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# Spectrophotometric determination of rupatadine in pharmaceutical dosage form using potassium ferricyanide

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**Abstract**

A new simple, accurate and precise spectrophotometric assay method was developed and validated for the quantitative determination of rupatadine in bulk and tablets dosage form using UV-visible spectrophotometer. In this method, methanol was used as solvent and potassium ferricyanide was used as ion-pair reagent. The yellow coloured complex was formed by the reaction between rupatadine and potassium ferricyanide, with the absorption maxima of 438 nm. The developed method obeyed Beer's law in the concentration range of 10-50 µg/ml with correlation coefficient of 0.999. The method showed good reproducibility and precision in this concentration range. The % recovery and %RSD values were found to be within the limits, indicating the method to be accurate and precise, respectively. The LOD and LOQ values were found to be 1.06 µg/ml and 3.20 µg/ml. The validation parameters tested in accordance with the requirements of ICH guidelines, prove the suitability of this method. The proposed method can be used for routine quality control analysis for the estimation of rupatadinein bulk and tablet dosage form.

## 1. Introduction

Rupatadine is chemically designated as 8-chloro-6,11-dihydro-11-[1-[(5-methyl-3-pyridinyl) methyl] piperidin-4-ylidene]-5H-benzo [5,6] cyclohepta [1,2-b] pyridine. It has a molecular formula $C_{26}H_{26}ClN_3$, molecular weight 416 g/mol and pKa value of 7.19 (Picado, 2006). It is a white powder, soluble in ethanol and methanol and used as antihistamine in the relieving the symptoms of allergic rhinitis such as sneezing, runny nose, itching in the eyes and nose (Keamand Plosker, 2007). Rupatadine is also used to relieve the symptoms associated with urticaria (an allergic skin rash), such as itching and hives (localised skin redness and swelling) (Mullol *et al.*, 2008). Literature survey reveals that there were few analytical methods developed for the estimation of rupatadine in pharmaceutical dosage form such as UV spectrophotometer (Anusha Gandi *et al.*, 2020; Shakir Basha *et al.*, 2019; Shaiba *et al.*, 2010), HPLC (Mazahar Farooqui, 2014), but no spectrophotometric method was developed for the determination of rupatadine using ion pair reagent. The present study aimed to develop and validate a spectrophotometric method for the determination of rupatadine in pharmaceutical dosage form using ion-pair reagent (Figure 1).

## 2. Materials and Methods

### 2.1 Chemical and reagents

The rupatadine working standard was procured from Vishnu Institute of Pharmaceutical Education and Research, Medak, Telangana. The tablet dosage form (Rupafin) was purchased from local pharmacy. All the solvents and reagents used for the development of method were of AR grade and purchased from Merck, Mumbai, India.

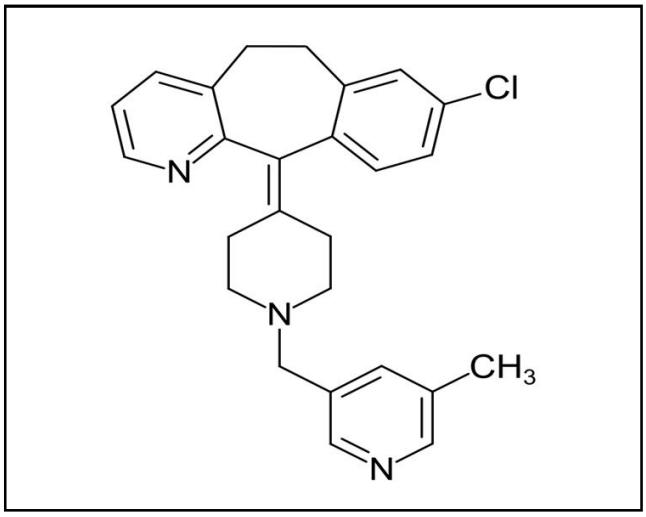


**Figure 1: Chemical structure of rupatadine.**

### 2.2 Instrumentation

T60 UV-visible spectrophotometer with 1cm matched quartz cuvettes was used for the estimation of rupatadine in pharmaceutical dosage form. The parameters were controlled by UV win software. Other instrument used for the method was electronic balance of Aczet make.

