ISSN:2249-1236

INTERNATIONAL JOURNAL OF RESEARCH AND REVIEWS IN PHARMACY AND APPLIED SCIENCES

Research Article

Received: 02-08-2011 *Accepted: 06-09-2011* *Published: 29-09-2011*

NEW RP-HPLC METHOD DEVELOPMETN AND VALIDATION FOR THE ANALYSIS OF LORATADINE IN FORMULATIONS

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ABSTRACT

A simple, precise and accurate RP-HPLC method was developed and validated for rapid assay of Loratadine in tablet dosage form. Isocratic elution at a flow rate of 1.0 ml/min was employed on a symmetry Chromosil C18 (250x4.6mm, 5µm in particle size) at ambient temperature. The mobile phase consisted of Methanol: TEA: 95:5% (V/V)pH adjusted with Ortho phosphoric acid.. The UV detection wavelength was 242 nm and 20µl sample was injected. The retention time for Loratadine was 4.2 min. The percentage RSD for precision and accuracy of the method was found to be less than 2%. The method was validated as per the ICH guidelines. The method was successfully applied for routine analysis of Loratadine in tablet dosage form and bulk drug.

Key words: Loratadine, RP-HPLC, UV detection, recovery, precise, 242 nm.

INTRODUCTION

Loratadine is H_1 histamine antagonist and it is used in treatment of allergies like hay fever (allergic rhinitis), urticaria (hives) and other skin allergies. Loratadine shows side effects like insomnia, nervousness, anxiety. Other possible side-effects include headache and antimuscarinic effects such as urinary retention, dry mouth, blurred vision, and gastrointestinal disturbances.[4][6] Loratadine causes less but still significant adverse effects like sedation and psychomotor retardation than the older antihistamines because it penetrates the blood brain barrier only to a smaller extent. Loratadine doesnot interact with alcohol. It has rapid first-pass hepatic metabolism. It is metabolized by isoenzymes of cytochrome P450 system including CYP3A4, CYP2D6.[9][10] Loratadine is almost totally (97–99%) bound to plasma proteins. Its metabolite desloratadine is largely responsible for the antihistaminergic effects. It binds to plasma proteins by 73–76%.[4]

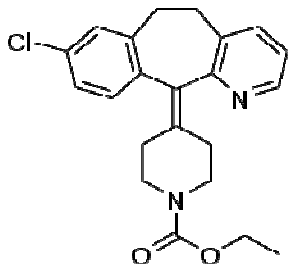


Figure.1: Chemical structure

EXPERIMENTAL

Materials

Working standard of Loratadine was obtained from well reputed research laboratories. HPLC grade water, methanol, Acetonitrile was purchased from E. Merck (Mumbai, India).

Apparatus

A Series HPLC system PEAK LC7000 isocratic HPLC with PEAK 7000 delivery system, Rheodyne manual sample injector with switch (77251), analytical column Chromosil C18 250×4.6mm, Electronic balance-DENVER (SI234), a manual Rheodyne injector with a 20 µl loop was used for the injection of sample. PEAK LC software was used. UV 2301 SPECOPHOTOMETER was used to determine the wavelength of maximum absorbance

Determination of wavelength of maximum absorbance

The standard solutions of Loratadine were scanned in the range of 200 -400 nm against mobile phase as a blank. Loratadine showed maximum absorbance at 242 nm. So the wavelength selected for the determination of Loratadine was 242 nm.

Chromatographic equipment and conditions

The development and validation of the assay was performed on A Series 200 HPLC system PEAK LC7000 isocratic HPLC with PEAK 7000 delivery system. Rheodyne manual sample injector with switch (77251), Analytical column Chromosil 100-5 C18 250×4.6mm, manual injector rheodyne valve) with 20µL fixed loop, PEAK LC software was used.

The mobile phase consisted of a Methanol, Triethylamine 95:5(v/v). Injections were carried out using a 20 µl loop at room temperature (20 + 2 °C) and the flow rate was 1.0 ml/min. Detection was performed at 242 nm with 8.0 min runtime.

