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Short Communication

Spectrophotometric determination of terbutaline and orciprenaline sulphate through diazo coupling with *o*-nitroaniline and *p*-aminobenzoic acid

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Introduction

Terbutaline sulphate and orciprenaline sulphate are sympathomimetic agents, used as bronchodilators. They have been determined by different techniques, including titrimetry [1, 2], spectrophotometry [3] and chromatography [5, 6]. The suggested method is a simple spectrophotometric one.

Experimental

Instrument

A Jasco-UVIDEC 320 spectrophotometer (Double beam) was used.

Materials and reagents

Terbutaline sulphate, orciprenaline sulphate, bricanyl tablets (labelled to contain 2.5 mg terbutaline per tablet), alupent tablets (labelled to contain 20 mg orciprenaline per tablet) and alupent injection (labelled to contain 0.5 mg orciprenalline per ampoule), were obtained from Cid Co. (Egypt). Working solutions of orciprenaline or terbutaline sulphate (25 mg/100 ml aqueous solution), *o*-nitroaniline solution (1 mg ml^{-1} of 1.5 N hydrochloric acid), *p*-aminobenzoic acid solution (1 mg ml^{-1} or 1.5 N hydrochloric acid), 1% aqueous solution of sodium hydroxide, 0.1% aqueous solution of sodium nitrite, and trimethylamine (Merck) were used.

Procedures

Procedure 1 (using diazotized o-nitroaniline).

(A) Pure orciprenaline and terbutaline sulphate. Pipette 1 ml of *o*-nitroaniline solution into a 25-ml volumetric flask. Add 2.5 ml of 0.1% sodium nitrite solution and mix. Add accurately measured aliquots of orciprenaline or terbutaline sulphate solution (equivalent to 0.05–0.35 mg), followed by 2.5 ml of 1% sodium hydroxide solution. Mix the contents, and dilute to volume with distilled water. Measure the absorbance at 455 nm against blank prepared in the same way neglecting the orciprenaline or terbutaline sulphate.

(B) Pharmaceutical preparations for tablets. Thoroughly triturate the contents of 20 tablets of terbutaline or orciprenaline sulphate, then accurately weigh a quantity equivalent to 2.5 mg of the drug. Transfer to a 50 ml beaker, and dissolve in sufficient distilled water. Filter into a 50 ml volumetric flask and complete to volume with distilled water. Proceed as mentioned under procedure 1(A).

(C) Pharmaceutical preparations for ampoules. Pipette an aliquot of alupent ampoule equivalent to 25 mg of orciprenaline sulphate into a 50 ml volumetric flask and complete to volume with distilled water. Proceed as mentioned under procedure 1(A).

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Procedure 2 (using p*-aminobenzoic acid).*
(A) Pure orciprenaline and terbutaline sulphate. Pipette 1 ml of *p*-aminobenzoic acid into a 25-ml volumetric flask. Add 2.5 ml 0.1% sodium nitrite solution, and mix well. Add accurately measured aliquots of orciprenaline or terbutaline sulphate solution (equivalent to 0.025–0.175 mg), followed by 3.5 ml of trimethylamine. Mix the contents and dilute to volume with distilled water. Measure the absorbance at 440 nm against a blank prepared in the same way neglecting the orciprenaline or terbutaline.

(B) Pharmaceutical preparations. Proceed as mentioned under procedure 1(B) to get the prepared solution from either tablets or ampoules. Then proceed as under procedure 2(A).

Calculation

Using the least-squares method the calibration graphs were described by the following regression equations:

Procedure 1 (using diazotized *o*-nitroaniline)

$A = 0.0127 + 0.8827C$

$r = 0.99995$

relative Y-intercept = 0.00253,

Procedure 2 (using diazotized *p*-aminobenzoic acid)

$A = 0.00696 + 1.368C$

$r = 0.995$

relative Y-intercept = 0.001851,

where C is the concentration in mg% in final solution.

