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ANALYTICAL METHOD DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF LORATADINE USING UV-SPECTROPHOTOMETER

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ABSTRACT

The UV-Spectrophotometric method can be used for routine analysis of Loratadine in API and Pharmaceutical dosage form. Pharmaceutical analysis is mainly focused in drug analysis, raw material and pharmaceutical formulation involving the determination of active components, impurities, excipients, content uniformity, solubility, dissolution rate and stability. The spectrophotometric method were successfully developed for the determination by using INFRADIGI IR-513C, solvent system was 0.1 N HCL, Ethanol, detection wavelength was 276nm. The analytical method was validated according to ICH guidelines (ICH, Q2(R1)). The linearity study for Loratadine was found in concentration range of 0.5-2.5µg/ml and correlation coefficient (r2) was found to be 0.999, The percentage mean recovery for Loratadine was found to be 96.83%. The precision study was precise, intermediate precision, and Method Precision. RSD% for intermediate precision was 1.4%. The %RSD method precision was found to be 0.4%. The degradation was determined by both analysed both drug solutions in the presence of acid, base, hydrogen peroxide, thermal and photosensitivity.

KEYWORDS: Loratadine, Antihistamine, Uv-spectrophotometer, Validation method, Absorbance, λmax wavelength.

INTRODUCTION[25]

A New method was established for estimation of Loratadine by UV-Spectrophotometric method. Loratadine, a piperidine derivative related to azatadine, is a long-acting, non-sedating antihistamine with no significant antimuscarinic activity. It is used for the symptomatic relief of allergic conditions such as runny nose, itchy or watery eyes, sneezing, and nasal or throat itching and chronic urticaria. Loratadine is well absorbed following oral administration with the peak plasma concentration usually attained in 1 hour. Loratadine is a second generation antihistamine used to manage the symptoms of allergic rhinitis. A lack of sedative and CNS adverse effect make loratadine, along with other second generation antihistamines, preferable over their 1st generation counterparts in many clinical situation.

Loratadine

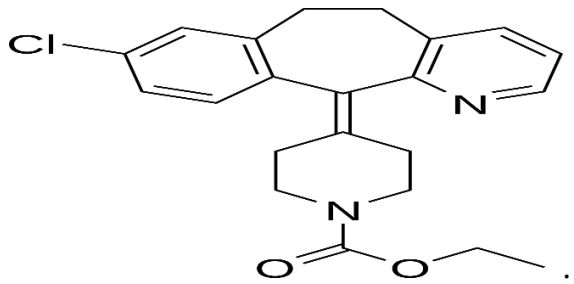

Figure 1.1: Structure of loratadine.

Chemical Name: Ethyl 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-1-piperidinecarboxylate.

Analytical method

Analytical method includes use of a specified techniques and detailed – stepwise instruction which are used in qualitative, quantitative or structural analysis of a sample for one or more analytes. Analytical method development allows to confirm that that accuracy and reliable potency measurement of Pharmaceutical Preparation can be prepared.

Method validation

The method of validation is used for identification tests, quantitative tests for impurities content, limit tests for control of impurities.

Method validation is a process of establishing documented evidence that provides high level of guarantee that the product that will meet the requirement of decide analytical application.

MATERIALS AND METHODS

List of instruments

Table 1.1: List of instrument.

Si. No	Instrument	Model
1	UV/VIS Spectrophotometer	Infradigi ir -513c
2	Ph meter	Elico
3	Weighing machine	Wensar
4	Pipettes and burettes	Borosil
5	Beakers	Borosil

List of chemicals

Table 1.2: List of chemical.

SI. NO	Chemical	Company name
1	Loratadine	Alaspan
2	Hydrogen peroxide	Merk
3	Ethanol	Krishna pharma
4	Hydrochloric acid	Merk
5	Sodium hydroxide	Merk

Method development[20][22][23]

Method development for simultaneous estimation of loratadine in pharmaceutical dosage form includes the following steps:

Assay procedure

Preparation of 0.1N Hcl: Pipette put 4.2ml of hydrochloric acid in 500ml distilled water.

