Spectrophotometric determination of cefixime by charge transfer complex formation

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Abstract:

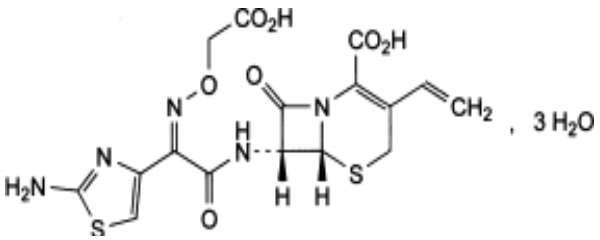
Simple, sensitive and economical spectrophotometric methods have been developed for the determination of cefixime in pure form. This method is based on the reaction of cefixime as n-electron donor with chloranil to give highly colored complex in ethanol which is absorb maximally at 550 nm. Beer's law is obeyed in the concentration ranges 5-250 µg ml^{-1} with high apparent molar absorptivities of 1.52×10^{3} $L.mole^{-1}.cm^{-1}$.

Key words: cefixime; chloranil ;charge-transfer complexes; aqueous solution.

Introduction:

The charge transfer complexes are formed between electron donors, having sufficiently low ionization potential, and acceptors, having sufficiently high electron affinity. The transfer of an electron from a donor to an acceptor is readily possible in the charge transfer process[1] .

Cefixime tri hydrate is 5-Thia-1-azabicyclo[4.2.0] oct-2-ene-2-carboxylic acid, 7-[[(2- amino-4-thiazolyl) [(caroxymethoxy)imino] acetyl] amino]-3-ethenyl-8-oxo-trihydrate fig (1)[2] Cefixime is effective against a wide spectrum of sensitive Gram –Ve, Gram +Ve and anaerobic bacterial pathogens including β- lactamase producing strains[3]. Cefixime is given by mouth in the treatment of susceptible infections including gonorrhoea, otitis media, pharyngitis, lower respiratory-tract infections such as bronchitis, and urinary-tract infections[4].



Chemical Structure of Cefixime M.wt. =507.5

Literature survey reveals that various high-performanceliquid chromatographic (HPLC) methods have been reported for the determination of cefixime. [2, 5-8] and by HPTLC[9] individually or with other drugs, spectrophotometric methods[10-11]

In this paper we report a simple, sensitive, and accurate, spectrophotometric method for the determination of cefixime in pure form and in pharmaceutical formulations

Materials and Methods:

Apparatus

All spectral measurements were performed on Shimadzu U.V-visible recording spectrophotometer (U.V-160), where as absorbance

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measurements were carried out on CECIL-CE-1021spectrophotometer.
pH measurements are carried out using a Philips PW 9420 pH meter.

Reagents

Chemicals used are of the highest purity available.

Chloranil solution: A saturated (1×10^{-3}M) ethanol solution was used.
Borate Buffer solution: borate buffer solution of pH 9 is obtained by preparation of (5×10^{-2}M) sodiumtetraborate in aqueous solution.

Standard solutions of cefixime: (1000µg/ml): 0. 1g is dissolved in ethanol, solution is transferred into a 100 ml volumetric flask, and diluted to the mark with absolut ethanol
Ethanol: Absolute(100 %) is used.

