Asian Journal of Chemistry Vol. 11, No. 3 (1999), 922–926

Extractive Spectrophotometric Determination of Dextromethorphan Hydrobromide and Triprolidine Hydrochloride from Liquid Dosage Form

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Two accurate methods have been developed for the simultaneous analysis of dextromethorphan hydrobromide and triprolidine hydrochloride from liquid dosage forms. First method depends on derivative spectrophotometry with zero crossing point technique of measurement, whereas another method is based on measurement of absorbances of sample solution at 278 and 300 nm. Beer's law is followed up to 180 μg/mL of dextromethorphan hydrobromide and 15 μg/mL of triprolidine hydrochloride. The methods have been validated statistically and by recovery studies.

INTRODUCTION

Dextromethorphan hydrobromide, chemically ent-3-methoxy-9a-methylmorphinan hydrobromide monohydrate, is a non-narcotic antitussive used for the relief of unproductive cough. It is official in IP[1], BP[2] and USP[3]. IP, BP and USP describe titrimetric assay procedure for the analysis of dextromethorphan hydrobromide in powder form. For its syrup formulation, IP and USP describe HPLC method. Few spectrophotometric[4–6] and HPLC[7] methods are reported in literature for its estimation in single as well as in combined dosage forms.

Triprolidine hydrochloride, chemically (E)-2-(3-pyrrolidin-1-yl-1-*p*-tolylprop-1-enyl) pyridine hydrochloride monohydrate, is an antihistaminic agent. It is official in IP[8], BP[9] and USP[10]. Non-aqueous titrimetric method has been described in IP, BP and USP for the analysis of triprolidine hydrochloride. For the formulations containing triprolidine hydrochloride, IP and BP describe spectrophotometric method, whereas USP describes HPLC method. Some other methods reported in literature for the analysis of triprolidine hydrochloride in single as well as combined dosage forms include spectrophotometry[11, 12] polarography[13] and HPLC[14, 15]. But no analytical method is reported for simultaneous analysis of dextromethorphan hydrobromide and triprolidine hydrochloride from combined dosage forms. The present communication describes two accurate and precise methods for the simultaneous determination of dextromethorphan hydrobromide and triprolidine hydrochloride from combined liquid dosage formulation.

EXPERIMENTAL

Shimadzu (Model UV 160A) instrument was used for spectral measurement using 10 mm matched quartz cells. Instrumental parameters chosen were: spectral

bandwidth: 2 nm, scan speed: 480 nm/min, wavelength range: 340–240 nm and wavelength sampling interval: 0.1 nm. Samples of dextromethorphan hydrobromide (IP) and triprolidine hydrochloride (IP) were procured from Nicholas Piramal India Limited. Hydrochloric acid (Ranbaxy, AR grade), *n*-hexane (Merck, spectroscopic grade), ammonia (Qualigens) and double distilled water were used in the present work.

Method I: Employing Derivative Spectrophotometry

Overlay spectrum of dextromethorphan hydrobromide and triprolidine hydrochloride is shown in Fig. 1 and overlay first order derivative spectrum ($\Delta\lambda = 7.2$ nm) of both the drugs in shown in Fig. 2.

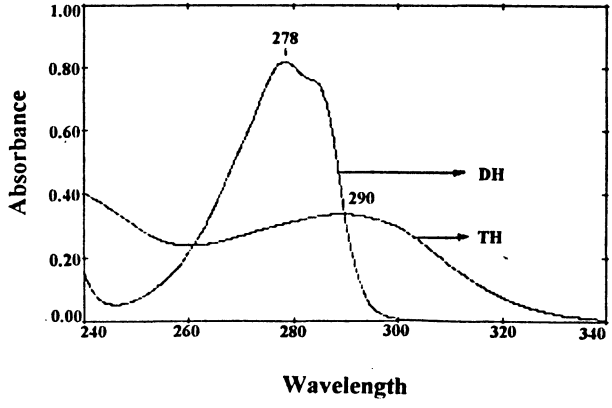

Fig. 1 Overlay spectrum of dextromethorphan hydrobromide (DH) and triprolidine hydrochloride (TH).

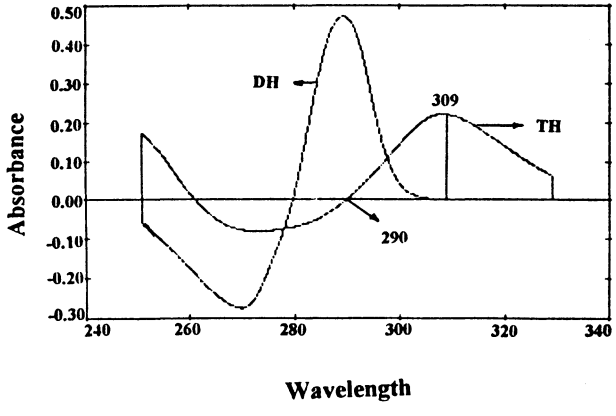

Fig. 2 First order derivative spectrum of dextromethorphan hydrobromide (DH) and triprolidine hydrochloride (TH).

First order derivative spectrum reveals that triprolidine hydrochloride shows absorbance maximum at 309 nm, where absorbance due to dextromethorphan

hydrobromide is zero. Similarly at the zero crossing point on the first derivative spectrum of triprolidine hydrocloride, *i.e.*, at 290 nm, dextromethorphan hydrobromide shows substantial absorbance. Hence 290 nm and 309 nm were the two wavelengths selected for the estimation of dextromethorphan hydrobromide and triprolidine hydrochloride respectively.

