March 2010 ISSN : 0974-7419 Volume 9 Issue 1

Trade Science Inc.

Analytical CHEMISTRY

An Indian Journal

Full Paper

ACAIJ, 9(1) 2010 [108-112]

A simple method for the spectrophotometric determination of cefixime in pharmaceuticals

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Received: 11th December, 2009 ; Accepted: 21st December, 2009

ABSTRACT

A simple specrtophotometric method for the determination of cefoxamide with variamine blue is presented. The determination is based on the hydrolysis of β-lactum ring of cefixime with sodium hydroxide which subsequently reacts with iodate to liberate iodine in acidic medium. The liberated iodine oxidizes variamine blue to violet colored species of maximum absorption at 572nm. The absorption is measured within the pH range of 4.0-4.2. Beer's law is obeyed in the range of 0.5-5.9μg/mL for Cefixime. The analytical parameter was optimized and the method is successfully applied for the determination of cefixime.

KEYWORDS

Cefixime;
Spectrophotometry;
Variamine blue.

INTRODUCTION

Cefixime is a semi-synthetic, broad-spectrum antibiotic in the third generation of the cephalosporin class, proven effective for common bacterial infections of the ear, sinus, throat, and skin. The key intermediate for semi synthetic production of a large number of cephalosporins is 7-aminocephalosporinic acid, which is formed by hydrolysis of cephalosporin produced by fermentation[1]. A few thousand semi-synthetic cephalosporins have been described in the science literature, but only a small number of these have shown clinical importance.

Cefixime is a β-lactum antibiotic possessing a broad spectrum of antibacterial properties[2,3]. Several methods have been reported for the quantitative determination of Cefixime. This include fluorimetric[4], polorograph[5] and isotachophotomrteic methods for determination of this analytic is chloronilic acid[3], paramolybdate anion[7], molybdophosphoric acid[8] formation of a complex with Cu(II)[9], a reaction with potassium iodated in acidic medium[10]. Cefixime was also determined in pharmaceuticals preparations[11-15], Urine[14,16-19] and human serum[20]. Recently a rapid development method of pharmaceuticals has been observed too[21,22].

The hydrolysis of β–lactum ring, which is the common feature for cephalosporins and penicillin, has been achieved by the sodium hydroxide addition. Major difficulties in the determination of Cefixime have been encountered at β–lactum ring hydrolysis step[23]. A β–lactum enzyme[24] has been used for the hydrolyzed product of the analyte reacts with iodated in acid medium and liberates iodine. The liberated iodine oxidizes

variamine blue to the voilet colored species is the basis for the specrtophotometric determination of the analytes. The reaction mechanism followed the course similar to the described for penicillin[25]. The proposed method has been successfully applied for the determination of Cefixime in pharmaceuticals.

EXPERIMENTAL

Apparatus

A systronics 2201 UV-VIS Double Beam Spectrophotometer with 1cm quartz cell was used for the absorbance measurements and a WTW pH 330, pH meter was used.

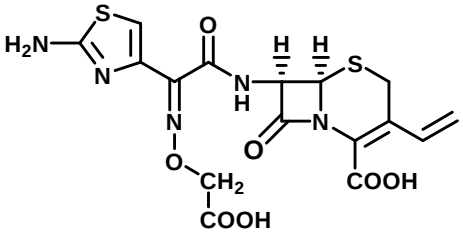
Reagents and solutions

All chemicals used were of analytical grade and doubly distilled water was used for dilution of the reagents and samples. Cefdinir stock solution (1000µg/mL) was prepared by dissolving standard sodium cefdinir in water. This compound chosen to represent cephalosporins. Cefixime (Agio Pharmaceuticals Ltd) was prepared freshly, as required, by dissolving an appropriate amount of antibiotic in water to provide a 1µg/ml solution. The standard solution must be protected from contact with light. The structure of the cephalosporines studied is listed in TABLE 1. Sodium hydroxide 0.1 mol/L aqueous solution, hydrochloric acid 1 mol/L aqueous solution were used through out.

