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Ultra-Violet Spectrophotometric Method for Validation of Rupatadine Fumarate from Bulk Drug and Pharmaceutical Formulation

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ABSTRACT

A simple, rapid, sensitive and precise UV spectrophotometric method has been developed for the estimation of rupatadine fumarate from bulk drug and pharmaceutical formulation. In this method rupatadine fumarate showed maximum absorbance at about 250 nm in absolute alcohol. Beer's law was followed in the concentration range of 1 to 30 µg/ ml. Regression equation was found to be y = 0.0257- 3x 10^{-5} and coefficient of correlation was 0.9999 . The proposed method is accurate, sensitive, reproducible and useful for the estimation of rupatadine fumarate from bulk drug and pharmaceutical formulation.

Keywords: Rupatadine fumarate**,** Absolute alcohol

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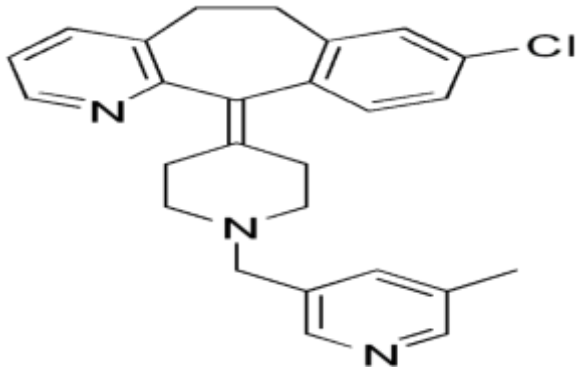
INTRODUCTION

In this communication the present work proposes a new UV spectrophotometric method for assay of rupatadine fumarate from its active pharmaceutical ingredients. Its chemical name is 8-chloro-6,11-dihydro-11-[1-[(5-methyl-3-pyridinyl)methyl]-4-piperidinylidene]-5H-benzo[5,6]cyclohepta[1,2 b]pyridine Fumarate. Rupatadine fumarate is a second generation of antihistamine and platelet activity factor (PAF) antagonist used to treat allergies. Rupatadine possesses anti-allergic properties such as the inhibition of the de-granulation of mast cells induced by immunological and non-immunological stimuli and inhibition of the release cytokines, particularly of the TNF in human mast cell[1]. Literature survey reveals the Spectrophotometric [2-4] titration [5, 6], HPLC[7-11] methods for the estimation of rupatadine fumarate. A simple, rapid and reliable UV spectrophotometric method is developed for the determination of rupatadine fumarate. This method can be used for the routine analysis. In the proposed method optimization and validation of this method are reported.

Structure of rupatadine



MATERIALS AND METHOD

Shimadzu UV-1800 was used with 10 mm matched quartz cell to measure absorbance of solution. A Shimadzu analytical balance with 0.01 mg was used.

Chemical and Reagents

Reference standard of rupatadine fumarate was obtained from reputed firm with certificate analysis. All spectral absorbance measurements were made on Shimadzu UV-1800 with 10 mm matched cell.

Preparation of Standard Solution

About 10 mg of standard rupatadine fumarate was weighed accurately and transferred in 100 ml of volumetric flask. About 30 ml of absolute alcohol was added and sonicated for 15 minutes. The volume was adjusted up to the mark with absolute alcohol to give concentration as 100 µg /ml.

Experimental

Into a series of 10 ml graduated flask, varying amount of standard drug rupatadine fumarate solutions were pipette out and volume was adjusted with absolute alcohol. Absorbance of the resulting solutions was measured at 250 nm using absolute alcohol as blank using calibration curve method. (Figure.1). The calibration curve was prepared in the concentration range of 2 to 10 µg/ml (Figure. 3).

Estimation from tablets

Twenty tablets were weighed accurately and average weight of each tablet was determined. Powder equivalent to 10 mg of rupatadine fumarate was weighed and transferred in 100 ml of volumetric flask. A 30 ml of absolute alcohol was added and sonicated for 15 minutes and filtered. The filtrate and washing were diluted up to the mark with absolute alcohol to give concentration as 100 µg /ml. Such solution was used for analysis.

