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EXTRACTIVE SPECTROPHOTOMETRIC AND CONDUCTOMETRIC ANALYSIS FOR DETERMINATION OF PROPANTHELINE BROMIDE FROM BULK DRUG AND ITS PHARMACEUTICAL FORMULATION.

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ABSTRACT

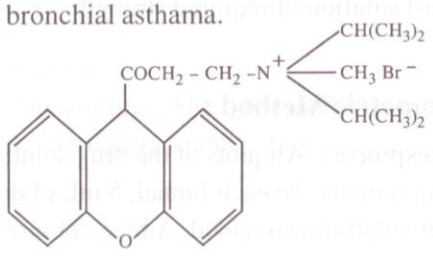
A simple extractive spectrophotometric and a sensitive conductometric method has been developed for the determination of propantheline bromide (P.B) from its bulk drug and pharmaceutical formulations. The method is based on the formation of a blue coloured ion–pair complex of drug and bromo phenol blue (BPB) in a solution buffered at pH 7.5 followed by its extraction in organic solvent (Chloroform). This light blue coloured complex has an absorption maximum at 600 nm which is stable upto 20 hrs. and Beer's law is obeyed in the concentration range 40 µg/mL to 140 µg/mL.

The conductivity measurements was carried out at different concentrations of PB before and after complexing it with BPB as it has different conductivities under non–complexing and complexing conditions. The advantage of the conductometric analysis of ion–pair complex lies in the fact that this method is applicable above 10 µg/mL whereas the direct conductometric measurements (non–complexing) can only be used for the quantitative estimation of PB above 500 µg/mL. Extractive spectrophotometric as well as conductometric methods were found to be precise and accurate for the determination of drug from its pharmaceutical and bulk form.

Key words : Propantheline Bromide, Extractive spectrophotometric, Conductometric analysis, Bromo phenol blue, Bulk drug, Pharmaceutical formulations

INTRODUCTION

Propantheline bromide i.e., N–N diisopropyl N–methyl– 2 [xanthane –9–4, carboxyl–oxy] ethyl ammonium bromide belongs to anti cholinergic group[1] used as antisecretry in preanaesthetic medication in bronchial asthama.



Propantheline bromide is official in Indian Pharmacopiea[2], literature cites only high performance liquid chromatographic (HPLC)[3–5] and gas chromatographic – mass spectrometric (GC –MS)[6] methods. No spectrophotometric and conductometric methods are cited in the literature.

Therefore the need for a fast, low cost relative method is obvious, specially for routine quality control analysis of bulk and pharmaceutical formulations containing propantheline bromide.

The present work is based on the extraction of a blue coloured ion pair complex formed with bromo phenol blue – an acid dye in presence of buffer solution at pH–7.5 in chloroform followed by its spectrophotometric and conductometric analysis . The proposed method gave reproducible results for determination of (PB) in pharmaceutical formulations as well as in bulk drug.

EXPERIMENTAL

Instruments : Chemita VIS spectrophotometer type CL 10 A 4 was used for all spectral measurements. Century Model–CP 901 pH meter was used for all the pH measurements CC 601 model of conductivity meter was used for the measurement of conductance as well as resistance of solution.

Reagents : All the chemicals used were of analytical grade. Conductivity water was used through out the experiment for conductometric analysis.

Preparation of bromo phenol blue solution : 0.05 g of bromo phenol blue is warmed with 30 mL of 0.05 N NaOH and 5 mL of alcohol (90%) after solution is effected to heat sufficient alcohol (20%) is added to produce 250 mL.

Buffer solution : Buffer solution of pH 7.5 was prepared by mixing 7.5 mL each of 0.1M citric acid and borax solution and diluting it to 100 mL with distilled water.

Drug solution (in bulk form) : Propantheline bromide solutions were prepared by dissolving appropriate amount of drug in distilled water.

Drug solution (in tablet form) : 100 mg of propantheline bromide from its tablet powder was accurately weighed and dissolved in 100 mL of distilled water in a standard volumetric flask to obtain a stock solution of 1 mg/ mL. The solution was further diluted with the distilled water to get working standard solution of required strength.

METHOD A
Extractive Spectrophotometric Method :

Linearity of detector response : Aliquots of the drug solution of PB were transferred into a series of 100 mL separating funnels. To each funnel, 5 mL of drug solution, 2 mL of BPB dye solution and 20 mL of buffer solution was added. A blue coloured complex is formed, which is

extracted with 30 mL of chloroform. The contents were shaken for thorough mixing of the two phases and were allowed to stand for clear separation of the layers. The absorbance of the separated chloroform layers was measured against their respective reagent blank at the wavelength of maximum absorbance i.e. 600 nm.

Assay procedure : Two types of tablets named as probanthine and seribenthine containing 15 mg of propantheline bromide were used as samples. The drug solution was suitably diluted with distilled water to obtain a final concentration of 75 mcg /mL of propantheline bromide.

Appropriate aliquots of drug solution were taken and the assay procedure was followed for analysis of drug content. The analysis was repeated three times for each sample and hence percentage label claims were also calculated and are compiled in Table 2. The amount of propantheline bromide per tablet was calculated by comparing the standard and sample at wavelength of maximum absorbance using the formula.

$$\text{Amount of PB mg/tablet} = \frac{A_2 \times D_1 \times W \times M}{A_1 \times D_2 \times S}$$

Where,

A_1 = Absorbance of the standard solution.

A_2 = Absorbance of the sample solution.

D_1 = Dilution factor for the standard solution.

D_2 = Dilution factor for the sample solution.

W = Weight of the standard taken.