Zeefix (Agio Pharmaceuticals Ltd.); A 0.05%solution of variamine Blue (E-Merck Limited, Mumbai) in (75:25) water –ethanol mixture was used and stored in an amber bottle.

Procedure

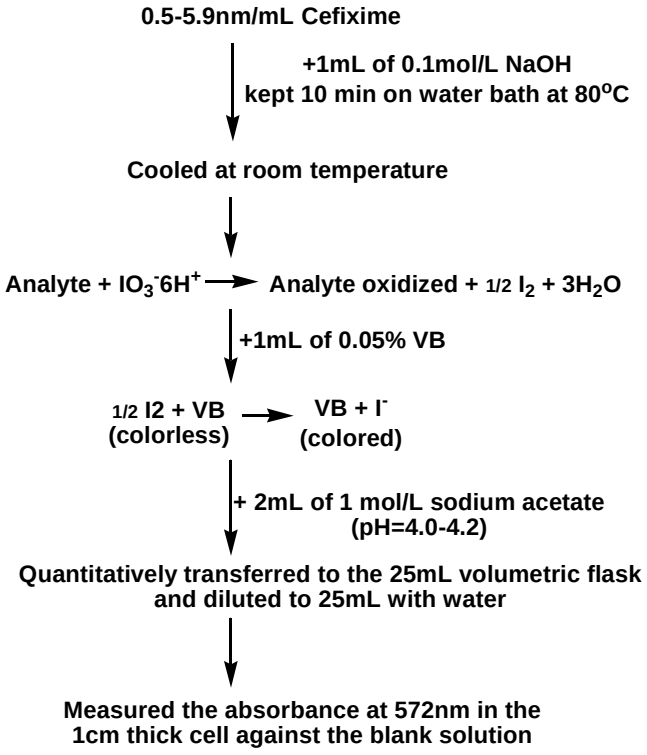
An aliquot of a sample solution containing 0.4-5.5µg/mL of Cefixime was transferred into a series of 25mL calibrated flasks, 1mL of 0.1ml/ L sodium hydroxide were added and the mixture was kept on a water bath (80° C) for 10 min .after being cooled to room temperature (27.2°C), 1.5mL of 0.1 mol /L potassium iodate and 2mL of 1 mol/L hydrochloric acid were added. The mixture was gently shaken until the appearance of yellow color, indicating the liberation of iodine, 1mL of 0.05% of variamine blue was then added to it followed by the addition of 2mL of 1 mol/L of acetate buffer of pH 4 and the reaction mixture was shaken for 2 min. the contents were diluted up to 25mL with distilled water and mix well. The absorbance of the oxidized species variamine blue formed was then measured at 572nm against the reagent blank prepared in the same manner, without the analyte. The amount of the Cefixime present in the volume taken



Structure of the cefixime

TABLE 1 : Maximum amount of tolerance of excipients for the determination of cefixime

Common excipients	Tolerance limit (mg)
Glucose	54.0
Fructose	35.5
Lactose	56.5
Sucrose	32.4
Starch	8.4
Citric acid	22.0
Sodium benzoate	21.3