Standard stock solutions of dextromethorphan hydrobromide (600 μg/mL) and triprolidine hydrochloride (50 μg/mL) were prepared separately in 0.1 N hydrochloric acid. By appropriate dilutions of standard stock solutions, six mixed standard solutions containing dextromethorphan hydrobromide and triprolidine hydrochloride in the concentration ratio of 30 : 2.5, 60 : 5, 90 : 7.5, 120 : 10, 150 : 12.5 and 180 : 15 (μg/mL) were prepared. These mixed standard solutions were scanned in the range of 340 to 240 nm and first derivative amplitudes at 290 and 309 nm were recorded. These spectral amplitudes were used to prepare calibration curves for dextromethorphan hydrobromide and triprolidine hydrochloride respectively. Coefficient of correlation for dextromethorphan hydrobromide and triprolidine hydrochloride was found to be 0.9996 and 0.9999 respectively.

Analysis of Commercial Formulation: 2 mL of commerical syrup sample containing dextromethorphan hydrobromide (12 mg) and triprolidine hydrochloride (1 mg) was pipetted in separating funnel. To it, 20 mL of water and 3 mL of 1 N hydrochloric acid was added and shaken well. It was extracted thrice with 25 mL portions of *n*-hexane. Solvent *n*-hexane layer was discarded.

Aqueous layer was made alkaline with 10 mL of ammonium hydroxide, and the resulting solution was extracted with three 25 mL portions of *n*-hexane. The combined *n*-hexane layer was washed with two 10 mL portions of water, and then extracted with successive amounts of 0.1 N hydrochloric acid (20, 20, 20, 20 and 10 mL), each time collecting the aqueous layer in 100 mL volumetric flask. Volume was made up to 100 mL with 0.1 N hydrochloric acid. Spectrophotometric analysis of resulting solution was carried out and concentration of dextromethorphan hydrobromide and triprolidine hydrochloride were obtained from calibration curves plotted. The results of replicate analysis with two different batches of the formulation and results of recovery studies are presented in Table-1.

TABLE-1
ANALYSIS OF COMMERCIAL FORMULATIONS

Method	DH			TH		
	Mean (%)* estimated ±S.D.	S.E.	R.S.	Mean (%)* estimated ±S.D.	S.E.	R.S.
Method I	99.90 (±1.02)	0.29	98.9–100.8%	99.94 (±0.74)	0.21	99.1–100%
Method II	100.52 (±1.14)	0.33	98.7–101.4%	100.02 (±0.80)	0.23	98.9–101%

*Average of six determinations each on two different batches of formulation:
H: Dextromethorphan hydrobromide TH: Triprolidine hydrochloride
SD: Standard deviation RS: Recovery studies.

Method II: Method based on the Property of Additivity of Absorbances

Standard calibration curve of triprolidine hydrochloride was plotted at 300 nm in the concentration range of 0–15 μg/mL. Standard calibration curves of dextromethorphan hydrobromide (0–180 μg/mL) and triprolidine hydrochloride (0–15 μg/mL) were plotted at 278 nm.

Triprolidine hydrochloride shows nearly an absorbance peak at 300 nm, where dextromethorphan hydrobromide shows zero absorbance. Hence, concentration of triprolidine hydrochloride in sample solution was obtained from the absorbance of the sample solution at 300 nm and calibration curve plotted at 300 nm.

Dextromethorphan hydrobromide shows an absorbance peak at 278 nm. Concentration of dextromethorphan hydrobromide in the sample solution was obtained from the absorbance contribution of dextromethorphan hydrobromide to the sample solution at 278 nm as follows:

$$A_1 = A - A_2$$

where

A_1 = absorbance contribution of dextromethorphan hydrobromide to the sample solution at 278 nm.

A = absorbance of the sample solution at 278 nm.

A_2 = absorbance contribution of triprolidine hydrochloride to the sample solution at 278 nm.

Absorbance contribution of the triprolidine hydrochloride to the sample solution (A_2) is obtained from the concentration of the triprolidine hydrochloride in the sample solution (which has been estimated earlier) and its calibration curve plotted at 278 nm.

Syrup sample solution was prepared as described under method I. Absorbances of the sample solution at 300 and 278 nm were noted and quantities of dextromethorphan hydrobromide and triprolidine hydrochloride present in the sample solution were calculated. Replicate analysis of two different batches of the formulation using the method showed impressive statistical parameters. The recovery studies were also satisfactory (Table-1).

RESULTS AND DISCUSSION

The proposed methods were found to be accurate and precise for routine simultaneous analysis of the two drugs in their combined dosage forms.

The first method, derivative spectroscopic method, requires spectral data processing. Wavelength range of 340 to 240 nm and derivative interval of 7.2 nm was selected keeping in view the sensitivity of measurements and spectral responses. Standard deviation values (1.02 for dextromethorphan hydrobromide and 0.74 for triprolidine hydrochloride) were satisfactory. Recovery studies close to 100% were indicative of the accuracy of the method.

The second method is a very simple method, which can be employed for analysis of these drugs in combined dosage forms using simplest form of

instrument. This method employs the fact that absorbance in an additive property. After recording the absorbances at the selected wavelengths, the concentration of the drugs can be found out by simple calculations. Standard deviation values obtained (1.14 for dextromethorphan hydrobromide and 0.80 for triprolidine hydrochloride) were somewhat higher than the first method. The recovery studies were close to 100% indicating the accuracy of the method.

ACKNOWLEDGEMENTS

Authors thank the Director, S.G.S.I.T.S., Indore and the Head, Department of Pharmacy, S.G.S.I.T.S., for providing experimental facilities for the work. One of the authors (S.G.) thanks CSIR, New Delhi, for the financial assistance provided. Authors are also thankful to Nicholas Piramal India Limited for gift samples of dextromethorphan hydrobromide and triprolidine hydrochloride.

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(*Received*: 28 January 1999; *Accepted*: 3 April 1999) AJC-1717