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ANALYTICAL METHOD DEVELOPMENT AND ITS VALIDATION FOR DETERMINATION OF RUPATADINE HCL IN BULK AND FORMULATION BY U.V. SPECTROMETRIC METHOD

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ABSTRACT

A simple, sensitive, spectrophotometric method in UV region has been developed for the determination of RupatadineFumarate in bulk and tablet dosage form. The method have been developed and validated for the assay of Rupatadine. Solution of Rupatadine Fumaratein Solvent shows maximum absorbance at 273.5 nm in zero order spectrum method, in first order derivative spectra show sharp peak at 261.5 nm, calculation of area under curve (AUC) for analysis of Rupatadine in wavelength rangebetween 268.5 nm to 278.5 nm. The Beer-Lambert'slaw was obeyed in the concentration range of 1 to 6 µg / ml. Result of analysis were validated statically and were found to be satisfactory. Parameters of the analysis were chosen according to ICH [Q2 (R1)] guideline.

Keywords: RupatadineFumarate, UV spectroscopy, Zero order Derivative, First order derivative, Area under curve method.

INTRODUCTION

Rupatadine HCl 8-Chloro-6, 11-dihydro-11-[1-[(5-methyl-3-pyridinyl) methyl]-4-piperidinylidene]-5Hbenzo [5, 6] cyclohepta [1, 2-b] pyridine fumarate. 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 [1]. It is potent and orally active that was developed as a therapeutic agent for the treatment of seasonal allergic rhinitis and chronic idiopathic urticarial [2]. It acts as a long acting, non-sedative antagonist at histaminergic H1-receptors and also antagonizes the platelet-activating factor (PAF) [3-6]. Rupatadine fumarate belongs to a class of medications called Anti allergic, Antihistaminic [7]. Montelukast is a CysLT1 antagonist; it blocks the action of leukotriene D4 (and secondary ligands LTC4 and LTE4) on the cysteinyl leukotriene receptor CysLT1 in the lungs and bronchial tubes by binding to it [8]. This drug is not officially reported in pharmacopeias [9]. Recent studies reveal that the treatment of` asthma with concomitant administration of antileukotriene (Montelukast) and an antihistamine (Rupatadine) [10].

Literature survey reveals that there are few methods like UVSpectroscopy, HPTLC, RP-HPLC [11-13], Potentiometric Titration [14], Titrimetric method[15] has been reported for estimation of Rupatadine Fumarate, but at different wavelength and use of different solvent system hence the

objective of work is to develop simple, precise, accurate, sensitive and rapid cheap UV-Visible spectrophotometer in bulk and pharmaceutical formulation.

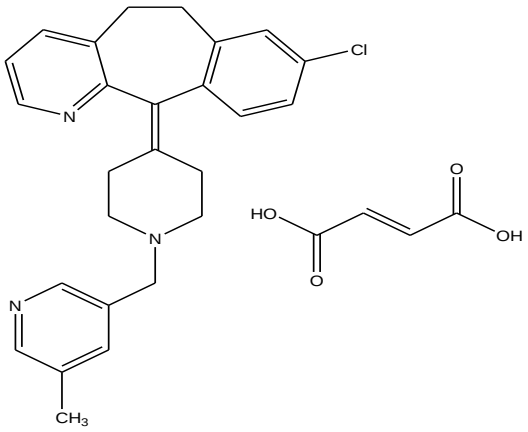

Figure 1: Structure of Rupatadine Fumarate

MATERIALS AND METHODS

Instrument

Shimadzu UV-1800 was used with 10 mm matched quartz cell of 1cm to measure absorbance of solution.

A Shimadzu analytical balance with 0.01 mg was used.

Materials

Standard gift sample of was procured from Gain Pharmaceuticals Ltd. Bhosari, Pune.

