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HPLC DETERMINATION AND VALIDATION OF LORATADINE IN PHARMACEUTICAL PREPARATIONS

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ABSTRACT

An accurate, simple and reproducible HPLC method was developed for the estimation of Loratadine. Separation of the drug was achieved on a reversed phase using a LiChrosorb® RP-8 column with a flow rate of 1.4 ml/min. Mixture of Methanol, Acetonitile and Buffer solution (pH=3.5) (200:395:405 v/v) was used as mobile phase. The detection was at 215 nm wavelength. The proposed method was validated as per the ICH guidelines for linearity, accuracy, precision, limit of detection and limit of quantification. The linear range of determination of Loratadine was 20-160µg/ml with a correlation coefficient of 0.999. The retention time of Loratadine was 4.358 min. The percentage recovery of Loratadine was obtained within a range of 99.33-100.4%. The method is suitable for routine quality control analysis of Loratadine in tablet dosage forms.

Keywords: Loratadine, Validation, estimation, RP-HPLC

INTRODUCTION

Loratadine (L) is a non-sedating H_1-antihistamine with the chemical name 4-(8-chloro-5, 6-dihydro-11 H-benzo [5,6] cyclohepta [1, 2-b] pyridin-11-ylidene)-1-piperidinecarboxylic acid ethyl ester **(Figure 1)**. It is a potent and orally active antihistamine that was developed as a therapeutic agent for the treatment of seasonal allergic rhinitis **[1]**. Among the second generation antihistamines, loratadine is free from sedation at the recommended dosages **[2]**.

Its active metabolite – desloratadine (DL) prolongs the effect of the drug **[3]**. Loratadine is commercially available in the form of tablets and syrups, the latter always containing different preservatives. Loratadine was analysed in pharmaceutical formulations alone **[4-11]**, in the presence of its degradation product **[12]**, in mixtures with related impurities **[13-15]**, and with other drugs, for example desloratadin **[16]**, pseudoephedrine **[17-21]**, montelukast **[22]**, pseudoephedrine and dexbrompheniramine **[23]**, and pseuodoephedrine and ibuprofen **[24]**. Literature reveals the use of different analytical techniques to determine L and /or DCL in plasma, voltammetry **[25]**, radioimmunoassay **[26]**, gas chromatography with nitrogenphosphorous **[27]**, high-performance liquid chromatography (HPLC)-UV **[28-30]** and fluorescence detection **[31–35]**, and liquid chromatography–tandem mass spectrometry (LC–MS–MS) **[36–45]**. The present paper is dedicated to the development and validation of a HPLC method for the identification and quantification of loratadine in pharmaceutical preparations.

MATERIALS AND METHODS

Reagents

All chemicals and reagents were used of HPLC. Loratadine reference standard was obtained from Sigma Aldrich. Tablet formulation containing Loratadine 10 mg was purchased at the local market. HPLC grade Acetonitrile and Methanol were procured from Merck Ltd. All other chemical reagents were of analytical grade.

Instrumentation

A Shimadzu HPLC system consisting of the following components was utilized: pump LC – 20 AD, vacuum degasser unit DGU – 20 A_5 and a UV/VIS variable detector SPD – 20 A. Separation was carried out on a LiChrosorb C 8 column (250 x 4.6 mm, particle size 10 µm) under reversed phase partition chromatographic conditions. The equipment was controlled by a PC using chromatographic software.

Chromatographic Conditions

The mobile phase was a 200:395:405 % v/v, Methanol: Acetonitrile: Phosphate buffer (3.85 g sodium dihydrogen phosphate in 500 ml water, adjusted with orthophosphoric acid, pH=3.5±0.1). The mobile phase was filtered through 0.45 µm membrane filter and degassed by using sonicater for about 10 min before use. The sample solutions were also filtered using 0.45 µm membrane filters. The mobile phase was delivered isocratically at a flow rate 1.4 ml/min. The column was maintained at a temperature of 35ºC. The injection volume was a 20 µl and the total run time was 6 minutes. The detection was carried out at 215 nm.

Preparation of the Standard Solution

Accurately weighed quantity of 20 mg Loratadine was transferred in 100 ml volumetric flask, dissolved with 50 ml methanol and made up with the same solvent, having the concentration 200 µg/ml. From the stock solution by further dilutions were prepared standard solutions with the required concentrations.