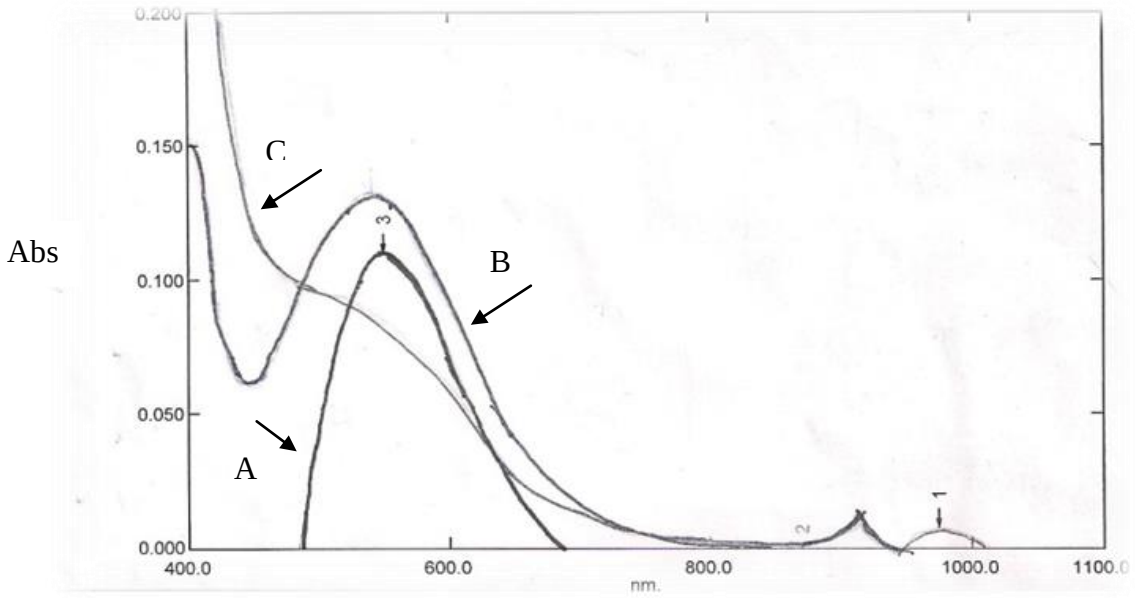
Recommended procedure

Aliquots of standard cefixime solutions were transferred separately into a series of 25ml calibrated flasks. To each of these were added 2.0 ml of 1×10^{-3}M chloranil followed by addition 2 ml of borate buffer solution and the solutions were heated at 30°C for 5 min., then the solutions were cooled to room temperature and diluted to the mark with ethanol. The absorbances of the products was measured at 550 nm against corresponding reagent blank.

Results and Discussion:

Absorption spectra

cefixime reacted with chloranil reagent in the presence of a base and produced a yellow color with chloranil having maximum absorption at 550 nm against respective reagent blank (Fig. 1).



Wavelength(nm)

A= (S& b) , B= (S &w) , C = (b & w)

Fig(1.) Absorption spectra of cefixime (30 µg/25ml) complex with chloranil reagent (1×10^{-3} M)

Study of the optimum reaction conditions

The effect of various parameters on the absorption of the coloured CT complex formed with chloranil have been investigated and the reactions conditions have been optimized for cefixime.

1. Effect of pH and buffer solutions on the absorbance

The effect of pH on the absorption of cefixime – chloranil product was studied using different concentrations of HCl and NaOH of pH ranging from 5-10. It was found that the product cefixime –chloranil formed in the final pH9 in the presence of sodium hydroxide. Different buffers of pH9 namely bicarbonate, borate, phosphate buffers were prepared to examine the sensitivity of cefixime –chloranil product. (Table 1) shows that maximum absorption is obtained by using a borate buffer solution. However, the optimum amount of this buffer has been investigated and it was found that 2ml of aliquots gave maximum absorbance and selected in subsequent experiments.

Table (1): Effect of different buffers of pH

Buffer	Bicarbonate	Borate	Phosphate
Absorbance	0.261	0.355	0.245

2. Effect of reaction time and temperature

The reaction time was determined by following the colour development at room temperature and in thermostatically controlled water-bath at different temperatures. The absorbance was measured against reagent blank treated similarly at 550 nm. It was observed that the absorbance reached maximum after addition of the reagent solutions after 5min at(35°C) (Table 2). These temperature and reaction time was chosen for colour development.

Table (2): Effect of reaction time& temperature on absorbance

Temp °C	Absorbance								
	Time (min)								
	immediately	5	10	15	20	25	30	35	40
0	0.213	0.211	0.210	0.210	0.210	0.210	0.210	0.210	0.210
25	0. 350	0.350	0.351	0.351	0.351	0.351	0.351	0.351	0.351
30	0. 350	0.358	0.358	0.358	0.358	0.358	0.358	0.358	0.358
35	0.361	0.363	0.363	0.363	0.363	0.363	0.363	0.363	0.363
40	0. 361	0.362	0.363	0.363	0.364	0.363	0.632	0.363	0.363
45	0.360	0.361	0.363	0.364	0.363	0.363	0.363	0.362	0.363

3. Effect of reagent concentration

The effect of changing the reagent concentration on the absorbance of solution containing a fixed amount of cefixime was studied, It was found, as shown in (Table 3), that absorbance increases with increasing choranil concentration and reached their maximum value on using 2ml of 1×10^{-3}M of chloranil which was used in subsequent experiments.

Table (3) Effect of the reagent concentration on absorbance

Chloranil(1×10^{-3}M)ml	1	1.5	2	2.5	3
Absorbance	0.357	0.360	0.365	0.362	0.359

4. Effect of surfactant

Effect of various anionic, cationic and neutral surfactants including sodium dodecyl sulphate (SDS), , cetavlon (CTAB), and triton X-100 were tested for the investigation of the sensitivity of the method. The results reveal that the presence of the

surfactants has no remarkable effect on the intensity of the colour. Therefore, the methods have been carried out without using surfactants.

5. Effect of order of addition

In order to obtain the high colour intensity, the order of addition of reagents should be followed as given in the recommended procedures, otherwise a loss in colour intensity was observed.

