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ISSN: 2278-1862

Journal of Applicable Chemistry

2018, 7 (4): 1040-1046

(International Peer Reviewed Journal)

Spectrophotometric Determination of Cetirizine Hydrochloride in a Pharmaceutical Formulation Using Potassium Permanganate and Sulphanilic Acid as an Analytical Reagent

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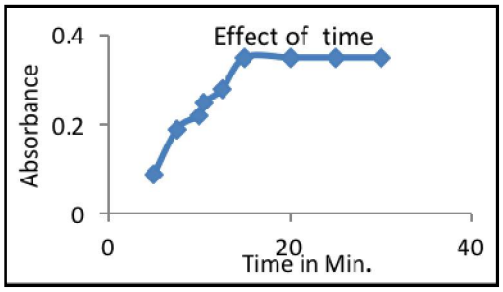
Accepted on 2nd July 2018

ABSTRACT

For the determination of Cetirizine hydrochloride two simple and sensitive spectrophotometric methods are developed. The first method A is based on the addition of excess $KMnO_4$ of known concentration in the presence of 2M H_2SO_4, reactants are allowed to react and the unreacted $KMnO_4$ is estimated with a fixed amount of Methyl Orange by measuring the absorbance at 510 nm. Beer's law was obeyed in the concentration range of 0.5- 5µg mL^{-1}. Molar absorptivity was found to be 1.818 X 10 ^{4} L $mol^{-1}cm^{-1}$. The second method B is based on the formation of orange color dye because of reaction between drug and diazotized Sulphanilic acid the absorbance of the resulting solution was measured at 510 nm. All parameters affecting the development of the color were investigated and the conditions were optimized. Under the optimum condition, Beer's law was obeyed in the concentration range 1.0 - 8.0 µg mL^{-1}. Molar absorptivity was found to be 0.7534 X 10 ^{4}L $mol^{-1}cm^{-1}$. The proposed methods are well suited for determination of Cetirizine hydrochloride in pharmaceutical formulations.

Graphical Abstract



Effect of contact time for the formation of color product in method A.

Keywords: Cetirizine hydrochloride, Diazotizedsulphanilicacid, Spectrophotometric, Methyl orange, Oxidation.

INTRODUCTION

Cetirizine is an antihistamine. It works by blocking a certain natural substance (histamine) that our body makes during an allergic reaction. It acts as a selective antagonist of the histamine H_1 receptor. Cetirizine used to relieve allergy symptoms such as watery eyes, runny nose, itching eyes/nose, sneezing, hives, and itching. It is widely used in the comprehensive management of allergic rhinitis, the symptoms of which include itching, sneezing and nasal congestion.

Cetirizine is second-generation antihistamines and is less able to cross the blood–brain barrier and therefore have diminished effects on the central nervous system compared to first-generation drugs. Hence, it is less likely to cause drowsiness or memory impairment. Thus, it displays a series of advantages over its predecessors as it is free of both sedative and cholinergic effects and has potent antiallergic activity [1-3]. Cetirizine hydrochloride is a piperazine derivative and its chemical name is (±)–[2-[4-[(4- chlorophenyl) phenyl methyl]-1-piperazinyl] ethoxy] acetic acid, dihydrochloride its molecular formula is $C_{21}H_{27}Cl_3N_2O_3$. Its molar mass is 388.89 g mol^{-1}. Literature survey reveals a variety of analytical methods for determination of Cetirizine in pharmaceutical formulations such as Acid base titration and TLC or HPTLC [4–6], HPLC [7–13], spectrophotometry/colorimetry [14–16] and other sophisticated methods such as LC-MS/MS [17–18], ion-selective electrodes [19].

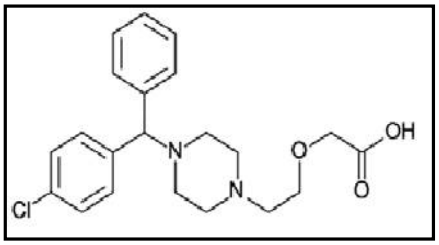


Figure 1. Structure of Cetirizine hydrochloride.

There is a need for a simple spectrophotometric method for the analysis of Cetirizine in pharmaceutical formulations. $KMnO_4$ and Sulphanilic acid are used for development of spectrophotometric method level determination of many drug at micro gram level [20-22].

