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SIMPLE EXTRACTIVE SPECTROPHOTOMETRIC DETERMINATION OF RUPATADINE AS RUPATADINE FUMARATE FROM PHARMACEUTICAL FORMULATION

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ABSTRACT

Simple, sensitive and accurate extractive spectrophotometric methods have been developed for the estimation of rupatadine as rupatadine fumarate from pharmaceutical dosage form. The methods were based on the formation of coloured complexes by the drug with reagents like bromothymol blue, bromophenol blue and methyl orange in acidic medium. The ion associated complexes were formed and quantitatively extracted under the experimental condition in chloroform. The absorbance values were measured at 416, 418 and 422 nm, respectively. The proposed methods were validated statistically. Recoveries of methods were carried out by standard addition methods. The linearity was found to be 1.0-12.0 μg/mL, 1.0-16.0 μg/mL and 1.0-28.0 μg/mL for methods I, II and III, respectively. The low values of standard deviation and percentage RSD indicate high precision of methods. Hence, these methods are useful for routine estimation of rupatadine as rupatadine fumarate in tablets.

Key words: Rupatadine, Bromothymol blue, Bromophenol blue, Methyl orange.

INTRODUCTION

Rupatadine is 8-chloro-6, 11-dihydro-11-[1-(5-methyl-3-pyridinyl) methyl-4-piperidinyllidene]-5 H-benzo [5, 6] cyclohepta [1, 2-b] pyridine. It acts as a long acting, non sedative antagonist at histaminergic H_1-receptors and also antagonizes the platelet-activating factor (PAF). Both histamine and PAF cause broncho-constriction and lead to an increase in vascular permeability, acting as a mediator in the inflammatory process, which is responsible for the bronchial hyperactivity.

This drug is not official reported in pharmacopeia. In literature survey HPLC[1-3] and HPTLC[4] methods were reported.

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EXPERIMENTAL

Materials and methods

A Shimadzu-160 A double beam UV-Visible recording spectrolphotometer with pair of 10 mm matched quartez cell was used to measure absorbance of solutions. A Shimadzu analytical balance was used.

Bromothymol blue, bromophenol blue, methyl orange, hydrocholoric acid, potassium hydrogen phthalate and chloroform of A.R. grade were used in the study.

Prepartion of standard solution and reagents

Stock solution of rupatadine as rupatadine fumarate (100 μg/mL) was prepared in distilled water. From this stock solution, working standard (10 μg/mL) was prepared by diluting 10 mL stock solution to 100 mL with distilled water. 0.1% w/v solution of bromothymol blue, bromophenol blue and methyl orange solutions were prepared in distilled water, respectively.

Potassium hydrogen phthalate buffer solution of pH 4.01 was prepared in distilled water. Diluted hydrochloric acid was used to adjust desired pH of buffer solution.

Method I (with bromothymol blue)

Into a series of separating funnels, appropriate amounts of the working standard drug solutions were pipetted out. To each funnel, 2.0 mL of buffer (pH = 3.5) and 2.0 mL of 0.1% (w/v) bromothymol blue were added. 10 mL of chloroform was added to each funnel. The solutions were shaken for thorough mixing of the two phases and were allowed to stand for clear separation of the layers.

The absorbance values of the chloroform layers were measured against their respective reagent blank at the wavelength of the maximum absorbance (λ_{max} 416 nm) (Fig. 1).

Method II (with bromophenol blue)

Into a series of separating funnels, appropriate amounts of the working standard drug solutions were pipetted out. To each funnel, 2.0 mL of buffer (pH = 3.0) and 2.0 mL of 0.1 % (w/v) bromophenol blue were added. 10 mL of chloroform was added to each funnel. The

solutions were shaken for thorough mixing of the two phases and were allowed to stand for clear separation of the layers.

The absorbance values of the chloroform layers were measured against their respective reagent blank at the wavelength of the maximum absorbance (λ_{max} 418 nm) (Fig. 2).

Method III (with methyl orange)

Into a series of sparating funnels, appropriate amounts of the working standard drug solutions were pipetted out. To each funnel, 3.0 mL of buffer (pH = 3.0) ad 3.0 mL of 0.1% (w/v) methyl orange were added. 10 mL of chloroform was added to each funnel. The solutions were shaken for thorough mixing of the two phases and were allowed to stand for clear separation of the layers.

The absorbance values of the chloroform layers were measured against their respective reagent blank at the wavelength of the maximum absorbance (λ_{max} 422 nm) (Fig. 3).

