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Research Article

METHOD DEVELOPMENT AND VALIDATION OF RUPATADINE FUMARATE IN BULK BY UV SPECTROSCOPY

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ABSTRACT

A simple, rapid, precise and economical spectrophotometric method has been developed for quantitative analysis of rupatadine fumarate in bulk form. The objective of the present work is to develop and validate stability indicating simple and accurate method for the determination of Rupatidine fumarate using accurate UV spectroscopic method. The solutions of standard were prepared in methanol. Based on the solubility and physical parameters of the drug the standard stock solution of the drug was prepared and wavelength maxima were determined. The λmax was found to be 232nm. Based on the absorbance maxima of the drug dilutions were prepared and in the formulation estimated was carried out. The method can be adopted in routine analysis of Rupatadine fumarate in bulk form and it involves relatively low cost solvents and no complex extraction techniques. The drug showed linearity in the range of 2-10µg/ml with a correlation co-efficient of 0.999. The ruggedness was found to be 0.28%. The detection limit and quantification limit of the method were calculated as the 0.4714µg/ml and 1.5557µg/ml. The method validated for different validation parameters such as linearity, accuracy, precision, detection limit, quantization limits, robustness, ruggedness and the results were found to be within the acceptance limits as per the guidelines of International Conference on Harmonisation (ICH).

KEYWORDS: Rupatadine fumarate, Spectroscopy, Method development.

INTRODUCTION

Rupatadine fumarate is a dual histamine H1 receptor and platelet activating factor receptor antagonist that is used for symptomatic relief in seasonal and perennial rhinitis as well as chronic spontaneous urticaria in adults and children. The chemical name of Rupatadine fumarate is (2E)-but-2-enedioicacid; 13chloro-2- {1-[(5-methylpyridin-3-yl)methyl] piperidin-4-ylidene}- 4azatricyclo [9,4,0,0 {3,8}] pentadeca-1 (15), 3(8),4,6,11,13-hexaene. It has a molecular formula of $C_{30}H_{30}ClN_3O_4$. Rupatadine fumarate is a white coloured crystalline powder having solubility in methanol, ethanol, chloroform. The melting point of rupatadine fumarate is >187^{0}C.[1]

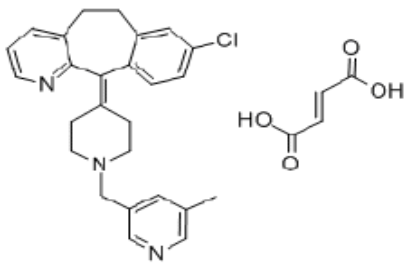


Figure 1: Structure of Rupatadine fumarate[2]

It is having the purity 98.8-99%. It is available under the brand name Rupafin, Rupax. It was stored in dark place at 0-4^{0}c for days to weeks and at 20^{0}c for months to years.

Rupatadine fumarate has a dual mechanism of action. It acts as a long acting, non sedative antagonist at histaminergic H1 receptors by competitively binding to it which is present on uterus, bronchus and large blood vessels etc. It is also antagonizing the platelet activating factor. Both histamine and PAF causes broncho-constriction and lead to an increase in the vascular permeability, acting as a mediator in the inflammatory process, which is responsible for the bronchial hyper reactivity.[3]

MATERIALS AND METHODS

Drug, solvents, chemicals

Rupatadine fumarate was obtained as a gift sample from Hetero Pharmaceutical private limited, Nakkapalli. Methanol and distilled water are used as solvents for this method and were procured from the local market.

INSTRUMENTS

Instruments employed for the study were

- WENSAR weighing scales limited (weighing balance).
- ELICO-Double beam SL-210/UV-Visible spectrophotometer with pair of 10 mm matched quartz cells.

Preparation of reagents

Preparation of stock 1 solution

Weigh accurately 100mg of Rupatadine fumarate in a 100ml volumetric flask and dilute with upto the mark to get concentration of 1000µg/ml.

