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DEVELOPMENT AND VALIDATION OF LORATADINE IN BULK AND PHARMACEUTICAL DOSAGE FORM BY UV SPECTROSCOPIC METHOD

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ABSTRACT

A simple UV spectroscopic method was developed and validated for the estimation of loratadine in bulk and pharmaceutical dosage form using acetonitrile as solvent. The quantification was achieved at 250nm. Beers law was obeyed in the concentration range of 4-24 µg/ml. The results of analysis have been validated statistically and recovery studies carried out in the range 80-120% to confirm the accuracy of the proposed method. The relative standard deviation was found to be less than 2.0%. The assay result of marketed formulation was found to be 99.46% pure. The present result shows that the proposed method can be successfully implemented for estimation of loratadine in bulk and its marketed formulations.

Keywords: UV Spectroscopy, Loratadine, Acetonitrile.

INTRODUCTION

Loratadine is a tricyclic antihistamine, which acts as a selective inverse agonist of peripheral histamine H1-receptors [1]. Loratadine is Ethyl 4-(8-chloro-5, 6-dihydro- 11Hbenzo[1,2-b]pyridin-11ylidene)piperidine-1-carboxylate. It shows molecular formula as C22H23ClN2O2 with molecular weight 382.9. It is official in USP1, BP2; IP3. Loratadine is given orally, is well absorbed from the gastrointestinal tract, and has rapid first-pass hepatic metabolism it is metabolized by isoenzymes of the cytochromeP450 system, including CYP3A4, CYP2D6, and, to a lesser extent, several others. Loratadine is almost totally (97–99%) bound to plasma proteins. Its metabolite desloratadine, which is largely responsible for the antihistaminergic effects, binds to plasma proteins by 73–76%. Loratadine's peak effect occurs in 1–2 hours, and its biological half-life is on average 8 hours (range 3–20 hours) with desloratadine's half-life being 28 hours (range 9–92 hours), 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 unmetabolizedloratadine can be found in the urine [2].

Literature review reveals that some of the UV [2-4, 8, 9], HPLC [1, 5-7]methods have been reported for the estimation of loratadine. Very few assay indicating methods are reported; hence the present work has made an attempt for quantification of Loratadine individually in its bulk and tablet formulation by UV spectroscopy as per ICH guidelines.

MATERIALS AND METHODS

Instrumentation

Absorption spectral measurements were carried out with a UV – Visible spectrophotometer (Elico Model 159) with spectral bandwidth of 1nm and wavelength accuracy of 0.3 nm (with automatic wavelength correction with a pair of 5 cm matched quartz cells.

Chemicals

Acetonitrile used for dilution was of analytical grade. Loratadine pure drug was obtained from Vasudha

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Pharmaceuticals, Visakhapatnam. Tablet formulations [Alaspan, Encore health care Pvt. Ltd., Paithan, Aurangabad district-Maharashtra] were procured from a local pharmacy with labeled amount 10 mg per tablet.

Preparation of Standard stock solutions

Accurate quantity of 25mg pure loratadine drug was weighed and taken in a clean and dry 25ml volumetric flask. The drug was dissolved in some amount of acetonitrile and made up to the mark with the same solvent to give 1000µg/ml solution**.**

Selection of λ max

The standard stock solution was further diluted with Acetonitrile to get a 10 µg/mL of concentration (1 ml to 100 ml).The solution was scanned between 200 and 400 nm using acetonitrile as blank. The UV spectrum had shown highest peak at 250nm.Hence 250nm was selected as λ max for analysis.

Validation parameters

Linearity

A linear relationship should be evaluated across the range of the analytical procedure. It was demonstrated directly on the drug substance (by dilution of a standard stock solution) and using the proposed procedure [10].

Accuracy

Accuracy was established across the specified range of the analytical procedure. Accuracy is the closeness of the test results obtained by the method to the true value. Recovery studies were carried out by addition of standard drug to the sample at 3 different concentration levels taking into consideration percentage purity of added bulk drug samples.

Precision

Precision was determined as repeatability and interday and intraday precision, in accordance with ICH guidelines. Variation of results within the day (intraday), variation of results between the day (interday) were analyzed. Intraday precision was determined by analyzing Loratadine for six times in the same day at 250nm.

