ISSN : 0974-7419 Volume 9 Issue 4

Trade Science Inc.

Analytical CHEMISTRY

An Indian Journal

Full Paper

ACAIJ, 9(4) 2010 [408-412]

# A simple spectophotometric method for the determination of cefdinir in pharmaceuticals

**B.S.Virupaxappa[1], K.H.Shivaprasad[1]*, M.S.Latha[2]**

[1]Department of Chemistry PG Centre, Bellary, Gulbarga University, Gulbarga, Karnataka, (INDIA)

[2]Department of Chemistry G M Institute of Technology, Davangere, Karnataka, (INDIA)

E-mail: virupaxb@gmail.com; lathamschem97@gmail.com

*Received: 13th May, 2010 ; Accepted: 23rd May, 2010*

## ABSTRACT

A simple spectophotometric method for the determination of Cefdinir with Thionin is presented. The determination is based on the hydrolysis of β-lactum ring of Azithromycin with sodium hydroxide which subsequently reacts with iodate to liberate iodine in acidic medium. The liberated iodine bleaches the violet colored Thionin species of maximum absorption at 610 nm. The absorption is measured within the pH range of 4 -4.3. Beer's law is obeyed in the range of 0.6-6.3 μg/mL for Azitrhomycin. The analytical parameter was optimized and the method is successfully applied for the determination of Cefdinir. 

## KEYWORDS

Cefdinir;
Spectrophotometry;
Thionin.

## INTRODUCTION

Cefdinir 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 is 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.

Cefdinir is a β-lactum antibiotic possessing a broad spectrum of antibacterial properties[2,3]. Several methods have been reported for the quantitative determination of Cefdinir. These include fluorimetry[4], polarographic[5] and isotachophotometric methods[6]. Determinations, also, have been carried out at using chloronilic acid[3], paramolybdate anion[7], and molybdophosphoric acid[8] and by complexes with copper[9,11]. A reaction with potassium iodated in acidic medium is also reported[10]. Cefdinir was also determined in pharmaceutical preparations[11-15], Urine[14,16-19] and human serum[20]. Recently, a rapid deformation method for Cefdinir in pharmaceutical preparations has been developed[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 Cefdinir 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 forms the basis for the spectrophotometric determination of the analyte. The reaction mechanism followed the course

similar to the one described for penicillin[25,26]. The proposed method can be successfully applied for the determination of Cefdinir in pharmaceuticals.In the present investigation, an attempt has been made to develop a simple, accurate, and reproducible spectrophotometric method for estimation of Cefdinir in pharmaceutical formulations.

## EXPERIMENTAL

### Apparatus

A systronics 2201 UV-VIS Double Beam Spectrophotometer with 1 cm 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. Cefdinir (Abbott 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 studied Cefdinir is listed in Figure 1. Sodium hydroxide 0.1 mol/L aqueous solution, hydrochloric acid 1 mol/L aqueous solution were used through out.

Omnicef (Abbott Pharmaceuticals Ltd.); a 0.05%solution of Thionin in used.

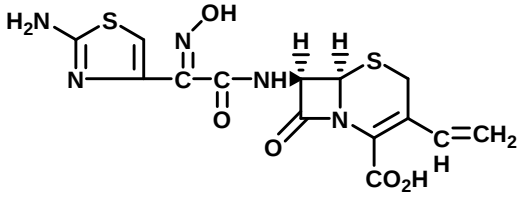


**Figure 1 : Structure of the cefdinir studied.**

### Procedure

An aliquot of a sample solution containing 0.6-6.3 µg/mL of Cefdinir was transferred into a series of 25 mL calibrated flasks, 1 mL of 0.1ml/ L sodium hydroxide were added and the mixture was kept on a water bath (80° C) for 15 min .after being cooled to room temperature (24°C), 2.0 mL of 0.1 mol /L potassium iodate and 2 mL of 1 mol/L hydrochloric acid were added. The mixture was gently shaken until the appearance of yellow color, indicating the liberation of iodine, 1 mL of 0.05% of Thionin was then added to it followed by the addition of 2 mL 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 25 mL with distilled water and mix well. The absorbance of the resulting solution was then measured at 610 nm against the reagent blank prepared in the same manner, without the analyte. The absorbance corresponding to the bleached color that in turn corresponds to the analyte concentration was obtained by substracting the absorbance of the blank solution of that test solution. The amount of the Cefdinir present in the volume taken was computed from the calibration graph.

### Analysis of injection solution

An appropriate amount of antibiotic was dissolved in ethanol so as to prepare 1 µg/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.