Scheme 1 : Determination of cefdinir

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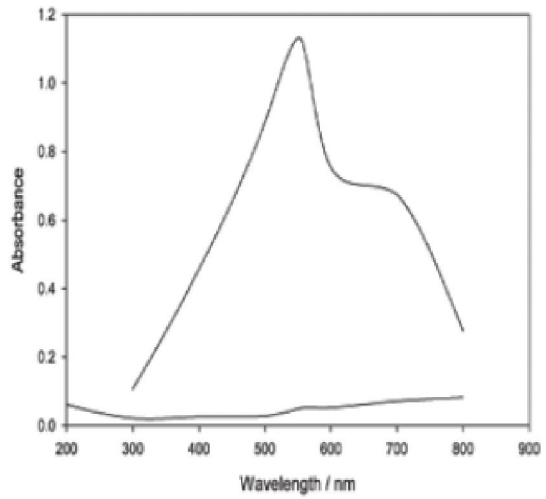
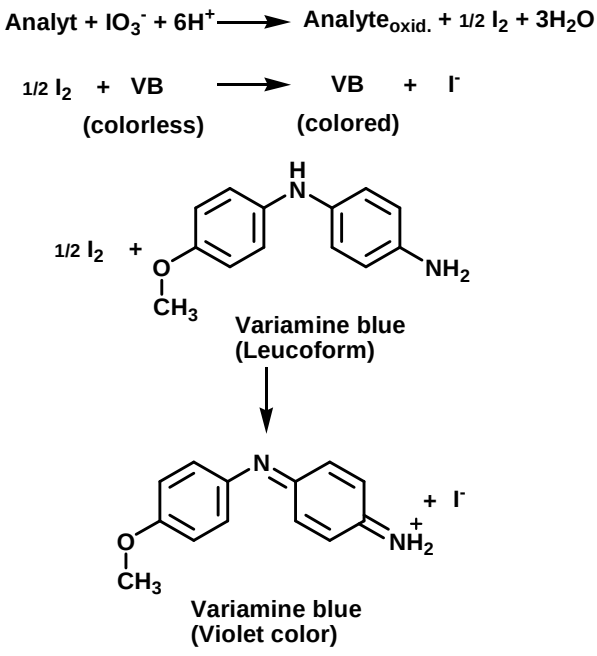


Figure 1 : Absorption spectra of the oxidized form of variamine blue with reagent blank



Scheme 2

was computed from the calibration graph.

Analysis of injection solution

An appropriate amount of antibiotic was dissolved in water so as to prepare 1µg/mL solution and then the recommended procedure was followed without modification. The presence of other substances causes no significance interference with the determination of antibiotic.

Analysis of formulation

Weighed an amount of the sample equivalent to about 250mg Cefixime and was dissolved in a sufficient amount of distilled water. The solution was shaken and filtered of through whatman No.1 filter paper and washed with water. Filtrate was diluted up to 100mL. The general procedure was applied with no modification and the presence of excipients in the sample such as glucose, lactose, fructose, starch, citric acid and sodium benzoate, because no interference in the determination and process of separation was not required.

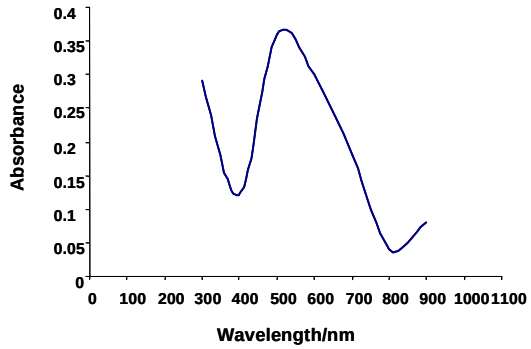


Figure 2 : Absorption spectra of colored species of variamine blue with cefixime against reagent blank (Variamine blue) = 0.05%, (Cefixime) = 2µg/mL

RESULT AND DISCUSSION

This method is based upon the hydrolysis of β–lactum ring of the analyte on heating with sodium hydroxide and the reaction of the hydrolyzed product with potassium iodate in the acidic media which liberates iodine. The liberated iodine oxidizes variamine blue to violet colored species of maximum absorption at 572nm. The reagent blank had negligible absorption at this wavelength. Beer's law is obeyed in the range of 0.5-5.9µg/mL for cefdinir. Determination of cefdinir as represent in Scheme 1. The absorption spectra of the oxidized form of variamine blue is presented in figure 1, the absorption spectra of colored species of variamine blue with cefdinir against reagent blank in the range of 300-800nm are illustrated in figure 2. The maximum absorption is at 572nm and reaction system is presented in Scheme 2.