S = Weight of the sample taken.

M = Average Weight of the tablet.

Recovery experiments: To study the accuracy and precision of the method recovery experiment was carried out using standard addition method. The pre–analyzed tablet solutions of three different batches containing 75 µg/mL was added and analyzed by the same procedure. The analysis was done thrice for each sample and results are compiled in Table 3 and percent recovery for added standard was calculated using the formula.

$$\% \text{ Recovery} = \frac{N(\Sigma XY) - (\Sigma X)(\Sigma Y) \times 100}{N(\Sigma X^2) - (\Sigma X)}$$

Where,

N = number of observations.

X = Amount of the standard drug added per tablet.

Y = Amount of the standard drug found per tablet.

METHOD B

Conductometric Method (complexation method): In this method, conductivity was followed by the addition of 0.5mL of bromo phenol blue to 20 mL of drug solution in presence of buffer solution, Observation of change in conductivity indicated that complex is formed. A calibration curve is obtained by measuring conductivity of different concentrations of solution of propantheline bromide drug under the optimum conditions as mentioned in Table 1 and then a curve was plotted between different concentration of drug taken and the conductivities obtained.

Assay procedure: Two types of tablets named as probanthine and seribenthene containing 15 mg of propantheline bromide were used as samples. The drug solution was suitably diluted with distilled water to obtain a final concentration of 20 mcg /mL of propantheline bromide. Appropriate aliquots of drug solution were taken and the assay procedure was followed for analysis of drug content same as above and percentage label claim was calculated as in method A.

Recovery experiments: As an additional check on accuracy and precision of the method, recovery experiments were carried out using standard addition method. The pre–analyzed tablet solutions of three different batches containing 20 µg/mL was added and analyzed by the same procedure as above and percent recovery was calculated as in method A.

METHOD C

Conductometric Method (Direct method) : In this method, conductivity of the propantheline bromide drug was directly measured in conductivity water. 1 mL of the drug solution containing 500 µg/mL of propantheline bromide was added from burette to 50 mL conductivity water. Thus, conductivity was followed and calibration curve was obtained.

Assay procedure : For analysis of tablets, a final concentration of 1µg/mL of drug was used and conductivity was measured. The percentage label claims were calculated as in Method A and Method B.

Recovery studies : Recovery studies were performed by the addition of 2 mg of pure drug to the tablet solution and percent recovery was calculated as in method A and method B.

RESULTS AND DISCUSSION

The optimum conditions were established by varying one parameter at a time and keeping the others fixed by observing the effect produced on the absorbance of the coloured species. The various parameters involved in the colour development like, the concentrations of various reagents and time involved for maximum colour development were optimized for each method and recorded in Table 1.

The light blue coloured complex was formed by the addition of bromo phenol blue and was found to be stable for about 20 hrs. This complex was extracted in chloroform and estimated spectrophometrically without interference at 600 nm, Beer's law was found to be obeyed in the range of 40 µg/mL to 140 µg/mL.

In conductometric methods, conductivity of drug after complexation and without complexation (direct method) was measured at different concentrations. The linearity of the concentration and conductivity of the drug was found to be above 10µg/mL and above 500µg/mL for complexometric method and direct method, respectively.

Table 1. Optimum conditions and results of the proposed method for the determination of propantheline bromide

Reagent	Method A	Method B	Method C
Drug solution taken (µg/mL)	10–200	20–200	500
Volume of buffer solution (mL)	20	40	–
pH of buffer solution	7.5	7.5	–
Volume of [BPB] mL	2.0	0.5 (from burette)	–

Table 2. Estimation of propantheline bromide in commerical products by three methods.

S. No.	Tablet sample	Label claim (mg/ tab)	% Label Claim					
			Method A	S.D.	Method B	S.D.	Method C	S.D.
1.	Probanthine							
	Batch I	15	101.106	1.078	101.650	1.563	100.000	0.514
	Batch II	15	99.710		98.335		100.600	
	Batch III	15	98.466		98.335		99.340	
2.	Seribenthine							
	Batch I	15	98.880	1.546	101.650	1.353	100.000	1.11
	Batch II	15	102.213		100.000		102.600	
	Batch III	15	98.990		98.335		102.000	
Range of analysis			40–140 µg/mL		10 µg/mL		500 µg/mL	

The recovery studies conducted by way of standard addition to a commercial sample gave satisfactory results by all the three methods (Table 3). The reliability of the proposed method was checked on commercial products by all methods and the results were compiled in Table 2. The values of standard deviations are low, indicating high accuracy and reproducibility of the methods. Interference studies revealed that the common excipients and other additives usually present in the dosage form did not interfere in the proposed methods. The proposed extractive

spectrophotometric and conductometric methods of the estimation of propantheline bromide are simple, sensitive, cheap and accurate and have their application in the routine quality control analysis and quantitave determination of (propantheline bromide) in its pharmaceutical preparations as well as in bulk form.

Table 3. Recovery study data

S. No.	Tablet sample	Label claim (mg/ tab)	% Recovery Formulation					
			Method A	S.D.	Method B	S.D.	Method C	S.D.
1.	Probanthine							
	Batch I	15	100.00	1.028	98.36	1.235	102.50	1.690
	Batch II	15	97.50		100.83		101.80	
	Batch III	15	99.00		100.83		98.60	
2.	Seri banthine							
	Batch I	15	100.00	1.406	98.33	0.794	101.25	0.946
	Batch II	15	98.16		100.03		99.35	
	Batch III	15	101.60		98.36		99.15	
Range of analysis			40–140 µg/mL		10 µg/mL		500 µg/mL	

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