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## 2.3 Experimental work

### 2.3.1 Solubility studies

Different solvents such as ethanol, methanol, chloroform, acetonitrile, 0.5N sodium hydroxide solution were used for the solubility studies.

### 2.3.2 Selection of suitable solvent

One of the above solvents will be selected based on the solubility studies.

### 2.3.3 Selection of ion-pair reagents

Ferric chloride and potassium ferricyanide, one of them was used as ion-pair reagent based on the solubility.

### 2.3.4 Selection of detection wavelength

The standard solution of 10 µg/ml was prepared and scanned in the wavelength range of 400-800 nm.

### 2.3.5 Preparation of standard and sample solution

Accurately weighed and transferred an amount of 100 mg of rupatadine working standard into 100 ml of clean volumetric flask. 70 ml of the methanol was added to dissolve the drug. The volume was made upto the mark using methanol. 10 ml of the stock solution was diluted to 100ml with distilled water. Later the 3 ml of the above solution and 1ml of potassium ferricyanide solution was diluted to 10 ml with distilled water.

Average weight of 20 tablets of rupafin was calculated and an amount equivalent to 100 mg was weighed and transferred into 100 ml of clean volumetric flask. 70 ml of the methanol was added to dissolve the rupatadine. Finally, make up the volume to 100 ml with methanol. The solution was filtered and 10 ml of the solution was diluted to 100 ml with distilled water. 3 ml of the above solution and 1ml of potassium ferricyanide solution was diluted to 10 ml with distilled water.

### 2.3.6 Method validation (ICH, 2005; ICH, 2003; ICH, 1996)

#### 2.3.6.1 Linearity

Serial dilutions of standard rupatadine in the range of 10 µg/ml and 50 µg/ml were prepared and placed in the system. A linearity graph was plotted between concentration and absorbance.

#### 2.3.6.2 Accuracy

The solutions were prepared in three different concentration levels of 50%, 100% and 150%, placed in the system and % recoveries were calculated.

#### 2.3.6.3 Precision

The precision of the method was determined by intra and inter-day precision studies. The standard solution was placed six times on the same day (intra-day) as well as on different day (inter-day) and the % RSD was calculated.

#### 2.3.6.4 Specificity

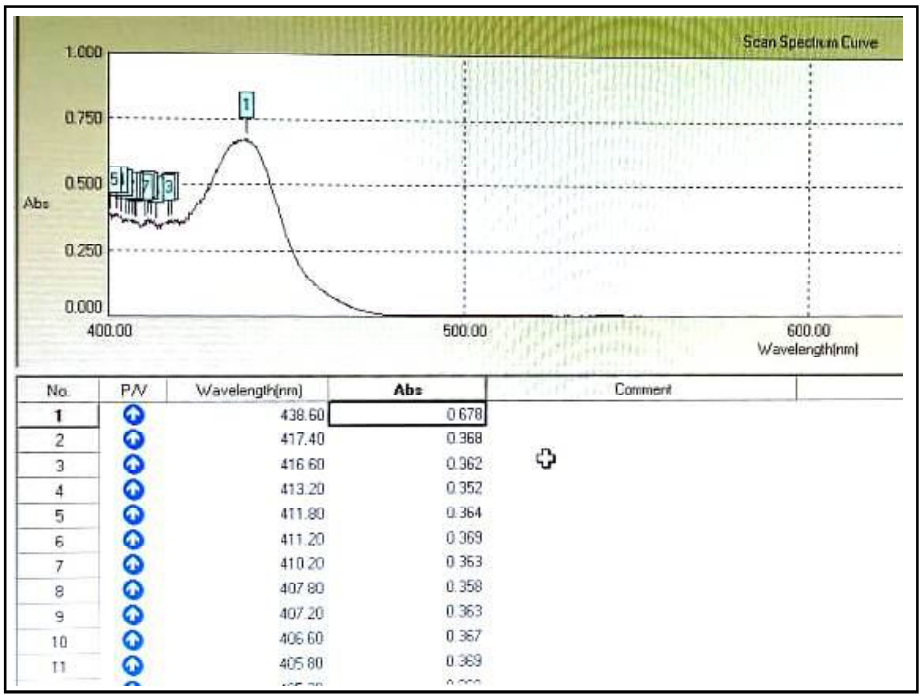
The specificity of the method was determined by placing the placebo solution and comparing with standard solution for the interference with rupatadine peak.