Diluent preparation: 0.1N Hcl and Ethanol (9:1)

Preparation of loratadine Standard & Sample solution

Standard solution preparation

Accurately weigh and transfer 0.1g of loratadine working standard into a 10ml clean dry volumetric flask add ethanol and sonicate to dissolve it completely and make volume up to the mark with same solvent (stock solution). Further pipette 1ml of loratadine of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent up to the mark with diluent. Further pipette 1ml of loratadine of the above stock solution into 10ml volumetric flask and dilute up to the mark with diluents.

Sample solution preparation

Accurately weigh and transfer 0.1g of loratadine working sample into a 10ml clean dry volumetric flask add small amount of ethanol and sonicate it up to 30mins to dissolve it completely and make volume up to the mark with same solvent (stock solution). Then it is filtered using whattman filter paper. Further pipette 1ml of loratadine of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent up to the mark with diluent. Further pipette 1ml of loratadine of the above stock solution into 10ml volumetric flask and dilute up to the mark with diluents.

Procedure: keep standard, sample into the uv system and measure the absorbance for the loratadine peaks and calculate the % assay by using the formulate. The assay absorbance are shown in Table 1.3

Analytical method validation

Accuracy

Accurately weigh and transfer 0.1g loratadine working standard into a 10ml clean dry volumetric flask add ethanol and sonicate to dissolve it completely and make up to the mark with the same solvent (stock solution). Further pipette 1ml loratadine of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluents. Further, pipette 1ml of loratadine of the above stock solution into a 10ml volumetric flask and diluent. The results are shown in Table 1.5

Preparation of sample solution

For preparation of 80% solution (With respect to target assay concentration)

Accurately weigh and transfer 0.4g loratadine working standard into a 10ml clean dry volumetric flask add ethanol and sonicate it up to 30mins to dissolve it completely and make up to the mark with the same solvent. Then filter it through whattman filter paper (stock solution).

Further, pipette 1ml loratadine of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluents. Further pipette 1ml of loratadine of the above stock solution into a 10ml volumetric flask and diluent.

For preparation of 100% of solution (With respect to target assay concentration)

Accurately weigh and transfer 0.5g loratadine working standard into a 10ml clean dry volumetric flask add ethanol and sonicate it up to 30mins to dissolve it completely and make up to the mark with the same solvent. Then filter it through whattman filter paper (stock solution).

Further, pipette 1ml loratadine of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluents. Further pipette 1ml of loratadine of the above stock solution into a 10ml volumetric flask and diluent.

For preparation of 120% of solution (With respect to target assay concentration)

Accurately weigh and transfer 0.6g loratadine working standard into a 10ml clean dry volumetric flask add ethanol and sonicate it up to 30mins to dissolve it completely and make up to the mark with the same solvent. Then filter it through whattman filter paper (stock solution).

Further, pipette 1ml loratadine of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluents. Further pipette 1ml of loratadine of the above stock solution into a 10ml volumetric flask and diluent.

Precision

Accurately weigh and transfer 0.1g of loratadine working standard into a 10ml clean dry volumetric flask add ethanol and sonicate to dissolve it completely and make volume up to the mark with same solvent (stock solution). Further pipette 1ml of loratadine of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent up to the mark with diluent. Further pipette 1ml of loratadine of the above stock solution into 10ml volumetric flask and dilute up to the mark with diluents.

Procedure: keep standard into the UV system and measure the absorbance for the loratadine peaks for five times. The % RSD for the absorbance of five replicates were found to be within the specified limits.

Intermediate precision

To evaluate the intermediate precision (also known as ruggedness) of the method, precision was performed on different day.

Preparation of stock solution

Accurately weigh and transfer 0.1g working standard into a 10ml clean dry volumetric flask add ethanol and sonicate to dissolve it completely and make up to the mark with the same solvent (stock solution).

Further, pipette 1ml loratadine of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluents. Further, pipette 1ml of loratadine of the above stock solution into a 10ml volumetric flask and diluent.

Procedure: The standard solutions prepared in the precision was performed on the other day, for five times and measured the absorbance for all five replicates in UV. The % RSD for the absorbance of five replicates were found to be within the specified limits.

Method precision

To evaluate the method precision five individual sample solution were prepared and calculate the % of assay.

