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Original Article

Polarographic determination of certain cephalosporins in pharmaceutical preparations

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Abstract

Polarographic methods have been developed for the determination of two cephalosporins namely cefotaxime (CTX) and ceftriaxone (CTR) in pharmaceutical formulations. Well defined peaks at potentials –1.432 V vs. SCE for CTX and –1.627 V vs. SCE for CTR were obtained in the presence of tungsten (VI). The method has been successfully applied for the determination of above mentioned cephalosporins in commercial dosage forms. The salient features of this investigation are presented in this communication.

Keywords: Polarographic method; Cefotaxime; Ceftriaxone; Dosage forms

INTRODUCTION

Cephalosporins are beta-lactams used for treatment of infections caused by both gram-negative and gram-positive bacteria (1,2). Thousands of semisynthetic cephalosporins have been reported in the literature, but only a few of these have clinical significance. A wide variety of analytical methods have been reported for the determination of cephalosporins in pure form and in pharmaceutical preparations. A variety of techniques i.e. spectrophotometry (3-6), spectrofluorimetric (7,8), chemiluminiscence (9,10), HPTLC (11), HPLC (12,13), atomic absorption spectrometric (14), electrochemical (15-19) were reported in the literature for the analytical determination of cephalosporins. A number of polarographic methods for the determination of cephalosporins were reported from these laboratories (20,21). It is well known that most of the sulphur containing compounds produce characteristic polarographic catalytic waves when complexed with transition metal ions such as Co (II), Cr (IV) and W (VI) (22-24). The proposed article describes a catalytic polarographic method for the determination of hydrolysed cephalosporins namely cefotaxime (CTX) and ceftriaxone (CTR) in the presence of W (VI).

MATERIALS AND METHODS

Apparatus

An Elico Polarograph Model CL 357 was employed for the polarographic investigations.

General procedure

Twenty five tablets of the drug (each 100 mg) were ground into fine powder. A quantity of powder equivalent to 100 mg of the tablet was weighed and taken into a 100 ml standard flask. Fifty ml of 5 M HCl was added and heated in a water bath for 30 min. The solution was cooled and made up to the mark with double distilled water. Ten ml of this solution was neutralized with 10 ml of 2.5 M NaOH and the solution was diluted to 100 ml to obtain a final concentration of 0.1 mg/ml. The solution was diluted appropriately for further studies. Tungstate solution of concentration 0.01 M was prepared in double distilled water.

Required volume of hydrolysed cephalosporin was taken into a 25 ml volumetric flask. 7.5 ml of 1 M sulphuric acid and 2.5 ml of 1 M KCl were added. Required amount of tungstate solution was added and made up to the mark with double distilled water. The solution taken

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into the polarographic cell was deaerated with nitrogen for about 15 min.

RESULTS

The polarograms of (a) hydrolysed cephalosporin (b) tungsten solution and (c) a mixture of the both recorded in 0.3 M sulphuric acid in presence of 0.1 M KCl supporting electrolyte are shown in Fig. 1 and 2. The polarograms reveal that mixture of drug and the metal ion produced a wave at potentials –1.432 V vs. SCE for CTX and –1.627 V vs. SCE for CTR.

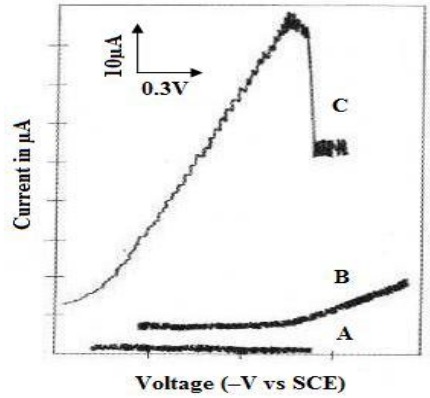


Fig. 1. Polarogram of CTX – W (VI) system.
[H_2SO_4] = 0.3 M; [KCl] = 0.1 M; Ep = -1.432 V vs. SCE
A) [CTX] = 3×10^{-6} M: B) [W (VI)] = 3×10^{-6} M and C) [CTX] = 3×10^{-6} M; [W (VI)] =3×10^{-6} M; Starting potential = - 0.832

Effect of different acids

The polarograms were recorded in different acid media and the data is shown in Fig. 3. It is clear that the behavior of polarograms was prominent in sulphuric acid medium.

