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QUANTITATIVE DETERMINATION OF TROVENTOL FROM AEROSOLS BY REVERSED PHASE LIQUID CHROMATOGRAPHY

V.G. Nayak, V.B. Malkar, C.D. Gaitonde*, A.J. Vaidya and M.G. Gangrade

Research & Development Laboratory,
CIPLA LTD.,Vikhroli, Bombay 400 083, India.

ABSTRACT

Troventol, an anticholinergic agent and a derivative of atropine was estimated quantitatively from the samples of aerosols. An isocratic, reversed-phase liquid chromatographic method was developed using a C6, 5-um column with mobile phase acetonitrile-water-diethylamine-phosphoric acid (40:60:0.1:0.1, v/v) filtered through 0.45-micron and degassed before use. Salbutamol in combination with troventol from an aerosol preparation was also determined simultaneously by the present method. Recoveries obtained for troventol as well as for salbutamol were in the range 98.0 to 102.0% from aerosols, monitored at wavelength 215 nm. A flow rate of 1.0 mL/min was maintained throughout the analysis.

INTRODUCTION

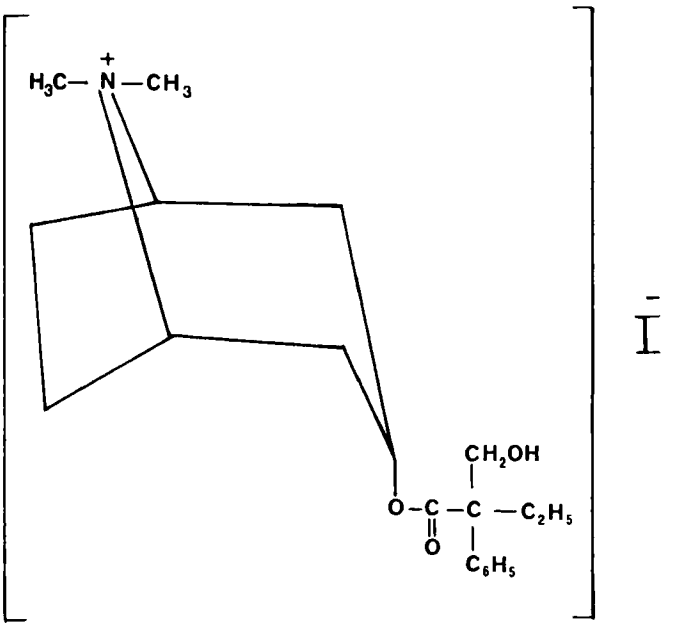
The importance of antiasthamatics and anticholinergic agents in treating asthama related diseases has burgeoned both in medical and pharmaceutical science. An important question entails the activity of anticholinergic agents when monitored from an aerosol preparation. A great increase in the use of compounds like salbutamol sulfate, terbutaline sulfate , metaproterenol sulfate from an aerosol inhalation has gained popularity since a decade.

In just 5 years or so, new entities, derivatives of atropine, namely ipratropium bromide (1-4) and troventol (5,6) has emerged successfully for their use in the management of asthama. Troventol, shown in Figure 1, exhibits remarkable anticholinergic activity when administered in the form of an aerosol. There are no known methods published in the literature for the estimation of troventol.

The purpose of this work is to develope a HPLC method for determining troventol from an aerosol cannister quantitatively. The same method was extended for determining salbutamol base from a combined formulation of troventol and salbutamol.

EXPERIMENTAL

Apparatus: A liquid chromatograph (TOSOH Corporation, Japan) consisting of CCPE, dual-piston reciporcating pump, UV 8011, UV-visible detector and a Rheodyne injector fitted with a 100-μL loop. The column used was MEDPHARMEX, C6, 250 mm X 4.6 mm, 5 micron from Medpharmex Inc., CA, U.S.A. Data



TROVENTOL

FIGURE 1 : Structure of Troventol

acquisition was accomplished by using an integrator, CHROMATCORDER from TOSOH.

Reagents and Chemicals: Analytical reagent grade diethylamine, orthophosphoric acid (85%), HPLC grade acetonitrile (E. Merck India Ltd., Bombay, India) and distilled deionised water prepared in our laboratory was used to prepare the mobile phase.

Reference Standards: Standards of troventol (purity 99.8%, 250 µg/mL), salbutamol base (purity 99.9%, 1 mg/mL) were prepared in water and water-methanol(1:1) mixture respectively. The calibration curve for troventol as well as salbutamol was prepared in the range 20 to 100 µg/mL.

