RESEARCH ARTICLE

Spectrophotometric Estimation of Cefixime *via* Oxidation Reaction using Sodium Hypochlorite

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ABSTRACT

A sensitive and simple spectrophotometric method has been proposed to estimate cefixime in its pure form and in pharmaceutical preparations. The method depends on the oxidation of cefixime by sodium hypochlorite in the acidic medium in the presence of a methyl red pigment where the color of the dye appears after the oxidizing agent has run out with the drug as the dye absorption was measured at the wavelength of 524 nm and the method follows law with a concentration range of 0.5- 7 $\mu g.mL^{-1}$ with a correlation coefficient of( ), molar absorptivity of (10.44942×10^{4}) "l $mol^{-1}.cm^{-1}$ and the Sandell`ssensivity" (0.0048) $\mu g.cm^{-2}$". The method was successfully applied to pharmaceutical preparations.

Keywords: Cefixime, Methyl red, Oxidation, Sodium Hypochlorite, Spectrophotometry.

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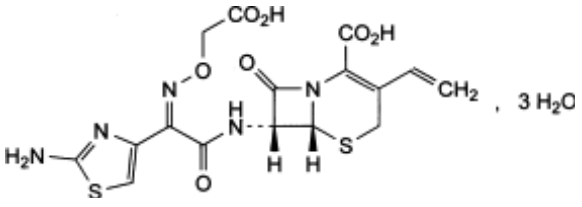
INTRODUCTION

Cefixime is a synthetic fluoroquinolone antibiotic and chemically is (6*R*,7*R*)-7-{[2-(2-amino- 1,3-thiazol-4-yl)-2-(carboxymethoxyimino) acetyl]amino}-3-ethenyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-5-thia-1-azabicyclo[4.2.0] oct-2-ene-2- carboxylic acid tri hydrate,[1] Figure 1. Cefixime is effective against a wide range of sensitive Gram-Ve and Gram + Ve anaerobic bacterial pathogens, including lactamase-producing strains.[2] Cefixime is given by mouth in the treatment of susceptible infections, including "gonorrhea," otitis media, pharyngitis," lower respiratory tract infections such as bronchitis, and urinary tract infections.[3]

Literature survey reveals that various high-performance liquid chromatographic (HPLC) methods have been reported for the determination of cefixime.[4] Individually or with other drugs, by HPTLC[5] and spectrophotometric methods.[6-8] In this paper, we present a simple, sensitive and accurate spectroscopic method for determining cefixime in its pure form and in pharmaceutical.



"$C_{16}H_{15}N_5O_7S_2,3H_2O$ш 507.5"

Figure 1: Chemical Structure of Cefixime

EXPERIMENTAL

Apparatus

- Shimadzu UV-Vis 1800 Spectrometer (Japan) was used with a Quartz cell of 1.0 cm for absorbance measurements.
- Sartorius BL 210S sensitive Scientific balance.

"Reagents and Materials" Used

All the chemicals were highly pure, and their solutions were prepared as follows:

1-Standard Cefixime Solution (100 ppm)

A total of 0.01 g of pure furosemide was dissolved in 5 mL ethanol, then complete the volume with distilled water in a 100mL calibrated flask.

2-Red methyl Solution (0.01%)

Prepare the solution by dissolving 0.0100 g of the dye in ethanol and complete the volume to a mark is in a 100 mL volumetric flask with ethanol and kept in the dark vial.

3- Sodium Hypochlorite Solution (0.01)

Prepare the solution by diluting 0.2 mL of concentrated sodium hypochlorite (5%) with distilled water to the mark in a 100 mL volumetric flask.

4- Sulphuric Acid(0.01N)

Prepare by diluting 0.271 mL of concentrated sulphuric acid 18.38 N with distilled water to the mark in a 500 mL volumetric flask.

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Table 1: Effect of type of the acid:

Type of acid 0.01N))	HCl	H_2SO_4	CH_3COOH	HNO_3
Absorbance	0.780	0.831	0.711	0.722

Table 2: Effect of the amount of H_2SO_4

Volume of H_2SO_4 (0.01N)	0.25	0.5	0.75	1	1.5	2.0
Absorbance	0.775	0.821	0.815	0.801	0.742	0.712

Table 3: Effect of the red methyl dye

Volume of M.R (0.01%)	*Absorbance*
0.25	0.272
0.5	0.430
0.75	0.752
1	0.851
1.5	1.040
2	0.950

Table 4: Effect of the (0.01%) sodium hypochlorite

Volume of NaOCl (0.01%)	*Absorbance*
0.25	0.383
0.5	0.655
0.75	0.882
1	1.001
1.5	1.020
2	1.061
2.5	1.040

Table 5: Effect of oxidation time

Time of oxidation (min)	*Absorbance*
0	1.001
5	1.121
10	1.115
15	1.101
20	0.955
25	0.824
30	0.714

5-Interference Solutions 1000 ppm

Prepared by taking 0.5 g of each interfering substance and dissolving it with distilled water, then the volume is completed to 500 mL in a volumetric flask.

