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Simple 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 bromocresol green , eriochrome black-T and solochrome dark blue 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 nm, 511 nm and 527 nm respectively. The proposed methods were validated statistically. Recoveries of methods were carried out by standard addition methods. The linearity was found to be 1-12 µg/ml, 2.5 – 50 µg/ml and 100-600 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, bromocresol green, eriochrome black-T, solochrome dark blue.

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 pharmacopeias. In literature survey HPLC methods [1-5], HPTLC method [6] , spectrophotometric method [7] and titrimetric method [8] were reported.

MATERIALS AND METHODS

A SHIMADZU –UV-1800 double beam UV-VISIBLE recording spectrophotometer with pair of 10 mm matched quartz cell was used to measure absorbance of solutions.

A SHIMADZU analytical balance with capacity 0.01 mg was used. Bromocresol green, eriochrome black-T, solochrome dark blue , hydrochloric acid, potassium hydrogen phthalate and chloroform of A.R. grade were used in the study.

Preparation of standard solution and reagents
Stock solution of rupatadine as rupatadine fumarate (1000 µg /ml) was prepared in distilled water. From this stock solution working standard (100 µg/ml) was prepared by diluting 10 ml stock solution to 100 ml with distilled water.

A 0.1% w/v solution of bromocresol green, eriochrome black-T and solochrome dark blue solutions were prepared in distilled water respectively.

Potassium hydrogen phthalate buffer solution of pH 4.0 was prepared in distilled water. Dilute hydrochloric acid was used to adjust desired pH of buffer solution.

Method I(with bromocresol green) : Into a series of separating funnels appropriate amount 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 bromocresol green were added. A 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 eriochrome black-T) : Into a series of separating funnels appropriate amount of the working standard drug solutions were pipetted out. To each funnel 2.0 ml of buffer (pH = 3.5) and 1.0 ml of 0.1% w/v eriochrome black-T were added.A 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} 511 nm).Fig. 2.

Method III(with solochrome dark blue) : Into a series of separating funnels appropriate amount of the working standard drug solutions were pipetted out. To each funnel 2.0 ml of buffer (pH = 1.5) and 6.0 ml of 0.1 % w/v solochrome dark blue were added.A 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} 527 nm.) Fig. 3.

Estimation from tablets
Twenty tablets of labelled 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 sonicated with 50 ml of distilled water and filtered. The filtrate and the washing were collected in a 100.0 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 and II 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 curve. The recovery experiment was carried out by standard addition method. Results of analysis are given in table no 1.

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 from its formulations 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 time and keeping the other parameters fixed by observing the effect produced on the absorbance of the colour species. The 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 - $mole^{-1}$ cm^{-1}), co-relation coefficient (r) and sandell sensitivity (µg/cm^2/0.001) were calculated and are also summarized in table 1. Assay results of recovery studies are given in table no. 2.

Results are in good in agreement with labelled value. 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 1: Optical and regression of drug in different methods

Parameter	Methods		
	I	II	III
λ_{max} (nm)	416	511	527
Beer Law Limits (µg/ml)	1.0-12.0	2.5-50.0	100-600
Molar absorptivity(l/mol.cm)	3.3401 x10^2	7.4498 x 10^2	3.32 x 10^4
Sandell's sensitivity	0.0125	0.0541	1.2195
Correlation coefficient(r^2)	0.9998	0.9996	0.9998
Regression equation (y=b+ac)			
Slope (a)	0.0803	0.1791	0.0008
Intercept	0.0013	0.0009	0.0006

Table 2: Results of recovery of drug

Reagent	Amount of drug added µg/ ml	Amount of standard drug µg/ml	Total amount recovered	Percentage recovery	Standard deviation	Percentage of relative standard deviation
Bromocresol green	1	0	1.0107	101.07	0.0584	5.7782
	1	1.0	1.9982	99.91	0.0275	1.3762
	1	2.0	3.0264	100.88	0.0270	0.8921
	1	3.0	4.0053	100.13	0.0173	0.4319
Eriochrome black-T	10	0	9.9999	99.99	0.0987	0.9870
	10	10	19.9692	99.85	0.0751	0.3761
	10	20	29.9999	99.99	0.1282	0.4273
	10	30	39.9846	99.96	0.1345	0.3364
Solochrome dark blue	100	0	99.8257	99.83	1.3037	1.3059
	100	100	201.7528	100.88	2.5401	1.2590
	100	200	304.6045	101.53	3.3352	1.0949
	100	300	400.3527	100.09	4.4919	1.1219

The proposed methods are simple, sensitive, accurate, precise and reproducible. They are directly applied to drug to form chromogen. 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.