Into series of 10 ml graduated flask, varying amount of sample solutions of rupatadine fumarate were pipette out and volume was adjusted with absolute alcohol. Absorbance of the resulting solutions was measured at 250 nm using absolute alcohol as blank. The concentration of the drug in the given sample was calculated using calibration curve. The results of analysis are given in table 1.

VALIDATION

Accuracy:

Accuracy of the proposed methods was carried as on the basis of recovery studies. It is performed by the standard addition method. Recovery studies were performed by adding standard drug at different levels to the pre-analyzed tablets powder and the proposed method was followed. From the amount of the drug estimated, the percentage recovery was calculated. The results of the analysis are shown in table 2.

Precision:

The method precision was established by carrying out the analysis of homogenous powder blend of tablets. The assay was carried out of drug using proposed analytical method in six replicates. The value of relative standard deviation lie well within the limits indicated the sample repeatability of the method. The results obtained are tabulated in table 3.

Inter-day and intra-day precision:

An accurately weighed quantity of tablets powder equivalent to 10 mg of rupatadine fumarate was transferred to 100 ml of volumetric flask, sonicated for 15 minutes with absolute alcohol and diluted up to mark with absolute alcohol to get stock solution of concentration as 100 µg /ml.

The contents were filtered through whatmann filter paper no. 41. Aliquots portions were further diluted with absolute alcohol to get concentration of 10 µg /ml. of rupatadine fumarate. The absorbance of final solutions was read after 0 hr., 3 hrs. and 6 hrs. in 10 mm cell at 250 nm. Similarly the absorbance of the same solution was read on 1st, 2nd and 5th day. The amount of rupatadine fumarate was estimated by comparison with standard at 250 nm. The results are recorded in table 4.

Limit of Detection (LOD) and Limit of Quantification (LOQ)

The limit of detection (LOD) is defined as the lowest concentration of an analyte that an analytical process can reliably differentiate from back-ground levels. In this study, LOD and LOQ were based on the standard deviation of the response and the slope of the corresponding curve using the following equations-

$$LOD = 3.3\ \sigma/S \text{ and } LOQ = 10\ \sigma/S$$

Where σ is the standard deviation of the signal to noise ratio of the sample and S is the slope of the related calibrations graphs.

The limit of quantification (LOQ) is defined as the lowest concentration of the standard curve that can be measured with an acceptable accuracy, precision and variability .The values of LOD and LOQ are given in table 5.

RESULTS AND CONCLUSION

The proposed method was validated statistically and by recovery studies. The molar absorptivity and Sandell's sensitivity values show the sensitivity of methods while the precision was confirmed by the %RSD (relative standard deviation). Assay results of recovery studies are given in table 2. Results are in good agreement with labeled value. The reproducibility, repeatability and accuracy of this method were found to be good, which is evidenced by low standard deviation.

UV spectrophotometric method[3] suggested in literature is applicable in concentration range of 10-50 µg /ml by using 0.1 N hydrochloric acid as solvent. The proposed method is applicable in the concentration range of 1-30 µg /ml by using absolute alcohol as solvent and intra-day and inter-day study are carried out. It showed good recovery and relative small value of % RSD. The proposed method is applicable with concentration range from 1 to 30 µg/ ml

The proposed method is simple, sensitive, accurate, precise and reproducible. Hence it can be successfully applied for the routine estimation of rupatadine fumarate in bulk and pharmaceutical formulation even at very low concentration as 1 µg /ml. In conclusion the proposed method is simple, sensitive and accurate. It can be used for routine estimation of rupatadine fumarate in bulk

drug and pharmaceutical formulation.