Solvent used: 0.1N HCL, Distilled Water

Experimental

Preparation of drug stock solution:

Weigh accurately about 10mg of Rupatadine Fumarate and transferred to 100ml volumetric flask. To it 20ml of distill water was added to dissolve the drug completely with vigorous shaking then the volume was made up with 0.1N HCLup to mark to give the drug stock solution of concentration 100µg/ml.

Method A: Zero order derivative method

A series volumetric flask of 10 ml capacity was arranged. To each of these flasks 1, 2, 3, 4, 5, 6 µg/ml of the drug stock solution were added. The volume was made up with glass distilled water. The absorbance was measured at 267.5 nm against reagent blank. A linear graph of absorbance vs. concentration was obtained. The concentration range over which the drugs obeyed Beer – Lambert's law was found to be 1 to 6 µg/ml for Rupatadine.

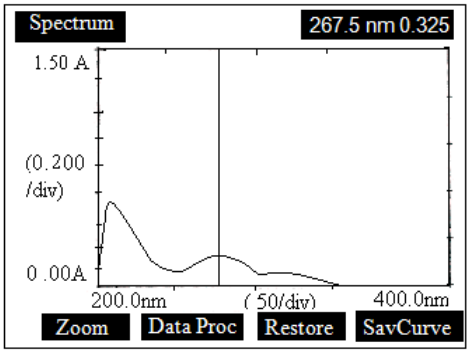

Figure 2: Zero order spectra

Method B: First order derivative method

A series of volumetric flasks of 10 ml capacity were arranged. To each of these up with glass HCl. The solutions were scanned in the first order derivative mode with (n=1) and the difference in the absorbance were measured at 218 nm against reagent blank. A linear graph of absorbance Vs concentration was obtained. The concentration range over which drug obeyed Beer-Lambert's law was chosen as the analytical concentration range (1 to 6 µg/ml) for Rupatadine HCl. The standard calibration of Rupatadine absorbance difference against concentration of the drug showed linearity.

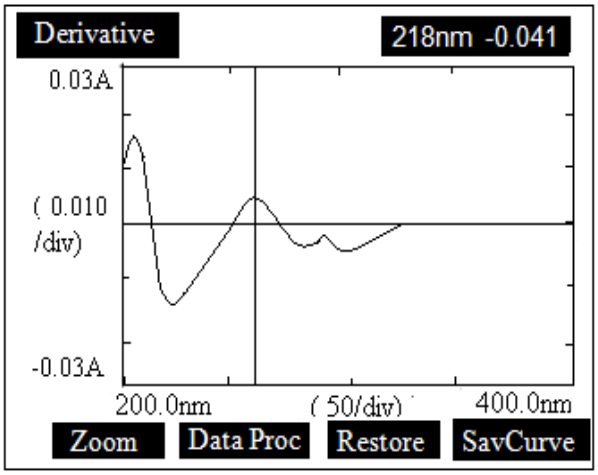

Figure 3: First order spectra

Method C: Area under Curve (AUC) Method

Suitable concentrations of solutions were prepared accurately to determine the range of Rupatadine HCl for analysis. The standard solutions were scanned in the spectrum mode of the instrument from 400 nm to 200 nm. The absorbance maxima of these solutions were obtained at wavelength273.5nm. The area under the curve between 265 nm to 270 nm was selected for the calculation because the linearity was obtained within these areas with good reproducibility of results.

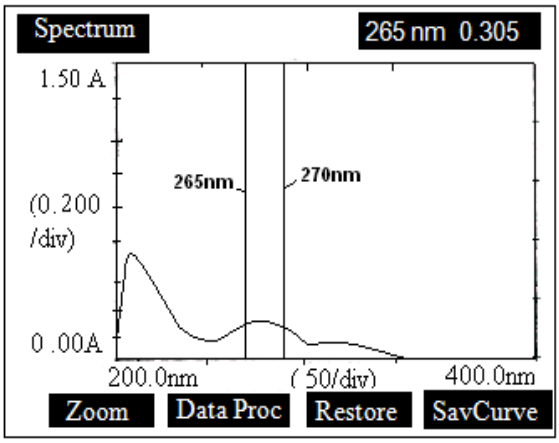

Figure 4: Area under Curve spectra

RESULT AND DISCUSSION

Analysis of tablet formulation

For estimation of Rupatadine in tablet formulation by three methods, twenty tablets were weighed. The tablet content was weighted and triturated to fine powder. Tablet powder equivalent to 10 mg.