Preparation of standard solution: Accurately weigh and transfer 0.1g of loratadine working standard into 10ml clean dry volumetric flask add ethanol and sonicate to dissolve it completely and make volume up to the mark with the same solvent (stock solution).

Further pipette 1ml of loratadine of the above stock solution into a 10ml volumetric flask and dilute, further pipette 1ml of loratidine of the above stock solution into 10ml volumetric flask and dilute up to the mark with diluents.

Linearity

Stock solution

Accurately weigh and transfer 0.1g of loratadine working standard into a 10ml clean dry volumetric flask add ethanol and sonicate to dissolve it completely and make volume up to the mark with the same solvent (stock solution). Further pipette 1ml of loratadine of the above stock solution into 10ml volumetric flask and dilute up to the mark with diluents.

Procedure: Chart each level into the spectroscopic system and measure the peak absorbance. Plot a graph of peak absorbance versus concentration (on X-axis concentration and on Y-axis peak absorbance) and calculate the correlation coefficient. The results are tabulated in Tables

1.4 and the calibration curve for loratadine is shown in Fig 1.4 and overlay uv spectrum of loratadine is shown in Fig 1.5

RESULT AND DISCUSSION

The spectroscopic method development for the estimation of loratadine were optimized by several trials for various parameters as solvent system finally, the optimized spectroscopic methods was selected for the separation and quantification of loratadine in API and pharmaceutical dosage form by uv-spectroscopic method.

Selection of solvent

We have tired some solubility test with different solvents like toluene, chloroform, benzene, phenol, ethanol with 0.1N HCL. Hence we used ethanol and 0.1 N HCL (1:9) as a solvent.

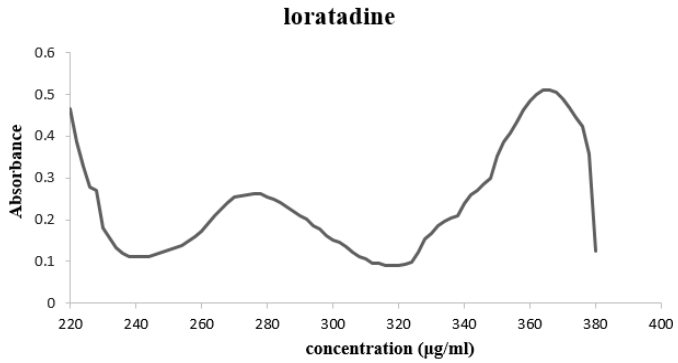

Figure 1.2: UV Specturm of standard loratadine.

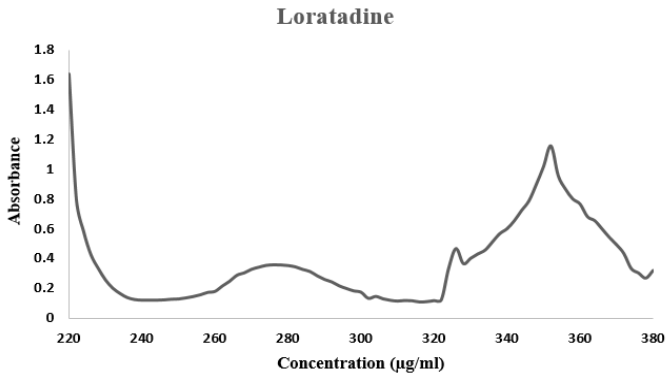

Figure 1.3: UV Spectrum of sample drug loratadine.

Observation: Compared to other four trails, trail 5 has proper spectrum and peak concentration.

Assay calculation for loratadine

The assay study was performed for the loratadine.

Assay results: For loratadine is shown in table 1.3

Table 1 3: Assay absorbance.

Solution	Absorbance
Standard	0.358
sample	0.465

$$\% \text{ PURITY} = \frac{0.358}{0.465} \times \frac{0.01}{10} \times \frac{10}{1} \times \frac{10}{1} \times \frac{99.8}{100} \times \frac{0.1}{0.01} \times 100 = 98.69\%$$

Validation results

Linearity

The linearity study was performed forth concentration of 0.5ppm to 2.5ppm. Each level was charge into Spectroscopy system. The area of each level was used for used for calculation of correlation coefficient.