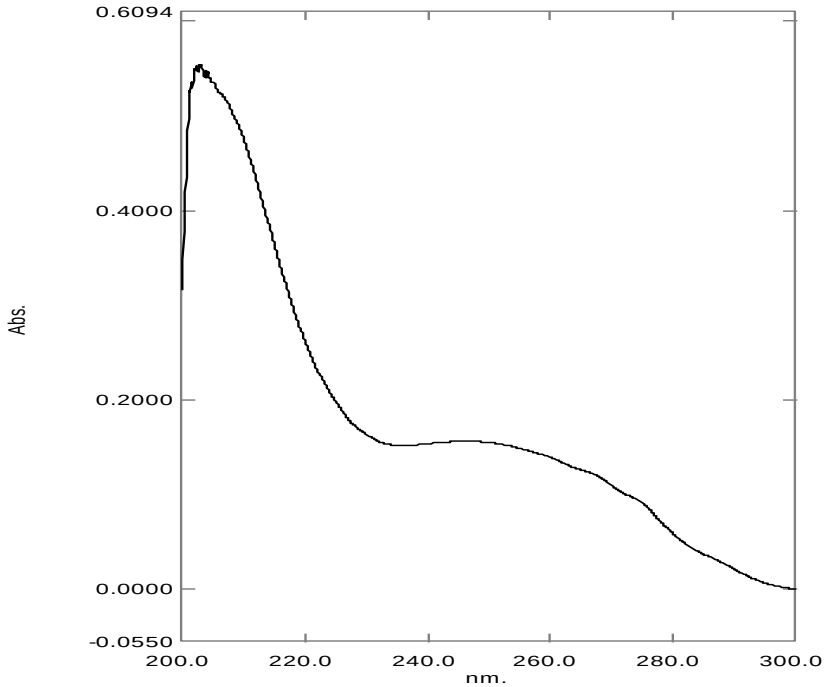


Figure 1. (a)UV spectrum of standard rupatadine fumarate (Pure drug) (6µg/ ml)

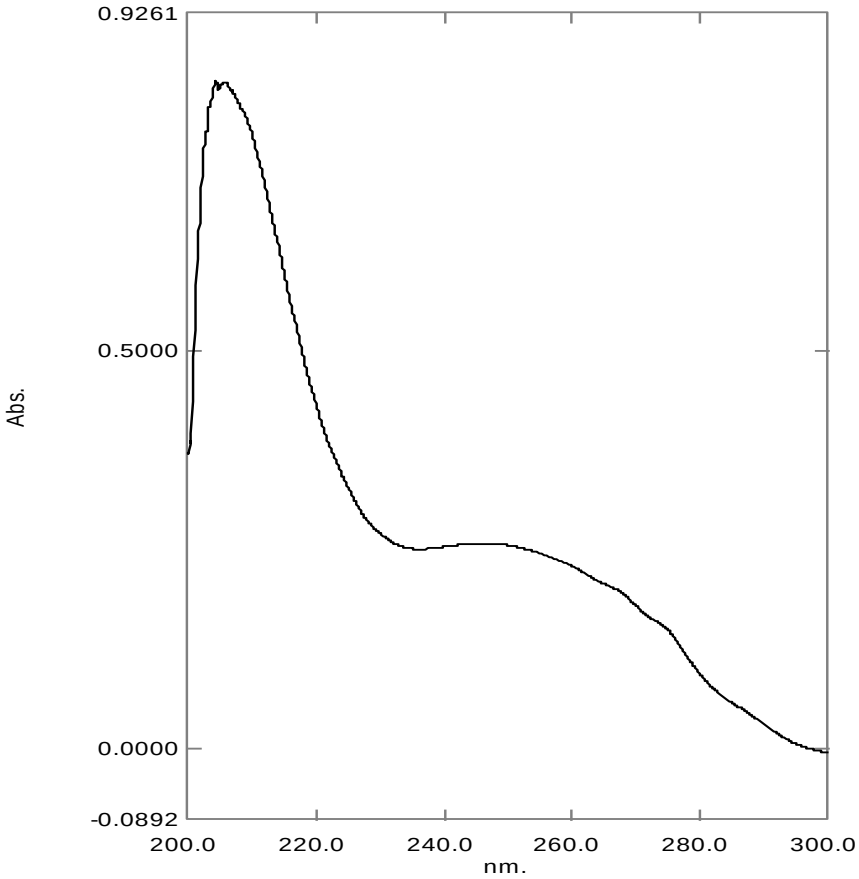


Figure 2. UV spectrum of rupatadine fumarate (Sample) (10 µg/ ml)

