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Original Article

UV SPECTROPHOTOMETRIC DETERMINATION OF RUPATADINE FUMARATE IN BULK AND TABLET DOSAGE FORM BY USING SINGLE POINT STANDARDIZATION METHOD

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ABSTRACT

Objective: To develop and validate a simple, selective, precise and accurate method for the estimation of rupatadine fumarate in bulk and tablet dosage form by using the single point standardization method as per international conference on harmonization (ICH) guidelines.

Methods: In this proposed method, the absorbance of a standard solution of known concentration and a sample solution was measured. From this, the concentration of the unknown can be calculated.

Results: Rupatadine fumarate showed maximum absorbance at 246 nm with methanol. Linearity was checked in different concentrations. The calibration curve was obtained in the range of 2-10 µg/ml. The slope, intercept and correlation coefficient (R^2) values of Rupatadine fumarate were found to be 0.047, 0.0034 and 0.9995 respectively. Intra-day and inter-day precision studies were carried out and there % RSD values were found within limits i.e. less than 2%. The recovery studies were carried out by adding a known amount of standard drug to preanalysed formulation and % Recovery was found to be within 99.7-101.6%. LOD and LOQ of Rupatadine fumarate were found to be 0.1 µg/ml and 0.3 µg/ml respectively. Robustness studies were performed at different wavelengths and the % RSD was found within the limits i.e. less than 2 %.

Conclusion: The developed single point standardization method for the estimation of Rupatadine fumarate was found to be simple, precise, accurate, reproducible and cost-effective. Statistical analysis of the developed method confirms that the proposed method is an appropriate and it can be useful for the routine analysis. The proposed method gives the basic idea to the researcher who is working in the area like product development.

Keywords: Rupatadine fumarate, Standardization, Robustness, Reproducible

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INTRODUCTION

Rupatadine fumarate [(E)-but-2-enedioic acid: 8-chloro-11-[1-[(5-methylpyridine-3-yl) methyl] piperidin-4-ylidene] 5, 6-dihydrobenzo [1, 2] cyclo hepta [2, 4-b] pyridine], with molecular weight of 532.037 g/mol [1]. It is a second generation antihistamine and a PAF antagonist used to treat allergies. It blocks H_1 and PAF (platelet activating factor) receptor and prevents their mediators from exerting their effects and reduces the severity of allergic symptoms [2].

UV spectrophotometric analysis is based on measuring the absorption of monochromatic light by colorless compounds in the near of the UV path of the spectrum [200-400 nm]. The photometric method of analysis is based on beer's-lamberts law, which states that the absorbance of a solution is directly proportional to the concentration of the absorbing species in the solution and the path length [3]. Thus, for a fixed path length, UV spectroscopy can be used to determine the concentration of absorber in a solution [4-5].

As per the past literature survey, Rupatadine fumarate was estimated by different spectroscopic and chromatographic techniques such as, UV-Visible spectroscopic method by using different reagents [6-7], UV spectroscopic method for the estimation of Rupatadine fumarate in tablet dosage form [8], AUC and first-order derivative methods [9] and RP-HPLC technique [10, 11]. Hence the present study aims to develop and validate a simple, precise, and accurate UV spectrophotometric method for the estimation of Rupatadine fumarate in bulk and tablet dosage form by using the single point standardization method.

MATERIALS AND METHODS

Chemicals and reagents

Rupatadine fumarate was obtained as a gift sample from Medrich pharma company, Bangalore. Methanol-AR grade and Distilled water.

Instruments used

Electronic weighing balance-SHIMADZU-model-ELB300, sonicator-Ultrasonicator-model-2200MH, agilent UV-Visible spectrophotometer-model-Cary 60.

Method used

The single point standardization procedure involves the measurement of the absorbance of a sample solution and of a standard solution of a reference substance having the same concentration. From this concentration of the sample was calculated [12].

Experimental work

Selection of solvent

The solubility of the drug was performed with different solvents. Rupatadine fumarate was freely soluble in methanol. The drug showed a good absorbance spectrum and was stable in methanol, hence methanol was selected as the solvent. The solubility profile of Rupatadine fumarate was given in table 1.