## 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 bleaches the vio-

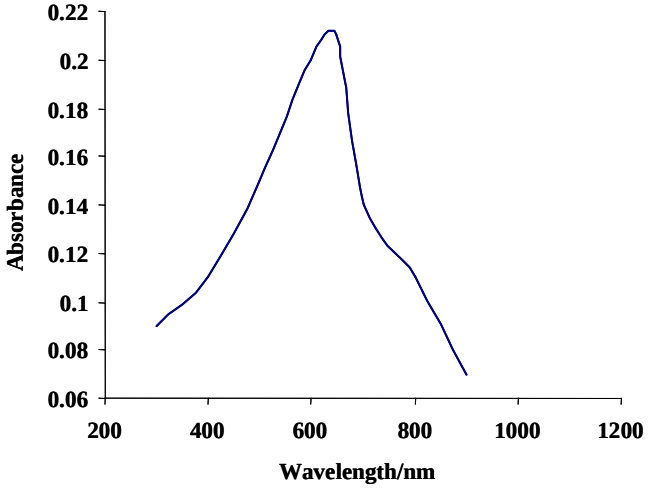


**Figure 2 : Absorption spectrum of coloured species of thionin with reagent blank**

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let colored thionin of maximum absorption at 610 nm. The reagent blank had negligible absorption at this wavelength. Beer's law is obeyed in the range of 0.6-6.3µg/mL for Cefdinir. Determination of Cefdinir as represented in Scheme 1. The absorption spectra of the Thionin is presented in Figure 2, the absorption spectra of colored species of Thionin with Cefdinir against reagent blank in the range of 300-800nm are illustrated in Figure 3. The maximum absorption is at 610 nm and reaction system is presented in Scheme 2.

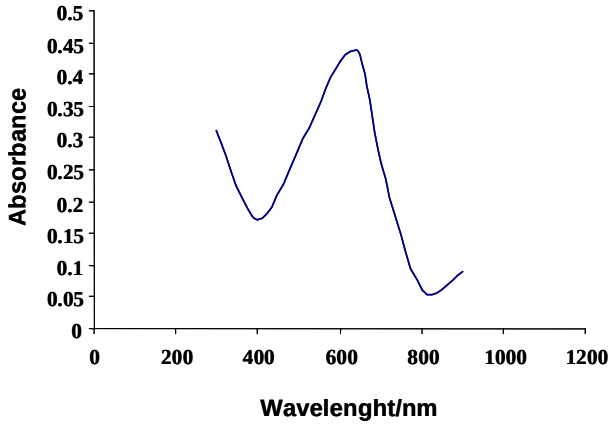
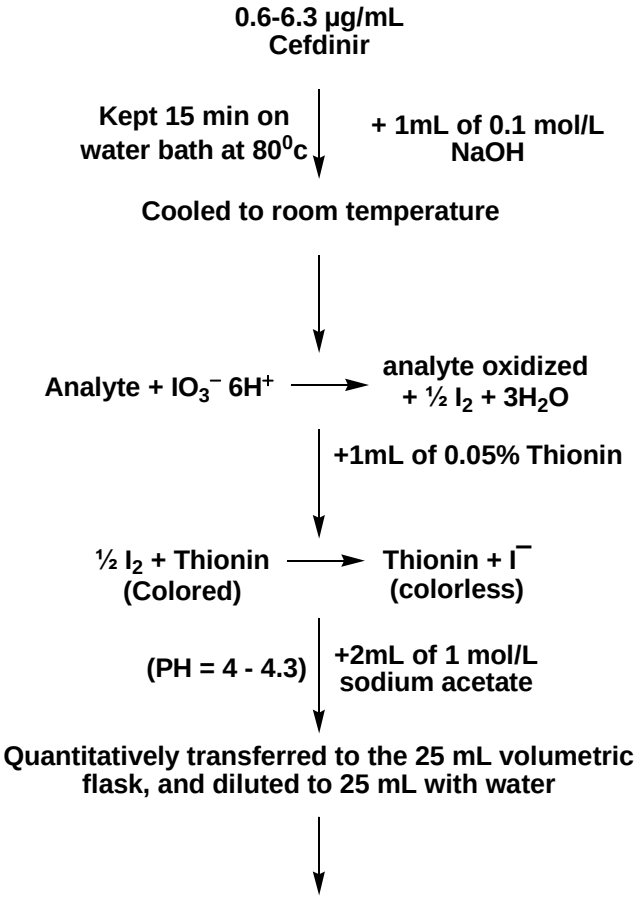


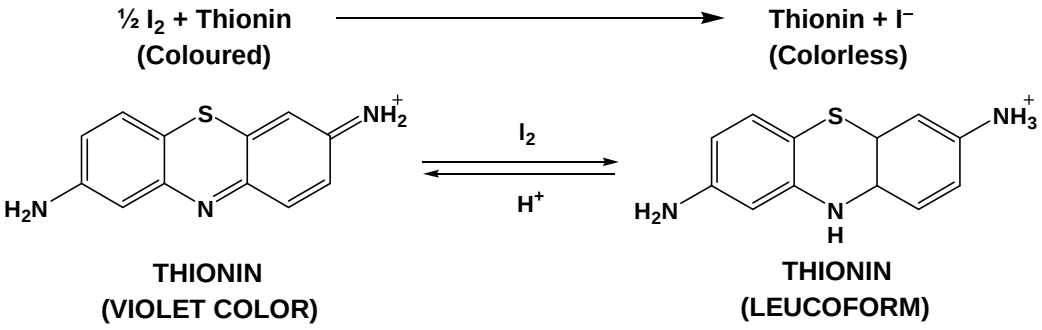

**Figure 3 : Absorption spectra of coloured species of thionin with cefdinir against reagent blank**

## Effect of sodium hydroxide concentration

The effect of sodium hydroxide concentration on the absorption was studied with 2µg /mL of Cefdinir. Volumes from 0.5-2.0 mL of 0.1 mol/mL NaOH solution were examined. The investigation showed that 1.0-1.5 mL of 0.1 mol/mL NaOH solution gave maximum absorbance and 1.0 mL of 0.1 mol/mL NaOH solutions was chosen for the procedure.