Effect of sulphuric acid concentration

In order to establish the optimum concentration of the acid employed, studies were carried out with sulphuric acid of different concentrations. The optimum concentration of acid was found to be 0.3 M. The relevant results are shown in Fig. 4.

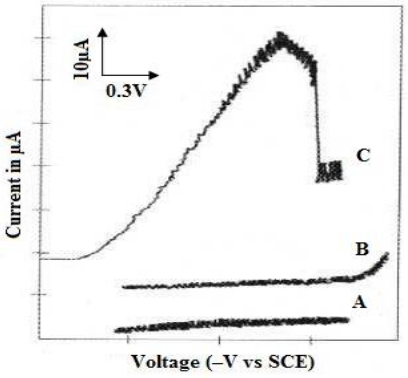


Fig. 2. Polarogram of CTR – W (VI) system.
[H_2SO_4] = 0.3 M; [KCl] = 0.1 M; Ep = -1.627 V vs. SCE
A) [CTR] = 3×10^{-6} M**: B)** [W (VI)] = 1.5×10^{-6} M and **C)** [CTR] = 3×10^{-6} M**;** [W (VI)] = 1.5×10^{-6} M; Starting potential = -0.920 V

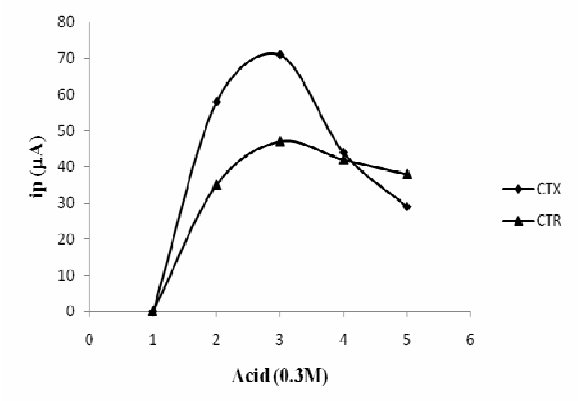


Fig. 3. Effect of different acids on peak current.
1: No acid, 2: HCl, 3: H_2SO_4, 4: HNO_3, 5: CH_3COOH.
[CTX] or [CTR] = 3×10^{-6} M; [W (VI)] = 3×10^{-6} M with CTX and 1.5×10^{-6} M with CTR; [KCl] =0.1 M; Ep = - 1.432 V vs. SCE with CTX and -1.627 V vs. SCE with CTR

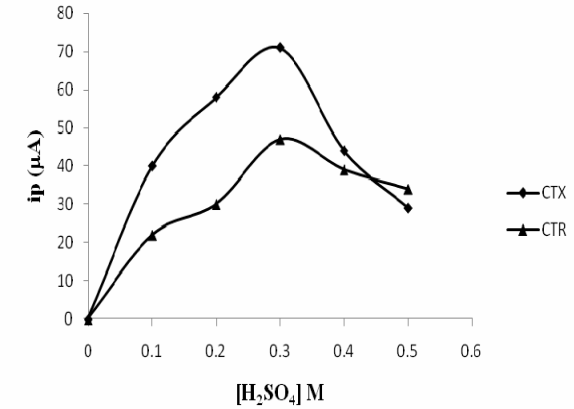


Fig. 4. Effect of sulphuric acid concentration on peak current.
[CTX] or [CTR] = 3×10^{-6} M; [W (VI)] = 3×10^{-6} M with CTX and 1.5×10^{-6} M with CTR; [KCl] = 0.1 M; Ep = -1.432 V vs. SCE with CTX and -1.627 V vs. SCE with CTR

Table 1. Effect of electrolyte on peak current.

Electrolyte (20 % by weight)	i_p (μA)	
	CTX	CTR
None	60	32
KCl	71	47
NH_4Cl	46	36

[CTX] or [CTR] = 3×10^{-6} M; [W(VI)] = 3×10^{-6} M with CTX and 1.5×10^{-6} M with CTR; [H_2SO_4] = 0.3 M