#### 2.3.6.5 Limit of detection (LOD) and limit of quantitation (LOQ)

LOD and LOQ are determined by standard deviation (SD) and slope of the calibration curve. The limiting values are calculated as per the following equations: LOD = (3.3 × SD)/Slope and LOQ = (10 × SD)/Slope.

## 3. Results

The visible spectrum was shown in Figure 2.




| No. | P/V | Wavelength(nm) | Abs | Comment |
|---|---|---|---|---|
| 1 | | 438.60 | 0.678 | |
| 2 | | 417.40 | 0.368 | |
| 3 | | 416.60 | 0.362 | |
| 4 | | 413.20 | 0.352 | |
| 5 | | 411.80 | 0.364 | |
| 6 | | 411.20 | 0.369 | |
| 7 | | 410.20 | 0.363 | |
| 8 | | 407.80 | 0.358 | |
| 9 | | 407.20 | 0.363 | |
| 10 | | 406.60 | 0.367 | |
| 11 | | 405.80 | 0.369 | |

**Figure 2: Visible spectrum of rupatadine.**

The optical characteristics were calculated and results were presented in Table 1.

**Table 1: Optical characteristics**

| S.No. | Parameters | Result |
|---|---|---|
| 1 | Absorption maximum | 438 nm |
| 2 | Linearity range | 10-50 µg/ml |
| 3 | Regression equation | y = 0.015x+0.003 |
| 4 | Slope | 0.015 |
| 5 | Intercept | 0.003 |
| 6 | Correlation coefficient (r) | 0.999 |
| 7 | Molar extinction coefficient ($L.mol^{-1} cm^{-1}$) | $6.368\times10^{3}$ |
| 8 | Sandell's sensitivity ($\mu g/cm^2$ - 0.001absorbance units) | 0.0653 |
| 9 | Accuracy (% recovery) | 99.76 %-101.96 %, |
| 10 | Precision(Intra-day) % RSD (Inter-day) %RSD | 0.170.29 |
| 11 | LOD | 1.06 µg/ml |
| 12 | LOQ | 3.20 µg/ml |
| 13 | Standard error | 0.004803 |

The linearity results were summarised in Table 2 and linearity plot was shown in Figure 3.

**Table 2: Linearity results**

| S. No. | Concentration (µg/ml) | Absorbance |
|---|---|---|
| 1 | 10 | 0.153 |
| 2 | 20 | 0.313 |
| 3 | 30 | 0.454 |
| 4 | 40 | 0.603 |
| 5 | 50 | 0.756 |
| | Regression coefficient ($r^2$) | 0.999 |
| | Correlation coefficient (r) | 0.999 |

