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New Simple Spectrophotometric Methods for Determination of Cetirizine in Presence of Its Oxidative Degradate in Pure Form and Pharmaceutical Dosage Form

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ABSTRACT

Four, simple, accurate, selective and sensitive spectrophotometric methods were developed for the determination of cetirizine (CTZ) in presence of its oxidative degradate without previous separation. Method A, Bivariate method using optimum wavelengths (211 and 231 nm) which formed by Kaiser's method, with mean percentage recovery of 100.81±0.560. Method B, Area under curve method using two wavelength regions (220− 230 nm) and (240−250 nm) with mean percentage recovery of 100.43±1.068. Method C, Dual wavelength method using two wavelengths 230 nm and 244 nm with mean percentage recovery of 100.07±0.549. Method D, Simultaneous equation method, using two wavelengths one for maximum absorbance of drug and one for degradate at 230 nm and 258 nm respectively. Results were statistically compared to a reported method and no significant difference was noticed regarding accuracy and precision.

1. INTRODUCTION

Cetirizine hydrochloride (Figure 1) is a piperazine derivative and its chemical name is (±) - [2-[4- [(4-chlorophenyl) phenyl methyl] -1- piperazinyl] ethoxy] acetic acid, dihydrochloride.Cetirizine drug is considered as a member of the second generation antihistamines and used for the symptomatic relief of hypersensitivity reactions including rhinitis and chronic urticaria[1,2]. Its H1-antagonist activity is primarily due to its R- enantiomer, levocetirizine which can be considered as the third-generation non-sedative antihistamine, developed from the second-generation antihistamine cetirizine. Chemically, levocetirizine is the active enantiomer of cetirizine, in which it works by blocking histamine receptors[3]. It also reduces asthma attacks in children by 70%[4] and slightly crosses the blood-brain barrier, eliminating the sedative side-effect common with older antihistamines; however it still causes mild drowsiness[5]. Several analytical techniques have been reported for the determination of cetirizine which include liquid chromarography[6-10], gas chromarography[11], spectrophotometry[12-14], capillary electrophoresis[15], and voltammetry [16], fluorimetry [17]. Most of these methods, however, utilize expensive instrumentation, involve careful control of the reaction conditions or derivatization reactions, and require time-consuming pretreatment steps which affect their usefulness for routine analysis. On the other hand, application of potentiometric sensors in the field of pharmaceutical and biomedical analysis have been advocated[18-20]. The approach provides simple, fast, and selective technique for various drugs[21,22]. Some potentiometric sensors for assessment of cetirizine were reported[23-25]. The present work describes preparation, characterization and application of three potentiometric sensors for static and continuous monitoring of cetirizine in pharmaceutical preparations. The sensors exhibit high accuracy, high analytical throughput and good response stability with short measurement time, low limit of detection and high selectivity in the presence of many interferents and its oxidative degradation product.

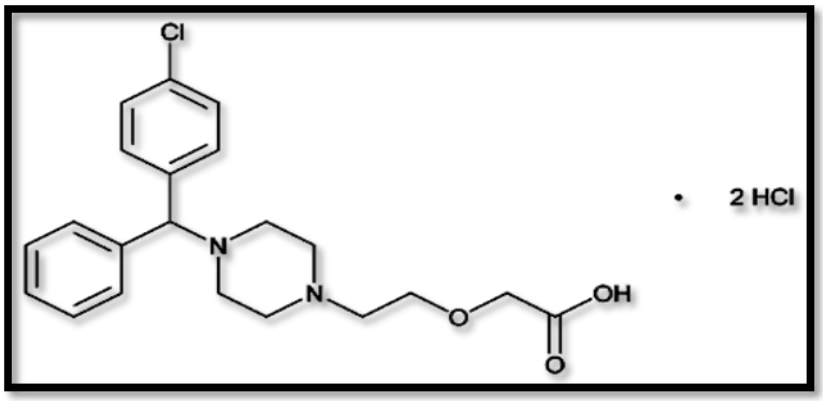

Figure (1) Structural formula of Cetirizine hydrochloride

Reviewing the literature on the determination of cetirizine in presence of its degradate revealed the lack of any stability indicating spectrophotometric methods. The aim of this work is to develop a simple, economic, rapid, sensitive, accurate and precise stability indicating methods for determination of **CTZ** in presence of its degradate without sophisticated instruments or any separation steps.

2. Theory

2.1. Theory of Bivariate calibration method:[26]

The principle of bivariate calibration is the measurement of two components (A and B) at two selected wavelengths (λ_1 and λ_2) to obtain two equations:

$$A_{AB1} = m_{A1}C_A + m_{B1}C_B + e_{AB1} \quad (1)$$

$$A_{AB2} = m_{A2}C_A + m_{B2}C_B + e_{AB2} \quad (2)$$

The resolution of such equations set allows the evaluation of C_A and C_B values:

$$C_A = (A_{AB1} - e_{AB1} - m_{B1}C_B) / m_{A1} \quad (3)$$

$$C_B = [m_{A2} (A_{AB1} - e_{AB1}) + m_{A1} (e_{AB2} - A_{AB2})] / m_{A2}m_{B1} - m_{A1}m_{B2} \quad (4)$$

Where:

- C_A, C_B are the concentration of component A, component B.
- m_{A1}, m_{A2} are the slope values of component A at λ_1, λ_2.
- m_{B1}, m_{B2} are the slope values of component B at λ_1, λ_2.
- A_{AB1}, A_{AB2} are the absorbance values of the binary mixture at λ_1, λ_2.
- e_{AB1}, e_{AB2} are the sum of the intercepts of components A, B at λ_1, λ_2.

This simple mathematic algorithm allows the resolution of the two components by measuring the absorbance of their mixture at two selected wavelengths and using the parameters of the linear regression functions evaluated individually for each component at the same wavelengths.