Preparation of stock 2 solution

Take 1.0ml of above stock-1 solution and dilute with methanol in 100ml of volumetric flask to get concentration of 10µg/ml.

Preparation of stock 3 solution

From stock-1 solution, take 1.0ml and dilute with methanol in 10ml volumetric flask to get concentration of 100µg/ml.

Preparation of NaOH solution (0.1N):

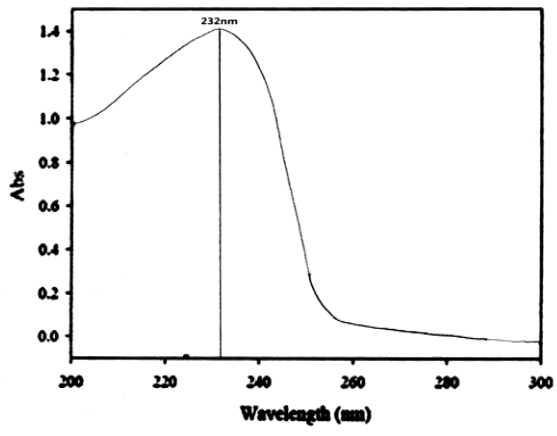
Accurately weighed 4.0gms of NAOH and dissolved in few ml of water and final volume is make upto 1000ml with distilled water and standardized.

Preparation of 0.1N HCL solution

Accurately measured 8.3ml of HCL and diluted in few ml of water and final volume is make upto 1000ml with distilled water and standardized.

METHODOLOGY

Method Development



Based on the solubility and physical parameters of the drug the standard stock solution of the drug was prepared and wavelength maxima were determined. The λ max was found to be 232nm.

Based on the absorbance maxima of the drug, different dilutions were prepared and the formulation estimation was carried out.[5]

Selection of solvent

The solubility of rupatadine fumarate was determined in a variety of solvents as per Indian pharmacopeia standards. Solubility test for rupatadine fumarate was carried out in different polar solvents. From the solubility studies, methanol was selected as suitable solvent for proposed method.[4]

Selection of λ max

The standard stock solution was further diluted with methanol to get 10µg/ml concentrations. The solution was scanned between 200-400nm range using methanol as blank. From the UV spectra 232nm was selected as for analysis of rupatadine fumarate.

Figure 2: UV absorption spectrum of rupatadine fumarate at 232nm

METHOD VALIDATION

Linearity

In this methanolic stock solution of rupatadine fumarate (0.2-1.0ml of 10µg/ml) were transferred into 100ml volumetric flask and made upto the mark with methanol. The absorbance of different concentration solutions were measured at 232nm against blank. The sample was found to be linear from 2-10µg/ml the calibration curve was plotted using concentration v_s absorbance. The curve obtained was linear in the concentration range of 2-10µg/ml.

Preparation of 2µg/ml solution

From stock-3 solution, take 1.0ml and dilute with methanol in 50ml volumetric flask to get concentration of 2µg/ml.

Preparation of 4µg/ml solution

From stock-3 solution, take 2.0ml and dilute with methanol in 50ml volumetric flask to get concentration of 4µg/ml.

Preparation of 6µg/ml solution

From stock-3 solution, take 3.0ml and dilute with methanol in 50ml of volumetric flask to get concentration of 6µg/ml.

Preparation of 8µg/ml solution

From stock-3 solution, take 4.0ml and dilute with methanol in 50ml of volumetric flask to get concentration of 8µg/ml.

Preparation of 10µg/ml solution

From stock-3 solution, take 5.0ml and dilute with methanol in 50ml volumetric flask to get concentration of 10µg/ml.