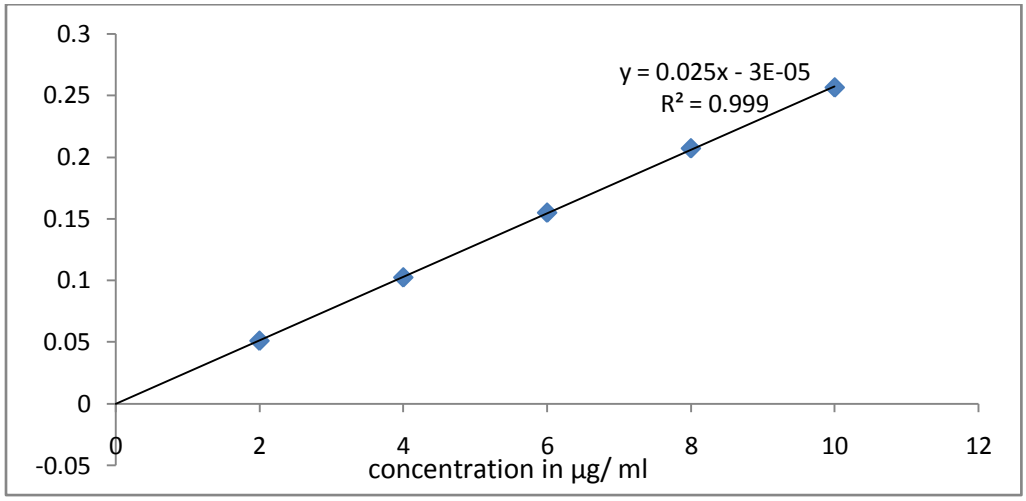


Figure 3: Calibration curve of standard Rupatadine Fumarate

Table 1: Values of results of optical and regression of drug.

Parameter	Values
λ max (nm)	250
Beer Law Limits (µg/ml)	1-30
Molar absorptivity(L/mol.cm)	1.069 X 10^4
Sandell's sensitivity	0.0390
Regression equation (y=b+ac)	
Correlation coefficient(r^2)	0.9999
Slope (a)	0.0257
Intercept	0.00003

Table 2: Results of recovery of Rupatadine fumarate in bulk drug

Amount of Sample Added in (µg/ml)	Amount of Standard Added in (µg/ml)	Total amount recovered	Percentage recovery(%)	Standard deviation	Percentage of relative standard deviation(C.O.V.)
2	0	1.965	99.50	0.01275	0.6405
2	2	4.063	99.25	0.0463	1.167
2	4	5.957	99.99	0.0364	0.608
2	6	8.040	99.88	0.0230	0.288
				Mean=0.02961	Mean =0.6758

Table 3: Precision- method precision

Experiment no.	Weight of rupatadine fumarate taken in mg.	Content in mg. of rupatadine fumarate
1	10	10.149
2	10	10.010
3	10	10.135
4	10	9.966
5	10	9.987
6	10	10.011

Standard deviation= 0.07858 ,C.O.V.= 0.7824

Table 4: Summary of validation parameter for intra-day and inter-day

Sr. no.	Parameters	Percentage
1	Intra-day precision (n=3)	99.60
	Amount found ± %RSD	0.5443
2	Inter-day precision (n=3)	98.484
	Amount found ± %RSD	0.8882
3	Ruggedness	100.12
	Analyst to analyst (n=3) %RSD	0.3845

Table 5: Values of results of LOD and LOQ

Parameters	(µg/ml)
Limit of Detection	0.0410
Limit of Quantification	0.1245

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