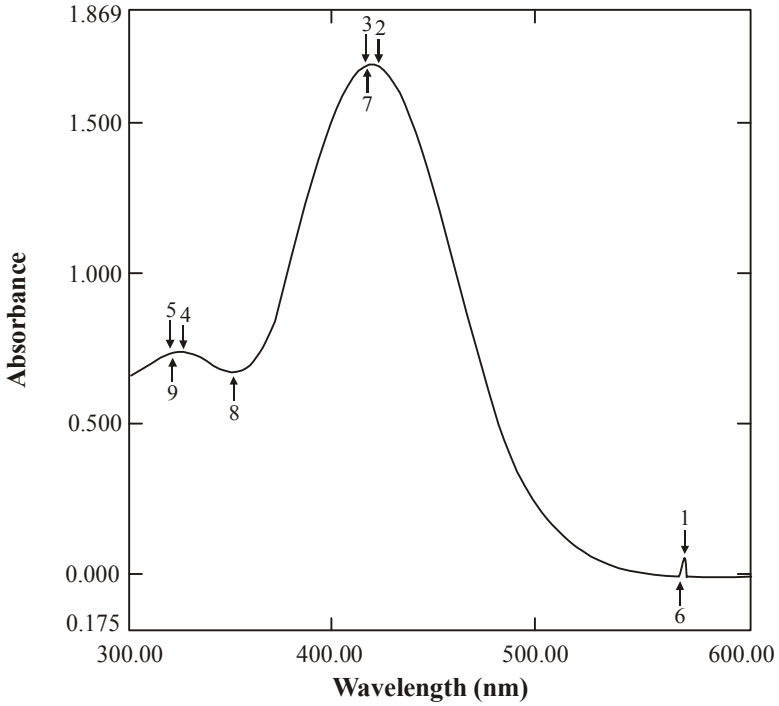

Fig. 1: Spectrum with bromothymol blue

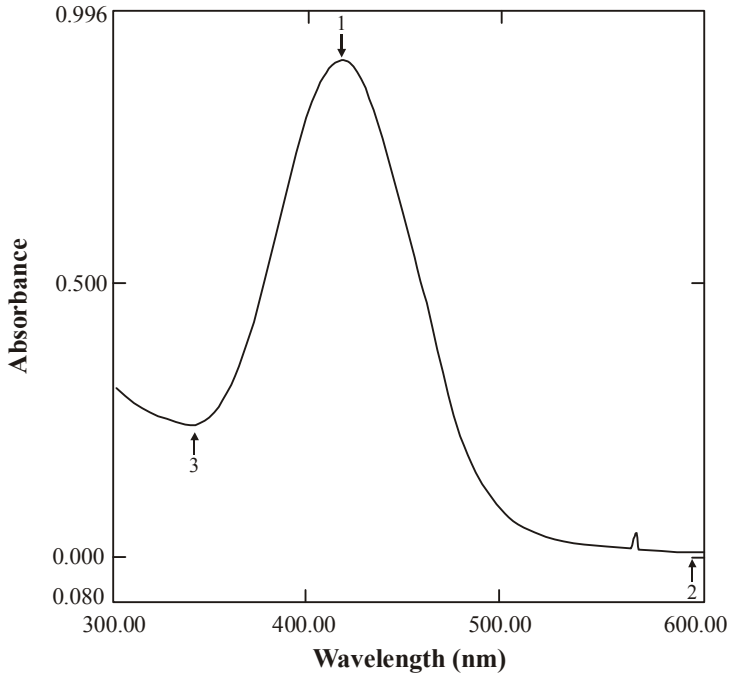

Fig. 2: Spectrum with bromophenol blue

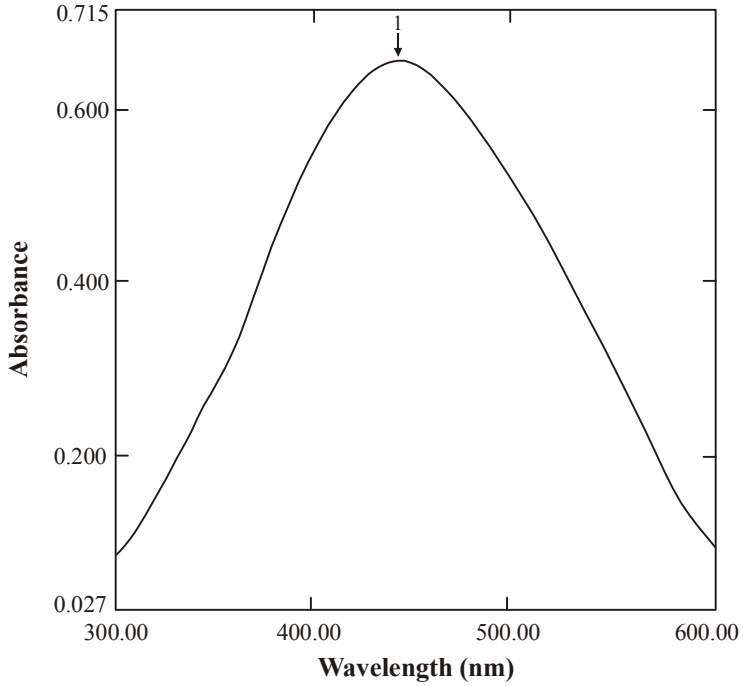

Fig. 3: Spectrum with methyl orange

Estimation from tablets

Twenty tablets of labeled claim 10 mg of rupatadine were weighed accurately. Average weight of each tablet was determined. Tablets were crushed into fine powder. An accurately weighed quantity of powder equivalent to 10 mg of rupatadine (Rupatadine fumarate) was transferred into a beaker and it was shaken with 50 mL of distilled water and filtered. The filtrate and the washing were collected in a 100 mL volumetric flask. This filtrate and the washing were diluted up to the mark with distilled water to obtain final concentration as 100 μg/mL. This solution was further diluted to give 10 μg/mL. Such solution was used for methods I, II and III, respectively.

Appropriate aliquots of drug solution were taken and the individual assay procedures were followed for the estimation of drug contents in tablets. The concentration of the drug in the tablets was calculated using calibration curves. The recovery experiment was carried out by standard addition method. Results of analysis are given in Table 1.

Table 1: Optical and regression of drug in different methods

Parameter	Method		
	I	II	III
λmax (nm)	416	418	422
Beer law limits (μg/mL)	1.0-12.0	1.0-16.0	1.0-28
Molar absorptivity (L/mol. Cm)	2.26698 x 104	2.953 x 104	1.0398 x 104
Sandell's sensitivity	1.818 x 10-3	1.408 x 10-2	3.846 x 10-2
Correlation coefficient (r^2)	0.9995	0.9999	0.9999
Regression equation (y = b + ac)			
Slope (a)	0.0545	0.071	0.025
Intercept	0.0022	0.0040	0.003

RESULTS AND DISCUSSION

The extractive spectrophotometric methods are popular due to their sensitivity in assay of the drug and hence, ion pair extractive spectrophotometric methods have gain considerable attention for quantitative determination of many pharmaceutical preparations. These proposed methods are extractive spectrophotometric methods for the determination of

rupatadine by using chloroform as solvent form its formulation i.e. tablets.