According to Kaiser method, the slope values of the linear regression equations for both components at different wavelengths were used to calculate the sensitivity matrices (K**)** to find out the optimum pair of wavelengths (highest matrix value) at which the binary mixture was determined.

$$K = \begin{vmatrix} m_{A1} & m_{B1} \\ m_{A2} & m_{B2} \end{vmatrix} \qquad (5)$$

2.2 Theory of area under curve method [27]

Area under curve method utilizes two wavelength ranges. From the overlain spectra of both drugs, the area under curve is determined at both the selected analytical wavelength ranges.

Within the above-selected wavelength ranges, the area under curve was determined for both the drugs and analysis was performed using "Cremer's Rule'' and "Matrix Method''.

Consider a binary mixture consisting of two components X and Y, from the spectra of two components, following information is obtained:

- $AUC^{X}_{\lambda 1-\lambda 2}$: Area under curve for component X at the wavelength range λ_1 - λ_2.
- $AUC^{X}_{\lambda 3-\lambda 4}$: Area under curve for component X at the wavelength range λ_3 - λ_4.
- $AUC^{Y}_{\lambda 1-\lambda 2}$: Area under curve for component Y at the wavelength range λ_1 - λ_2.
- $AUC^{Y}_{\lambda 3-\lambda 4}$: Area under curve for component Y at the wavelength range λ_3 - λ_4.

The total area under the curve of a mixture at a particular wavelength range is equal to the sum of area under curve of the individual components at same wavelength range. The area under curve of the mixture containing component X and Y can be given as follows:

$$AUC_{\lambda 1-\lambda 2} = AUC^{X}_{\lambda 1-\lambda 2} + AUC^{Y}_{\lambda 1-\lambda 2} \qquad \textbf{(1)}$$

$$AUC_{\lambda 3-\lambda 4} = AUC^{X}{}_{\lambda 3-\lambda 4} + AUC^{Y}{}_{\lambda 3-\lambda 4} \quad (2)$$

Now the above equations can also be written as follows:

$$AUC_{\lambda 1-\lambda 2} = A^{X}{}_{\lambda 1-\lambda 2}\, bC^{X} + A^{Y}{}_{\lambda 1-\lambda 2}\, bC^{Y} \quad (3)$$

$$AUC_{\lambda 3-\lambda 4} = A^{X}{}_{\lambda 3-\lambda 4}\, bC^{X} + A^{Y}{}_{\lambda 3-\lambda 4}\, bC^{Y} \quad (4)$$

Where,

$$A_{\lambda 1-\lambda 2} = AUC_{\lambda 1-\lambda 2} / Conc.in\ \mu g/ml$$

$$A_{\lambda 3-\lambda 4} = AUC_{\lambda 3-\lambda 4} / Conc.in\ \mu g/ml$$

By applying "Cramer's Rule'' and "Matrix Method'', the concentration of component X and component Y can be determined as follows:

$$C^{X} = (A^{Y}{}_{\lambda 1-\lambda 2}\ AUC_{\lambda 3-\lambda 4}) - (A^{Y}{}_{\lambda 3-\lambda 4}\ AUC_{\lambda 1-\lambda 2})/(A^{Y}{}_{\lambda 1-\lambda 2}\, A^{X}{}_{\lambda 3-\lambda 4}) - (A^{Y}{}_{\lambda 3-\lambda 4}\ A^{X}{}_{\lambda 1-\lambda 2}) \quad (5)$$

$$C^{Y} = (A^{X}{}_{\lambda 1-\lambda 2}\ AUC_{\lambda 3-\lambda 4}) - (A^{X}{}_{\lambda 3-\lambda 4}\ AUC_{\lambda 1-\lambda 2})/(A^{Y}{}_{\lambda 1-\lambda 2}\, A^{X}{}_{\lambda 3-\lambda 4}) - (A^{Y}{}_{\lambda 3-\lambda 4}\ A^{X}{}_{\lambda 1-\lambda 2}) \quad (6)$$

2.3 Theory of Dual wavelength method[28]

Dual wavelength spectroscopy offers an efficient method for analyzing a component in presence of an interfering component. For elimination of interference, dual analytical wavelengths were selected in a way to make the absorbance difference zero for one drug in order to analyses the other drug. This technique has been successfully applied for simultaneous determination of certain drugs in their binary mixtures.

2.4 Theory of simultaneous equation method [29]:

Consider a multicomponent system consisting of two components X and Y, each of which absorbs at the λ_{max} of the other.λ_1 being the wavelength of maximum absorbance of **X** and λ_2

being the wavelength of maximum absorbance of **Y**, it may be possible to determine both components by the technique of simultaneous equation method.

- The absorptivities of **X** at λ_1 and λ_2, a_{X1} and a_{X2} respectively.
- The absorptivities of **Y** at $\lambda 1$ and $\lambda 2$, a_{Y1} and a_{Y2} respectively.
- The absorbance of the diluted sample at $\lambda_1$and λ_2, A_1 and A_2 respectively.
- C_X And C_y be the concentrations of **X** and **Y** respectively in the diluted sample.

Thus, the absorbance of the mixture at λ_1 and λ_2 may be expressed as follows:

$$At\ \lambda_1 \quad A_1 = a_{X1}bC_X + a_{Y1}bC_Y \qquad (1)$$

$$At\ \lambda_2 \quad A_2 = a_{X2}bC_X + a_{Y2}bC_Y \qquad (2)$$

For measurements in 1 cm cell, b = 1, rearrange eq. **(2)**:

$$C_Y = A_2 - a_{X2}C_X/a_{Y2}$$

Substituting for C_Y in eq. (1) and rearranging gives

$$C_X = A_2a_{Y1} - A_1a_{Y2}/a_{X2}a_{Y1} - a_{X1}a_{Y2} \qquad (3)$$

$$C_Y = A_1a_{X2} - A_2a_{X1}/a_{X2}a_{Y1} - a_{X1}a_{Y2} \qquad (4)$$

Using the above two equations (3, 4) the concentration of component X and component Y in the sample mixture can be determined.

