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NOTE

Extractive Spectrophotometric Estimation of Ambroxol

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Three simple and sensitive extractive spectrophotometric methods have been developed for the determination of ambroxol in pure and in its dosage forms. The developed methods involve formation of colored chloroform extractable complexes of drug with orange II, bromocresol green, bromophenol blue in acidic medium. Extractable complexes showed absorption maximum at 490 nm, 430 nm and 420 nm and showed linearity in concentration ranges of 5 to 40 μg/mL, 2.5 to 25 μg/mL and 5 to 40 μg/mL respectively. Results were validated statistically and were found to be reproducible.

Ambroxol (AXL) is chemically trans-4-2-(2-amino-3,5-dibromo benzylamino) cyclohexanol[1], a bromohexine metabolite. It has significant importance as a potent expectorant acting primarily by increasing bronchial secretions and reducing the viscosity of sputum. Literature survey revealed few analytical methods for the estimation of AXL which includes HPLC[2,3], UV[2], LC[4], colorimetry[5] and automatic extraction spectrophotometric method[6]. In the present investigation AXL forms yellowish orange coloured molecular ion complex with orange II (method A) extractable into chloroform showing maximum absorption at 490 nm. The yellowish coloured molecular ion complex was produced using bromocresol green (method B) or bromophenol blue (method C), extractable into chloroform exhibiting absorption maximum at 430 nm or 420 nm respectively.

Spectral and absorbance measurements were made on Systronics UV/Vis spectrophotometer-117. All the reagents used were of analytical grade.

1. Buffer solution of pH 2.5 was prepared as per I.P. by mixing appropriate quantities of 0.2 M potassium hydrogen phthalate and 0.2 M sodium hydroxide.
2. Orange II (0.5%) solution was prepared by dissolving 500 mg in distilled water.
3. Bromocresol green (0.04%) solution was prepared by dissolving 40 mg of bromocresol green in a mixture of 0.72 mL of 0.1 M NaOH and 20 mL of alcohol (95%) and made up to 100 mL with distilled water.
4. Bromophenol blue (0.1%) solution was prepared by dissolving 0.1 g of bromophenol blue in 1.5 mL of 0.1 M sodium hydroxide and 20 mL of

ethanol (95%) with gentle heating and added sufficient water to produce 100 mL.

Standard and sample solutions: About 100 mg of AXL pure drug or formulation was accurately weighed and dissolved in water and made up to 100 mL with distilled water. Further dilutions were made with distilled water to get the working standard solutions of 100 μg/mL.

Assay procedures: Volumes of standard AXL (1 mL = 100 μg) solution ranging from 0.5 mL to 4 mL for method A and C or 0.25 mL to 2.5 mL for method B, were transferred into a series of 150 mL separating funnels. To that 1 mL of orange II dye (0.5%) for method A or 3 mL of bromocresol green (0.04%) for method B and 0.5 mL of HCl (0.1 N) were added, whereas for method C, 4 mL of bromophenol blue (0.1%) and 1 mL of buffer (2.5 pH) were added and the total volume of the aqueous phase was made up to 10 mL with distilled water. About 10 mL of chloroform was added to each funnel and the contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of chloroform layer was measured at 490 nm, 430 nm and 420 nm for methods A, B and C respectively against reagent blank. The amount of AXL present in the sample solution was computed for its calibration curve.

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, stability of the colored species, per cent relative standard deviation (calculated from eight separate samples containing 3/4th amount of the upper Beer's law limits of AXL in each method), per cent range of error (0.05 and 0.01 confidence limits), correlation coefficient, slope and intercept of regression analysis using least square method were calculated and summarized in Table-1.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION

Parameters	Method A	Method B	Method B
Beer's law limit (μg/mL)	5.0–40.0	0.25–2.5	5.0–40.0
Sandell's sensitivity (μg/cm^2/0.001 absorbance unit)	0.06593	0.03484	0.05525
Molar extinction coefficient (l mole^{-1} cm^{-1})	0.5734×10^4	$1.0.851 \times 10^4$	0.6843×10^4
% Relative standard deviation	0.63241	0.4826	0.4107
%Range of error:			
0.05 confidence limits	± 0.5287	± 0.3966	± 0.3434
0.01 confidence limits	± 0.7825	± 0.5969	± 0.5081
Correlation coefficient	0.9987	0.9998	0.9925
Regression equation (Y*):			
Slope (a)	0.0157	0.02855	0.04624
Intercept (b)	0.0025	0.0008	0.0166

Y* = b + aC, where "C" is concentration in μg/mL and Y is absorbance unit.

The values obtained for the determination of AXL in several pharmaceutical formulations (Tablets) by the proposed and the reported methods are compared in Table-2. To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analyzed pharmaceutical formulations and the mixtures were analyzed by the proposed methods and the recoveries (average of six determinations) are given in Table-2. Interference studies reveal that the common excipients and the additives usually present in the dosage forms did not interfere in the proposed methods.

TABLE-2
ESTIMATION OF AMBROXOL IN PHARMACEUTICAL FORMULATIONS

Sample	Labelled amount (mg)	Amount obtained (mg)				Per cent recovery of the proposed method		
		Reported method[5]	Proposed method					
			A	B	C	A	B	C
1	30	29.4	29.8	29.5	29.4	99.3	98.3	98.0
2	30	29.6	29.6	29.7	29.9	98.6	99.0	99.6
3	30	29.5	29.7	29.8	29.7	99.0	99.3	99.0

The coloured complexes which are being extracted into chloroform layer are due to the formation of drug : dye complexes between the acidic dyes and basic drug AXL, in the ratio of 1 : 1, 1.25 : 1 and 1 : 1 for method A, method B and method C respectively. The results indicate that the proposed methods are simple, sensitive, reproducible and accurate and can be used for the routine determination of AXL in bulk and dosage forms.

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