Fig. 1: Spectrum with bromocresol green

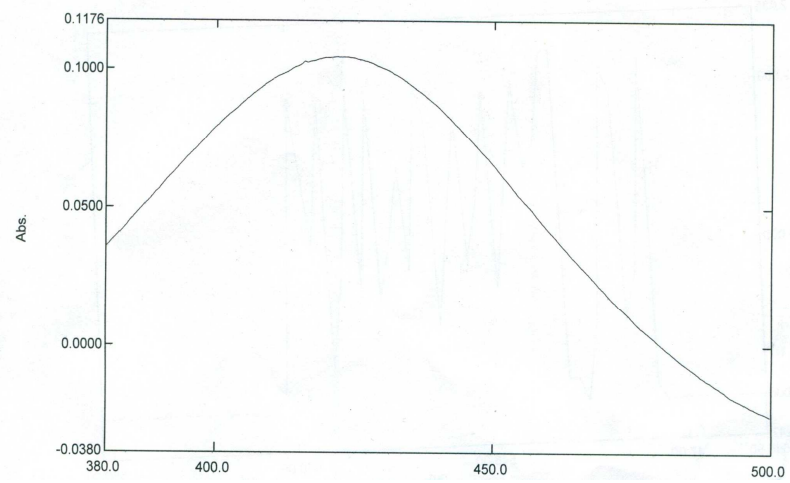


Fig.2: Spectrum with eriochrome black T

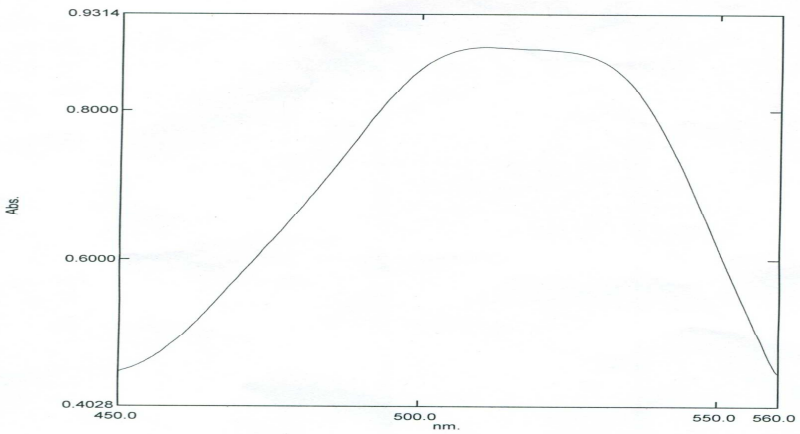
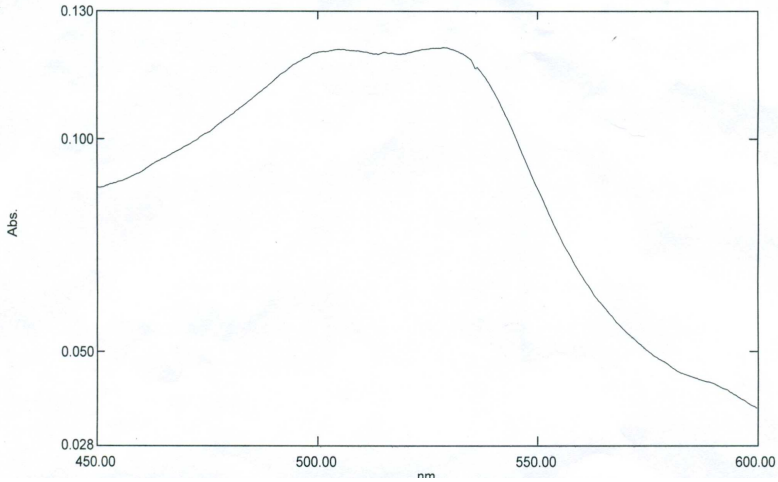


Fig. 3: Spectrum with solochrome dark blue



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

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