Sample Preparation

Twenty tablets were accurately weighed and powdered. Quantity equivalent to the average mass of one tablet (10 mg of Loratadine) was weighed and transferred into a 50 ml volumetric flask. Approximately 30 ml of diluents (methanol) was added and the mixture was sonicated for 10 minutes. Then mixture was diluted to volume with methanol. The solution was filtered through a 0.45 µm filter paper discarding the first few ml of filtrate. From the stock solution by further dilutions were prepared the required working solutions.

Placebo Solution Preparation

The placebo solution was prepared by using 100.0 mg of the following excepients: lactose monohydrate, maize starch, silicon dioxide colloidal, Mg-stearate, cellulose and povidone, dissolved in 30 ml methanol and the mixture was sonicated for 10 minutes. The mixture was diluted to 50 ml volume with methanol as solvent. The solution was then filtered through a 0.45 µ filter paper discarding the first few ml of filtrate. This solution was injected to HPLC system.

RESULTS AND DISCUSSION

All of the analytical validation parameters for this proposed method were determined according to ICH guidelines as follows.

Placebo Analysis

The placebo solution was injected twice according to the parameters stated under the developed method. It was found that there was no interference between the analyte and placebo solutions **(Figure 2)**.

Linearity

The **Table 1** presents the equation of the regression line, correlation coefficient (r^2) values of the slope and intercept between the peak areas and concentrations of 20-160 µg/ml with r^2=0.999 **(Figure 3)**. The calibration curve equation shows a good linearity curve which means that the linearity test is validated.

Limit of Detection and Quantification

The detection limit (LOD) is the lowest amount of analyte in the sample, which can be detected but not necessarily quantified as an exact value. The quantification limit (LOQ) is the lowest amount of analyte in the sample, which can be quantitatively determined with suitable precision and accuracy. The LOD and LOQ are calculated as given in **Table 1**.

Precision

For determination of the precision, the standard solution was consecutively injected 6 times according to the above method. Assay % and RSD % values obtained are within the range of 98 %- 102 % (±2). The data given in Table 2 show a precise and valid method of analysis.

Accuracy

The accuracy test was applied at three different levels of concentrations with triple injecting for each sample **(Table 3)**, the % of recovery equation is:

% Accuracy = [(recovered amount / actual amount) X 100]

The accepted limits of recovery are 98 %- 102 % according to USP and all observed data are within the required range that indicates good recovery values. Typical chromatogram of Loratadine is displayed in **Figure 4**.

