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RESEARCH ARTICLE

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SIMULTANEOUS ESTIMATION OF AMBROXOL HYDROCHLORIDE AND LORATADINE IN TABLET DOSAGE FORM BY USING UV SPECTROPHOTOMETRIC METHOD

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ABSTRACT

A novel, simple, rapid, precise, accurate, cost effective and reproducible spectrophotometric method has been developed for simultaneous estimation of ambroxol hcl and loratadine in combined tablet dosage form. The method employs measurement of absorbance at two wavelengths,308nm and 245nm, of ambroxol and loratadine respectively. Beer´s law obeyed in the concentration range of 10-50µg/ml and 10-50µg/ml for ambroxol and loratadine respectively.. The proposed method is recommended for routine analysis since it is rapid, simple, accurate, and also sensitive and specific. Results of percentage recovery studies confirmed the accuracy of the proposed method. The present uv spectroscopic method was validated following the ICH guidelines[17-18].

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KEY WORDS

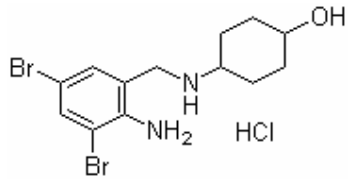
Ambroxol , Loratadine, Simultaneous equation method, Uv spectroscopy.

INTRODUCTION

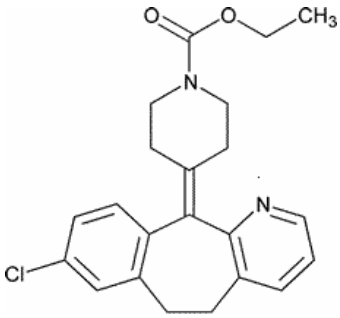
Ambroxol hydrochloride[1] is chemically, 1 ({[2 – Amino – 3, 5 dibromo phenyl] methyl} amino) cyclohexanol monohydrochloride which is a semi synthetic derivative of vasicine from the Indian shrub "Adhatoda vasica". It is an expectoration improver and a mucolytic agent used in the treatement of bronchial asthama and chronic bronchitis. Ambroxol hydrochloride has also been reported to have a cough suppressing effect and anti inflammatory action. Recently the inhibition of nitric oxide dependent activation of soluble guanylate cyclase was suggested one of the molecular mechanism of the therapeutic action of ambroxol hydrochloride, also used in pulmonary alveolar proteinosis in pulmonary distress and infant respiratory distress syndrome.

Loratidine[13] is chemically 4-[8-chloro-5, 6-dihydro-11Hbenzo [5, 6] cyclohepta [1, 2-b] pyridin-11-ylidene]-1-piperidinecarboxylic acid ethyl ester with a potent antihistaminic agent used in the treatment of utricaria and allergic rhinitis. . Literature survey showed that very few analytical methods have been reported for the estimation of Loratidine and Ambroxol Hydrochloride individually and in combination with other drugs like uv-visible spectrophotometry[12], liquid chromatography with flouroscence[11] , LC-MS/MS[5], RP-LC[13],capillary electrophoresis[8], HPLC with potentiometric detection[2], etc. However, there is no uv method reported for the simultaneous estimation of these drugs in combined dosage forms. fixed dose combination containing ambroxol hydrochloride (60mg) and loratadine (5mg)is available in the tablet dosage form in the market.

The objective of present study was to develop simple, precise, accurate and validated, economic and analytical methods for estimation of Ambroxol Hcl and Loratadine in tablet dosage forms.



Structure of Ambroxol hydrochloride:



Structure of Loratadine:

MATERIALS AND METHODS

APPARATUS:

All absorbance measurements were made on shimadzu uv-visible double beam spectrophotometer model shimadzu pharmaspec uv-1700 was employed with spectral band width of 0.5nm and wavelength accuracy of ±0.3nm with automatic wavelength corrections with a pair of 1cm uv matched quartz cells.

MATERIALS

The pure drug samples of ambroxol hydrochloride and loratadine were obtained from franco Indian pharma, Mumbai, india. Methanol AR grade was used throughout the experimental work.Tablets were purchased from local market(Lorfast-am) tablets containing ambroxol hydrochloride 60mg and loratadine 5mg per tablet.