Discussion

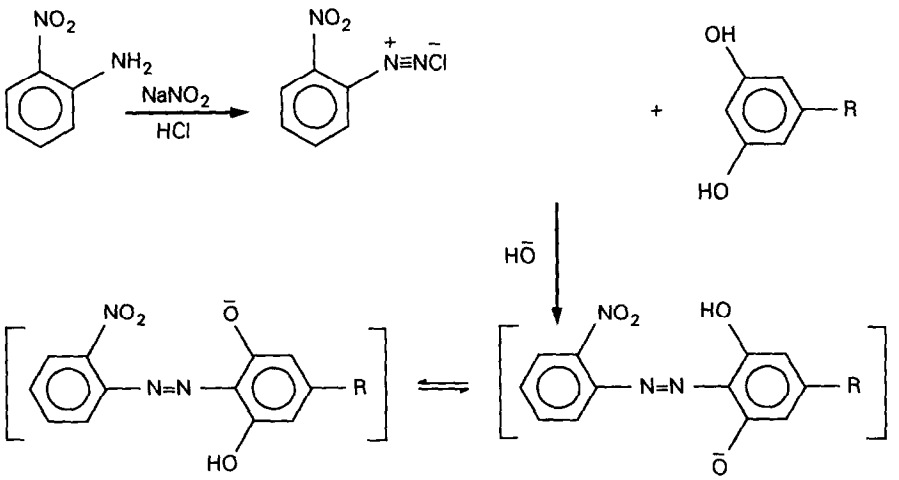
The utility of diazotized *o*-nitroaniline and *p*-aminobenzoic acid as chromogenic reagents for the determination of orciprenaline and terbutaline sulphate is investigated here. Generally, the coupling reaction between diazonium salts and phenolic compounds takes place in *para-* and *ortho-* positions to OH— group in the molecule. Thus the reaction may be represented by Scheme 1.

The optimum conditions for the procedures have been studied. Maximum absorption for orciprenaline and terbutaline azodyes was found to be the same applying both reactions. Coupling with diazotized *o*-nitroaniline and *p*-aminobenzoic acid produces azodyes having a maximum at 455 and 440 nm, respectively.

The effect of 0.1% sodium nitrite solution was studied and maximum absorbance occurred upon addition of 2 ml in both procedures. An alkaline medium is essential for the incidence of the coupling reaction, addition of 2.5 ml of sodium hydroxide solution is optimum for procedure 1, but it is unsuitable for procedure 2, it gives unstable colour. Many trials were carried out and it was found that triethylamine gives a stable colour, and maximum absorbance occurs upon addition of 3 ml of triethylamine base (Figs 1 and 2).

For further study of the reaction, the molar ratio of terbutaline or orciprenaline sulphate to

Using *o*-nitroaniline:



Scheme 1

Table 1
Statistical analysis of results obtained using the proposed methods and official methods for the analysis of authentic samples

	Orciprenaline sulphate				Terbutaline sulphate			
Statistic	Proposed method (1)	BP 1980 method	Proposed method (2)	BP 1980 method	Proposed method (1)	USP 1980 method	Proposed method (2)	USP 1980 method
Mean recovery, % ($p = 0.05$)	100.64 ± 0.99	101.3 ± 1.22	100.00 ± 1.26	98.91 ± 1.45	99.66 ± 0.74	100.6 ± 0.92	100.92 ± 1.03	99.30 ± 1.21
SD	1.041	1.277	1.317	1.52	0.779	0.964	1.085	1.269
N	5	5	5	5	5	5	5	
Variance	1.083	1.632	1.735	2.31	0.608	0.931	1.777	1.611
t-test	0.896 (2.131)		1.21 (2.13)		1.696 (2.131)		2.13 (2.31)	
F-test	1.51 (6.39)		1.33 (6.39)		1.53 (6.39)		1.37 (6.39)	

Table 2
Statistical analysis of the results obtained for pharmaceutical dosage forms using the proposed method (1) compared with official methods

	Orciprenaline sulphate				Terbutaline sulphate	
	Tablets		Injections		Tablets	
Statistic	Proposed method	BP 1980 method	Proposed method	BP 1980 method	Proposed method	USP 1980 method
Mean recovery, % ($p = 0.05$)	99.10 ± 0.496	100.0 ± 0.916	99.70 ± 0.47	99.20 ± 0.87	100.16 ± 0.65	101.05 ± 0.97
SD	0.603	0.961	0.659	0.918	0.680	1.017
N	&6	5	6	5	5	5
Variance	0.364	0.952	0.324	0.844	0.463	1.036
t-test	1.818 (2.26)		1.106 (2.26)		0.837 (2.13)	
F-test	2.54 (5.19)		2.605 (6.30)		2.237 (6.39)	

