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Original Article

SIMULTANEOUS ESTIMATION OF LORATADINE AND AMBROXOL HYDROCHLORIDE IN BULK AND PHARMACEUTICAL FORMULATIONS BY SIMPLE UV SPECTROPHOTOMETRY

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ABSTRACT

Objective: The simple, rapid, accurate, precise and cost-effective UV spectrophotometric methods have been developed and validated for simultaneous estimation of Loratadine and Ambroxol Hydrochloride in tablet dosage form.

Methods: The UV methods have been developed utilizing concept of standard addition utilizing Methanol: Water (50:50%, v/v) as a solvent. Method is estimation using simultaneous equation method at 305 nm (λ_{max} of Loratadine) and 242 nm (λ_{max} of Ambroxol Hydrochloride).

Results: Linearity was observed in range of 5-25 µg/ml each for Loratadine and Ambroxol Hydrochloride, respectively for methods. The correlation coefficient (r^2) value was found to be values in the range of 0.9941-0.9961. The assay result of marketed formulation was found to be 99.98 % and 100.07 % of Loratadine and Ambroxol Hydrochloride.

Conclusion: The present result shows that the proposed method can be successfully implemented for estimation of Loratadine and Ambroxol Hydrochloride in bulk and its marketed formulations. Methods were statistically validated as per ICH guidelines and can be successively applied for analysis for tablets formulation.

Keywords: Loratadine, Ambroxol hydrochloride, Simultaneous estimation, ICH guidelines

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INTRODUCTION

The Loratidine is chemically identified as "Ethyl-4-(8-chloro-5, 6-dihydro-11H-benzo-cyclohepta [1,2-b] pyridin-11-ylidene) piperidine-1-carboxylate (fig. 1). The Loratidine is a second-generation long-acting, non-sedative tricyclic antihistamine (piperidine derivative) that selectively inhibits H1-receptors [1, 2].

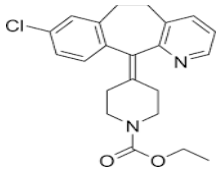

Fig. 1: Chemical structure of loratidine

Loratadine is a tricyclic antihistamine which acts as a selective inverse agonist of peripheral histamine H1-receptors [3]. Loratadine peak effect occurs in 1–2 h, and its biological half-life is on average 8 h (range 3–20 h), with desloratadine's half-life being 28 h (range 9–92 h), accounting for its long-lasting effect [citation needed] About 40% is excreted as conjugated metabolites into the urine, and a similar amount is excreted into the feces. Traces of unmetabolized Loratadine can be found in the urine [4].

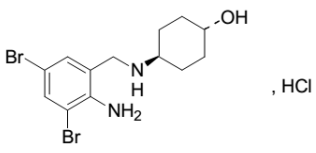

Fig. 2: Chemical structure of ambroxol hydrochloride

Ambroxol hydrochloride [AMB HCl] (fig. 2) official in Indian Pharmacopoeia and British Pharmacopoeia, is chemically Trans-4-[(2-amino-3, 5-dibromobenzyl) amino]-cyclohexanol hydrochloride. It is a white or yellowish crystalline powder. It is sparingly soluble in water; soluble in methanol; practically insoluble in methylene chloride [5, 6].

Ambroxol hydrochloride is a potent mucolytic and mucokinetic, capable of inducing bronchial secretion. Itdepolymerises mucopolysaccharides directly as well as by liberating lysosomal enzymes network of fibres in tenacious sputum is broken. It is particularly useful in if mucus plugs are present. Ambroxol hydrochloride (AMB) is a semi-synthetic derivative of vasicine obtained from Indian shrub Adhatoda vasica. It is a metabolic product of bromhexine. Used in a variety of respiratory disorders, including chronic bronchitis, also used in the treatment of cough [7].

MATERIALS AND METHODS

Apparatus and instrument

A double UV Visible Spectrophotometer (UV-1800 Shimadzu, Japan) was used. Absorption and spectra of both test and standard solutions were recorded over the wavelength range of 200-400 nm using 1 cm quartz cell at fast scanned speed and a fixed slit width of 1.0 nm. All weighing of ingredients were done on digital weighing balance (DV 215 CD Ohaus, USA) and bath sonicator (PCI analytical Pvt. Ltd) was also used in study. Glasswares used in each procedure were soaked overnight in a mixture of chromic acid and sulphuric acid, rinsed thoroughly with double distilled water and dried in hot air oven.

Chemicals and reagents

All the reagents and solvents were of analytical grade high-purity deionized water. Loratidine was obtained as a gift from Spectrum Labs, Hyderabad. Ambroxol Hydrochloride and were supplied as gift sample by Trojan Pharma Baddi, Himachal Pradesh, India.

