derivatized spectrophotometric study (^{0}D, ^{2}D, ^{4}D) of solutions containing a fixed concentration of salbutamol sulfate (20 μg/ml) and varying quantities of gelatin (1–8 μg/ml and 10–80 μg/ml) produced the following results. Setting 1.0% as the maximum limit of error, the drug (2.0×10^{-5} g/ml) can be analyzed in the presence of gelatin to an extent of only 1.0×10^{-6} g/ml by ^{0}D, 2.0×10^{-5} g/ml by ^{2}D and up to 8.0×10^{-5} g/ml by ^{4}D.

References

Collier, G.L. and Singleton, F., *J. Appl. Chem.*, 6 (1956) 495.
Fasanmade, A.A. and Fell, A.F., *Analyst*, 110 (1985) 1117–1124.

Fell, A.F., *Proc. Anal. Div. Chem. Soc.*, 15 (1978) 260.
Giese, A.T. and French, C.S., *Appl. Spectrosc.*, 9 (1955) 78.
Hammand, V.J. and Price, W.C.J., *J. Opt. Soc. Am.*, 43 (1953) 924.
Martin, A.E., *Nature*, 180 (1957) 231.
Martin, A.E., *Spectrochim. Acta*, 14 (1959) 97.
Morrison, J.D., *J. Chem. Phys.* 21 (1953) 1967.
O'Haver, T.C. and Green, G.L., *Int. Lab.*, 5 (1975a) 11.
O'Haver, T.C. and Green, G.L., *Int. Lab.*, 6 (1975b) 11.
Shibata, S., *Angew. Chem. Int. Ed. Eng.*, 15 (1976) 673.
Shiga, T., Shiga, K. and Kuroda, M., *Anal. Biol. Chem.*, 44 (1971) 291.
Thomas, E.C., Robert, E.S. and Harry, L.P., *Anal. Chem.*, 49 (1977) 876.