3. Experimental:

3.1. Instrument

Spectrophotometer: A double beam UV-Visible spectrophotometer (Shimadzu 1800, Japan) and it is connected to IBM compatible computer. The software UV-Probe Ver. 2.43.

3.2. Materials

A Pure cetirizine (99.3%) was kindly supplied by GlaxoSmithKline Pharmaceutical Company, Cairo, Egypt.

B Zyrtec® tablet: each tablet claimed to contain 10 mg cetirizine hydrochloride (B.No. 3345, manufactured by GlaxoSmithKline Pharmaceutical Company), purchased from local market.

C Water used throughout the procedures was freshly double distilled.

D Analytical grade, methanol and hydrogen peroxide (30%) from (El-Nasr Company, Egypt).

3.3. Standard solutions:

A stock standard solution of cetirizine (100µg/ml) was prepared by dissolving 10 mg of the drug powder in 50 ml of methanol and complete to 100 ml with the same solvent. Working standard solution (10µg/ml) was prepared by dilution of the stock solution with methanol.

A stock solution of cetirizine oxidative degradate: 100 mg of pure cetirizine hydrochloride powder were dissolved in 45 ml of distilled water and transferred to a 100-ml round-bottomed flask to which 10 ml of 30% H_2O_2 were added. The solution was heated under reflux for 5 hours at 70-80^{0}C and evaporated to dryness under vacuum. The obtained residue was extracted with methanol (2×10 ml), filtered into a 100-ml volumetric flask and diluted to volume with methanol to obtain a stock solution labeled to contain degradate derived from 1 mg/ml of cetirizine hydrochloride[30]. Working solution of degradate (100 µg/ml) was obtained by further dilution of the stock solution with methanol.

3.4. Pharmaceutical formulation:

Ten **Zyrtec®** tablets (10 mg/ml) were mixed well. An amount of powder equivalent to 10 mg of cetirizine hydrochloride was transferred into 100-ml volumetric flask and was dissolved in 50 mL of methanol with shaking for 30 min and filtered. The filtrate was diluted to 100 mL with methanol to obtain a solution labeled to contain 100 µg/ml of cetirizine hydrochloride. Determine cetirizine content of the tablets from the corresponding regression equation.

4. Procedures

4.1. Construction of calibration curves:

Accurately measured aliquots equivalent to (0.6−2.7 ml) of **CTZ** from stock solution (100 ug mL^{-1}) were, separately, transferred into a series of 10 ml volumetric flasks and accurately measured aliquots equivalent to (0.9 − 2.4 ml) of **its degradate** from stock solution (100 ug mL^{-1}) were, separately, transferred into the other series of 10 ml volumetric flasks , each flask was completed to the mark with pure methanol , yielding concentration range of (6− 27 ug mL^{-1}) and concentration range of (9−24 ug mL^{-1}) of **CTZ** and **degradate** respectively **(Table 1).** The zero-order absorption spectra of cetirizine and its oxidative degradate show a certain degree of overlapping, which does not permit direct determination of cetirizine in presence of its degradate as shown in figure (1).

4.1.1. For determination of CTZ in presence of degradate using bivariate technique:

Different aliquots equivalent to (60–270) µg of cetirizine hydrochloride and (90–240) µg of it's degradate were accurately transferred from their standard solutions (100 µg/ ml) into two separate series of 10-ml volumetric flasks and completed to volume with methanol. The absorption spectra (from 200 to 400 nm) of these solutions were recorded using methanol as a blank.

To choose the optimum pair of wavelengths at which measurements were done, calibration curves at different wavelengths; 211, 216, 221, 226, 231, and 236 nm were constructed for each drug and the regression equations were derived. The slope values of the linear regression equations for cetirizine (component A) and it's degradate (component B) at each pair of wavelengths were used to calculate the sensitivity matrices (K) to find out the optimum pair of wavelengths (highest K value). The absorbance was measured at 211 and 231 nm and then the corresponding regression equations were computed at selected wavelengths for both cetirizine hydrochloride and its degradate.

4.1.2. For determination of CTZ in presence of its degradate using area under curve technique (AUC):

Different aliquots equivalent to (60–270) µg of cetirizine hydrochloride and (90–240) µg of cetirizine degradate were accurately transferred from their standard solutions (100 µg/ ml) into two separate series of 10-ml volumetric flasks and completed to volume with methanol. The absorption spectra (from 200 to 400 nm) of these solutions were recorded using methanol as a blank. Area under the curve for the wavelength ranges selected for determination of cetirizine hydrochloride and cetirizine degradate are 220-230 nm (λ_1-λ_2) and 240-250 nm (λ_3-λ_4) were recorded, the absorptivity 'A' values of each of the two drugs were determined at the selected wavelength ranges. The absorptivity 'A' values were determined as, A= area under curve of component (from 220 to 230 nm or 240 to 250 nm)/concentration of the component (in g/l).

4.1.3. For determination of CTZ in presence of its degradate using Dual wavelength technique:

Different aliquots of cetirizine standard solution ranging from (60–270) µg were transferred to 10-ml volumetric flasks and completed to volume with methanol. The absorption spectra (from 200 to 400 nm) of these solutions were recorded using methanol as a blank. The difference in the absorbance was measured at 230 and 244 nm.