of Rupatadine was weighed and transferred to 100 ml volumetric flask and dissolved in 10 ml of 0.1N HCL. It was kept for ultrasonification for 30 min. finally the volume was made up to the mark with distilled water. further pipette out 1ml from above solution and dilute up to 10 ml with distilled water this was then filtered through what man filter paper no. 41 to get tablet stock solution of concentration of 10 µg/ml. various dilution of the tablet solution were prepared and analyzed for six times and concentration was calculated by using the calibration curve for three method. All these method were validated according to ICH guidelines by carrying out analysis of six replicate samples of the tablets (Table 1), Recovery studies were carried out at two different level i.e. 80%100%, 120% by adding the pure drug (8, 10, and 12 mg respectively) to previously Analyzed tablet powder sample from the amount of drug found percentage recovery was calculated (Table 2).

Table 1: Estimation of Rupatadine formulation Tablet

Sr. No.	Tablet sample	Label Claim (Mg/tab)	Label Claim Found (Mg/tab)	% mean	S.D*	C.O.V.*	S.E.M*
A	T_1	10	9.97	99.7	0.8779	0.8805	0.3584
B	T_1	10	10	100	0.5762	0.5762	0.2352
C	T_1	10	10.03	100.03	0.8733	0.8730	0.3565

*Average of six determinations

Table 2: Recovery Study Data

Sr. No.	Tablet sample	Level of recovery (%)	Percentage (mean)	S.D.*	C.O.V.*	S.E.*
1	T_1	80	99.71	0.5948	0.01	0.3434
2		100	100.1	0.03055	0.07751	0.01764
3		120	100.01	0.03055	0.0245	0.01765
4	T_2	80	99.71	0.5948	0.596	0.3434
5		90	100.05	0.0871	0.086	0.0503
6		100	99.98	0.0251	0.025	0.0145
7	T_3	80	100.17	0.5948	0.200	0.3440
8		90	100.64	0.03045	0.140	0.01745
9		100	100.60	0.03090	0.114	0.01785

*Average of six determinations

The Methods A, B, C were developed for estimation of Rupatadine fumarate in tablet dosage form and found to be accurate and reproducible. These proposed methods are spectrophotometric methods for the determination of Rupatadine by using 0.1N HCl as solvent from its formulations i.e. tablets. Beer- lambert's was obeyed in the concentration range of 1- 6ug/ml in all these methods .The values of standard deviation were satisfactory and the recovery studies were close to 100%. .The molar absorptivity 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}), correlation coefficient (r) and were calculated and are also summarized in (table no.3). Assay results of recovery studies are given in (table no.1). 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. These methods can be useful in the routine analysis of Rupatadine fumarate in bulk drug and formulation.

Table 3: Optical Calibration Curve of Rupatadine

Parameters	**Method A**	**Method B**	**Method C**
λ_{max} (nm)	267.5	218	265-270
Beer's – Lambert's range (µg/ml)	1-6µg/ml	1-6µg/ml	1-6µg/ml
Coefficient of correlation (r^2)	0.9992	0.9996	0.9995
Regression equation : Y = mx + c	0.0825x+0.0	-0.0081x+0.00	0.1766x+0.0
a – Slope (m)	0.0825	-0.0081	0.1766
b – Intercept (c)	0.0	0.0	0.0
LOD µg/ml	0.004	0.051	0.005
LOQ µg/ml	0.013	0.172	0.016
Molar absorptivity	0.036×10^{-3}	0.024×10^{-3}	0.029×10^{-3}

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