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ACIDIC DYES AS ION–PAIRING REAGENTS FOR THE DETERMINATION OF AMBROXOL IN PHARMACEUTICAL FORMULATIONS

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ABSTRACT

Simple and sensitive extractive spectrophotometric methods for the determination of Ambroxol in pharmaceutical preparations is described. The method is based on the formation of yellow coloured ion–pair complexes of the drug with acidic dyes like tropaeolin OO (TPO) (M_1), bromothymol blue (BTB) (M_2) and bromophenol blue (BPB) (M_3) in acidic medium. The ion–pair complexes formed are quantitatively extracted into chloroform under experimental conditions and estimated by spectrophotometry. The method is found to be precise and accurate.

Key words: Acidic dyes, Ion–pairing reagent, Ambroxol, Pharmaceutical formulations, Spectrophotometric determination.

INTRODUCTION

Ambroxol (ABH) is a new semisynthetic derivative of vascine obtained from the indian shrub, Adhatoda vasaka and chemically the drug is trans–4(2–amino–3,5 dibromo benzyl–amino) monohydrochloride[1]. It is a potent expectorant and mainly used as mucolytic agent in the treatment of respiratory disorders[2]. The drug is not official in any pharmacopoeia. Literature survey reveals two RP–HPLC methods[3–4], two gas chromatographic methods[5,6], a uv method[7] and two spectrophotometric methods[8,9] reported for the estimation of the drug. The two reported visible spectrophotometric methods are based on oxidative coupling reactions with MBTH, cerric ammonium sulphate and ferric chloride. The functional groups of the drug have not been fully exploited. Extractive spectrophotometric procedures are normally adopted for the assay of drugs because of higher sensitivity, reproducibility and accuracy of these methods. Usually these methods have higher λ_{max} and less interference from the associated impurities[10,11]. Hence, the present paper describes simple and accurate extractive spectrophotometric method based on the formation of ion–pair complexes of the drug with acidic dyes in the acidic medium.

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EXPERIMENTAL

Instrument

An Elico SL 171 spectrophotometer with 1 cm matched quartz cells was used in the present study. An Elico L–120 digital pH meter was used for pH measurements.

Reagents

All reagents used were of analytical grade.

Dye solutions: 0.1% solutions of tropaeolin OO, bromothymol blue and bromophenol blue were prepared in distilled water, filtered and used.

Buffer solution: Potassium hydrogen phthalate buffer solution of pH 2.4 to 4.0 was prepared as per Briton and Robinson method[12].

Preparation of Drug Solutions

a) **Standard drug solution:** Twenty mg of the standard drug (base) is dissolved in distilled water and made up to mark in a 100 mL calibrated volumetric flask (0.2 mg/mL).

b) **Sample drug solution:** The sample (tablet, powder or syrup) equivalent to 20 mg of the drug is transferred into a beaker and dissolved in 100 mL distilled water. The solution is filtered through Whatman filter paper No.42 into a 100 mL calibrated volumetric flask (0.2 mg/mL).

Procedure

Aliquots of drug solutions representing 10–160 µg in case of M_1, 10–140 µg in case of M_2 and 20–160 µg in case of M_3 are transferred into a series of separating funnels, 4 mL of buffer solution and 2 mL of dye solution are added successively to each separating funnel and total volume of the aqueous phase is brought to 10 mL with distilled water in each separating funnel. 10 mL chloroform is added and the contents are shaken for 2 min and two phases are allowed to separate and the chloroform layer is passed through anhydrous sodium sulphate. The absorbance of the chloroform layer is measured at the respective absorption maxima of 420, 420 and 418 nm against reagent blanks. The amount of ABH present in each sample solution is computed from the calibration curve.

RESULTS AND DISCUSSION

Optimum operating conditions used in the procedures were established adopting variation of one variable at a time (OVAT) method. The optical characteristics of the methods are presented in Table 1. The precision and accuracy of the methods was tested by measuring six replicate samples of the drug in Beer's law limits. Commercial formulations containing ABH were successfully analysed by the proposed methods. The results are presented in Table 2. None

of the usual excipients employed in the formulation of dosage forms interfere in the analysis of ABH by the proposed methods. As an additional check of accuracy, recovery experiments were performed by standard addition method. The stoichiometric ratio of drug to dye was determined with slope ratio method[13] and was found to be 2 : 1.

Table 1. Optical characteristics and precision of the proposed method

Parameter	M_1	M_2	M_3
λ_{max} (nm)	420	420	418
Beer's law Limit (µg/ mL)	10–160	10–140	20–160
Molar absorptivity (L mol^{-1} cm^{-1})	6.12×10^4	6.02×10^4	6.40×10^4
Sandell's sensitivity (mg cm^{-2}per 0.001 absorbance unit)	0.0666	0.052	0.108
Regression equation (y = a + bC)* Slope (b)	1.49×10^{-2}	1.90×10^{-2}	9.10×10^{-3}
Intercept (a)	1.90×10^{-3}	-4.66×10^{-4}	-2.40×10^{-3}
Correlation coefficient (r)	0.9999	0.9998	0.9999
Relative standard deviation (%)**	0.461	0.922	0.531
% Range of error (confidence limits–95%)**	0.797	0.746	0.520

* Y = a + bC, where C is concentration of analyte and Y is absorbance unit, ** average of six determinations.

Table 2. Assay of Ambroxol in pharmaceutical formulations by the proposed method

Drug*	Label Claim mg/tablet	Amount found by Proposed Method **			Reference Method[7] (mg)	% Recovery by proposed method ***
		M_1	M_2	M_3		
Tablet 1	30	29.92	29.91	29.93	29.92	99.60 ± 0.71
Tablet 2	30	30.10	29.90	29.92	29.92	99.70 ± 0.61
Syrup 1	50	49.98	49.99	49.98	49.98	99.98 ± 0.20
Syrup 2	50	49.99	49.98	49.97	49.99	99.99 ± 0.10

* Drugs from different pharmaceutical companies; ** Average ± Standard deviation of 6 determinations; *** Recovery of 10 mg added to the preanalysed pharmaceutical dosage forms (average of 3 determinations).

CONCLUSION

The proposed method is advantageous over the other reported visible spectrophotometric methods for these drugs because of the higher sensitivity and higher λ_{max} exhibited by the association complex. The proposed method is simple, convenient, accurate, sensitive and reproducible. It can be employed for routine analysis of ABH in bulk drug and formulations.

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