4.1.4. For determination of CTZ in presence of its degradate using Simultaneous equation technique:

Different aliquots equivalent to (60–270) µg of cetirizine hydrochloride and (90–240) µg of cetirizine degradate were accurately transferred from their standard solutions (500 µg/ ml) into two separate series of 10-ml volumetric flasks and completed to volume with methanol. The absorption spectra (from 200 to 400 nm) of these solutions were recorded using methanol as a blank. The absorbance values were measured at 230 and 258 nm from which the absorptivity values for both drugs at the selected wavelengths were calculated.

4.2. Accuracy.

Accuracy was assured by carrying out the previously mentioned procedures under (section 4.1.1.) for each technique, for the determination of different concentration of pure **CTZ**. The concentrations were calculated from the corresponding equations of each technique.

4.3. Precision.

4.3.1. Intra-day precision (Repeatability).

Three concentrations of **CTZ** were analyzed three times intraday using the previously mentioned procedures for each technique. The percentage of recoveries of each concentration of **CTZ** and its relative standard deviation were calculated using the suggested methods **(Table 2)**.

4.3.2. Intermediate precision.

Three concentrations of **CTZ** were analyzed on three successive days using the previously mentioned procedures for each technique. The percentage of recoveries of each concentration of **CTZ** and its relative standard deviation were calculated using the suggested methods **(Table 2)**.

4.4. Limit of detection (LOD) and limit of quantification (LOQ):

The LOD and LOQ parameters were determined from regression equation,

$$LOD = 3.3\ S_y / a$$

$$LOQ = 10\ S_y / a$$

Where (S_y) is a standard error of the calibration curve and (a) is the slope of the corresponding calibration curve **(Table 1)**.

Since, Bivariate method depends upon two wavelengths found by (Kaiser's method) as mentioned in **section 4.1.1.,** area under curve method depends upon two wavelength areas as mentioned in **section 4.1.2.,** Dual wavelength and Simultaneous equation methods depend upon two wavelengths as mentioned in **section 4.1.3.** So that, LOD and LOQ should be applied at the two wavelengths for each method.

4.5. Application to laboratory prepared mixtures:

Laboratory prepared mixtures containing different concentration of CTZ were prepared, keeping the ratio between CTZ and its degradate within their calibration ranges. The spectra of these mixtures were recorded and the procedures under construction of calibration curves were then followed. Recoveries were calculated as previously mentioned in accuracy.

4.6. Application to pharmaceutical formulation:

Different concentrations within calibration range of each method (Bivariate, area under curve, Dual wavelengths and Simultaneous equation methods) were prepared from the solution of the pharmaceutical preparation, the spectra and optical density of these prepared concentrations were recorded and procedures under construction of calibration curves were followed using the recorded spectra and optical density of the pharmaceutical formulation prepared solution.

5. RESULTS AND DISCUSSION

Simple spectrophotometric methods were developed for the determination of **CTZ** in presence of its degradate without previous separation.

5.1. The bivariate method [31]:

Bivariate calibration spectrophotometric method is a direct method which has been proposed for the resolution of binary mixture. The principle of bivariate calibration is the measurement of two components (A and B) at two selected wavelengths (λ_1 and λ_2) to obtain two equations as mentioned before in (section 2.4.). The calibration curve equation and their respective linear regression coefficient are obtained directly with the aim of ensuring the linearity between the signal and the concentrations. The slope values of the linear regression were estimated for both **CTZ** and **its degradate** at the selected wavelengths and used for determination of the sensitivity matrics K, proposed by Kaiser's method. A series of sensitivity matrices K, were created for **CTZ** and **its degradate** and for every pair of pre-selected wavelengths:

$$K = \begin{pmatrix} m_{A1} & m_{B1} \\ m_{A2} & m_{B2} \end{pmatrix}$$

Where $m_{A1,2}$ and $m_{B1,2}$ are the sensitivity parameters (Slope) of the regression equations of A and B at two selected wavelengths (λ_1 and λ_2). The determination of these matrics were calculated as shown in **(Table 4).** The wavelength set was selected for which the highest matrix determinant value was obtained.

For bivariate determination of **CTZ** in presence of **its degradate,** wavelengths 211 and 231 nm were found to give the maximum value of K and thus can be used for the analysis, using the following linear regression calibration equations:

- **For cetirizine (component A):**

$$y_{211} = 0.0415\,x + 0.0327 \qquad (r^2 = 0.9997).$$

$$y_{231} = 0.0313\,x + 0.0188 \qquad (r^2 = 0.9997).$$

- **For cetirizine degradate (component B):**

$$y_{211} = 0.0300\,x - 0.0327 \qquad (r^2 = 0.9995).$$

$$y_{231} = 0.0119\,x + 0.0101 \qquad (r^2 = 0.9993).$$

Where A is the absorbance at the selected wavelength, X is the concentration in ug mL^{-1} and r is the correlation coefficient.

5.2. The area under curve method [32]:

Suitable dilution of standard stock solution of **CTZ** and **its degradate** were prepared separately in methanol in the concentration range of (6−27 ug mL^{-1}) and (9−24 ug mL^{-1}) respectively. The solutions of drugs were scanned in the range of 200−400 nm. For area under curve (AUC) method, sampling wavelength ranges which selected for estimation of **CTZ** in presence of **its degradate** were 220−230 nm ($\lambda_1 - \lambda_2$) and 240−250 nm ($\lambda_3 - \lambda_4$), areas under the curves were integrated between these selected wavelength ranges for both drugs **(Fig.2)** and **(Fig.3),** which show linear response with increasing concentration. The same wavelength ranges were used for preparation of calibration curve and estimation of tablet formulation by measuring the absorptivity of each component according to each area under the curve with corresponding concentration of each one, we can measure the concentration of the proposed component by using equation which mentioned before in **(section 2.5.).**

