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Research Article

SPECTROPHOTOMETRIC ESTIMATION OF RUPATADINE FUMARATE AND MONTELUKAST SODIUM IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

A simple, precise and reproducible UV spectrophotometric method, Q-value analysis method, have been developed and validated for the simultaneous estimation of Rupatadine fumarate and Montelukast sodium. The combination is used as anti-asthmatic, anti-allergic and is available in tablet dosage form.. The method is based on the measurement of absorbance of Rupatadine fumarate and Montelukast sodium at 260 nm which is the Isobestic point and 244 nm the λmax of Rupatadine fumarate. The method obeyed Beer's law in the concentration range of 4-24 µg /ml for Rupatadine fumarate and Montelukast sodium. The results of analysis have been validated statistically and recovery studies confirmed the accuracy of the proposed method. The method was successfully applied to the determination of these drugs in pharmaceutical dosage forms.

Keywords: Rupatadine fumarate, Montelukast sodium, Q-Analysis method, UV Spectrophotometry.

INTRODUCTION

Rupatadine fumarate (RUPA) 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 is a non-sedating H_1-antihistamine (second generation) and platelet-activating factor inhibitor. It is potent and orally active that was developed as a therapeutic agent for the treatment of seasonal allergic rhinitis and chronic idiopathic urticaria.[1]. The structure of RUPA is shown in Fig.1. Montelukast sodium (MONT) is [R-(E)]-1-[[[1-[3-[2-(7-chloro-2quinolinyl) ethenyl] phenyl]-3-[2-(1-hydroxy-1-methylethyl) phenyl] propyl] thio] methyl] cyclopropane aceticacid, monosodium salt. Montelukast is a specific cysteinyl leukotriene receptor antagonist belonging to a styryl quinolines series. It is developed as a therapeutic agent for the treatment of bronchial asthma[2]. The structure of MONT is shown in Fig. 2

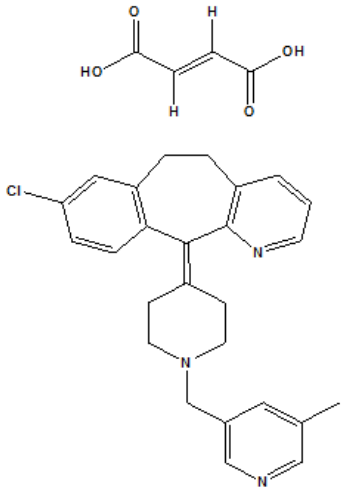

Fig. 1: It shows structure of Rupatadine

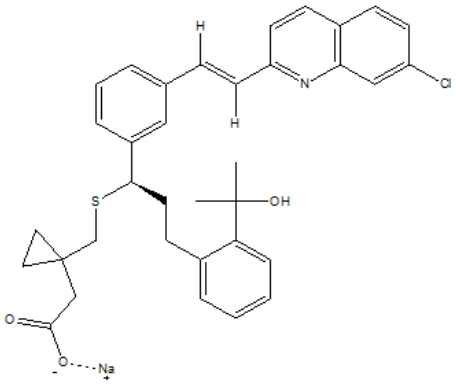

Fig. 2: It shows structure of Montelukast

Fumarate[1] Sodium[2]

The literature review reveals only one analytical method for the simultaneous estimation of Rupatadine fumarate and Montelukast sodium by UV-visible Spectrophotometry[3]. Literature review reveals few analytical techniques like Spectrophotometry[3-8], RP-HPLC [9-14] and HPTLC [15-16] estimations of either Montelukast sodium or Rupatadine fumarate.

The combination is not official in any Pharmacopoeia. In view of the need for a suitable method for routine analysis in combined formulations, attempts are being made to develop simple, precise and accurate analytical methods for simultaneous estimation of title ingredients and extend it for their determination in formulation.

MATERIALS AND METHODS

Materials

Rupatadine fumarate and Montelukast sodium was generous gift samples from Hetero Health Care Ltd. (Mumbai, India). A commercial tablet formulation Rupanex-M from Dr. Reddy's Laboratories Ltd, (Hyderabad, India) containing 10mg of RUPA and 10mg of MONT was purchased from local market and used within their shelf life period. All other chemicals used were of pharmaceutical or analytical grade.

Instrumentation

A Jasco double beam UV–visible spectrophotometer, Model: V-630, with a fixed bandwidth (1.5nm) and 1-cm quartz cell was used for

Spectral and absorbance measurements. In addition, electronic balance, micropipette and sonicator were used in this study.

Procedure

Preparation of standard stock solution

Standard stock solutions of Rupatadine fumarate and Montelukast sodium were prepared by dissolving 25 mg of drug in 25 ml of methanol to get standard stock solution of 1000 µg/ml. This solution was further diluted to get standard solution of concentration 100 µg/ml of RUPA and MONT.