Preparation of standard stock solution

The reference standard Loratadine (10 mg) and Ambroxol hydrochloride (10 mg) were weighed and transferred into two separate 10 ml volumetric flasks and dissolved in diluent, the contents of the flask were mixed and volume was made up to the

mark with diluent. From this 1 ml of Ambroxol hydrochloride and 1 ml of Loratadine was diluted to 10 ml with the same solvent to obtain a standard solution of Loratadine and Ambroxol hydrochloride each of 100 µg/ml [8].

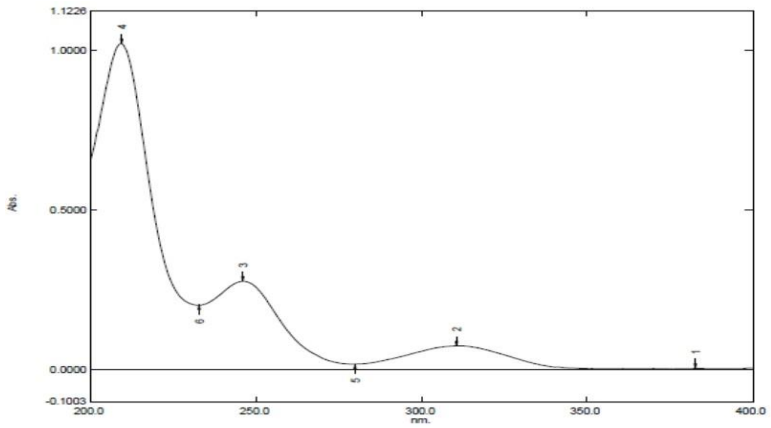

Fig. 3: Ambroxol hydrochloride shows λ_{max} at 242 nm

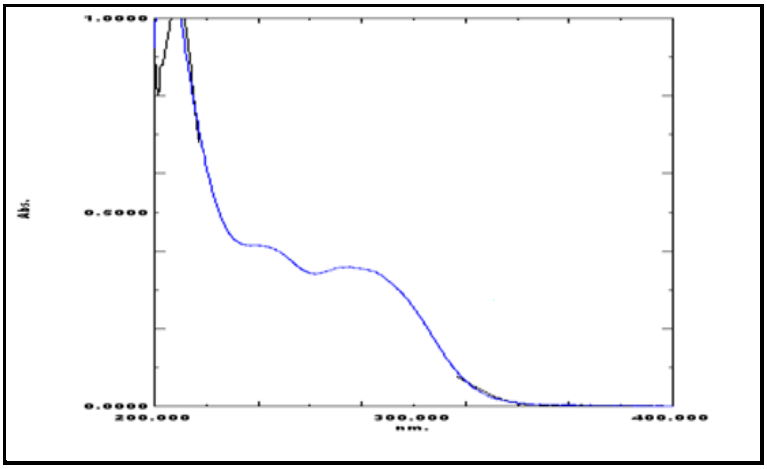

Fig. 4: Wavelength of loratadine shows λ_{max} at 242 nm

Selection of analytical wavelength

Standard solution of Loratadine and Ambroxol hydrochloride have diluted appropriately with diluent to obtain a solution containing 10 µg/ml of Loratadine and 10µg/ml of Ambroxol hydrochloride. These diluted solutions were scanned in range 200-400 nm separately using diluent as blankLoratadine showed λ_{max} at 305 nm and Ambroxol hydrochloride shows λ_{max} at 242 nm.

Procedure for analysis of tablet formulation

Twenty tablets containing 5 mg of Loratadine and 60 mg of Ambroxol hydrochloride from the marketed formulation were taken and accurately weighed. The average weight was calculated and tablets were crushed into fine powder. The powder equivalent to 10 mg of Loratadine and Ambroxol hydrochloride was weighed and transferred into 10 ml volumetric flask containing diluent. The solution was sonicated for 15 min, shaken vigorously and the volume made up to the mark with diluent. The solution was flittered utilizing Whatman filter paper (No. 41) and 0.6 ml of filtrate was transferred into 10 ml volumetric flask to prepare a working sample solutioni. e5 µg/ml of Loratadine and 60 µg/ml of Ambroxol hydrochloride. This solution was used for estimation of Loratadine and Ambroxol hydrochloride. The amount of Loratadine and Ambroxol hydrochloride present in the sample solution were determined by substituting derivative responses into the equation of straight line representing the calibration curves of Loratadine and Ambroxol hydrochloride.

The absorbance at λ1 and λ2 was measured and the concentration was calculated using following formula;

$$Cx = \frac{A2ay1 - A1ay2}{ax2ay1 - ax1ay2}$$

$$Cy = \frac{A1ax2 - A2ax1}{ax2ay1 - ax1ay2}$$

Where,

Cx and Cy are the concentrations of Loratadine and Ambroxol hydrochloride, respectively, A1 and A2 are the absorbances of sample at λ1 and λ2, respectively, ax1 and ax2 are the absorptivity of Loratadineat λ1 and λ2, respectively, ay1 and ay2 are the absorptivity of Ambroxol hydrochloride at λ1 and λ2, respectively.