Inter day precision was determined by analyzing the drug for three different days at 250 nm. Repeatability was performed by analyzing concentration of drug (12 µg/ml, 16µg/ml) for six times.

Ruggedness

Ruggedness is done by changing analyst to confirm the reproducibility of results.This was validated by analyzing the amount of drug recovered by two different analyst under the same conditions.

Limit of detection (LOD)

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value. For spectroscopic techniques or other methods that rely upon a calibration curve for quantitative measurements, the IUPAC approach employs the standard deviation of the intercept (Sa), which may be related to LOD and the slope of the calibration curve, b, by

$$LOD = 3\ Sa / b$$

Limit of quantitation (LOQ)

The LOQ is the concentration that can be quantitated reliably with a specified level of accuracy and precision. The LOQ represent the concentration of analyte that would yield a signal-to-noise ratio of 10.

$$LOQ = 10\ Sa / b$$

Where, Sa is the standard deviation of the peak area ratio of analyte to IS (5 injections) of the drugs and b is slope of the corresponding calibration curve.

RESULTS AND DISCUSSION

Linearity

In this method Loratadine was estimated by using ultraviolet spectroscopy. The method obeys Beer lamberts law in the concentration range of 4-24 µg/ml and its wavelength of detection was 250nm. Correlation coefficients of loratadine were found to be 0.999 with a straight line equation Y=0.052X+0.017.The absorbance values are given in Table 1 and figure 2 indicates that the method is linear.

Accuracy

The accuracy of the proposed methods was assessed by recovery studies at three different levels i.e. 80%, 100%, 120%.The values of recovery (%), RSD (%) listed in Table 3 indicate the method is accurate.

Precision

The intra & inter day variation and repeatability of the method was carried out and the standard deviation and % RSD (% RSD < 2%) within a day and day to day variations for Loratadine listed in Table 4 and Table 2 ,indicates the proposed method is precise.

Ruggedness

Influence of small changes in parameter such as change in analyst was performed to determine the ruggedness of the method and the % RSD values listed in Table 5 indicates they are within the limits.

LOD & LOQ

The Minimum concentration level at which the analyte can be reliable detected (LOD) & quantified (LOQ) were found to be 0.57 & 1.9 µg/ml respectively.

Assay of Marketed Formulation

Twenty tablets of formulation were weighed and finely powdered. The powder equivalent to 10 mg of Loratadine was accurately weighed. It was then transferred to volumetric flask of 10 ml capacity containing 5 ml of acetonitrile and sonicated for 10 min. The flask was shaken and the solution was filtered through filter paper into 10 ml volumetric flask. Volume was made up to the mark with acetonitrile to give a solution of 1000 µg/ml (Stock solution A). From this stock solution A, 1 ml was taken and placed in 10 ml volumetric flask. The volume was made up to the mark using acetonitrile to give a solution of 100 µg/ml(Stock solution B). From the stock solution B, 2.0 ml was taken and diluted to 10 ml to give 20 µg/ml and it was further used for the estimation of loratadine.% purity of the marketed formulation was found to be 99.46 and results of assay method is represented in Table 6.

Table 1.Linearity Results

Sl. no	Concentration of drug taken (100µg/ml)	Concentration range (µg/ml) in 10ml	Absorbance Range at 250nm
1	0.4ml	4	0.228
2	0.8 ml	8	0.449
3	1.2 ml	12	0.654
4	1.6 ml	16	0.857
5	2.0 ml	20	1.04
6	2.4 ml	24	1.226

Table 2. Results for Repeatability

Concentration	12µg/ml	16µg/ml
Absorbance	0.613	0.857
	0.61	0.855
	0.615	0.862
	0.611	0.87
	0.615	0.882
	0.613	0.866
Mean	0.613	0.865
SD	0.002	0.010
RSD	0.333	1.141

Table 3. Results of Accuracy Studies by UV spectroscopy

Level of recovery	Amount of sample (µg/ml)	Amount of drug added(µg/ml)	Amount of drug recovered (µg/ml)	% Recovery	SD	%RSD
80%	12	9.6	9.46	98.5	0.0035	0.67
100%	12	12	11.76	98.07	0.0018	0.289
120%	12	14.4	14.15	98.2	0.0043	0.565