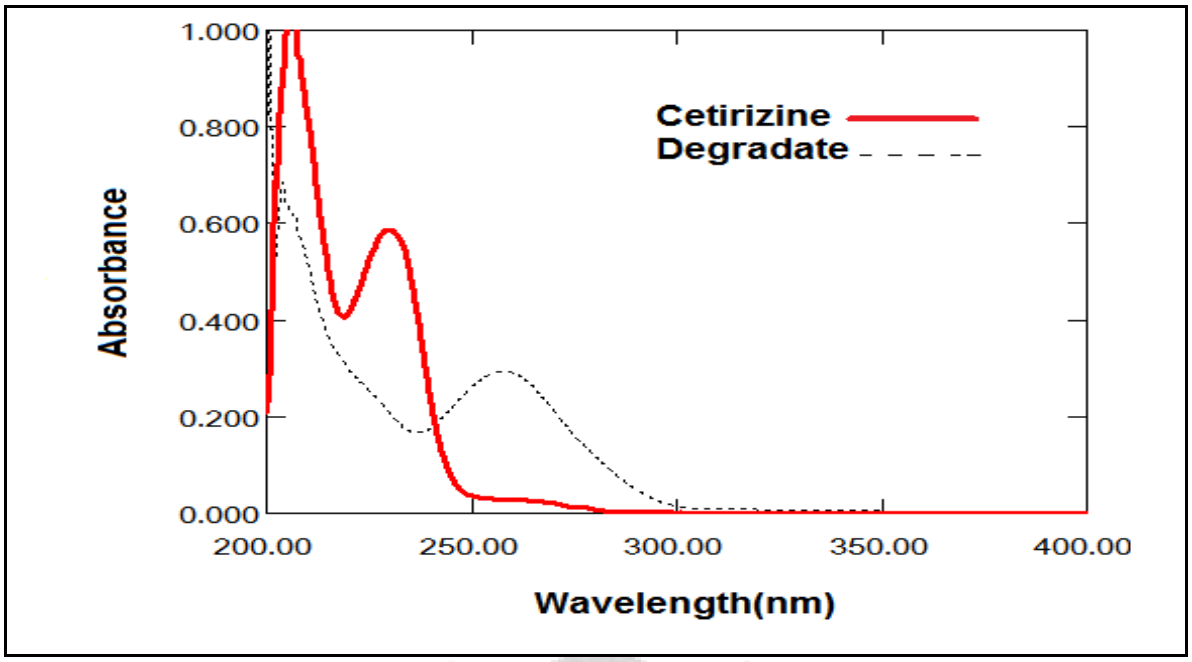

Figure (1): Zero-order absorption spectra of cetirizine hydrochloride (18 µg/ ml) and its oxidative degradate (18 µg/ ml) in methanol.

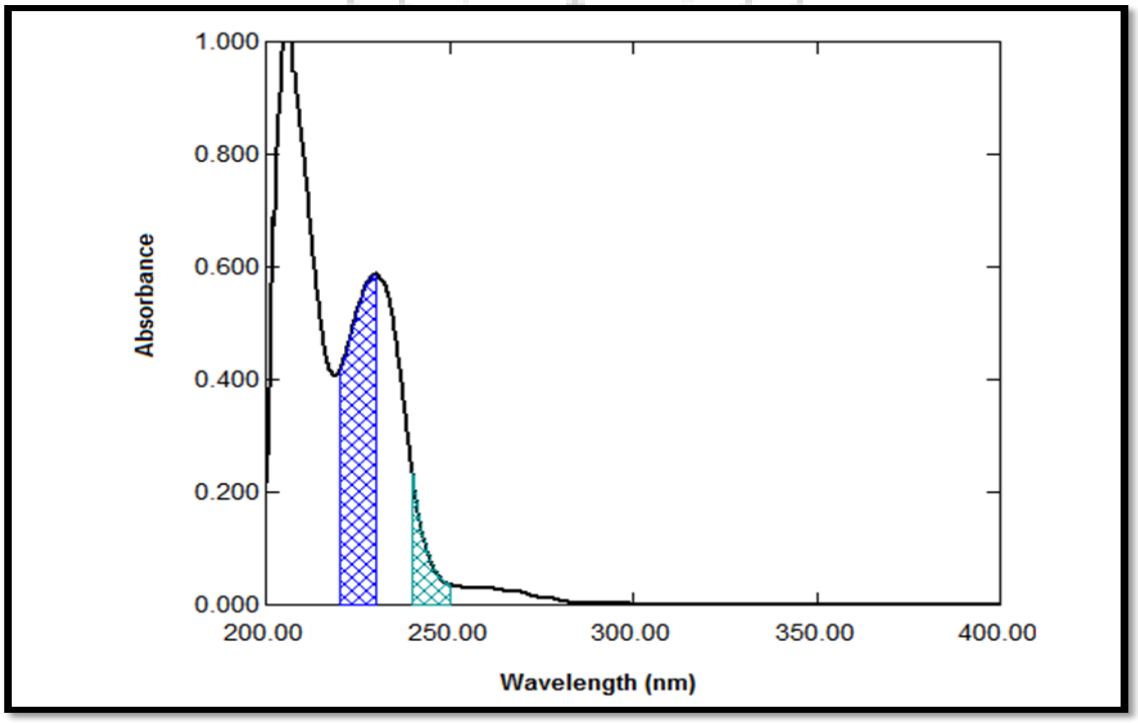

Figure (2): Zero order spectrum of cetirizine 18 µg/ml showing area under the curve over the range (220:230) and (240:250) nm.