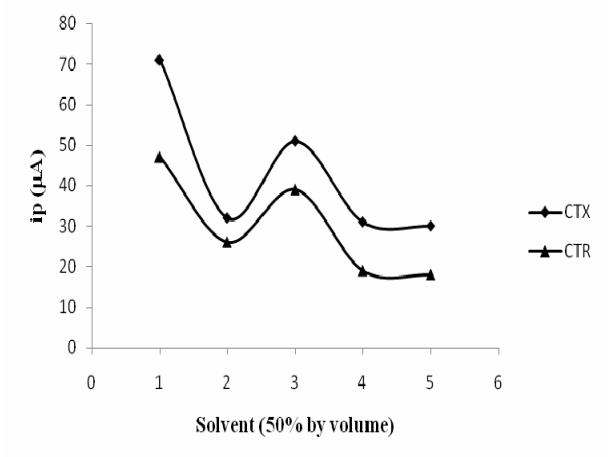


Fig. 5. Effect of solvent on peak current.
1: None, 2: Methanol, 3: Dimethylformamide, 4: Dioxane, 5: Acetonitrile.
[CTX] or [CTR] = 3×10^{-6} M**;** [W (VI)] = 3×10^{-6} M with CTX and 1.5×10^{-6} M with CTR**;** [H_2SO_4] = 0.3 M**;** [KCl] = 0.1 M

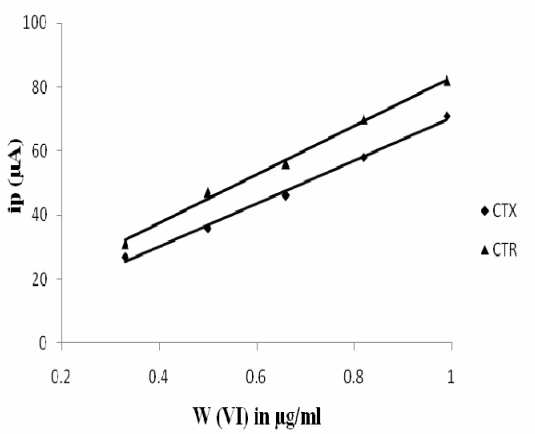


Fig. 6. Effect of metal ion concentration on peak current.
[Drug] = 3×10^{-6} M for CTX and 6×10^{-6} M for CTR; [H_2SO_4] = 0.3M; [KCl] = 0.1 M; Ep = -1.432 V vs. SCE for CTX -1.627 V vs. SCE for CTR

Effect of electrolyte

Studies relevant to the effect of supporting electrolyte reveal that 0.1 M KCl supporting electrolyte has given well defined peak (Table 1). Hence, further studies were carried out employing 0.1 M KCl as supporting electrolyte.

Studies on influence of organic solvent namely dimethylformamide, methanol, acetone, acetonitrile and dioxane (50% by volume) on the peak current reveal that aqueous medium was highly favorable for complex formation. The relevant data is shown in the Fig. 5.

Effect of metal ion

The effect of metal ion concentration on the peak current was studied and the calibration plot drawn between the peak current and concentration of metal ion is shown in the Fig. 6. The studies reveal that tungsten (VI) can be determined in the concentration range of 0.33 to 0.99 μg/ml.

Construction of calibration plot

Studies relating to the effect of varying concentration of drug reveal that CTX and CTR can be determined in the concentration ranges of 0.47 to 1.47 μg/ml and 1.23 to 3.69 μg/ml, respectively. The calibration plots constructed between the drug concentration and the peak current are shown in Fig. 7A and 7B, respectively for CTX and CTR. The pertaining regression parameters are shown in the Table 2.

It is also noticed from Fig. 8 that mercury column height did not affect the peak current.

Application to dosage forms

The proposed method was applied for determination of CTX or CTR in pharmaceutical formulations. The pertaining results are listed in the Table 3. The results are found to be satisfactory. The proposed method can be successfully applied for the microdetermination of CTX or CTR in pharmaceutical formulations.