Effect of sodium hydroxide concentration

The effect of sodium hydroxide concentration on the absorption was studied with 2µg /mL of cefdinir. Volumes from 0.5-2.0mL of 0.1 mol/mL NaOH solution were examined. The investigation showed that 1.0-

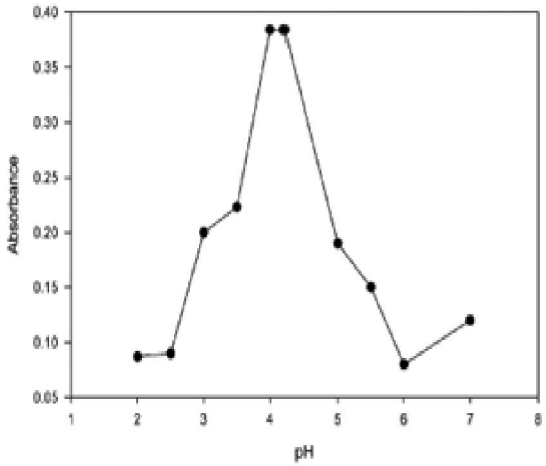


Figure 3 : Effect of pH on color intensity for cefotaxime (2µg/mL)

TABLE 2 : Determination of cefixime in pharmaceuticals preparations

Pharmaceuticals	Declared quantity (µg /mL)	Found in the sample a (µg/mL)± S.D
Zeefix1	2.00	1.984±0.03
Zeefix 2	4.00	3.975±0.02
Zeefix3	5.00	5.454±0.02

Average of three determinations

1.5mL of 0.1 mol/mL NaOH solution gave maximum absorbance and 1.0mL of 0.1 mol/mL NaOH solutions was chosen for the procedure.

Effect of temperature, time and pH

The effect of different variables such as temperature, time and pH on the coloration was studied with 2µg/mL of cefdinir. It was observed that the optimum reaction temperature is 80°C-90°C, lower or higher temperature gives inaccurate results, and the reaction time for complete hydrolysis of β–lactum ring was 10-15 min. constant and maximum absorbance values were obtained in the pH=4.0-4.2 hence the pH of the reaction system was maintained at pH=4.0-4.2 throughout the study by adding 2mL of 1mol/L sodium acetate solution. Effect of pH on color stability is presented in figure 3.

Calibration graph

The aqueous sample of solution containing 0.5-5.9µg/mL of cefdinir, the reagents was added as described above. Within the studied concentration ranges, the measured absorbance values changed linearly. The correlation coefficients foe cefdinir were

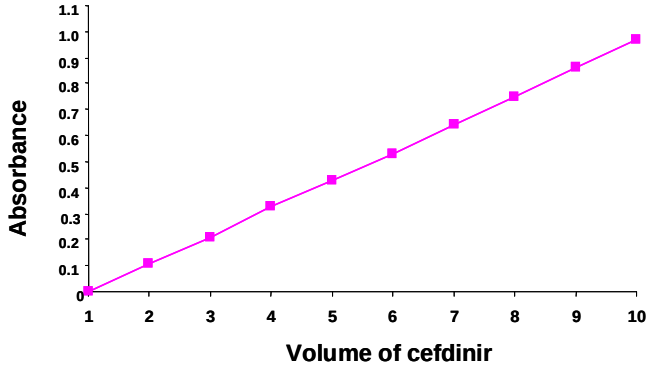


Figure 4 : Calibration graph of cefixime

found to be 0.9980. The following regression coefficient was calculated: for cefdinir a= 0.2239 b= 0.014. The following relative molar absorption coefficient was obtained: 1.07×10^5 L/mol/cm for cefdinir. A calibration graph for the determination of cefdinir is presented in figure 4.

Effect of foreign substance

The influence of foreign substance was examined by the proposed method. The maximum tolerance (in mg)in the determination of 100µg/mL cefdinir was 54.0 for glucose, 35.5 for fructose, 56.5 for lactose, 32.4 for sucrose, 8.4 for starch, 22.0 for calcium, 22.0 for citric acid and 21.3 for sodium benzoate. The tolerance limits of foreign substance are summarized in TABLE 2.

Application

The proposed method has been successfully applied to the determination of studied cefdinir in pharmaceuticals. Cefdinir was determined in 1g of Zeefix. The content in the investigated drug sample was calculated from the calibration curve mentioned above are found to be in a good agreement with the labeled amounts (TABLE 2) the results, listed in TABLE 2 compared favorably with those from a reference method[26]. The precision of the proposed method was evaluated by replicate analysis of 3 samples containing cefdinir at different concentration.