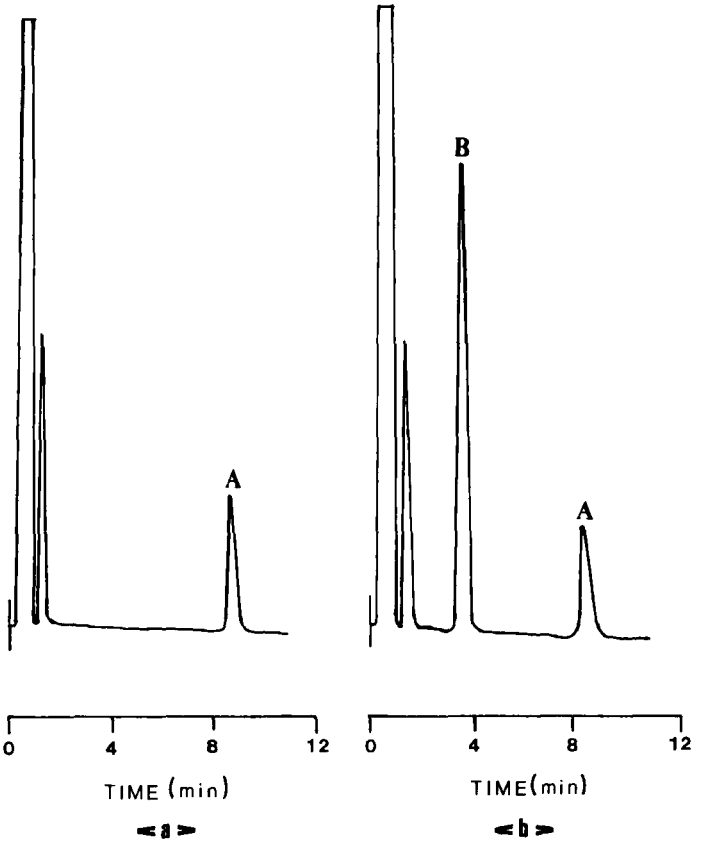


FIGURE 2 : **(a)** A chromatogram of troventol (A) from an aerosol formulation (100-µL), **(b)** A chromatogram of troventol (A) plus salbutamol (B) from an aerosol formulation (100-µL). For chromatographic conditions see text.

Sample preparation: (Troventol aerosol spray and with combination of salbutamol sulfate)

In a 100-mL beaker containing 50-mL acetonitrile, 50 sprays of troventol were actuated The contents were then warmed at 50°C for 5 min. The final solution was cooled to ambient temperature, diluted to 50 mL with acetonitrile and directly used for analysis. The container was shaken after actuation

TABLE I

RECOVERY OF TROVENTOL AND SALBUTAMOL FROM AEROSOL CANNISTERS

Conc. Added (µg/spray)	Conc. Found (µg/spray)	%Recovery (Mean ± S.D. n = 3)	Coefficient of variation (%)
FOR TROVENTOL (WITHIN-DAY STUDY)			
10.0	9.88	98.8 ± 1.28	1.29
20.0	20.10	100.5 ± 1.55	1.54
FOR TROVENTOL (DAY-TO-DAY STUDY)			
10.0	9.92	99.2 ± 1.41	1.42
20.0	19.82	99.1 ± 1.38	1.39
FOR SALBUTAMOL (WITHIN-DAY STUDY)			
5.0	5.05	101.0 ± 1.81	1.79
10.0	9.80	98.0 ± 1.70	1.73
FOR SALBUTAMOL (DAY-TO-DAY STUDY)			
5.0	4.94	98.8 ± 1.69	1.71
10.0	10.06	100.6 ± 1.29	1.28

of every 10 sprays. Similar procedure was followed for combination aerosol : troventol plus salbutamol.

RESULTS AND DISCUSSION

The determination of troventol from aerosol evolved problems of investigating a suitable mobile phase that would separate the drug from the excipients. However,

addition of diethylamine to the mobile phase gave sufficient selectivity to achieve the separation of troventol from salbutamol as well from excipients. This is evident from a chromatogram obtained from an aerosol sample as shown in Figures 2 (a) and (b).

Quantitative determination was accomplished by the external standardisation method. The response of the detector was found to be linear with a regression equation Y = 0.14051 x + 0.91099 (r=0.998) for troventol individual and Y = 0.13517 x + 0.92456 (r=0.997), Y = 0.24908 x - 0.22069 (r=0.998) for troventol plus salbutamol respectively. Detection levels of troventol were estimated to be 5 µg/mL monitored at 215 nm, 0.05 A.U.F.S.

The recovery of troventol as well as combination with salbutamol was assessed by comparing peak areas from the standard stock solutions of the drug added to the preanalysed samples. For confirming the precision of the assay method reproducibilities for within-day and day-to-day variations were determined. Results are summarised in Table I.

The method described is rapid and precise and can be conveniently adapted for routine quality control analysis.

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