The present investigation describes two Spectrophotometric methods for the determination of cetirizine by using $KMnO_4$ as an oxidizing agent and Sulphanilic Acid as a coloring reagent respectively. Simplicity, sensitivity, accuracy, wide linear ranges, mild experimental conditions and above all cost effectiveness characterize the proposed methods. The proposed methods are comparable with reported method with respect to sensitivity moreover; the methods require neither extraction nor prior separation of the drug.

MATERIALS AND METHODS

Apparatus: A Systronics UV-VIS Spectrophotometer-118 Model with 1cm length quartz coated optics; Wavelength range190-1000nm: High stability, linearity, precision instrument is used for all the spectral measurements, which is calibrated by standard method.

Reagents and Materials: For this research project, all chemicals used were of analytical grade and double distilled water was used to prepare all the solutions.

Preparation of Standard solution of drug: An accurately weighed 5 mg of cetirizine dissolved in 50 mL of ethanol. The final volume is adjust with distilled water to 100 mL in standard flask.

Preparation of reagents

Method A: A stock solution of methyl orange (160 µg mL^{-1}) was prepared by dissolving the dye (Himedia Laboratories Pvt, Limited, Mumbai) in distilled water. The dye solution was diluted to 80

µg mL^{-1}. Potassium permanganate (0.001) mol L^{-1} was prepared by dissolving about 0.0158 gm of chemical (Merck, Mumbai, India) in water and diluting to 100 mL and standardized [23] using H.A Brights Procedure (A.I. Vogel, 3rd edition, 1961, p.no.280). Stock solution of $KMnO_4$ was further diluted to get the working concentration of 63.2 µg mL^{-1}(4 x10^{-4} M) concentrated H_2SO_4 (SD. Fine Chem Limited, Mumbai) diluted appropriately with distilled water to get 2M acid solution.

Method B: Diazotized Sulphanilic Acid, In a 100 mL volumetric flask 200 mg of sodium nitrite taken and dissolved in 60 mL of distilled water. 1 mL of hydrochloride acid added and then allowed to stand for 1 h. 500 mg of Sulphanilic acid added and the final volume made up to the mark with distilled water. This reagent used after 30 min of preparation. This reagent should be freshly prepared for analytical work.

Experimental procedure

Method A: Aliquots of a drug solution (1 to 5 mL, 20 µg mL^{-1}) were transferred into a series of 10 mL calibrated flask. To each flask, 1 mL of 2M H_2SO_4 added, followed by 1 mL of $KMnO_4$ solution (63.2 µg mL^{-1}). The contents mixed and the flasks were set aside for 15 min under occasional shaking. Finally, 1 mL of Methyl Orange solution (80 µg mL^{-1}) was added to each flask, diluted to the mark with water and the absorbance of solution was measured at 510 nm against a reagent blank.

Method B: With the help of burette, into a series of 25 mL calibrated flasks (1 to 8 mL, 20 µg mL^{-1}) of pure cetirizine was taken and 10 mL of coloring reagent was added. The final volume made to 20 mL with NaOH (1M). The absorbance measured at 510 nm after 5 min after dilution [21, 22].

Assay Procedure for Tablet: Ten tablets accurately weighed and powdered. A portion of tablet powder equivalent to 5 mg of was cetirizine accurately weighed and transferred into 100 mL beaker and then shaken with 50 mL ethanol by following standard method. The resultant solution filtered into 100 mL standard flask and volume adjusted with 50% ethanol. Suitable aliquots of this solution used for the determination of cetirizine contents by both the as procedure describe earlier.

RESULTS AND DISCUSSION

Method Development

Method A: The proposed spectrophotometric method is indirect after allowing the reaction between $KMnO_4$ and drug the excess amount of $KMnO_4$ is determined spectrophotometrically. The excess of $KMnO_4$ made to react it with a fixed amount of methyl orange dye. $KMnO_4$ bleaches the dye by causing oxidative destruction of the dye. Drug the process increasing concentrations to a fixed concentration of $KMnO_4$, consumes the $KMnO_4$ proportionally and there occurs a fall in the concentration of $KMnO_4$ (Fig. 2). When a fixed concentration of dye is added to decreasing concentrations of $KMnO_4$ there is increase in the concentration of dye. Thus, a proportional increase in the absorbance at the respective λ max observed with increasing concentration of drug (Fig. 3).