Table 1.4: Lineartiy results of loratadine.

S. No	Linearity Level	Concentration (µg/ml)	Absorbance at 276nm
1	I	0.5	0.024
2	II	1	0.049
3	III	1.5	0.072
4	IV	2	0.097
5	V	2.5	0.121
Correlation Coefficient			0.9999

Acceptance criteria: Correlation coefficient should not be less than 0.999.

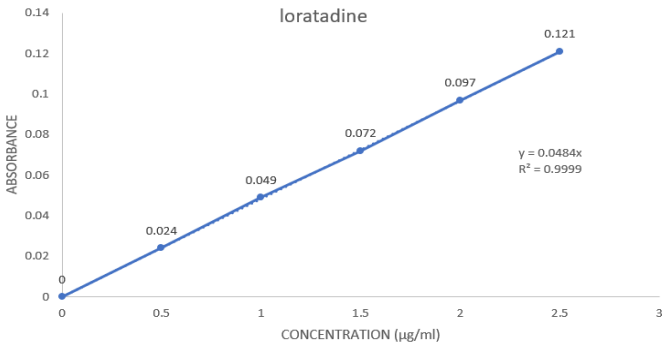

Figure 1.4: Calibration curve for loratadine.

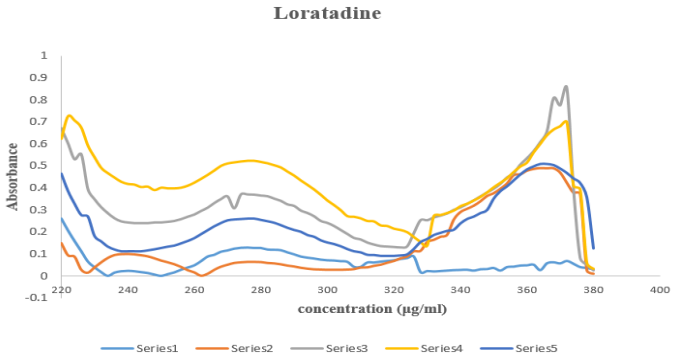

Fig. 1.5: Overlay UV spectrum of loratadine.

Accuracy test results of loratadine

Table 1.5: Accuracy test result of loratadine.

%Concentration (at specification level)	Amount added(mg)	Amount found (mg)	% recovery	Mean
80%	4	4.99	89.9	96.83
100%	5	5.01	100.1	
120%	6	4.05	100.5	

Degradation studies

Table 1.6: Degradation studies.

Parameter	Loratadine
Acid	0.064
Base	0.045
Hydrogen Peroxide	0.371
Thermal	0.261
Photo	0.064

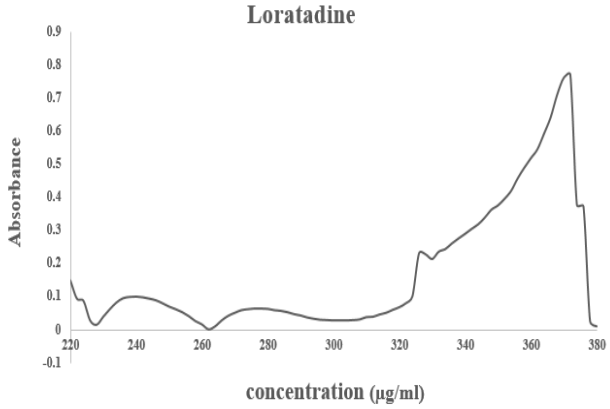

Figure 1.6: Hydrolytic degradation under acidic condition.

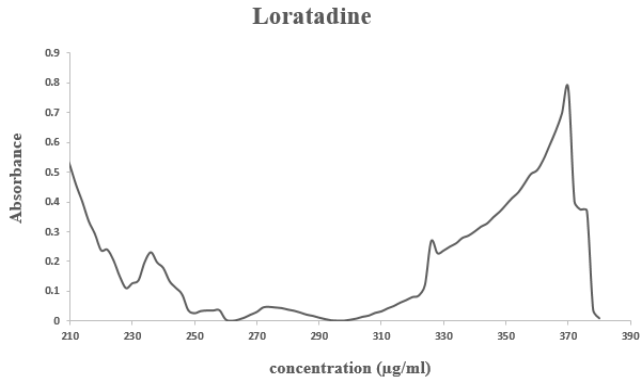

Figure 1.7: Hydrolytic degradation under alkaline condition.