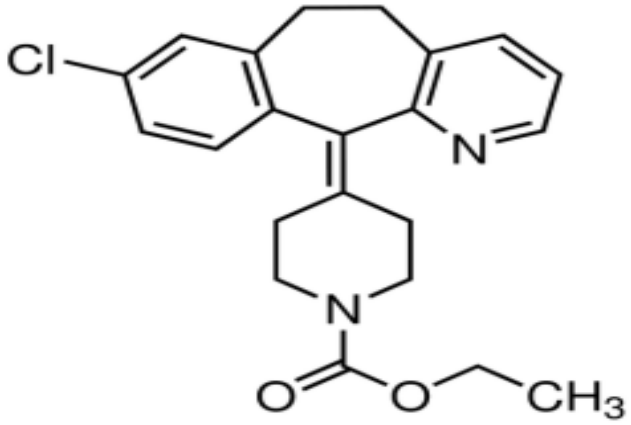

Figure 1: Structure of Loratadine

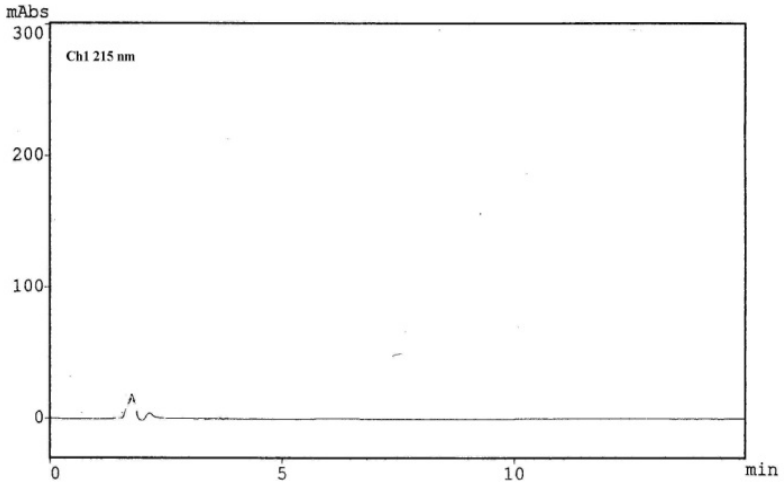

Figure 2: Placebo Chromatogram

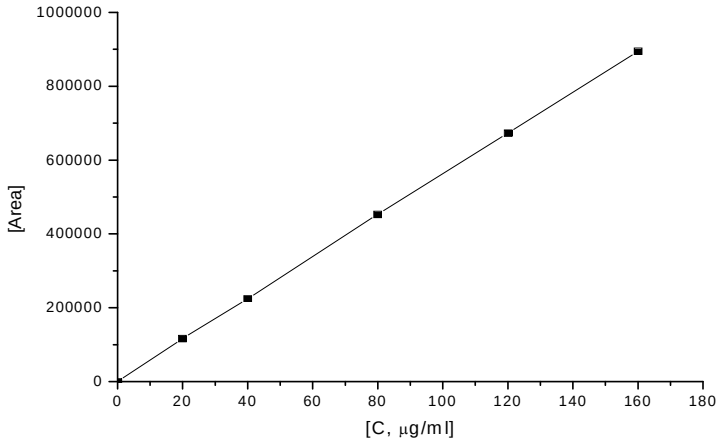

Figure 3: Linearity of Loratadine

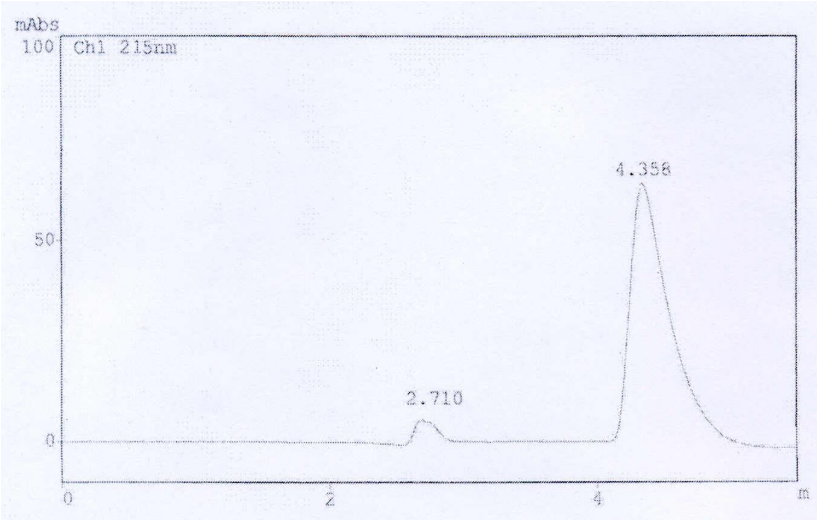

Figure 4: Chromatogram of Loratadine Sample

Table 1: Linearity Results, Limit of Detection (LOD) and Limit of Quantification (LOQ)

Compounds	r^2	Calibration curve equation	LOQ ng	LOD ng
Loratadine	**0.999**	**Y=55703,8X+241,6**	**3**	**8**

Table 2: Results of Formulation and Recovery Studies

Drug	Amount (mg/1 tabl)		Percentage Recovery*
	Label Claim	Found ±S.D.*	
Loratadine	**10 mg**	**10.19 (± 1.168)**	**100.1_5 (± 1.179)**

***Average of 6 Determinations**

Table 3: Accuracy of Loratadine

Parameters	% Taken	Mass taken (mg/1 tabl.)	Mass found (mg/1 tabl.)	% Found	% Recovery
		5.00	5.02	50.20	100.4
	50.00	5.00	5.01	50.10	100.2
		5.00	4.99	49.90	99.80
		10.00	9.93	99.93	99.93
	100.0	10.00	10.02	100.2	100.2
		10.00	9.93	99.93	99.93
		15.00	14.90	149.0	99.33
	150.0	15.00	14.95	149.5	99.67
		15.00	15.07	150.7	100.5
X					99.99
SD					±0.370
% RSD					0.370

CONCLUSION

An accurate, sensitive and precise HPLC method with ultra violet detection was developed and fully validated for quality control analysis of Loratadine in tablets. The proposed method is very rapid, where the total analytical run time is less than 6 min.

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