Validation

Linearity and range

In this method Loratadine and Ambroxol hydrochloride was estimated by using ultraviolet spectroscopy. From the above standard stock solution 100µg/ml prepare various concentration given below in table 1. The method both drug obeys Beer lamberts law in the concentration range of 5-25 µg/ml [9]. 5 concentrations of loratadine and Ambroxol hydrochloridevarying concentrations ranging from 5 to 25 µg/ml were made. The sample preparations are given as below; X ml of Loratadineand Y ml of Ambroxol hydrochloride was diluted to 10 ml.

Table 1: Different concentration of loratadine and ambroxol hydrochloride

X ml of loratadine	Y ml of ambroxol hydrochloride	Diluted to	Conc. of loratadine (µg/ml)	Conc. of ambroxol hydrochloride (µg/ml)
0.5 ml	0.5 ml	10 ml	5	5
1 ml	1 ml	10 ml	10	10
1.5 ml	1.5 ml	10 ml	15	15
2 ml	2 ml	10 ml	20	20
2.5 ml	2.5 ml	10 ml	25	25

Limit of detection (LOD) and limit of quantification (LOQ)

LOD is the lowest amount of analyte in a sample that can be detected but not necessarily quantify under the stated experimental conditions. LOQ is the lowest concentration of analyte in a sample that can be determined with the acceptable precision and accuracy under stated experimental conditions (table 5).

The LOD and LOQ for Loratadine and Ambroxol hydrochloride were determined according to ICH guideline

$$LOD = 3.3\ \sigma/S \quad LOQ = 10\ \sigma/S$$

Where,

σ = Standard deviation of the y-intercept of calibration curves

S = Slope of the calibration curve

Precision

Precision was studied to find out intra and inter-day variations in the test method of Loratadine and Ambroxol hydrochloride. Intra-day precision was determined by analyzing three replicate measurements of 100% concentrations within linearity range of drugs on three different times in the same day. Inter-day precision was conducted during routine operation of the system over a period of 3 consecutive days. The precision of an analytical method is expressed as % RSD of a series of measurements, which should be less than 2 % (table 6-9) [10, 11].

Accuracy

Accuracy of the methods was determined at three different concentration levels i. e.50%, 100% and 150% in triplicate for each drug as per ICH guidelines. From the total amount of drug found, the percentage recovery was fond in range of 99.29–101.20 % (table 10).

RESULTS AND DISCUSSION

The proposed methods for simultaneous estimation of Loratadine and Ambroxol hydrochloride in tablet dosage forms were found to be simple, accurate, economical and rapid. The method was validated as per the ICH Q2 (R1) guidelines.

Table 2: Analysis of tablet formulation by proposed methods

Drug	Alastin-AM	Assay* ±SD
Loratadine	5 mg.	99.98694±0.502
Ambroxol hydrochloride	60 mg	100.0711±0.332