6-Pharmaceutical Solutions

Prepare with a weight of ten tablets, crushed and mixed well, and a sufficient weight of 0.01 gm of Cefixime 100 µg. mL^{-1} and dissolve it in 5 mL of absolute ethanol and 70 mL of distilled water, heat the solution, filter it into a 100 mL volumetric flask, then wash the filter paper several times with distilled water and then complete the volume up to the mark of the distilled water.

Principle of the Method

The principle of the method is the oxidation of cefixime by sodium hypochlorite in the acidic medium in the presence of methyl red dye. The drug is oxidized by hypochlorite in the acid medium. The color of the dye appears when added, indicating the depletion of the oxidizing agent with the drug.

Preliminary Study

In a 25 mL volumetric flask, add 1 mL of (0.01%) of sodium hypochlorite to 1 mL of 100 ppm of cefixime. After making the medium acidic by added 1 mL of (0.01 N) sulphuric acid, wait 5 minutes, then add 1 mL 0.01% red methyl dye, was noted for the appearance of the color of the dye, which gave the highest absorption at the wavelength of 524 nm, against the reagent blank.

RESULTS AND DISCUSSION

Optimization of the Experimental Conditions

Study the effect of the different parameters affecting the intensity of absorption of the oxidative product formed between sodium hypochlorite and cefixime at a concentration of (4 ppm), to reach the best conditions for interaction in the volumetric flask of 25 mL.

Effect of type of the Acid

Experiments showed that process takes place in an acidic medium to form colored product was studied in the estimation of cefixime, the result showed that sulphuric acid is the best, Table 1.

Effect of the Amount of H_2SO_4

The effect of increasing volumes 0.25–2.5 mL of (0.01N) H_2SO_4 solution was studied on the absorption of the formed product and the results show that a volume of 0.5 mL is the best for estimating, cefixime so it was used to complete "the rest of experiment" (Table 2).

Effect of the Red methyl Dye

The result has shown that 1.5 mL of 0.01% M.R It gives the maximum absorption, so it was used to complete the rest of the experiment Table 3.

Effect of the Amount of Sodium Hypochlorite

The effect of increasing volumes 0.25–2.0 mL of 0.01% NaOCl solution was studied on the absorption of the formed product, and the results show that a volume of 2 mL is the best for estimating, cefixime, so it was used to complete "the rest of experiment Table 4.

Effect of Oxidation Time

In a series of 25 mL "volumetric flask", the calculated amount of NaOCl was added to cefixime in acidic medium and left for different time periods 0–30 minutes, and, then dilute to the mark limit and measure absorption at the highest wavelength of 524 nm, and the results showed that a 5 minute period of oxidation of cefixime gives the best absorption, so this time period of oxidation was adopted in subsequent trials Table 5.

Table 6: Order of additions

Order number	*Order of addition*	*Absorbance*
1	C+R+O+H	0.710
2	C+O+H+R	1.121
3	C+R+H+O	0.585
4	R+O+H+C	0.044
5	C+H+O+R	1.066

Table 7: The effect of time on the stability of the formed product:

Cefxime 4µgmL^{-1} Room Temp	*Absorbance/time (min)*
After addition	1.121
5	1.121
10	1.120
15	1.120
20	1.119
25	1.119
30	1.118
35	1.118
40	1.119
45	1.119
50	1.119
55	1.119
60	1.119
Over night	1.115

Order of Additions

To obtain optimum results the effect of different orders of addition on the absorption of the colored product was studied, and the results showed in Table 6.

The Effect of Time on the Stability of the Formed Product

The effect of time on the stability of the formed product was studied, and the dye resulting after additions and dilution was found to be stable at room temperature for 60 minutes (Table 7).

Final Absorption Spectrum

Under optimal conditions previously established, the final absorption spectrum study of the dye resulting from the reaction of the oxidized Cefxime by NaOCl and in the presence of H_2SO_4, the absorption spectrum graph showed the highest absorption intensity of the dye at the wavelength of 524 nm, as shown in (Figure 2).

Procedure for Construction of Calibration Curve

Following the previously established optimal conditions Table 8, 1 mL of 0.01% sodium hypochlorite was added to increasing volumes of cefxime (100 µg/mL) in a series of 25 mL volumetric flask in acidic medium and waiting for 5 minutes added 2.0 mL of 0.01% of the dye solution. The volumes were completed by distilled water to the point of the mark. The intensity of absorption of the solutions against the formal solution was measured at the wavelength 524 nm.

Figure 3 shows the standard curve, which is consistent with Bear's law, in the range of concentrations (0.5–7 ppm).