The colour ion-pair complexes formed are very stable. The working conditions of these methods were established by varying one parameter at a time and keeping the other parameters fixed by observing the effect produced on the absorbance of the colour species. Various parameters involved for maximum colour development for these methods were optimized. The proposed methods were 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 % RSD (relative standard deviation). The optical characteristics such as absorption maxima (nm), molar absorptivity (lit. mol^{-1} cm^{-1}), correlation coefficient (r) and Sandell's sensitivity ($mg/cm^2/0.001$) were calculated and are also summarized in Table 1. Assay results of recovery studies are given in Table 2. Results are in good agreement with labeled values. The percent recovery obtained indicates non-interference from the common excipients used in the formulation. The reproducibility, repeatability and accuracy of these methods were found to be good, which is evidenced by low standard deviation.

Table 2: Results of recovery of drug

Reagent	Amount of drug added (μg/mL)	Amount of std. drug (μg/mL)	Total amount recovered	% Recovery	Std. deviation	% of relative std. deviation
Bromothymol blue	1.0	0	1.0026	100.26	0.01255	1.25266
	1.0	1.0	2.0026	100.13	0.01255	0.62714
	1.0	2.0	3.0078	100.26	0.01776	0.59051
	1.0	3.0	4.0052	100.13	0.01731	0.43222
Bromophenol blue	1.0	0.0	0.9980	99.800	0.00972	0.9749
	1.0	1.0	1.9960	99.800	0.01341	0.6719
	1.0	2.0	3.0020	100.066	0.00972	0.3241
	1.0	3.0	3.9980	99.950	0.015073	0.3770
Methyl orange	1.0	0	1.0055	100.55	0.02655	2.6405
	1.0	1.0	2.0056	100.28	0.02705	1.3487
	1.0	2.0	2.9944	99.813	0.04218	1.4092
	1.0	3.0	4.0112	100.28	0.03729	0.9296

The proposed methods are simple, sensitive, accurate, precise and reproducible. These are directly applied to drug to form chormogen. Hence, they can be successfully applied for the routine estimation of rupatadine in bulk and pharmaceutical dosage form even at very low concentration and determination of stability of drug in formulation such as tablets.

The strong recommendation is made here for the proposed methods to be used in determination of rupatadine as rupatadine fumarate from its formulation.

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