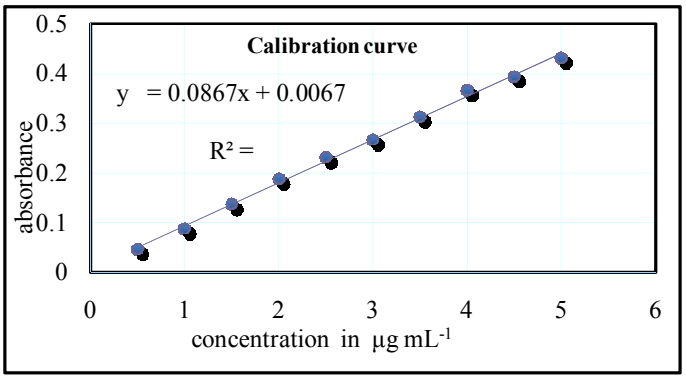


Figure 2. Calibration Curve for Method A.

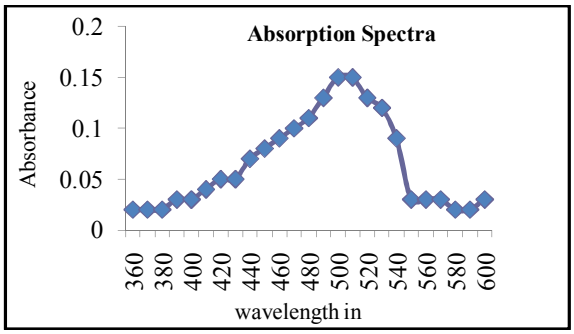


Figure 3. Absorption spectra showing λ max 510 nm for Method A.

Optimization of Parameters for Method A: Preliminary experiments were conducted in order to determine the maximum concentrations of methyl orange spectrophotometrically by measuring the absorbance of their acidic solutions at their respective λ max and 8 µg mL^{-1} of methyl orange was found to be the upper limits. $KMnO_4$ concentration of 6.32 µg mL^{-1} found to be sufficient to bleach the color of methyl orange upto concentration of 8 µg mL^{-1} methyl orange. Hence different amounts of drug was made to react with 6.32 µg mL^{-1} $KMnO_4$ in this method before determining the residual $KMnO_4$ as described under the respective procedure. Sulphuric acid found to be a convenient medium for these methods. For a quantitative reaction between drug and $KMnO_4$, a contact time of 15 min found sufficient. It is evident from the fig 4 given below.

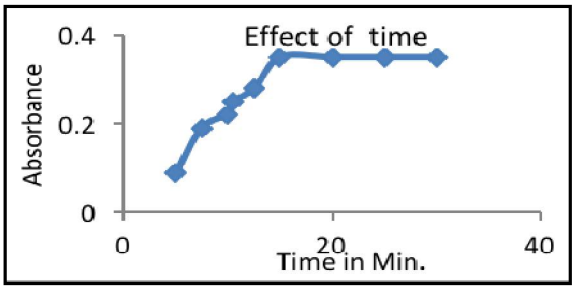


Figure 4. Effect of contact time for the formation of color product in method A.

Method B: Coloring reagent prepared by diazotization reaction with sulphanilic acid, in second method reaction proceeds with increasing absorbance. This reagent reacts with cetirizine to form orange colored complex

Optimization of Parameters for Method B: The optimum concentration of sulphanilic acid was 500 mg and of sodium nitrite 200 mg, optimum volume of coloring reagent 10 mL. The absorbance measured between first 10 min (Fig. 5).

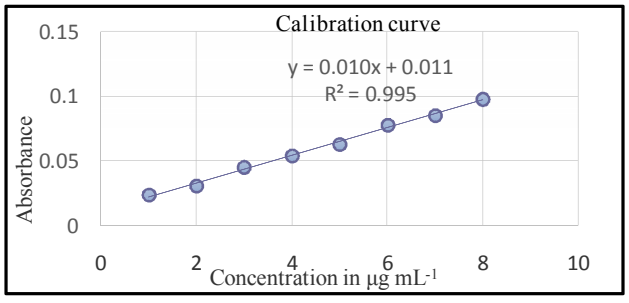


Figure 5. Calibration Curve for Method B.

The absorbance decreases after 15 min. It remains constant in first 10 min hence the absorbance was measured between first 10 min (Fig.6).

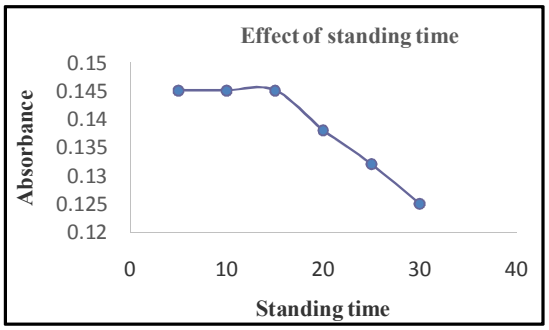


Figure 6. Standing time for Method B.