**Scheme 1 : Determination of cefdinir.**




**Scheme 2**

## 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 75⁰C-85⁰C, 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=4-4.3 hence the pH of the reaction system was maintained at pH=4 - 4.3 throughout the study by adding 2 mL of 1mol/L sodium ac-

etate solution. Effect of pH on color stability is presented in Figure 4.

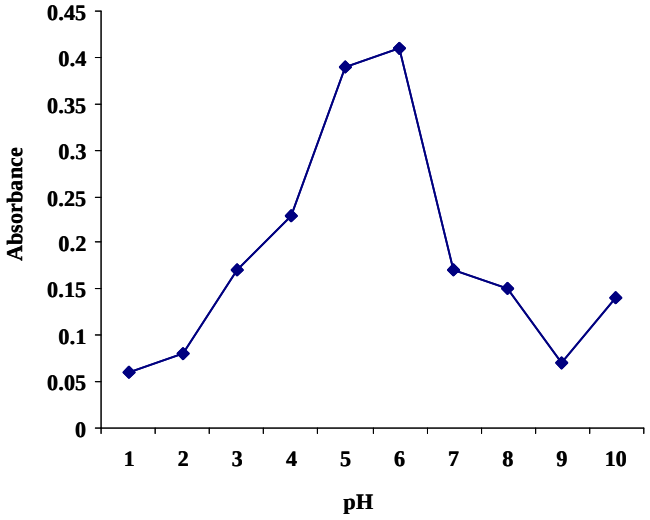



**Figure 4 : Effect of PH on color intensity for cefdinir**

## Calibration graph

The sample solution containing 0.6-6.3µg/mL of Cefdinir, the reagents was added as described above. Within the studied concentration ranges, the measured absorbance values changed linearly. The correlation coefficients for Cefdinir were found to be 0.9992. The following regression coefficient was calculated: for Cefdinir a= 0.1809 b= 0.0129. The following relative molar absorption coefficient was obtained: $1.02X10^5$ L/mol/cm for Cefdinir. A calibration graph for the determination of Cefdinir is presented in Figure 5.

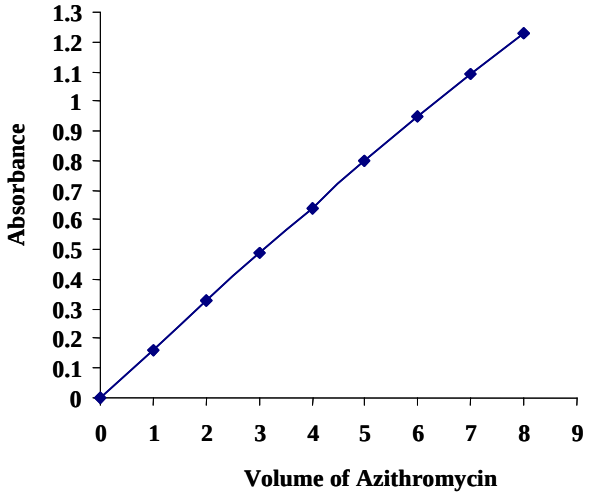



**Figure 5 : Calibration graph of cefdinir**

## Effect of foreign substance

The influence of foreign substance was examined by the proposed method. The maximum tolerance (in mg)in the determination of 100 µg /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 1.

**TABLE 1 : Maximum amount of tolerance of excipients for the determination of cefdinir.**

| Common excipients | Tolerance limit (mg) |
|---|---|
| Glucose | 59.0 |
| Fructose | 39.5 |
| Lactose | 51.5 |
| Sucrose | 36.4 |
| Starch | 9.4 |
| Citric acid | 26.0 |
| Sodium benzoate | 24.3 |

## Application

The proposed method has been successfully applied to the determination of studied Cefdinir in pharmaceuticals. Cefdinir was determined in 1 g of Omnicef. 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 1) 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 Azithromycin at different concentration.

**TABLE 2 : Determination of azithromycin in pharmaceuticals preparations.**

| Pharmaceuticals | Declared Quantity (µg /mL) | Found in the sample a (µg/mL)± S.D |
|---|---|---|
| Omnicef 1 | 2.00 | 1.988±0.03 |
| Omnicef 2 | 4.00 | 3.976±0.02 |
| Omnicef 3 | 5.00 | 5.457±0.02 |

**Average of three determinations**

## 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 bleaches

the violet color of Thionin is and measured at 610 nm. 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 Abbott pharmaceutical Ltd, Goa for the gift sample of Cefdinir.

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