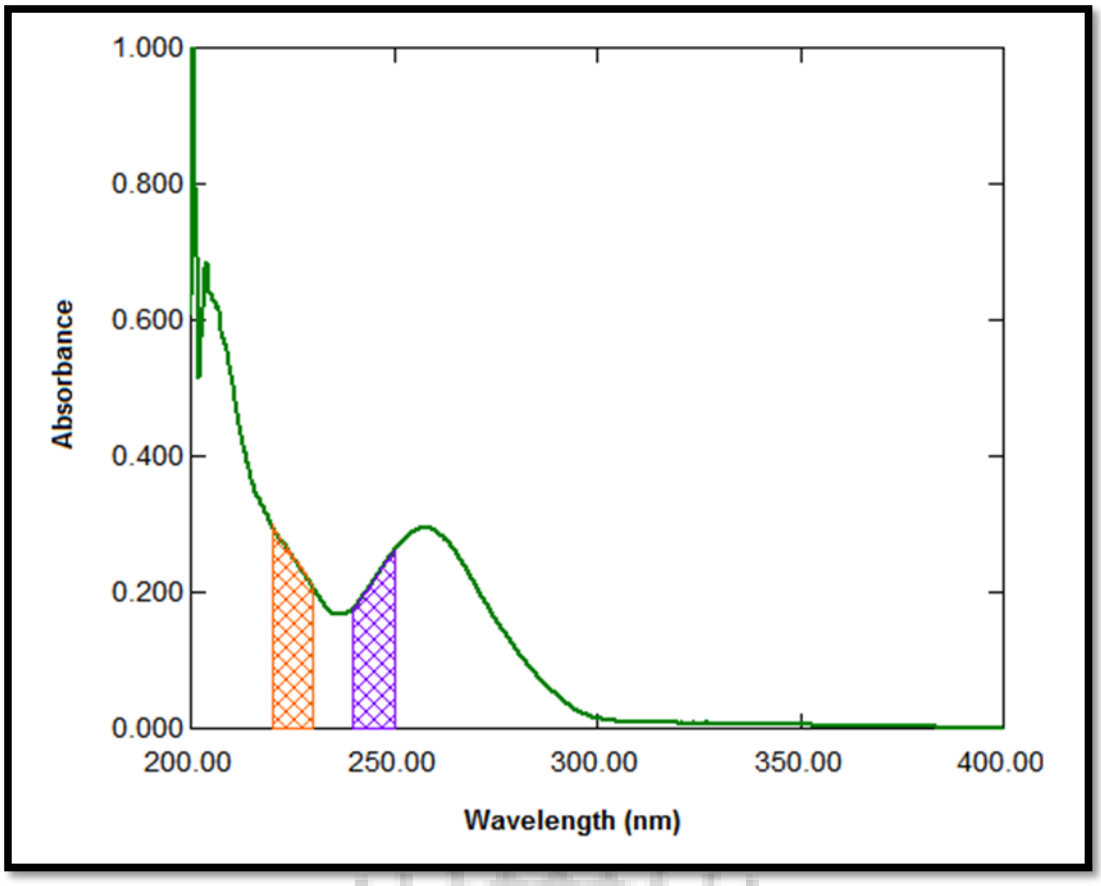

Figure (3): Zero order spectrum of cetirizine degradate 18 µg/ml showing area under the curve over the range (220:230) and (240:250) nm.

5.3. The Dual wavelength method [28]:

Under the described experimental conditions, the calibration graph for the method was constructed by plotting the differences in absorbance at 230 and 244 nm versus drug concentrations in µg/ml. The linear regression equation for the graph is:

$$y = 0.027\ x + 0.0063 \qquad (r2 = 0.9998).$$

Where y is the difference in absorbance at 230 and 244 nm, ***x*** is the drug concentration in µg/ml and r^2 is the squared correlation coefficient

5.4. For Simultaneous equation method:

In this method; for quantitative estimation of cetirizine hydrochloride in presence of it's degradate in binary mixture by simultaneous equation method, two wavelengths namely 230 nm (λ_{max} of intact cetirizine) and 258 nm (λ_{max} of cetirizine degradate) were selected. The absorbance value at two selected wavelengths (λ_1 and λ_2) of cetirizine hydrochloride in the concentration range 6-27 µg/ml was calculated. For cetirizine degradate absorbance value at two selected wavelengths (λ_1 and λ_2) in the concentration range 9-24 µg/ml was also calculated.

The Absorptivity coefficients were determined for both cetirizine hydrochloride and it's degradate and the average values were taken. Concentrations of cetirizine hydrochloride can be obtained by applying Cramer's rule and matrices in equations 1&2. Concentration of cetirizine hydrochloride in presence of its oxidative degradates was calculated according to the following equations:

$$At\ \lambda_1 = 230 \quad A_1 = 0.033\ C_{cetirizine} + 0.011\ C_{degradate} \qquad (1)$$

$$At\ \lambda_2 = 258 \quad A_1 = 0.0017\ C_{cetirizine} + 0.016\ C_{degradate} \qquad (2)$$

Where,

$C_{cetirizine}$ And $C_{degradate}$ are the concentrations of cetirizine hydrochloride and cetirizine degradate, respectively.

0.033 And 0.0017 are the absorptivity of cetirizine hydrochloride at λ_1 and λ_2, respectively.
0.011 And 0.016 are the absorptivity of cetirizine degradate at λ_1 and λ_2, respectively.
A_1 and A_2 are the absorption values of sample solutions at λ_1 and λ_2, respectively.

