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DISCRIMINATING DERIVATIVE SPECTROPHOTOMETRIC CONCURRENT QUANTIFICATION OF LORATADINE AND AMBROXOL IN TABLET DOSAGE FORM

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ABSTRACT: Understanding the preponderance of respiratory conditions with the symptoms like sore throat and cough being even more common, owing to the coronavirus outbreak. The improved resolution method was developed to quantify drugs Loratidine and Ambroxol from the most effective dosage regimen to treat sore throat and cough. An accurate, precise method was developed for concurrently estimating drugs from combined tablet dosage form by first-order derivative UV spectrophotometric method. Absorption maxima were determined as 265 nm for Ambroxol hydrochloride (ZCP for Loratadine) and 307 nm for Loratadine (ZCP for ambroxol hydrochloride), using 0.1 N HCl as a solvent for estimation. The analysis results were developed as per ICH guidelines and the drugs obeyed beer lambert's law in a concentration range of 10 – 125 µg/mL for Ambroxol hydrochloride and 2 – 12 µg/mL for Loratadine with a regression coefficient of 0.9994 and 0.999 respectively. The %RSD values (<2) in precision studies indicate the method's reproducibility. The LOD values were found to be 1.35µg/ml and 0.37µg/mL, and LOQ values were found to be 3.13µg/mL and 1.15µg/mL for Ambroxol hydrochloride and Loratadine, respectively. The simple and easy method can be applied for routine drug analysis in pharmaceutical quality control and biological samples.

INTRODUCTION: Ambroxol hydrochloride, the important treatment regimen for sore throat in bronchiectasis, bronchitis of trachea [1-3], bronchitis associated with emphysema, asthma and other pulmonary conditions was named chemically as " (1r, 4r)-4-{[(2-amino-3, 5 dibromophenyl) methyl] amino} cyclohexan-1-ol hydrochloride.

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"The ambroxol hydrochloride (60mg) is prescribed with an antihistamine agent Loratadine (5mg) in tablet dosage form to relieve sneezing, cough, and runny nose. The loratidine is chemically identified as "Ethyl4-(8-chloro-5, 6-dihydro-11H-benzo [5, 6] cyclohepta [1,2-b] pyridin-11-ylidene) piperidine-1-carboxylate.

"The loratidine is a second-generation long-acting, non-sedative tricyclic antihistamine (piperidine derivative) that selectively inhibits H1-receptors. A thorough review of literature in different databases like Pubmed, Embase, and Scopus discloses the availability of very few peer-reviewed articles to estimate the drugs Ambroxol hydrochloride and

Loratadine simultaneously in bulk and pharmaceutical dosage form by using UV and RP-HPLC [4–14]. But there is no available highly resolute first derivative spectroscopic method for simultaneous quantitative estimation of the combination of the drugs chosen. The increased differentiation between spectra in the derivative mode allows multicomponent analysis of a mixture of components with similar spectra that cannot be resolved in absorbance mode. Current research entails developing and validating the first-order derivative spectroscopic method for estimating ambroxal hydrochloride and loratidine.

MATERIAL AND METHODS:

Chemicals and Solvents: Pure drugs of ambroxal hydrochloride and Loratadine along with the combined dosage form (ALASPAN) composed of 60 mg ambroxal hydrochloride and 5mg loratadine respectively, were obtained from Hetero drugs private limited, Hyderabad India. The analytical grade solvent HCl was obtained from Sd fine Chemicals Limited., Mumbai.

Instruments: The Schimadzu (UV-1800) UV-visible spectrophotometer, Spincotech ultra sonicator, and Schimadzu AUX220 analytical balance were the instruments utilized for the experimentation.

Optimization of Solvent and Derivation Parameters: Ambroxol hydrochloride and loratadine drug samples were dissolved in different solvents like water, HCl, urea, sodium lauryl sulphate, methanol and NaCl to assess the solubility profile of the drugs. The bulk drug stock solutions of concentration 1mg/mL was prepared by dissolving 10 mg of ambroxol hydrochloride and loratadine bulk drug in 10 mL of solvent. From this 0.1 mL was pipetted into 10 mL volumetric flask and brimmed up to the mark with respective solvents to get the working concentration of both drug solutions. The bulk drug solutions were scanned in a spectrophotometer to obtain zero-order spectra, and then the zero-order spectra were transformed into first-order derivative spectra. The zero crossing point was best observed in solutions made of 0.1N HCl as a solvent for both the drugs, so 0.1 N HCl was considered the solvent of choice and then scaling factors, delta lambda were adjusted by trial and error method.