Method Validation: The developed methods validated for its accuracy, precision, reproducibility and selectivity. In addition, the experiment repeated three times in a day to determine intra-day precision and on three different days to determine inter-day precision. The percent relative standard deviation calculated at each concentration level and the results were tabulated. The reproducibility confirmed by repeating the three different analysts.

Limit of detection (LOD): LOD calculated based on standard deviation of response and the slope of calibration curve. The limit of detection expressed as

$$LOD= 3.3\times \sigma/S$$

Where σ is the standard deviation of intercept, S is the slope of calibration curve.

Limit of Quantitation (LOQ): LOQ calculated based on standard deviation of intercept and slope of calibration curve. In this method the limit of quantitation expressed as

$$LOQ= 10 \times \sigma/S$$

Where σ is the standard deviation of intercept, S is the slope of calibration curve.

The results summarized in table 2 above indicating good sensitivity of proposed method, according to USP validation guidelines (TUSP, 2002).

Accuracy and Precision of the proposed methods: Accuracy and precision checked according to USP validation guidelines (TUSP, 2002) at three concentration levels within the specified range, six replicates measurements recorded at concentration levels. The results are summarized in (table-1) below**.**

Table 1. Evaluation of precision of the proposed spectrophotometric methods for determination of cetirizine.

S. No	Amount taken (µg mL^{-1})	Amount found (µg mL^{-1}) Method A ($KMnO_4$ and Methyl orange)	Amount found (µg mL^{-1}) Method B (Sulphanilic acid)
1	2	2.016 ± 0.14719 variation with 95% confidence limit=0.11777	2.033 ± 0.10328 variation with 95% confidence limit=0.08264
2	5	5.00 ± 0.141421 variation with 95% confidence limit=0.1137	5.10667 ± 0.1169 variation with 95% confidence limit=0.08257

Table 2. Analytical parameters for spectrophotometric determination of cetirizine in the tablet form by applying methods A and B.

Parameters	Method A	Method B
Maximum Wavelength λ_{max}	510	510
Beer's Law Limits µg mL^{-1} (Linearity Range)	0.5- 5 µg mL^{-1}	1-8 µg mL^{-1}
Sandell's Sensitivity (µg cm^{2-1} /0.0001 Absorbance)	0.0213	0.05161
Molar Absorptivity L $mol^{-1}cm^{-1}$	1.818 X 10^4	0. 7534X 10^4
Slope(b)[a]	0.0867	0.0107
Standard Deviation on slope	0.001564	0.000288
Intercept(a)[a]	0.006733	0.0118
Standard Deviation on y intercept	0.004852	0.001452
LOD (µg mL^{-1})	0.1846	0.4478
LOQ (µg L^{-1}l)	0.559	1.357

APPLICATION

Application to formulation: The proposed methods applied to the determination of drugs in tablets. The results in table 3 showed that the methods are successful for the determination of drugs and that the excipients in the dosage forms do not interfere. The results compared with the available validated reported methods on each drug and the results agree well.

Table 3. Tablet of the cetirizine analyzed by the proposed method as per the procedure

Drug	Manufacturing company	Labelled amount(mg)	*Amount found by Proposed Method A(mg)	*Amount found by Proposed Method B (mg)	*Amount found by HPLC [11] Method(mg)
Acit	Savoy Biotech	10mg	9.79	9.76	9.89
Acet	Acto Pharmaceuticals Laboratories	10mg	9.86	9.76	9.91
Aglocet	Aglowmed Ltd	10mg	9.67	9.76	9.95

CONCLUSIONS

Two simple, rapid, accurate precise and sensitive spectrophotometric methods developed for the determination of cetirizine in bulk drug and in tablets. The methods are free, rigid over experimental conditions are characterized by wide linear dynamic ranges, has high sensitivity, employ inexpensive and easily available chemicals. The low detection, quantification limits, simplicity and selectivity make the method suitable for quality control in pharmaceutical industry for routine analysis

ACKNOWLEDGEMENTS

The authors gratefully acknowledged the use of central instrumentation facilities at V.E.S College of Arts Science and Commerce funded by FIST-DST (Ministry of Science & Technology, Department of Science and Technology) and DBT Star college scheme. The Authors are also thankful to the Principal, Dr. J.K. Phadnis, Vivekanand Educations Society's College of Arts Science and commerce Sindhi society, Chembur, Mumbai-400071 for providing all the necessary facilities to complete the above research project.

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