Table 3: Summary of linear regression analysis of loratadine

S. No.	Concentration	Absorbance
1	5	0.385
2	10	0.499
3	15	0.685
4	20	0.799
5	25	0.932

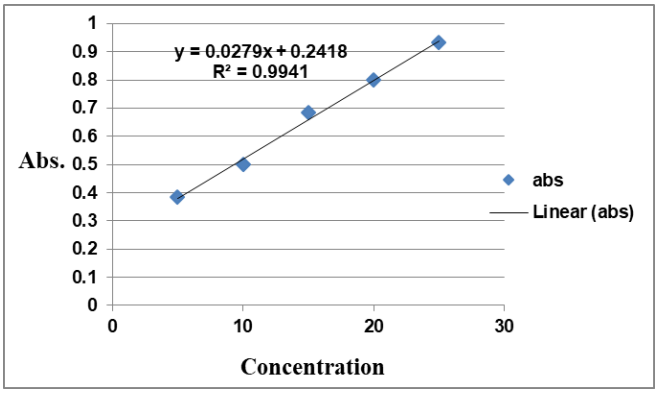

Fig. 5: Linearity for loratadine

Table 4: Summary of linear regression analysis of ambroxol hydrochloride

S. No.	Concentration	Absorbance
1	5	0.317
2	10	0.488
3	15	0.669
4	20	0.788
5	25	0.955

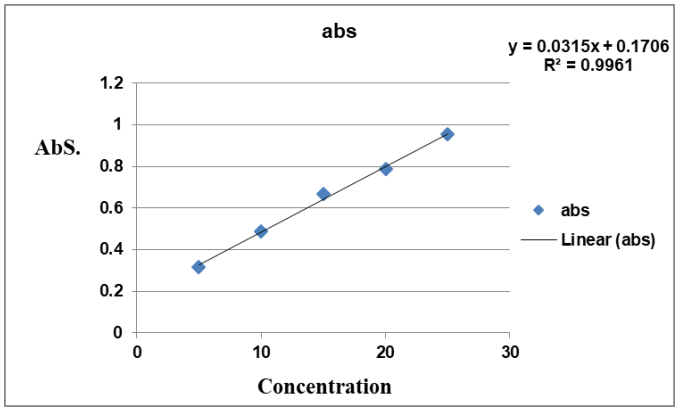

Fig. 6: Linearity for ambroxol hydrochloride

Standard calibration curves for Loratadine and Ambroxol hydrochloride were linear with correlation coefficients (r^2) values in the range of 0.9941-0.9961.

From the linear regression analysis, the correlation coefficient value (r^2) for Loratadine and Ambroxol hydrochloride. The calibration data given in table-3 and 4 for the drugs Loratadine and Ambroxol hydrochloride clearly depicts linearity of the method.

Range

5 to 25 µg/ml for Loratadine and 5 to 25 µg/ml for Ambroxol hydrochloride.

LOD and LOQ

Limit of detection and limit of quantitation was calculated on the basis of slope and standard deviation of response.

Table 5: LOD and LOQ of loratadine and ambroxol hydrochloride

Drug	LOD (µg/ml)	LOQ (µg/ml)
Loratadine	2.395	7.259
Ambroxol hydrochloride	0.617	1.870

The LOD and LOQ were found to be 2.395 and 7.259 µg/ml, respectively for Loratadine and 0.617 and 1.870 µg/ml for Ambroxol hydrochloride, respectively indicates sensitivity of the proposed method.

Table 6: Intraday precision for loratadine

Con.	Trial 1	Trial 2	Trial 3	Mean	SD	% RSD
5	0.385	0.388	0.39	0.387	0.0025	0.649
10	0.499	0.488	0.482	0.489	0.008	1.760
15	0.685	0.688	0.69	0.687	0.002	0.365
Mean					0.004	0.925

Table 7: Intraday precision for ambroxol hydrochloride

Con.	Trial 1	Trial 2	Trial 3	Mean	SD	% RSD
5	0.316	0.318	0.325	0.319	0.004	1.478
10	0.485	0.488	0.49	0.487	0.002	0.516
15	0.698	0.695	0.699	0.697	0.002	0.298
Mean					0.003	0.764

Table 8: Interday precision for loratadine

Con.	Trial 1	Trial 2	Trial 3	Mean	SD	% RSD
5	0.388	0.38	0.39	0.386	0.005	1.370
10	0.512	0.514	0.519	0.515	0.003	0.700
15	0.688	0.689	0.685	0.687	0.002	0.302
Mean					0.003	0.791

Table 9: Interday precision for ambroxol hydrochloride

Con.	Trial 1	Trial 2	Trial 3	Mean	SD	% RSD
5	0.395	0.387	0.39	0.390	0.004	1.034
10	0.488	0.489	0.491	0.489	0.001	0.312
15	0.69	0.692	0.698	0.693	0.004	0.600
Mean					0.003	0.649

The precision of an analytical method is expressed as %RSD of a series of measurements which should be less than 2 %.

Table 10: Accuracy of loratadine and ambroxol hydrochloride

Drug name	Level of recovery	Amount added (µg/ml)		Theoretical conc. (TC)	% Recovery
		Test	Standard		
Loratadine	50%	20	10	30	100.82 %
	100%	20	20	40	99.29 %
	150%	20	25	45	100.58 %
Ambroxol hydrochloride	50%	20	10	15	100.33 %
	100%	20	10	20	99.69 %
	150%	20	25	45	101.20 %

Precision

Intraday precision

Intraday precision was performed by analyzing three different concentrations within linearity range three times in a day.

Accuracy: (% Recovery)

Results of the analysis of pharmaceutical formulations reveal that the proposed methods are suitable for their simultaneous determination with virtually no interference of usual additive present in pharmaceutical formulations. Hence, the above methods can be applied successfully for simultaneous estimation of Loratadine and Ambroxol hydrochloride in marketed formulations.

CONCLUSION

The developed UV methods were found to be more accurate, precise and reproducible. The analysis of tablets containing two drugs gave satisfactory results. The statistical parameter of these methods showed good results. The recovery studies revealed excellent accuracy and high precision of the method. The method were found to be simple and time-saving. The proposed methods could be applied for routine analysis in quality control laboratories.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally

CONFLICTS OF INTERESTS

Declared none

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