Analytical Method Development:

Preparation of Standard Stock Solutions: The reference standard ambroxol hydrochloride (10 mg) and Loratadine (10 mg) were weighed and transferred into two separate 10mL volumetric flasks and dissolved in 0.1N HCl solution, the contents of the flask were mixed and volume was made up to the mark with 0.1N HCl solution. From this 1mL of ambroxol hydrochloride and 1mL of Loratadine was diluted to 10mL with the same solvent to obtain a standard solution of ambroxol hydrochloride and Loratadine each of 100 µg/mL

Selection of Wavelengths: Standard solution of ambroxol hydrochloride and Loratadine have diluted appropriately with 0.1N HCl to obtain a solution containing 10 µg/mL ambroxol hydrochloride and 10µg/mL of Loratadine. Spectra of these diluted solutions were scanned in the spectrum mode between 200 nm to 400 nm using 0.1N HCl as blank. These ambroxol hydrochloride and Loratadine zero order spectra was converted to corresponding first derivative spectra in 200 nm to 400 nm range**.**

Derivative Conditions: First order derivative spectra of ambroxol hydrochloride (10 µg/mL) and loratadine (10 µg/mL) were overlapped. The wavelength 265 nm was selected to quantify ambroxol hydrochloride (where the derivative response of Loratadine was zero). The wavelength 307 nm was selected to quantify Loratadine (where the derivative response of ambroxol hydrochloride was zero). The characteristic wavelengths (zero crossing points) of both drugs were confirmed by varying their concentrations.

Determination of Ambroxol Hydrochloride and Loratadine in Combined Tablet Dosage form (Assay): Twenty tablets containing 60 mg of ambroxol hydrochloride and 5 mg of Loratadine 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 ambroxol hydrochloride and Loratadine was weighed and transferred into 10 mL volumetric flask containing 0.1 N HCl. The solution was sonicated for 15 min, shaken vigorously and the volume made up to the mark with 0.1N HCl. The solution was flittered utilizing Whatmann filter

paper (No. 41) and 0.6 mL of filtrate was transferred into 10 mL volumetric flask to prepare a working sample solution. This solution was used for estimation of ambroxol hydrochloride and Loratadine. The amount of ambroxol hydrochloride and Loratadine present in the sample solution were determined by substituting derivative responses into the equation of straight line representing the calibration curves of ambroxol hydrochloride and Loratadine.

RESULTS AND DISCUSSION:

Analytical Method Development: The first-order derivative spectrum of ambroxol hydrochloride has zero absorbance at 307 nm, whereas Loratadine shows a significant derivative response. Similarly, the derivative spectrum of Loratadine has zero absorbance at 265 nm whereas ambroxol hydrochloride shows a significant derivative response. Therefore derivative, graphical method was developed for estimating ambroxol hydrochloride and Loratadine in the presence of each other at 265 nm and 307 nm, respectively. The zero order and first order UV overlaid spectrums of ambroxol and loratidine were shown in **Fig. 1** and **2.**