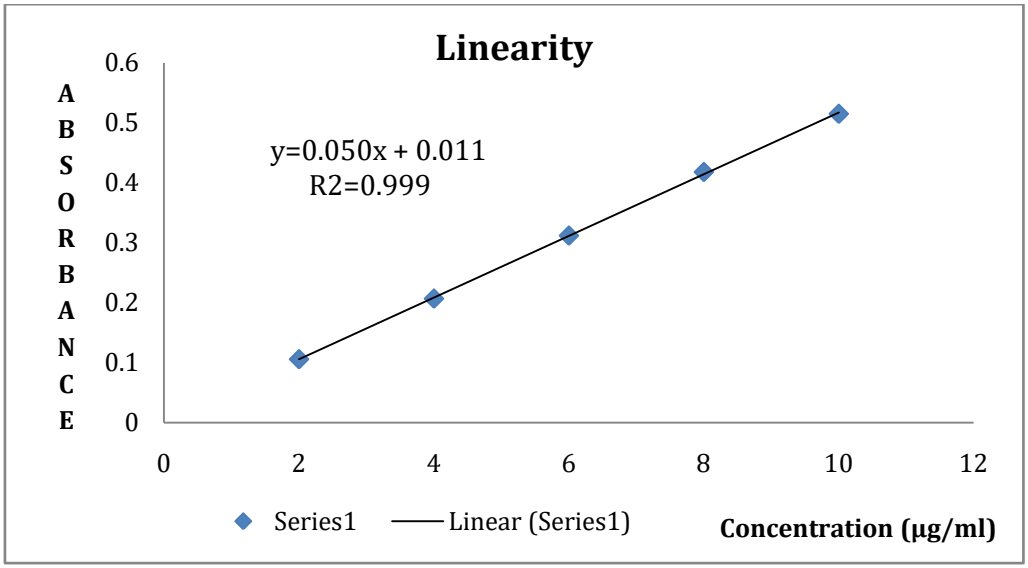


Figure 3: Calibration curve of Rupatadine fumarate

Precision

To evaluate the precision of the methods, pure drug solution (within working limits) was analyzed and being repeated 6 times of two different days. The relative error (%) and relative standard deviation (%) were found to be well within the acceptance criteria of below 2, indicate the high accuracy and precision for the proposed methods.

Preparation of 6µg/ml stock solution

From stock-3 solution, take 3.0ml and dilute with methanol in 50ml of volumetric flask to get concentration of 6µg/ml.

Table 1: Precision result

Precision	%RSD
Repeatability	0.22
Intraday precision	0.35
Inter day precision	0.31

Ruggedness

In order to determine this parameter the analysis was performed at same operational conditions and same environmental conditions but using different analysis.

Table 2: Ruggedness result

Parameter	% RSD
Ruggedness	0.28

Limit of detection (LOD) and limit of quantification (LOQ):

The detection limit and quantification limit of the method were calculated as the 0.4714µg/ml and 1.5557µg/ml respectively.

Table 3: Optical characteristics of Rupatadine fumarate by UV method

Parameters	Method values
Wavelength **λ** (nm)	232nm
Beer's law limit (µg/ml)	3-21
Sandell's sensitivity (µg/cm^2/0.001AU)	0.02296
Molar absorbtivity (L mol-1 cm-1)	1.0677x10^4
Correlation co-efficient (r)	0.999
Regression equation (Y=mx+c)	Y=0.050x +0.011
Slope (m)	0.050
Intercept (c)	0.011
LOD(µg/ml)	0.4714
LOQ(µg/ml)	1.5557
Standard error of mean of regression line	0.001565

RESULTS AND DISCUSSIONS

In the present work we have developed and validated UV spectroscopic method. The method was validated as per ICH guidelines. The linearity was found to be 2-10µg/ml for UV spectroscopic method showing the correlation coefficient of 0.999. The UV spectroscopic method was validated for linearity, precision, LOD, LOQ and ruggedness and the results were tabulated in table 1,2,3. All the results were found to be within the limits as per ICH guidelines and hence the proposed method was successfully employed for the determination of Rupatadine fumarate in its API for regular and routine analysis.

CONCLUSION

A simple, accurate, precise method was developed for the estimation of Rupatadine fumarate in bulk form. The method was validated as per ICH guidelines.

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