Table 3
Statistical analysis of the results obtained for pharmaceutical dosage forms using the proposed method (2) compared with official methods

	Orciprenaline sulphate				Terbutaline sulphate	
	Tablets		Injections		Tablets	
Statistic	Proposed method	BP 1980 method	Proposed method	BP 1980 method	Proposed method	USP 1980 method
Mean recovery, % ($p = 0.05$)	99.62 ± 0.57	100.52 ± 0.94	100.98 ± 0.57	101.7 ± 0.99	100.76 ± 0.49	100.35 ± 0.63
SD	0.593	0.991	0.593	1.035	0.512	0.664
N	5	5	5	5	5	5
Variance	0.352	0.984	0.352	1.072	0.263	0.441
t-test	1.74 (2.13)		1.34 (2.13)		1.09 (2.13)	
F-test	2.80 (6.39)		3.05 (6.39)		1.68 (6.39)	

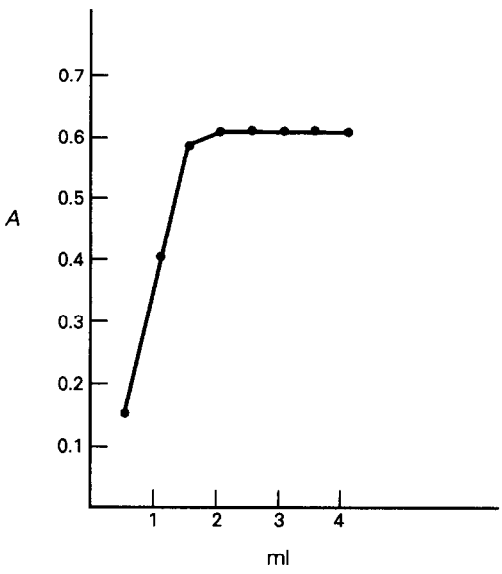


Figure 1
Effect of volume of 1.0% sodium hydroxide on the absorbance of orciprenaline sulphate (or terbutaline sulphate) — 0.7 mg% — coupled with diazotized *o*-nitroaniline.

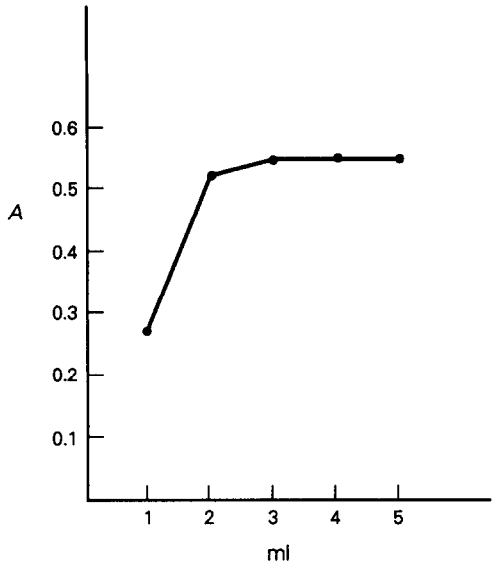


Figure 2
Effect of volume of trimethylamine on the absorbance of orciprenaline sulphate (or terbutaline sulphate) — 0.4 mg% — coupled with diazotized *p*-aminobenzoic acid.

diazotized *o*-nitroaniline and *p*-aminobenzoic acid has been determined and it was found to be 1:1.

Beer's law is obeyed in the range 2–14 μg ml^{-1} for both orciprenaline and terbutaline sulphate, applying procedure 1, and 1–7 μg ml^{-1} applying procedure 2.

The proposed methods were applied for the determination of different concentrations of terbutaline and orciprenaline sulphate in their pure forms, and results obtained were compared with the official USP colorimetric method [1] and BP spectrophotometric method [2], respectively. Statistical analysis of the results revealed that there is no significant difference regarding precision and accuracy as indicated by *t*- and *F*-tests, respectively (Table 1).

Applying the proposed methods for determination of orciprenaline in alupent tablets and injections, and terbutaline sulphate in bricanyl tablets, and the results obtained, are compared with official methods. Statistical analysis of the results, shows that the proposed method is equally precise and accurate as the official methods (Tables 2 and 3). Also, the proposed method has the advantage over the USP 1980 method, in that the produced colour is stable for several hours, whereas the colour produced in the official one is stable for only 75 s.

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