- **For cetirizine hydrochloride (component A):**

$$Y_{230} = 0.0315\ x + 0.0197 \qquad (r^2 = 0.9999).$$

$$Y_{258} = 0.0018\ x - 0.0006 \qquad (r^2 = 0.9995).$$

- **For cetirizine degradate (component B):**

$$y_{230} = 0.0117\ x - 0.0023 \qquad (r^2 = 0.9997).$$

$$y_{258} = 0.0167\ x - 0.0043 \qquad (r^2 = 0.9990).$$

5.5. Accuracy and Precision:

According to the ICH guideline, three replicate determination of three different concentration of the studied drug in pure form within their linearity ranges were performed in the same day (intra-day) and in three successive days (inter-day) for each method. Concentrations of (12, 18 and 24 ug mL^{-1}) were used. Accuracy as recovery percent (R%), and precision as percentage relative standard deviation (RSD%) were calculated and results were listed in **(Table 2).**

5.6. Specificity:

The specificity of the proposed methods was assured by applying the laboratory prepared mixtures of **CTZ** and **its degradate** as mentioned before in (section 4.5.)**.** The results were listed in **(Table 3).**

6. Pharmaceutical Applications:

The proposed methods were applied to the determination of the studied drug in Zyrtec ® **tablets**. The statistical comparison between the results obtained by applying the proposed methods and those obtained by applying the reported method [62]**,** showed less calculated t and F values revealing no significant difference in accuracy and precision, **(Table 5).**

7. CONCLUSION

The present work is concerned with the determination of CTZ in presence of its degradate. Reviewing the literature on the determination of CTZ in presence of its degradate (Binary mixture) revealed the lack of any stability indicating spectrophotometric for the determination of CTZ.

Bivariate, area under curve, Dual wavelength and Simultaneous equation spectrophotometric methods are well-established techniques that are able to enhance the resolution of overlapping bands.

Analysis of authentic samples containing CTZ and its degradate showed no interference from the common additives and excipient. Hence, recommended procedure is well suited for the assay and evaluation of drugs in pharmaceutical preparations. It can be easily and conveniently adopted for routine quality control analysis.

The suggested methods are found to be simple, accurate, selective and equally sensitive with no significant difference of the precision compared with the reported method of analysis [33].

8. ACKNOWLEDGMENT

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9. REFERENCES

[1] The Merck Index Merck research Laboratories. 13th edition **(2001)**
Martindale J O'Neil, Merck & Co, Inc, White house Station NJ. USA. 6281 and 2030.
[2] Martindale, the Extra Pharmacopoeia, the Pharmaceutical Press, London, Ed J.E.F. Reynolds **(1997).**
[3] Tillement JP, Testa B, Brée F, *Biochem. Pharmacol* (**2003)** 66, 1123.
[4] Pasquali M, Baiardini I, Rogkakou A, Riccio AM, Gamalero C, Descalzi D, Folli C, Passalacqua G, Clin. & Experim. Aller. **(2006**) 36 , 1161.
[5] Gupta A, Chatelain P, Massingham R, Jonsson EN, Hammarlund-Udenaes M, Drug Metab. Dispos. **(2006)** 34, 318.
[6] Dharuman J, Vasudhevan M, Ajithlal T J. Chromatog *B*, **(2011**) 879, 2624.
[7] Karakus S, Kucukguzel I, Kucukguzel SG J. Pharm. & Biomed. Anal. **(2008**) 46,295.
[8] Hadad GM, Emara S, Mahmoud WMM, Talanta*(***2009**) 79,1360.
[9] Kang SW, Jang HJ, Moorea VS, Parkb Ji, Kimb K,Youmc J, Hanc SBJ. Chromatog. B **(2010)** 878, 3351.
[10] Morita MR, Berton D, Boldin R, Barros F A P, Meurer EC, Amarante AR, Campos DR, Calafatti SA,Pereira R, Abib JrE, Pedrazolli Jr,
J. *Chromatog. B*,**(2008**) 862, 132.
[11] Baltes E, Coupez R, Brouwers L, Gobert J, J. *Chromatogr*.
Biomed, (**1988**) 74, 149.
[12] Prabu SL, Shirwaikar AA, Kumar CD, G. A. Kumar, G. A., *Indian* J. *Pharm.* Sci., (**2008**) 70, 236 .
[13] Choudhari V, Kale A, Abnawe S, Kuchekar B, Gawli V,
Patil N, J. Pharm. Tech. Res.,(**2010**) 2, 4 .
[14] El Walily A F M, Korany M A, El Gindy A, Bedair M F,
J. Pharm. & Biomed. Anal., (**1998**) 17, 435.
[15] Bajerski L, de Silva Sangoi M, Barth T, Diefenbach I F,
Simone Gonçalves Cardoso S L D E, Quim. Nova, **(2010**) *33*, 114 .
[16] Patil R H, Hegde R N, Nandibewoor S T, J. Colloids and Surfaces B Bioint.,(**2011**) 83, 133 .
[17] Melwanki M B, Seetharamappa J, Gowda B G, Sajjan A G, Chem. Warsaw Anal., (**2001**) 46,883.
[18] Kamel A H, J. Pharm. Biomed. Anal.,(**2007**) 45,341.
[19] Hassan S S M, Sayour H E M, Kamel A H, Anal. Chim.
Acta,(**2009**) 640, 75.
[20] Kamel A H, Mahmoud W H, Mostafa M S, Anal. Meth. ,
(2011) 957, 9.
[21] Kamel A H, Mahmoud W H, Mostafa M S, Eur. Chem.
Bull.,(**2013**) 2, 88.
[22] Hassan S S M, Kamel A H, Abd El-Naby H, Talanta, **(2013**)103 ,330.