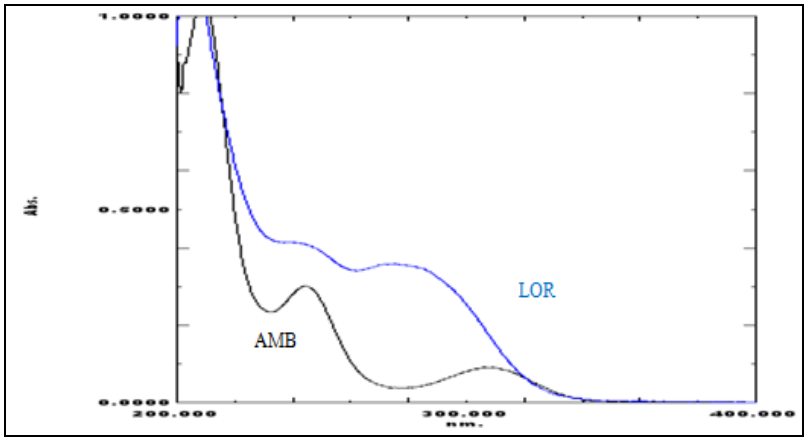

FIG. 1: ZERO ORDER UV OVERLAID SPECTRUM OF AMBROXOL HYDROCHLORIDE (10µg/mL) AND LORATADINE (10 µg/mL) IN 0.1N HCL

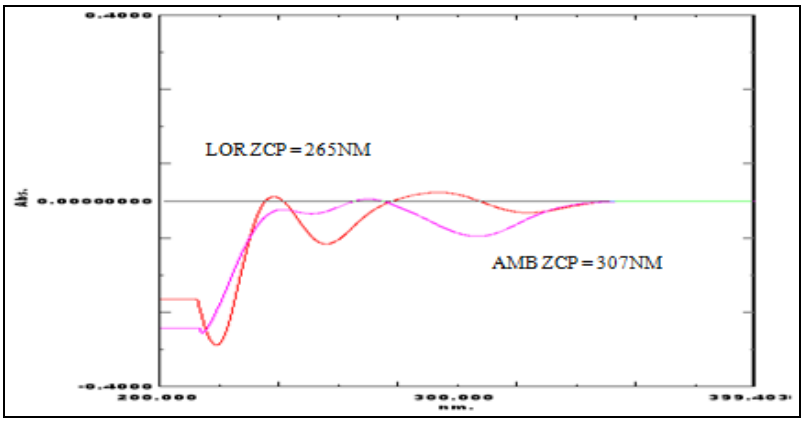

FIG. 2: UV FIRST ORDER OVERLAID SPECTRUM OF AMBROXOL HYDROCHLORIDE (10 µg/mL) AND LORATADINE (10 µg/mL) IN 0.1N HCL

Analytical Method Validation:

Ambroxol Hydrochloride and Loratadine Calibration Plot: Ambroxol hydrochloride and Loratadine as shown in overlaid spectrum **Fig. 3** were linear in the concentration range of 10 – 125 µg/mL and 2-12 µg/mL, respectively. From the linear regression analysis, the correlation coefficient value (r^2) for ambroxol hydrochloride is 0.9994 and for Loratadine is 0.999. The calibration data given in table-1 for the drugs ambroxol and loratidine clearly depicts linearity of the method.

The % recoveries of ambroxol hydrochloride and Loratadine were found to be in a range of 99.7–100.8% and 98.3-98.8%, respectively for ambroxol and loratidine. The %RSD of repeatability was <2% for both intra and inter day precision.

TABLE 1: OPTIMIZED CONDITIONS FOR THE PROPOSED METHOD

S. no.	Parameter	Ambroxol hydrochloride	Loratadine
1	Absorption maxima(nm)	265nm	307nm
2	Beer's law limit(µg/mL)	10 – 125 µg/mL	2 – 12 µg/mL
3	Slope	-0.0042	-0.006
4	Intercept	- 0.0102	- 0.0028
5	Correlation coefficient	0.9994	0.999
6	Regression equation	y = -0.0042x – 0.0102	y = -0.006x – 0.0028
7	LOD (µg/mL)	1.35	0.37
8	LOQ (µg/mL)	3.13	1.15

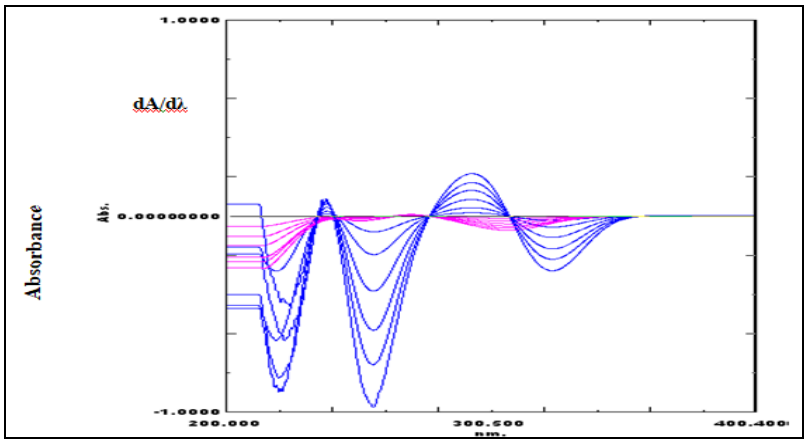

FIG. 3: FIRST-ORDER OVERLAID SPECTRUM OF AMBROXOL HCL AND LORATIDINE

Analysis of Commercial Tablets (Assay): The commercially available tablets (ALASPAN) containing ambroxol hydrochloride (60mg) and Loratadine (5mg) were assayed to determine the importance of the developed method. The results obtained for ambroxol hydrochloride and Loratadine was compared with the corresponding labelled amounts and results were in good agreement with the standards proposed The %RSD of the formulation was found to be less than 2 with 99.1% recovery for ambroxol and 98.9% for loratidine as indicated in **Table 2.**

TABLE 2: ANALYSIS OF COMMERCIAL TABLETS (ASSAY OF AMB AND LOR)

Formulation	% Amount found ± SD	%RSD
Ambroxol hydrochloride	99.1±0.023	0.51
Loratadine	98.9±0.045	0.32

CONCLUSION: The simple, accurate, precise first-order derivative spectrophotometric method for simultaneous estimation can be the best alternative to high-end chromatographic techniques due to its cost efficiency, and the method also indicated good resolution comparable to that of other peer-developed HPLC methods.

The result-driven derivative mode offers better quantification of drugs than the absorbance mode for simultaneous estimation of drugs from multicomponent mixtures in quality control samples, biological samples, and other drug formulations.

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CONFLICTS OF INTEREST: Nil

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