Preparation of standard stock solution

Weighed accurately about 50 mg Rupatadine fumarate reference standard and transferred into 50 ml volumetric flask. Then dissolved and diluted up to the mark with methanol to give a stock solution having strength 1 mg/ml or 1000µg/ml.

Determination of absorption maxima

The above stock solution was further diluted with distilled water to get a concentration of 10 µg/ml and scanned under UV between 200-400 nm by taking distilled water as blank. The maximum absorbance wavelength of Rupatadine fumarate was found at 246 nm as shown in (fig. 1).

Calibration curve

Working standard solutions of the drug having concentration 2, 4, 6, 8 and 10µg/ml were prepared by diluting the standard stock solution with distilled water. The absorbance of resulting solutions was measured against the solvent blank and a calibration curve was plotted to get the linearity and the regression equation [13] which was shown in (fig. 2) and the result was shown in table 2.

Single point standardization

Measurement of absorbance of the sample solution and a standard solution of a reference substance was done. It was observed that the concentration of the standard solution was close to that of the sample solution. The concentration of a substance in the sample was calculated from the proportional relationship that exists between absorbance and concentration [14]. The results were shown in table 3.

$$C_{test} = \frac{A_{test}}{A_{std}} X C_{std}$$

Preparation of sample solution

Weighed 20 tablets and powered it. The quantity of powder equivalent to 10 mg was taken and transferred into a 100 ml volumetric flask, dissolved in methanol and volume made with distilled water. From the above solution, 10 µg/ml solution was prepared by diluting with distilled water and measured under UV-Visible spectrophotometer at 246 nm. From this concentration was found by using an earlier equation. The amount of drug present in the formulation can be found by,

$$\text{Amount} = \frac{\text{Concentration X Dilution Factor X Average Weight}}{\text{Weight Taken}}$$

The results were shown in table 4.

Method validation

Specificity

By diluting the stock solution, 10µg/ml solution was prepared and the absorbance was measured at 246 nm against the blank. The result was shown in table 5.

Precision

Repeatability (Intraday precision)

2, 4 and 6 µg/ml solutions of Rupatadine fumarate was prepared, whose absorbance was measured six times at 246 nm at different time intervals and the relative standard deviation was calculated. The results were shown in table 6.

Reproducibility (Interday precision)

Six individual preparations of Rupatadine fumarate were prepared with different concentrations of 2,4 and 6 µg/ml and the absorbance were measured at 246 nm. The relative standard deviation was calculated. The results were shown in table 7.

Accuracy

A known quantity of the standard drug was added to the preanalysed sample formulation at 50%, 100% and 150% levels and the contents were reanalyzed by the proposed method. The results were shown in table 8.

$$\%R = \frac{\text{Amount of drug found after the addition of standard drug} - \text{Amount of drug found before the addition of standard drug}}{\text{Amount of standard drug added}} X100$$

Where, %R= % recovery

Limit of detection

It was performed by based on the visual evaluation method. It was determined by the analysis of the sample with a known concentration of analyte and by establishing the minimum level at which the analyst is reliably detected. The result was shown in table 9.

Limit of quantitation

It was performed based on the visual evaluation method. It was determined by the analysis of the sample with a known concentration of analyte and by establishing the minimum level of which the analyst can be quantified with acceptable accuracy and precision. The result was shown in table 10.

Robustness

10 mg/ml concentration of Rupatadine fumarate was prepared, whose absorbance was measured in three different wavelengths like 243, 246 and 249 nm closer to the λ_{max} of the drug. The results were shown in table 11.

RESULTS AND DISCUSSION

Method development parameters

Solubility studies

Rupatadine fumarate was freely soluble in methanol, ethanol and glacial acetic acid [GAA] partially soluble in chloroform and insoluble in water.

Determination of absorption maxima

The stock solution was further diluted with distilled water to get a concentration of 10µg/ml and scanned under UV between 200 nm-400 nm. The absorption maximum of Rupatadine fumarate was found at 246 nm.

Calibration curve

Calibration curve was performed in the concentration range of 2-10 µg/ml. Regression coefficient (R^2) was found to be 0.9995.

Single point standardization method

10 µg/ml concentration containing standard solution and equivalent to 10 µg/ml sample solution was prepared. The absorbance of both solutions was measured at 246 nm. From this, the sample concentration was found as 10.02 µg/ml.