CONCLUSIONS

A simple method for the determination of β–lactum antibiotic is described. The method is based on the reaction of iodate with the hydrolyzed product of β–lactum

antibiotics which liberates iodine, subsequently oxidizes variamine blue into violet colored species, and measured at 572nm. The developed method does not involve any stringent reaction conditions and offers the advantages of high stability of the reaction system (4 hours). The proposed method was applied to the determination of cefdinir in pharmaceuticals.

ACKNOWLEDGEMENTS

Authors are thankful to the Principal and Management, G.M.Institute of Technology, Davangere for the support to carry out the present investigations.

REFERENCES

[1] W.O.Foye, Lea.Febiger; Philadelpia, U.S.A., Principles of Medicinal Chemistry, 726 **(1975)**.
[2] J.K.Podlewsky, P.A.Chwalibogowaka; Drugs of the Modern Therapy. Split Trading., 45-47, **(1999)**.
[3] C.S.P.Sastry, T.E.Divakar, U.V.Pradad; Chem. Anal., **32**, 301 **(1987)**.
[4] J.Yang, G.Zhou, N.Jie, R.Han, C.Li, J.Hu; Anal.Chim.Acta, **325**, 195 **(1996)**.
[5] B.Ogoreve, V.Hudnik, S.Gomiseek, Z.Fresenius; Anal.Chem., **330**, 59 **(1988)**.
[6] A.Cieslak, E.Gwozdz, W.Holska; Chem.Anal., **36**, 363 **(1991)**.
[7] P.B.Issopoulos; J.Pharm.Biomed.Anal., **7**, 619 **(1989)**.
[8] P.B.Issopoulos; Analyst., **113**, 1083 **(1998)**.
[9] P.B.Issopoulos; J.Phar.Biomed.Anal., 6321 **(1988)**.
[10] S.A.Nabi, S.M.Eyad, A.Nameh, I.H.H.Murad; Chem.Anal., **42**, 881 **(1997)**.
[11] M.M.Ayad, A.A.Shalaby, H.E.Abdellatef, H.M. Elsaid; J.Pharm.Biomed.Anal., **20**, 557 **(1999)**.
[12] A.Shalaby, J.Liq; Chromatrogr.Relat.Technol., **21**, 3161 **(1998)**.
[13] S.Szarapkar, S.A.Shivalkar, A.A.Dhanvate, P.M.Desphande, S.S.Kolte; Indian Drugs., **32**, 232 **(1995)**.
[14] M.Hefnawy, Y.El-Shabrawy, F.Belal; J.Pharm. Biomed.Anal., **21**, 703 **(1999)**.
[15] Y.M.Issa, A.S.Amin; Mikrochim.Acta, **124**, 203 **(1996)**.
[16] H.Tan, R.Wang, W.Wei, S.Yao; Anal.Lett., **31**, 949 **(1998)**.
[17] H.Fabre, M.D.Blachin, D.Lerner, B.Mandrou; Analyst, **110**, 775 **(1985)**.
[18] J.A.Murill, J.M.Lemus, L.F.Garci; Anal.Lett., **27**, 1875 **(1994)**.
[19] M.Azza, M.Ali; Bioelectrochem.Bioenerg., **33**, 201 **(1994)**.
[20] P.Izquierdo, M.C.Gutierrez, H.A.Gomez, B.D.Perez; Anal.Lett., **23**, 487 **(1990)**.
[21] H.T.Pan, P.Kumari, J.Lim, C.C.Lin; J.Pharm.Sci., **81**, 663 **(1992)**.
[22] K.Matsubayashi, H.Tachzaw; J.Chromatogr., **515**, 47 **(1990)**.
[23] Z.H.Earle, D.T.Hurst, M.Viney; J.Chem.Soc., 2093 **(1969)**.
[24] B.M.Frantz; J.Pharm.Sci., **65**, 887 **(1976)**.
[25] M.I.H.Halaleh, R.M.Rahman, A.Q.Jamhour; Chem.Anal., **42**, 265 **(1997)**.
[26] F.Bhul, B.S.Sroka; Chem.Anal., **48**, 145 **(2003)**.