Table 4.Results for Precision

Concentration	Intraday Precision			Interday Precision	
	1st hour	2nd hour	3rd hour	1st day	2nd day
16µg/ml	0.757	0.857	0.888	0.85	0.8
	0.743	0.866	0.86	0.821	0.821
	0.736	0.862	0.865	0.823	0.813
	0.726	0.882	0.853	0.82	0.843
	0.747	0.855	0.852	0.806	0.822
	0.725	0.87	0.879	0.832	0.82
Mean	0.739	0.86533	0.86617	0.82533	0.81983
SD	0.01247	0.00987	0.01452	0.01469	0.01402
%RSD	1.68795	1.14089	1.67689	1.78018	1.71013

Table 5. Results for Ruggedness

Sample	Label claim(mg)	Analyst 1		Analyst 2	
		Amount found (mg)	% Recovery ±%RSD**	Amount found (mg)	% Recovery ±%RSD**
Loratadine	10	9.90	99.0% ±0.185	9.87	98.7% ±0.372

** Average of six determinations

Table 6. Analysis data of Tablet formulation by UV

Drug	Formulation	Amount of drug taken from tablet	Amount recovered	% Loratadine
Loratadine	Tablet(Alaspan10mg)	10mg	9.94mg	99.46%

Fig 1. Structure of Loratadine

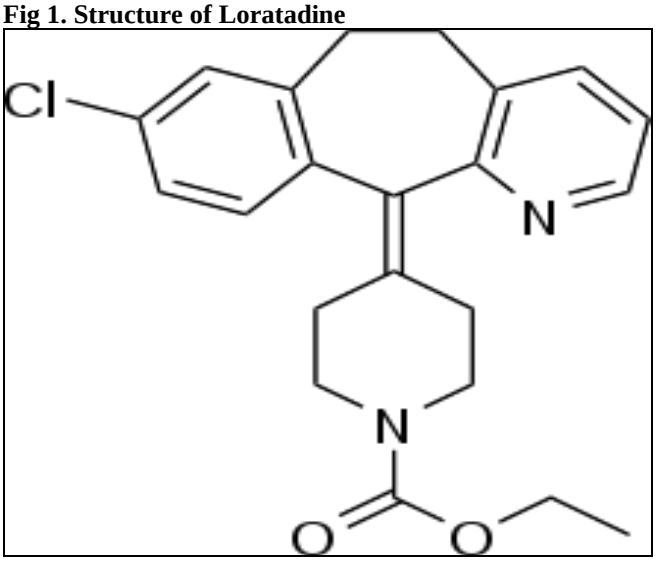
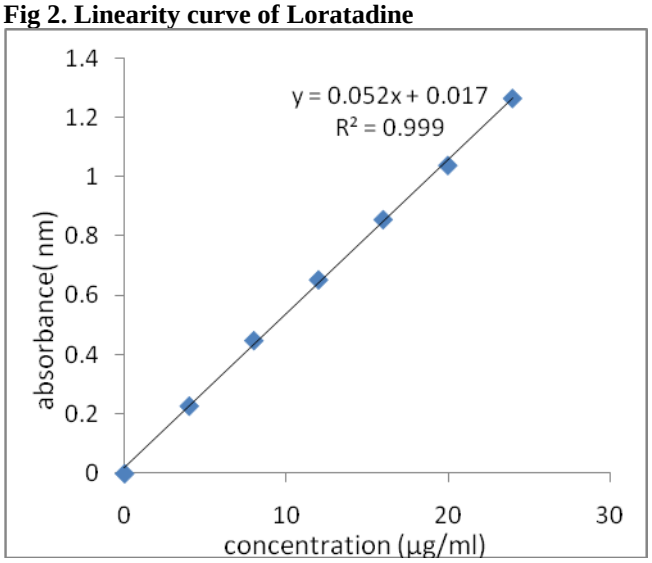


Fig 2. Linearity curve of Loratadine



CONCLUSION

The proposed method was found to be simple, selective and sensitive. The validation parameters were also found to be within the limits. The method showed acceptable linearity and accuracy and is highly sensitive therefore it could be used easily for the routine analysis of pure drugs and their formulations for Loratadine.

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