Quantification and Analytical Data

The results for the determination of cefixime is summarized in Table 4, which show the sensitivity, recovery and reproducibility of the proposed method. These are reasonably precise and accurate. The calibration graph is linear in the range of 5-250 $\mu g ml^{-1}$. The apparent molar absorptivities calculated is 1.52×10^{3} $mol^{-1}cm^{-1}$, Table 4 illustrates regression equations, and correlation coefficients (R^2) for the proposed methods. The reproducibility of the proposed method was checked by estimating three different concentration levels within the Beer's law limit in five replicates. The average recovery were 96.54 % reveal good accuracy for the method. The relative standard deviation can be considered to be very satisfactory.

Table (4). Quantitative parameters of the proposed method.

Parameter	Values
Beer's law limits (µg/ml)	5-250
Molar absorptivity ($l.mol^{-1}$ cm^{-1})	1.52×10^{3}
Slope, *a*	0.003
Intercept, *b*	0.006
Correlation coefficient (R^2)	0.9980
RSD[# #]	≤0.81
Average recovery %	100.49

550 λ_{max} (nm)

[#] ***Y = aX+ b*, where *X* is the concentration of cefixime in 1000 µg ml^{-1}.**

[# #] **Average of five determinations.**

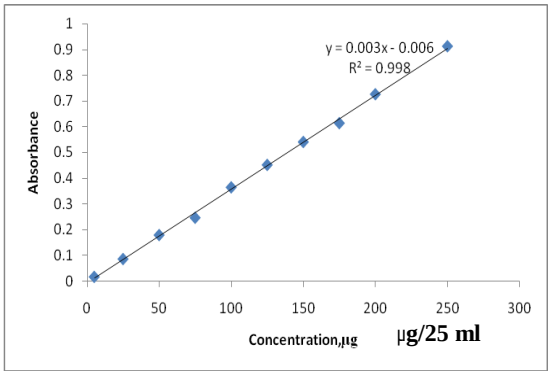


Fig. (2) Calibration graph for cefixime.

Accuracy and precision

The accuracy and precision of the method were evaluated by performing five replicate analyses of cefixime in pure form at four different concentration levels (5, 50, 100, 200 µ g.ml-1). The mean recovery (99.90%) and relative standard deviation (<0.81) can be considered to be very satisfactory.

Analytical application

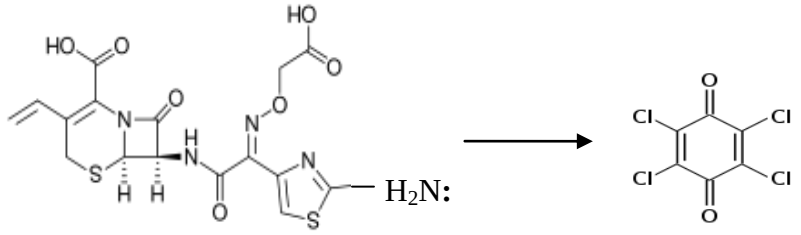
The contents of 5 tablets (200mg) were weighed and the powder was mixed. The accurately weighed portion of the powder equivalent to 100mg dissolved in amount of ethanol. The solution was filtered into a 100ml calibrated flask, the residue was washed with ethanol and the filtrate was diluted to the mark with ethanol. Different volumes of this solution were transferred to cover the concentrations 25,50,100 µg/ml of cefixime and proceeded as a procedure described above. The data are given in Table5.

Table (5.) Determinations of cefixime in tablets

Amount added (µg/ml)	Found(µg/ml)	Average recovery (%)	Recovery*(%)
25	24.86	100	98.80
50	50.89		100.89
100	101.9		101.42

*Average for five determinations

Stioicheiometry of the reaction :
The mole ratio method (12) was employed to establish the composition of the complex ,the result indicate the formation of a 1:1 complex between cefixime and chloranil at 550 nm .
Thus the suggested reaction might be written as;



Donor Acceptor

Conclusion:

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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التقدير الطيفي للسيفيكسيم بواسطة معقدات انتقال الشحنة

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الخلاصة:

تم تطوير طريقة طيفية تميزت بالبساطة والحساسية في تقدير سيفكسيم. اعتمدت الطريقة على تفاعل سيفكسيم بوصفه مانحا للإلكترونات نوع n مع كل من الكلورانيل بوصفه مستقبلا للإلكترونات نوع π لإعطاء معقد ملون في المحلول المائي يمتلك أقصى امتصاص عند الأطوال الموجية نانوميتر. أمكن تطبيق قانون بير للتراكيز 5 - 250 مايكروغرام/مللتر وبامتصاصيات مولارية 1.52×10^3 لتر.مول$^{-1}$سم$^{-1}$.