Standard and sample solutions

A 10 mg amount of Loratadine reference substance was accurately weighed and dissolved in 10 ml mobile phase in a 10 ml volumetric flask to obtain 1000 ppm concentrated solution. From standard solution by the serial dilution we prepared required concentrations of 100 ppm. From this 2 ml was taken and made upto 10 ml using mobile phase. A composite of 20 tablets was prepared by grinding them to a fine, uniform size powder. 10 mg of Loratadine was accurately weighted and quantitatively transferred into a 100 ml volumetric flask. Approximately 27 ml mobile phase were added and the solution was sonicated for 15 min. The flask was filled to volume with mobile phase, and mixed. After filtration, an amount of the solution was diluted with mobile phase to a concentration of 20 µg/ml.

Method validation

Method validation was performed following ICH specifications for specificity, range of linearity, accuracy, precision and robustness

RESULTS AND DISCUSSION

System Suitability

Having optimized the efficiency of a chromatographic separation the quality of the chromatography was monitored by applying the following system suitability tests: capacity factor, tailing factor and theoretical plates. The system suitability method acceptance criteria set in each validation run were: capacity factor >2.0, tailing factor ≤2.0 and theoretical plates >2000 13. In all cases, the relative standard deviation (R.S.D) for the analytic peak area for two consecutive injections was < 2.0%. A chromatogram obtained from reference substance solution is presented. System suitability parameters were shown in Table.1. Standard chromatogram was given in Figure.2

Table.1 System suitability parameters

Mobile phase	Methanol : TEA 95:5 (v/v)
Pump mode	Isocretic
pH	6.3
Diluents	Mobile phase
Column	Zodiac C18 column (250 X 4.6 mm, 5µ)
Column Temp	Ambient
Wavelength	242nm
Injection Volume	20 µl
Flow rate	1.0 ml/min
Run time	8 minutes
Retention Time	4.2 minutes