Table 8: Summary of optimal conditions obtained for Cefxime estimate

Material solution	*Concentration*	*Optimum amount (mL)*
M.R	0.01%	1.5
NaOCl	0.01%	2
H_2SO_4	0.01N	0.5
λ_{max} (nm)		524

Table 9: Analytical parameters of the proposed method

Limit of detection (LoD)*(µg/mL)	0.0236
Limit of quantitation (LoQ)*(µg/mL)	0.0718
Molar absorptivity (I.mol^{-1}.cm^{-1})	10.4494×10^4
Sandell's sensivity (µg/cm^2)	0.0048
Slope	0.2059
Intercept	0.1925

"Accuracy and precision":

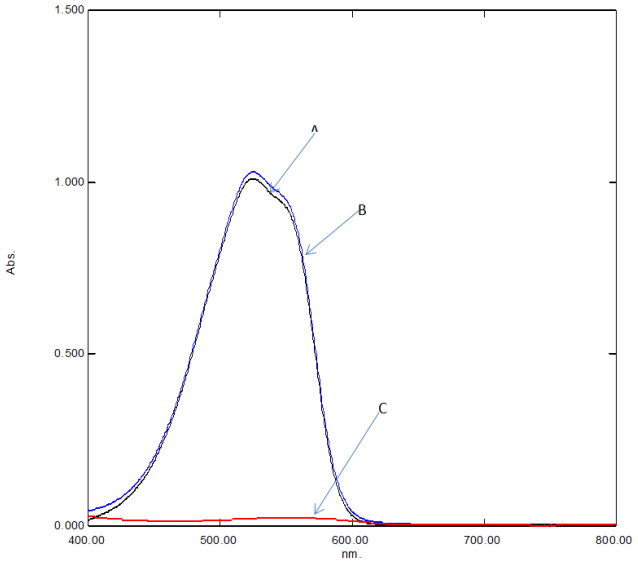

Figure 2: Final absorption spectrum of (4 PPM) solution of Cefxime: **A:** versus blank, **B:** versus "distilled water," **C:** blank versus "distilled water

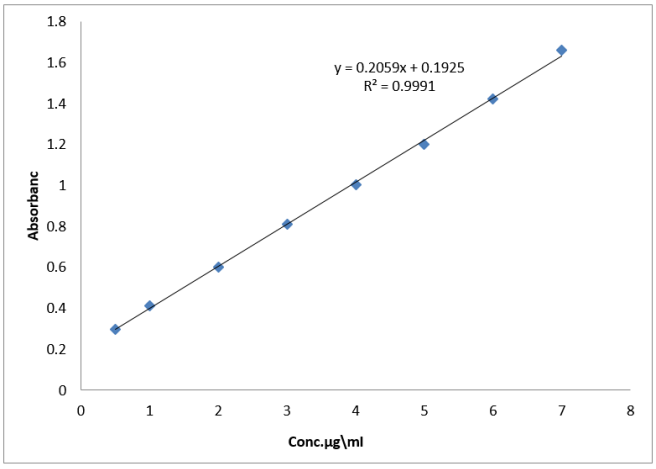

Figure 3: The standard curve for determination of Cefxime

The correlation coefficient indicates that the standard curve has excellent linear characteristics

Table 10: Accuracy and precision

Conc. of cefixime µg/mL	*Recovery* (%)*	*Relative error* (%)*	*RSD* (%)*
2	100.41	0.41	0.9
4	99.6	-0.35	0.3
5	98.95	-1.04	0.1

*For five determinations

Table 11: Estimation of cefxime in pharmaceutical preparations

Pharmaceutical preparation	*Amount taken µg/mL*	*Amount measured µg/mL*	*Recovery (%)*	*Relative error (%)*	*RSD (%)*
Cefxime Tabuk-Saudi Arabia	2	1.99	99.6	0.31	0.98
	4	4.07	101.8	1.80	2.36
	5	4.95	99.1	-0.87	0.93
Sancaklar –duzce -Turkey	2	2.003	100.1	0.16	3.2
	4	3.98	99.6	0.37	0.9
	5	4.99	99.9	-0.03	3.3

*Average of five determinations

The values for e_{max}, LoD, LoQ, Sandall's sensitivity, and correlation coefficient were calculated as shown in Table 9, where it is clear from the values of e_{max} that the method is "good"; also, the correlation coefficient value indicates the high linear specifications of the calibration curve.

An "accuracy and precision" were studied by measuring "absorption at 524 nm for three "different concentrations" (2,4,5 ppm) of the drug, and the results are shown in Table 10 show that the method is of good "accuracy" and precision."

Application in Pharmaceutical Preparations

The proposed method was applied to the pharmaceutical preparations of cefxime that were in the form of tablets by taking three different concentrations of the above-mentioned pharmaceutical solutions. Work steps were applied according to the method adopted in the optimal conditions and then calculated the values of relative error, recovery ratio and relative standard deviation and the results in the Table 11 Shows the "success of the proposed method" for estimating furosemide in the form of tablets, and that the method is of good "accuracy and precision."

CONCLUSIONS

It is thus concluded that the proposed method is simple, cost-effective, accurate, safe, free from pollution, and precise, and can be successfully employed in the routine analysis of this drug in pharmaceutical tablet dosage forms.

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