METHOD

PREPARATION OF STANDARD STOCK SOLUTIONS:

Standard stock Solutions of ambroxol hydrochloride and loratadine were prepared by dissolving 25mg of ambroxol and quantity of loratadine equivalent to ambroxol base 25mg separately in 10ml of methanol. It was then sonicated for 10minutes and the final volume of both the solutions were made up to 25ml with methanol to get stock solutions containing 1000µg/ml each of ambroxol and loratadine in two different 25ml volumetric flasks.

SELECTION OF WAVELENGTH

Ambroxol and loratadine soluitions 10 µg/ml solutions were prepared separately and λ max of both drugs was scanned individually in the range of 400-200nm to determine the wavelength of maximum absorption for both the drugs.for estimation two wavelengths were selected, 308nm for ambroxol and 245nm for loratadine in the respective solvent.

STUDY OF BEER LAMBERTS LAW

Ambroxol and loratadine showed linearity with absorbance in the range of 10-50µg/ml and 10-50µg/ml at their respective maxima. correlation coefficients of ambroxol and loratadine were found to be 0.9987 and 0.9991. For simultaneous estimation of ambroxol and loratadine, a series of standard solutions were prepared by diluting appropriate volume of standard stock solutions, like 10,20,30,40 and 50ug/ml. The soloutions were scanned in the range of 200-400nm against methanol as blank. Absorbance and absorptivities of series of standard solutions were recorded at selected wavelengths (λ1) and (λ2).

ANALYSIS OF TABLET FORMULATION

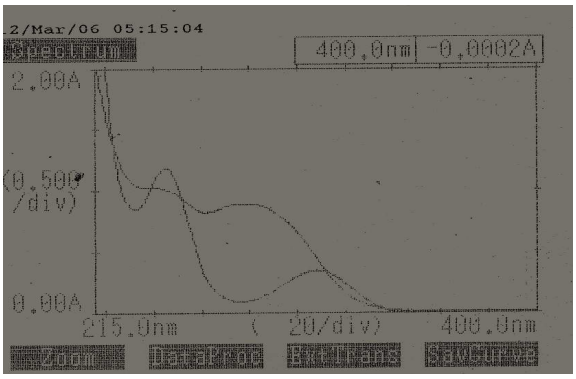
Twenty tablests of each containing 60mg of ambroxol hydrochloride and 5mg of loratadine were weighed accurately and finely powdered. From each triturate of the 20 tablets an amount equivalent to 50mg was weighed and transfer to 50ml volumetric flask. Containing 25ml methanol shaken for 10min, then volume was made up to50ml with methanol and filtered through whatman filter paper No41 in to another 50ml volumetric flask washed residue with double distilled water and added washings to filtrate, volume of filtrate was made to 50ml mark with double distilled water.

The final mixed sample solution were prepared, correspond to 80µg/ml of ambroxol hydrochloride and 20µg/ml of loratadine. The absorbance of resulting solutions were measured at 308nm and 245nm.The concentration of ambroxol and loratadine present in the sample solution was calculated directly from absorbance value at 245nm and 308nm from calibration curve prepared using standard drug solutions. The Results of analysis of the tablet formulation is presented in table no.1.

TABLE NO : 1
Results of analysis of tablet formulation

Analyte	label claim (mg/tab)	Estimated amount	%Label claim estimated * (Mean± S.D.)	%RSD
AMB HCL	60	59.46	99.18±0.0326	0.6275
LOR	5	4.83	99.83 ±0.0175	0.2301

**average of five determinations, R.S.D. relative standard deviation*



overlain spectrum of Ambroxl and Loratadine

SIMULTANEOUS EQUATION METHOD

Two wavelengths selected for the method are 308nm and 245nm that are absorption maxima of ambroxol and loratadine respectively in methanol. The absorbances were measured at the selected wavelengths and absorptivities (A1%,1cm) for both the drugs at both wavelengths were determined as mean of three independent determinations. Concentrations in the sample were obtained by using following equations

At λ1 $A_1 = ax_1bcx + ay_1bcy$(308nm)
At λ1 $A_2 = ax_2bcx + ay_2bcy$(245nm)

$$Cx = \frac{A_2ay_1 - A_1ay_2}{ax_2ay_1 - ax_1ay_2} \quad \text{.....eq. (i)}$$

$$Cy = \frac{A_1ax_2 - A_2ax_1}{ax_2ay_1 - ax_1ay_2} \quad \text{.....eq. (ii)}$$