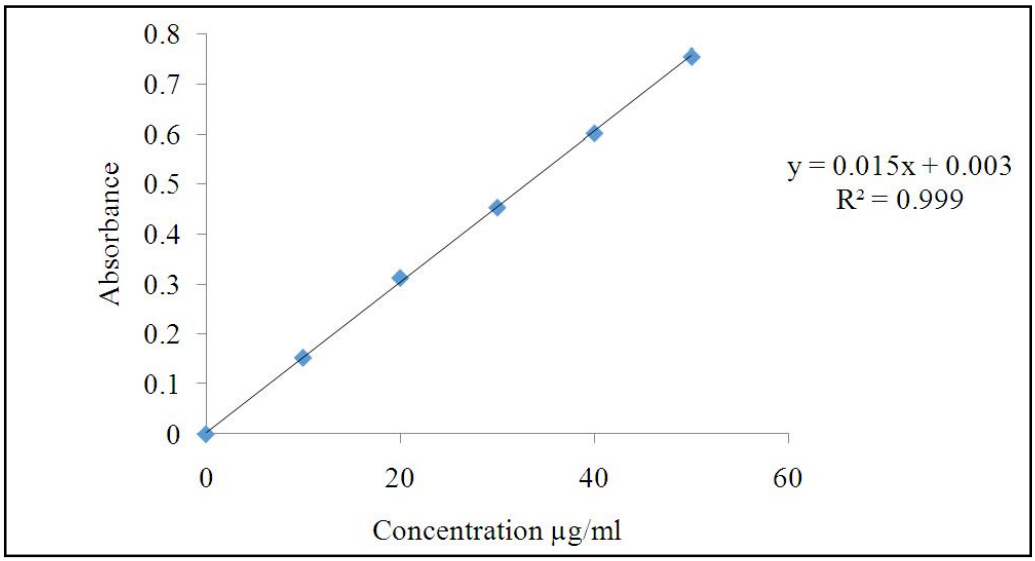



**Figure 3: Linearity plot of rupatadine.**

## 4. Discussion

Initially, the method was developed for the estimation of rupatadine in tablet dosage form by dissolving in different solvents such as ethanol, methanol, water, acetonitrile and 0.5 N sodium hydroxide solution. The drug was found soluble in methanol based on the solubility studies and methanol was selected as the suitable solvent for the development of method. For the selection of ion-pair reagent, various reagents such as ferric chloride and potassium ferricyanide were used. When ferric chloride solution was used, a turbid solution appeared whereas in potassium ferricyanide, a clear solution was observed. Hence, potassium ferricyanide was selected as ion-pair reagent. A yellow coloured complex was formed by the reaction of rupatadine with potassium ferricyanide. This complex has an absorption maxima at 438 nm when scanned in the wavelength range of 400-800 nm.

The standard solution and sample solution of rupatadine was prepared as mentioned above and placed in the spectrophotometer for the measurement of absorbance. The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity, sandell's sensitivity, slope (b), intercept (c), correlation coefficient (r) obtained from different concentrations, and per cent relative standard deviation values were calculated.

The developed method was validated as per the ICH guidelines. The method obeyed Beer's law in the concentration range of 10-50 µg/ml, with correlation coefficient of 0.999, indicating the method to be linear.

The % recovery for rupatadine was found to be 99.76 %-101.96 %, indicating the method to be accurate. For the determination of precision, the % relative standard deviation (RSD) was calculated for inter-day precision and intra-day precision. The % RSD for inter-day precision was found to be 0.29 and for intra-day precision, it was found to be 0.18, indicating the method to be precise.

The method was found to be specific when compared with the blank solution, as there was no interference of blank with the rupatadine peak in the spectrum. The LOD was found to be 1.06 µg/ml and LOQ was found to be 3.20 µg/ml.

## 5. Conclusion

A new accurate, precise and specific spectrophotometric method was developed for the quantitative estimation of rupatadine in pure drug and tablet dosage form using potassium ferricyanide reagent. The method was developed using methanol as solvent and the $\lambda_{max}$ were found to be 438 nm. The method was established according to ICH guideline and definition. Accuracy was investigated by analyzing marketed formulations and percentage recovery was found to be within the limits. Therefore, it can be said that the methods were highly accurate.The inter-day and intra-day relative standard deviation values with low percentage RSD values were obtained. This indicated that the precision of the method was found to be good. The method was validated with respect to linearity, precision, accuracy and sensitivity. The proposed method based on spectrophotometer is precise, accurate, simple to perform and economy in practice. It do not require expensive or sophisticated and chemicals in contrast with chromatographic method. Hence, the method can easily and conveniently adopt for the estimation of rupatadine for bulk and pharmaceutical dosage form. This spectrophotometric method developed can be used for the quality control and routine analysis of rupatadine in pharmaceutical formulations.

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## Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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