[23] Shoukry A F, Abdel-Ghani N T, Issa Y M, Ahmed H M,
Electroanalysis, (**1998**) 11, 443.
[24] Rizk N M H, Abbas S S, EL-Sayed F A, Abo-Bakr A, Int. J. Electrochem. Sci., **(2009**) 4, 396 .
[25] Javanbakht M, Eynollahi Fard S, Abdouss M, Mohammadi A, Ganjali M R, Norouzi P, Safaraliee L,Electroanalysis, (**2008**) 20, 2023.
[26] Darwish HW, Hassan SA, Salem MY, El-Zeany BA. Spectrochim Acta A Mol Biomol Spectrosc. 2013; 104:70-6.
[27] Rahman N, Nasrul Hoda M. J Pharm Biomed Anal. 2003; 31(2):381-392..
[28] Fernandes N, Nimdeo MS, Choudhar VP, Kulkarni RR, Pande VV, Nikalje AG. Int J Chem Sci. 2008;6(1):29-35.
[29] Chaudhary J, Jain A, Saini V. An overview. Int Res J Pharm. 2011; 2(12):81-83.
[30] Dyakonov T, Muir A, Nasri H, TOOPS d, Fatmi A. Pharm Res. 2010; (27)1318–24.
[31] D. Ramesh; S. Ramakrishna; Int. J. Pharm. Pharm. Sci. 2(2010) 215-219.N.
[32] R. Yashwanth; S. K. Shetty; A. Manzoor; Int. J. PharmTech. Res. 3 (2011) 1255-1259.
[33] Bobade T, Game M D, Iche PP. Int J Chem Tech Res. 2013; *5*(5), 2317-2321.

Table (1): Spectral data for determination of Cetirizine in presence of its degradate by proposed methods:

Parameters	Bivariate		Area under curve		Dual wavelength		Simultaneous equation	
Wavelength (nm)	211	231	220-230	240-250	230	244	230	258
Linearity range (µg ml^{-1})	6 — 27		6 — 27		6 — 27		6 — 27	
LOD (µg ml^{-1})	0.612	0.365	1.0404	0.013	1.068		1.245	0.154
LOQ (µg ml^{-1})	1.856	1.105	3.1527	0.039	3.237		3.773	0.468
Regression equation* Slope (*b*) Intercept (*a*)	0.0415 0.0327	0.0313 0.0188	0.2771 0.1738	0.0518 0.0276	0.027 0.0063		0.0315 0.0197	0.0018 -0.0006
Regression coefficient (r^2)	0.9997	0.9997	0.9997	0.9995	0.9998		0.9999	0.9995

* $y = a + bx$ where y is the response and x is the concentration.

Table (2): Intraday and interday accuracy and precision for the determination of Cetirizine by the proposed methods:

Method	Conc µg.ml^{-1}	Intraday			Interday		
		Found Conc. + SD	Accuracy (R%)	Precision (RSD%)	Found Conc. + SD	Accuracy (R%)	Precision (RSD%)
Bivariate	12	12.02±0.106	100.17	1.6	11.89±0.079	99.78	1.47
	18	18.1±0.2	99.82	1.59	17.92±0.159	100.19	1.34
	24	20.86±0.203	99.53	1.68	20.91±0.171	100.16	1.14
Area under curve	12	11.936±0.459	99.946	0.055	11.777 ± 1.87	99.93	0.224
	18	18.251±1.289	100.46	0.2309	17.85 ± 0.704	99.93	0.126
	24	24.025±0.569	99.46	0.137	23.73 ± 0.608	99	0.147
Dual wavelength	12	11.948±0. 198	99.56	1.658	11.93±0.056	99.49	0.473
	18	21.195±0.204	100.92	0.964	21.38±0.085	101.82	0.399
	27	26.948±0.127	99.808	0.472	27.19±0.235	100.73	0.864
Simultaneous equation	12	12.041±0.208	100.34	1.729	12.104±0.063	100.87	0.525
	18	17.819±0.054	98.99	0.309	17.956±0.204	99.76	1.137
	24	24.178±0.313	100.75	1.295	24.115±0.333	100.48	1.383

Table (3): Determination of CTZ in presence of its degradate in their laboratory mixtures by the proposed methods:

methods	CTZ (µg ml^{-1})	Degradate (µg ml^{-1})	CTZ found (µ ml^{-1})	Recovery % of CTZ
Bivariate	6	3	6.08	101.33
	9	6	8.9	98.89
	12	9	12.17	101.42
	15	12	14.74	98.27
	18	18	18.23	101.28
	Mean ± SD%			99.89 ± 1.61
Area under curve	6	21	5.967	99.46
	9	18	9.073	100.81
	12	15	12.173	101.44
	15	12	14.781	98.54
	18	9	17.681	98.23
	24	6	23.883	99.51
	Mean ± SD%			99.89 ± 1.26
Dual wavelength	6	21	5.9148	98.58
	9	18	9.1000	101.11
	12	15	12.2111	101.75
	15	12	14.9519	99.67
	18	9	17.9148	99.52
	24	3	24.1000	100.41
	Mean ± SD%			100.178 ± 1.151
Simultaneous equation	6	21	5.88	98.051
	9	18	8.93	99.329
	12	15	11.96	99.681
	15	12	14.76	98.431
	18	9	17.99	99.984
	Mean ± SD%			99.09 ± 0.832

Table (4): Values of the sensitivity matrix determinates calculated according to Kaiser's method (k x 106) for the mixture of cetirizine and its degradate:

λ/λ	211	216	221	226	231	236	λ/λ
211	0	430	99.5	325.5	445.15	325.3	211
216		0	94.42	234.16	198.79	411.38	216
221			0	246.5	352.22	359.36	221
226				0	90.72	381.2	226
231					0	156.34	231
236						0	236

Table (5): Statistical comparison between the results obtained by applying the proposed (spectrophotometric) and reported methods for determination of cetirizine in Zyrtec® tablets:

	Bivariate	**Area under curve**	**Dual wavelength**	**Simultaneous equation**	**Reported method**
N*	5	5	5	5	5
mean	100.002	99.015	99.87	100.28	99.88
SD	0.7876	0.741	0.895	1.105	1.43
RSD	0.7875	0.745	0.896	1.101	1.432
t-test	0.167 (2.31)	0.598 (2.31)	0.0051 (2.31)	0.503 (2.31)	———
F-value	3.29 (6.39)	1.871 (6.39)	2.55 (6.39)	1.67 (6.39)	———

** No. of experimental.*

t –test and F-value at (p= 0.05).