Where A_1 and A_2 are absorbance of mixture at308nm and 245nm respectively,ax1 and ax2 are absorptivities of ambroxol and loratadine at λ1 and λ2 respectively.cx and cy are concentrations of ambroxol and loratadine respectively. Figure 1 represents the overlain spectra of both the drugs in 1:1 ratio and the criteria for obtaininig maximum precision (i.e. absorbance ratio (A2/A1)/ax2/ax1 and ay2/ay1) by this method were calculated and found to be outside the range of 0.1-2.0 which is satisfied for both the ambroxol and loratadine in ratios of 1:1 and 1:2.

RECOVERY STUDIES[22-23]:

The method was validated according to ICH Q2B guidelines for validation of analytical

procedures in order to determine the linearity, precision, and accuracy for the analyte. Recovery studies by spiking different concentrations of pure drug in the pre analysed tablet samples with in the analytical concentration range of the proposed method. The added quantities of the individual drugs were estimated by above method. The results of recovery studies were found to be satisfactory and the results are presented in table no.2.

TABLE NO : 2
Determination of percentage recovery

Drug In Standard Mixture		% Recovery ±S.D.* Solution (µg/ml)	
AMB	LOR	AMB	LOR
10	10	99.37±0.43	99.04±1.20
20	20	100.93±0.90	99.66±0.63
30	30	100.25±0.78	99.87±1.38

S.D.* for standard deviation, the results of mean of three readings (n=3).

RESULTS AND DISCUSSION

PRECISION:
Assay of the method precision (inter day precision) was evaluated by carrying out 3independent assays of test samples of ambroxol and loratadine. The intermediate precision (inter day precision) of the method was also evaluated by using shimadzu uv-visible double beam spectrophotometer model [SHIMADZU PHARMASPEC UV-1700] was employed with spectral band width of 0.5nm and wavelength accuracy of ±0.3nm with automatic wavelength corrections with a pair of 1cm uv matched quartz cells.

ACCURACY:
Accuracy of the method was studied by recovery experiments. The recovery experiments were performed by adding known amounts to tablet. The recovery was performed at 100% level at 3 different standard concentrations.

The recovery samples were prepared in before mentioned procedure, three different concentrations of the samples were prepared for each recovery level. The solutions were then analysed, and the results of recovery studies were found to be satisfactory and the results are presented in table no:2.

LINEARITY:
The linearity of the response of the drugs was verified at 0-100ug/ml concentrations, the calibration graphs were obtained by plotting the absorbance versus the concentration data and were treated by linear regression analysis(table no) The equation of the calibration curve for ambroxol and loratadine obtained Y=0.008x+0.011 and Y=0.042x+0.016, the calibration curve were found to be linear in the afore mentioned concentrations. The correlation co-efficients (r^2)for ambroxol and loratadine were determined by 0.997 and 0.9991. Table no:3.

LIMIT OF DETECTION(LOD) AND LIMIT OF QUANTIFICATION (LOQ):
The LOD and LOQ of the ambroxol and loratadine were determined by using standard deviation of the response and slope approach as definded in ICH guidelines. The LOD and LOQ was found to be as in table no:3

Table No: 3

Regression And Optical Characteristics Of Ambroxol And Loratadine

Parameters	Value For AMB	Value For LOR
Beers law limit (µg/ml)	10-50	10-50
Correlation coefficient (r)	0.9987	0.9991
Regression equation	0.997	0.998
Slope	0.008	0.042
Intercept	0.011	0.016
LOD	2.31µg/ml	0.482 µg/ml
LOQ	7 µg/ml	1.463 µg/ml

DETERMINATION OF ACTIVE INGREDIENTS IN TABLETS

The validated method was applied to the determination of ambroxol and loratadine in tablets. The Tablets were assyased and the results shown in (table no:1) indicating that the amount of drug in tablet samples met with requirements(99-100%of the label claim)

CONCLUSION

The developed method was found to be simple, sensitive, accurate, precise, reproducible, and can be used for routine quality control analysis of ambroxol hydrochloride and loratadine in bulk and pharmaceutical formulations.

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