Table 1: Solubility profile of Rupatadine fumarate

S. No.	Solvents	Solubility
1	Methanol	Freely soluble
2	Ethanol	Freely soluble
3	Glacial acetic acid	Freely soluble
4	Chloroform	Partially soluble
5	Water	Insoluble

Table 2: Calibration curve values of Rupatadine fumarate

S. No.	Concentration (µg/ml)	Absorbance
1	2	0.0866
2	4	0.1898
3	6	0.2796
4	8	0.3707
5	10	0.4661

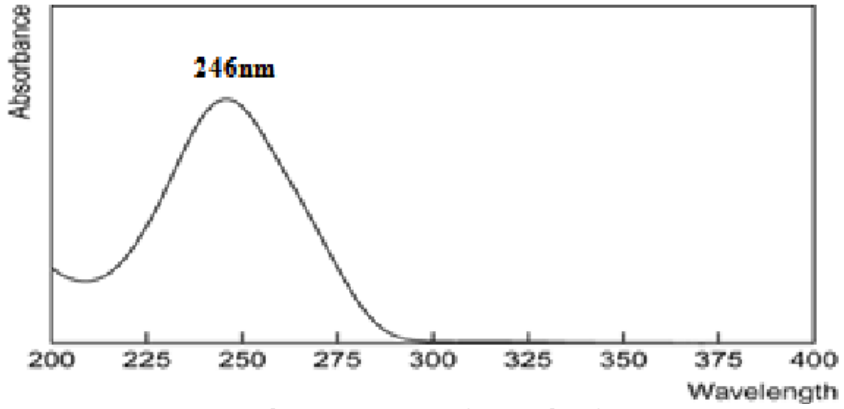

Fig. 1: UV absorption spectra of Rupatadine fumarate

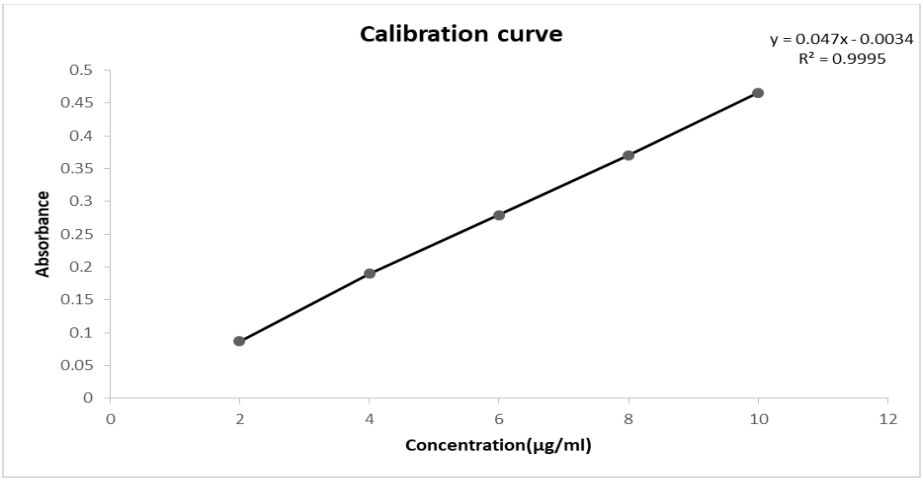

Fig. 2: Calibration curve of rupatadine fumarate

Table 3: Concentration of rupatadine fumarate in sample

S. No.	Concentration of standard (µg/ml)	Absorbance of standard	Absorbance of sample	Concentration of sample(µg/ml)
1	10	0.4564	0.4575	10.02

By substituting the concentration of sample solution in the formula which was mentioned in the methodology the amount was found as follows.

Table 4: Amount of rupatadine fumarate in sample

S. No.	Rupatadine fumarate	Label claim (mg)	Amount found (mg)	SD	%RSD
1	Tablet	10	10.2		
2	Tablet	10	10.3	0.1000	0.9801
3	Tablet	10	10.3		

SD= standard deviation, %RSD= relative standard deviation

Validation parameters

Specificity

Table 5: Specificity of rupatadine fumarate

S. No.	Wavelength(nm)	Concentration (µg/ml)	Absorbance	Mean	SD	%RSD
1	246	10	0.4576 0.4645 0.4572	0.4597	0.0041	0.8926

SD= standard deviation, %RSD= relative standard deviation

Precision

Intra-day precision

Intraday precision studies were performed in 2, 4 and 6 µg/ml concentrations and the relative standard deviation was found to be within limits i.e. less than 2%. Hence the performed parameter was validated.