Determination of iso-absorptive point and wavelength of maximum absorbance

The working standard stock solutions of RUPA and MONT were scanned in the range of 200 to 400 nm against methanol as a blank. Iso- absorptive point was found at 260 nm.

Preparation of Sample solution from tablet dosage form

For analysis of both RUPA and MONT in tablets, twenty tablets were accurately weighed and average weight was calculated. Tablets were finely powdered and mixed thoroughly. Quantity of tablet powder equivalent to 10 mg of RUPA and 10 mg of MONT was weighed accurately, dissolved in 50 ml methanol and sonicated for 20 min. The solution was filtered through Whatman filter paper (No. 41) and transferred to 100 ml volumetric flask and volume was made up to mark with methanol. The aliquot portion of filtrate was further diluted with methanol to get final concentration of about 10 µg/ml of both the drugs RUPA and MONT.

Calibration curve (Linearity)

A calibration curve was plotted over a concentration range of 4-24 µg/ml for both RUPA and MONT. Stock solutions for spectrophotometric measurements were prepared by dissolving RUPA and MONT in methanol to obtain concentration of 1 mg /ml for each compound. For calibration, series of above solutions were prepared containing RUPA 4.0-24.0 µg /ml and MONT 4.0-24.0 µg /ml. by diluting the stock standard solution with methanol in standard volumetric flasks (10ml). Calibration curves were constructed for RUPA and MONT by plotting absorbance versus concentrations at both wavelengths.

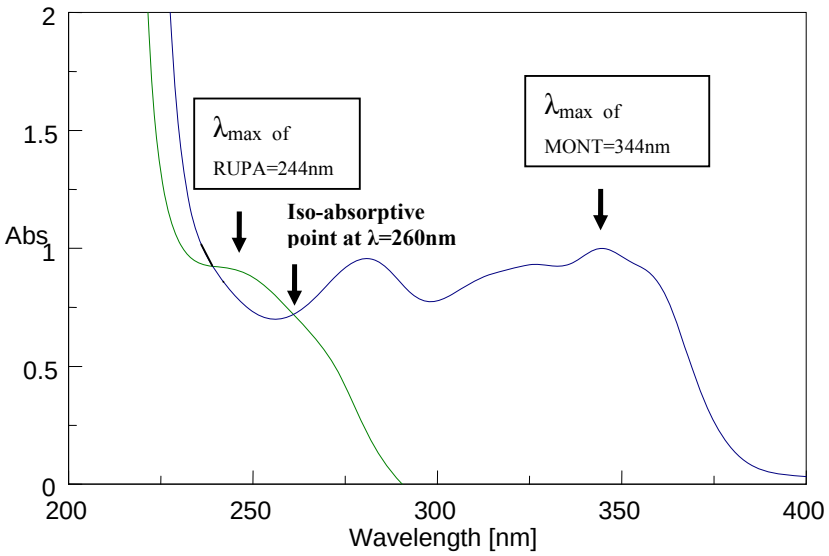

Fig. 3: It shows the overlay spectra of RUPA and MONT showing iso-absorptive point at 260 nm

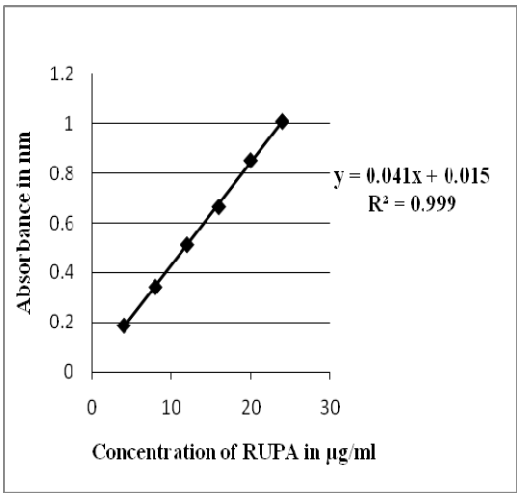

Fig. 4: It shows calibration curve of RUPA

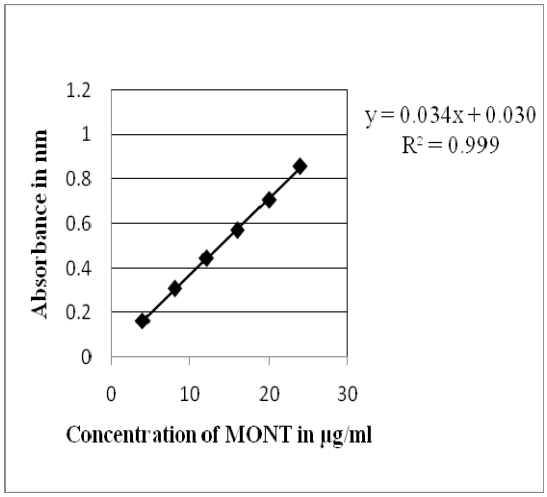

Fig. 5: It shows calibration curve for MONT

Q Value Analysis Method

From the overlain spectrum of RUPA and MONT which is shown in above Fig.3, the wavelengths selected for analysis are 260 nm (isobestic point) and 244 nm (λmax Rupatadine fumarate). The absorbance of the standard and sample solutions was measured. The absorptivity values for both standard drugs at the selected wavelengths were employed for determination of Q values .The concentrations of drugs in sample solution were determined by using the following formula.