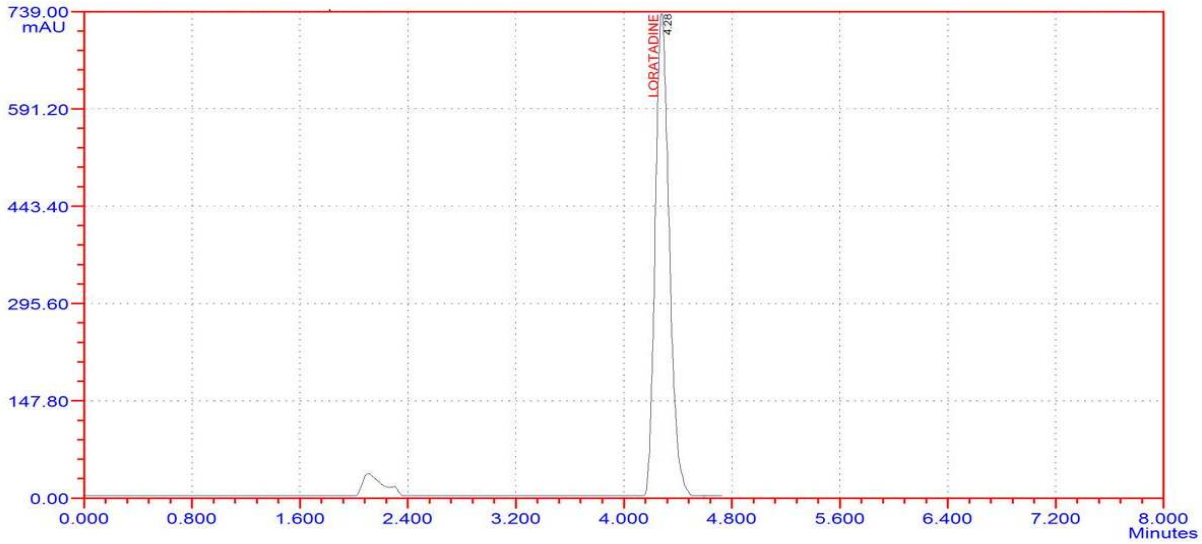


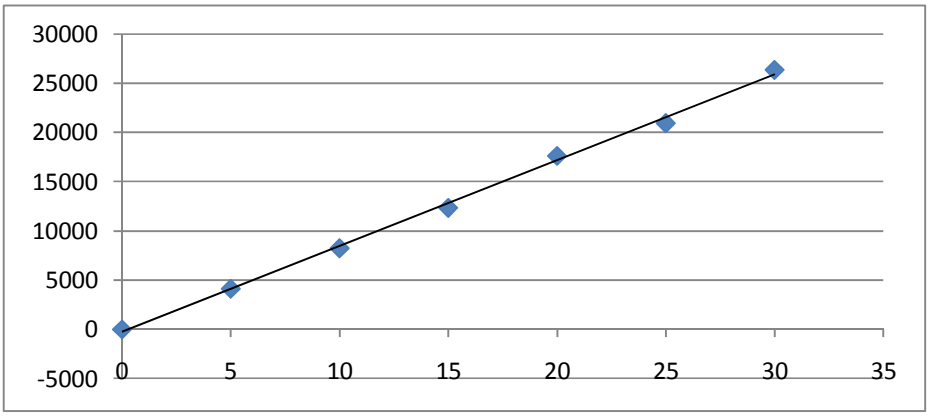
Figure.2: Standard solution

Range of linearity

Standard curves were constructed daily, for three consecutive days, using six standard concentrations in a range of 5, 10, 15, 20, 25, 30µg/ml for Loratadine. The linearity of peak area responses versus concentrations was demonstrated by linear least square regression analysis. The linear regression equation was y = 42598 + 6031x (r= 0.997). Linearity values can shown in Table: 2

Table.2: Linearity Results

Level	concentration of loratadine in ppm	Peak Area
Level 1	5	4132
Level 2	10	8249
Level 3	15	12356
Level 4	20	17639
Level 5	25	20967
Level 6	30	26378
Range 5 ppm to 30 ppm	Slope Intercept CorrealationCoefficient	872.8 274.92 0.9992



Graph.1: Linearity Graph

Precision

To study precision, six replicate standard solutions of Loratadine(20 ppm) were prepared and analyzed using the proposed method. The percent relative standard deviation (% RSD) for peak responses was calculated and it was found to be which is well within the acceptance criteria of not more than 2.0%. Results of system precision studies are shown in Table.3 and Table.4.

Precision Results for Loratadine:

Table.3: Precision Results

Sample	Conc. (in ppm)	Injection No.	Peak Areas	INTER DAY RSD (≤ 2.0%)
Loratadine	20	1	17618	0.42
		2	17522	
		3	17510	
		4	17639	
		5	17697	
		6	17658	
Sample	**Conc (ppm)**	**Inj No.**	**Peak Area**	**INTRA DAY RSD (≤ 2.0%)**
Loratadine	20	1	17540	0.33
		2	17632	
		3	17593	
		4	17645	
		5	17694	
		6	17550	

Limit of Detection and Limit of Quantification:

To determine the Limit of Detection (LOD) sample was dissolved by using Mobile phase and injected until peak was disappeared. After 0.02 ppm dilution Peak was not clearly observed, based on which 0.02 ppm is considered as Limit of Detection and Limit of Quantification is 0.05 ppm.

Table.5: LOD and LOQ results

Parameter	Measured Value
Limit of Quantification	0.05 ppm
Limit of Detection	0.02 ppm

Robustness

Typical variations in liquid chromatography conditions were used to evaluate the robustness of the assay method. In this study, the chromatographic parameters monitored were retention time, area, capacity factor, tailing factor and theoretical plates. The robustness acceptance criteria set in the validation were the same established on system suitability test describe above.

Table.6: Robustness Results

S.NO	PARAMETER	CONDITION	AREA	% OF CHANGE
1	Standard	Standard conditions	17639	100%
2	Mobile phase	Methanol 90%, TEA 10%	17629	99.9%
3	Mobile phase pH	6.1	17540	99.4%
4	Wavelength	240 nm	17697	100.3%

Recovery

Recover test was performed at 3 different concentrations i.e. 10ppm, 20ppm, 30ppm. Results are given in table.7

Table.7: Recovery Results

Recovery	Conc of sample	Recovery	% of recovery
50%	10	9.96	99.6%
100%	20	19.89	99.45%
150%	30	30.04	100.13%

Table.8: Formulation Analysis

S.NO	Tablet	Dosage	Sample conc	Sample estimated	% of Drug Estimated in Tablet
1	LORATIN	10 mg	10 ppm	9.98 ppm	99.8%

CONCLUSION

The proposed method for the assay of Loratadine in tablets or capsules is very simple and rapid. It should be emphasized it is isocratic and the mobile phase do not contain any buffer. The method was validated for specificity, linearity, precision, accuracy and robustness. Although the method could effectively separate the drug from its products, further studies should be performed in order to use it to evaluate the stability of pharmaceutical formulations.

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