Inter-day precision

Inter-day precision studies were performed in 2, 4, and 6 µg/ml concentrations and the relative standard deviation was found to be within limits i.e. less than 2%. Hence the performed a parameter was validated.

Accuracy

Accuracy studies were performed at 50%, 100%, and 150% levels by spiking 2, 4 and 6 µg/ml standard solutions to pre analysed sample solution. The % Recovery was found to be within the limits, i.e. in the range of 99.7-101.6.

Limit of detection

Limit of detection of Rupatadine fumarate was performed by the visual evaluation method and the result was found to be 0.1 µg/ml.

Limit of quantification

Limit of quantification of Rupatadine fumarate was performed by the visual evaluation method and result was found to be 0.3 µg/ml.

Table 6: Intraday precision of rupatadine fumarate

S. No.	Concentration(µg/ml)	Absorbance	Mean	SD	%RSD
		0.0852			
1	2	0.0856	0.0851	0.00034	0.40
		0.0849			
		0.0846			
		0.0853			
		0.0853			
		0.0851			
		0.1703			
2	4	0.1689	0.1695	0.00051	0.30
		0.1691			
		0.1693			
		0.1696			
		0.1698			
		0.2392			
3	6	0.2389	0.2370	0.000209	0.88
		0.2334			
		0.2365			
		0.2374			
		0.2368			

SD= standard deviation, %RSD= relative standard deviation

Table 7: Inter-day precision of Rupatadine fumarate

S. No.	Concentration (µg/ml)	Absorbance	Mean	SD	%RSD
		0.0789			
1	2	0.0785	0.0782	0.00078	0.99
		0.0778			
		0.0787			
		0.0785			
		0.0768			
		0.1709			
2	4	0.1715	0.1707	0.00101	0.59
		0.1694			
		0.1698			
		0.1721			
		0.1710			
		0.2436			
3	6	0.2415	0.2426	0.2426	1.44
		0.2396			
		0.2385			
		0.2478			
		0.2451			

SD= standard deviation, %RSD= relative standard deviation

Table 8: % Recovery of rupatadine fumarate

S. No.	level	Amount of drug in the sample (µg/ml)	Amount of standard drug added (µg/ml)	Amount of drug recovered (µg/ml)	%Recovery
1	50%	10	2	2.032	101.6
2	100%	10	4	4.012	100.6
3	150%	10	6	5.983	99.7

Table 9: Limit of detection of rupatadine fumarate

S. No.	LOD value	Absorbance
1	0.1 µg/ml	0.0145

LOQ= Limit of quantification

Table 10: Limit of quantification rupatadine fumarate

S. No.	LOQ Value	Absorbance
1	0.3 µg/ml	0.0423

LOQ= Limit of quantification

Robustness

Robustness of the method is its ability to remain unaffected by small changes in parameter such as changes in wavelength, changes in temperature, etc. robustness examine the effect of operational parameter on the analytical method. 10µg/ml concentration of Rupatadine fumarate was prepared, whose absorbance was measured in three different wavelengths like 243, 246 and 249 nm closer to λ_{max} of the drug. The % relative standard deviation was found within the limits i.e. less than 2%.

Table 11: Robustness of rupatadine fumarate

S. No.	Wavelength(nm)	Concentration(µg/ml)	Absorbance	Mean	SD	%RSD
1	243	10	0.4584 0.4676 0.4592	0.4617	0.0050	1.10
2	246	10	0.4614 0.4532 0.4512	0.4552	0.0054	1.18
3	249	10	0.4615 0.4632 0.4599	0.4615	0.0016	0.35

SD= Standard deviation, %RSD= %Relative standard deviation

CONCLUSION

The developed UV spectrophotometric method for the estimation of Rupatadine fumarate in bulk and tablet dosage form by using the single point standardization method was found to be simple, precise, accurate, reproducible and cost-effective. The statistical analysis of the developed method conforms that the proposed method is an appropriate and it can be used for routine analysis.

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Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally

CONFLICTS OF INTERESTS

There are no conflicts of interest

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