$$C_X = \frac{(Q_M - Q_Y) \times A_1}{(Q_X - Q_Y) \times aX_1} \quad \text{AND} \quad C_Y = \frac{A_1}{aX_1 - C_X}$$

Where,

A1 & A2 are the absorbance of the mixture at 260 nm & 244 nm respectively; aX1 and aY1 are absorptivity of RUPA and MONT respectively at 260 nm; aX2 and aY2 are absorptivity of RUPA and MONT respectively at 244 nm; QM=A2/A1, QX= aX2/ aX1 and QY= aY2/ aY1.

Validation of the Developed Method

The methods were validated with respect to linearity, accuracy, and precision.

Linearity

The linearity of an analytical method is its ability to elicit test results that are directly or by a well-defined mathematical transformation proportional to the concentration of analyte in samples within a given range. The range of analytical method is the interval between upper and lower level of analyte including levels that have been demonstrated to be determining with precision and accuracy using the method. The linear response of RUPA and MONT were determined by analysing five independent levels of the calibration curve in the range of 4-24 µg/ml. Result should be expressed in terms of Correlation co-efficient[20]

Accuracy (% Recovery)

Accuracy of an analysis is determined by systemic error involved. It is defined as closeness of agreement between the actual (true) value and analytical value and obtained by applying test method for a number of times. Accuracy may often be expressed as % Recovery by the assay of added amount of analyte. It is measure of the exactness of the analytical method. Recovery studies carried out for both the methods by spiking standard drug in the powdered formulations 80%, 100%, 120% amount of each dosage content as per ICH guidelines[20].

Precision

The reproducibility of the proposed method was determined by performing tablet assay at different time intervals (morning, afternoon and evening) on same day (Intra-day assay precision) and on three different days (Inter-day precision). Result of intra-day and inter-day precision is expressed in % RSD[20].

RESULTS AND DISCUSSION

In this method, the standard stock solutions of RUPA and MONT were prepared in methanol.

The Calibration curves for RUPA and MONT over concentration range of 4 – 24µg/ml were plotted and molar absorptivity for both the drugs were calculated at both the wavelengths of 244 nm (λ_{max} of RUPA) and 260 nm (iso- absorptive point). It is evident from the spectra of RUPA and MONT that these drugs obey the Lambert-beer's law at all the wavelength. The regression characteristics are reported in Table no.1. The assay was performed by measuring absorbance of the sample solutions at respective wavelengths for the formulation calculating Q-values for the drugs and then put these values in formula and determined content of each drug in formulation. The result of assay is reported in Table no.2. Recovery studies were carried out by spiking standard drug in the powdered formulations in 80%, 100%, 120% amount of each drug as per ICH guidelines. The results of the recovery analysis are reported in Table 4 which proved the good accuracy of the proposed methods.

Table 1: It shows linear regression data for calibration curves

Drug	Linearity range(µg/ml)	Correlation coefficient (r^2)	Slope (m)	Intercept (c)
RUPA	4-24 µg/ml	0.999	0.041	0.015
MONT	4-24 µg/ml	0.999	0.034	0.030

Table 2: It shows statistical evaluation of marketed formulation

% Mean amt. estimated*		± S.D.*		%RSD*		S.E.	
RUPA	**MONT**	**RUPA**	**MONT**	**RUPA**	**MONT**	**RUPA**	**MONT**
99.185	100.84	1.184	0.4777	1.1937	0.4737	0.4835	0.1950

*Average of six determinations

Table 3: It shows result of Intra-day and Inter-day precision

Sr. No.	Intra-day precision			Inter-day precision		
	SD	**%RSD**	**SE**	**SD**	**%RSD**	**SE**
RUPA	0.1097	0.412	0.853	0.1766	0.987	0.137
MONT	0.3451	1.078	0.1134	0.1427	0.876	0.198

Table 4: It shows result of Recovery study

RecoveryLevel	Drug	Conc. of (µg/ml)		Total conc. of Drug	Total amt. recovered (µg/ml)	% Recovery*
		Drug taken	Std drug added			
80	RUPA	10	8	18	18.2	101.1
100		10	10	20	19.9	99.5
120		10	12	22	21.8	99.09
80	MONT	10	8	18	17.99	99.94
100		10	10	20	20.5	102.2
120		10	12	22	21.9	99.54

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