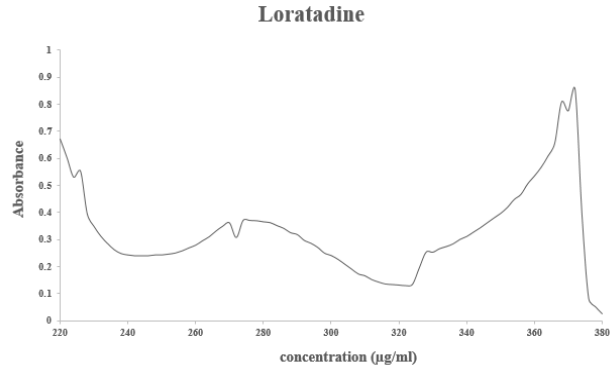

Figure 1.8: Oxidative degradation (Hydrogen peroxide).

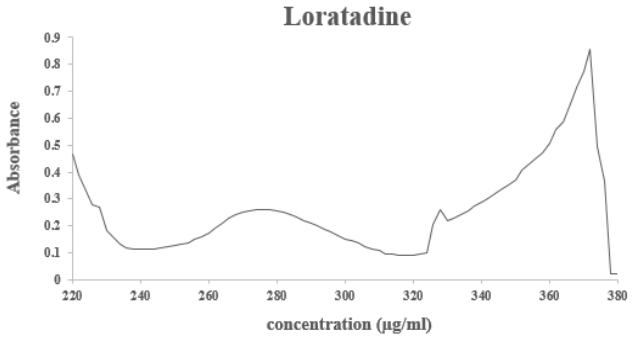

Figure 1.9: Thermal induced degradation.

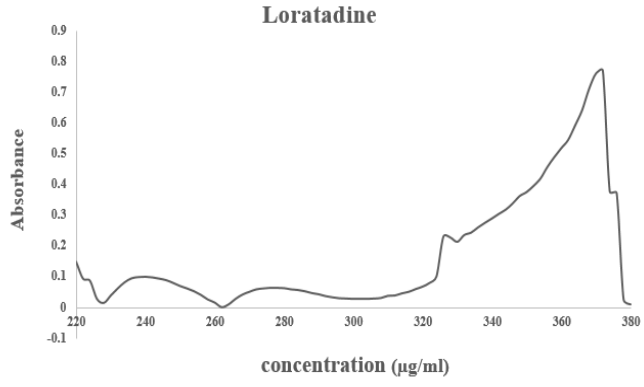

Figure 1.10: Photo degradation.

Sandell's Sensitivity

Sandell's sensitivity is the lowest concentration in ppm (µg/ml) which results in an absorbance of 0.01 in 0.1 cm path length.

$$\textbf{Sandel sensitivy} = \frac{0.001 \times 1\ (cm)}{slope\ (\frac{cm3}{\mu g})}$$

$$= \frac{0.001 \times 1}{0.048}$$

Sandel sensitivy = 0.02

CONCLUSION

From the above results and discussion, a new method was established for estimation of Loratadine by UV-Spectrophotometric method with using the solvent system 0.1N HCL, Ethanol detection wavelength was 276nm. The analytical method was validated according to ICH guidelines (ICH, Q2 (R1)). The linearity study for Loratadine was found in concentration range of 0.5-2.5µg/ml and correlation coefficient (r2) was found to be 0.999, The %mean recovery for Loratadine was found to be 96.83%. The precision study was precise, intermediate precision, and Method Precision. %RSD for intermediate precison was 1.4%. The %RSD method precison was found to be 0.4%. The degradation was determined by both analysed both drug solutions in the presence of acid, base, hydrogen peroxide, thermal and photosensitivity. Hence, the suggested UV-Spectrophotometric method can be used for routine analysis of Loratadine in API and Pharmaceutical dosage form.

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