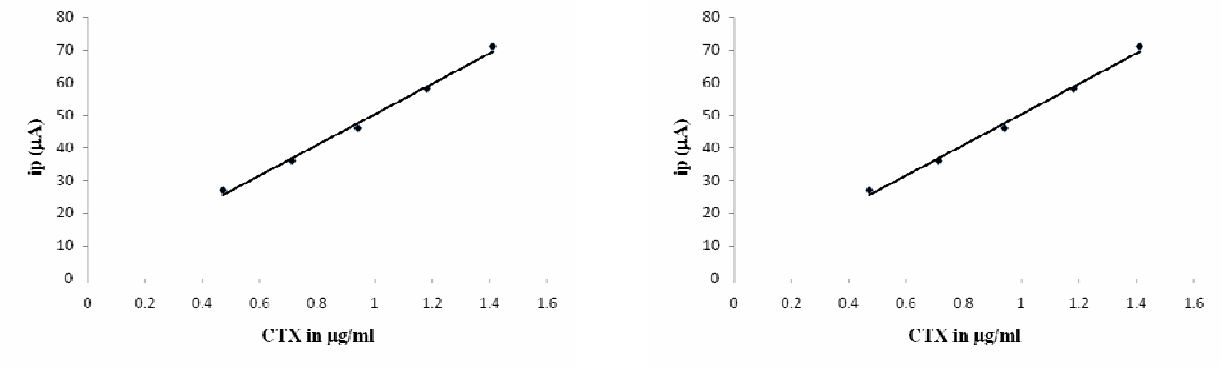


Fig. 7. Effect of drug concentration peak current.
A) [W (VI)] = 3×10^{-6} M; [H_2SO_4] = 0.3 M; [KCl] = 0.1 M; Ep = - 1.432 V vs. SCE for CTX.
B) [W (VI)] = 3×10^{-6} M; [H_2SO_4] = 0.3 M; [KCl] = 0.1 M; CTX; Ep = -1.627 V vs. SCE for CTR

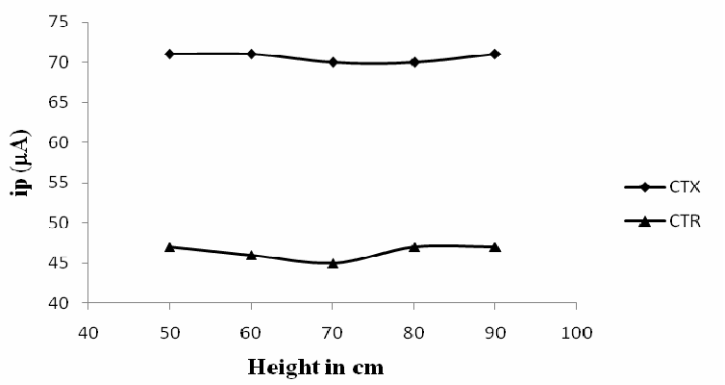


Fig. 8. Effect of mercury column height on peak current.
[CTX] or [CTR] = 3×10^{-6} M**;** [W (VI)] = 3×10^{-6} M with CTX and 1.5×10^{-6} M with CTR; [H_2SO_4] = 0.3 M; [KCl] = 0.1 M; Ep = -1.432 V vs. SCE with CTX and -1.627 V vs. SCE with CTR

Table 2. Regression parameters pertaining to proposed method**.**

System	To be determined	Regression equation	Correlation coefficient
CTX-W (VI)	CTX	y = 46.795x + 3.519	0.9968
	W (VI)	y = 67.06x + 3.63382	0.9964
CTR-W (VI)	CTR	y = 20.328x + 7.1513	0.9975
	W (VI)	y = 76.24x + 6.8781	0.9974

Table 3. Determination of CTX or CTR in pharmaceutical formulations.

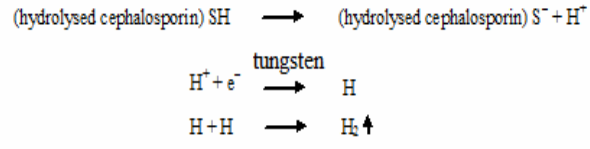
Sample	Labeled amount (mg/tab or cap)	Amount found (mg/tab or cap)	Recovery (%)*
Cefotaxime			
Desatax[a]	500	490	98
Cefantral[b]	125	130	104
Ceftrioxone			
Cefera[c]	250	257	102.8
Powercef[d]	125	123	98.4

*Average of six determinations, a and c = Plethico Pharmaceuticals Ltd., Indore, India and b and d = Lupin Laboratories Ltd., Mumbai, India

DISCUSSION

A careful observation of polarograms shown in Fig. 1 and 2 reveal that neither the drug nor the metal ion produced a current of appreciable magnitude whereas their mixture produced a wave at potentials –1.432 V vs. SCE for CTX and –1.627 V vs. SCE for CTR. Further it was observed that polarograms of the metal-cephalosporin system were well defined in the media of pH 6 and 7. Hence, a pH of 7 was considered to be optimum for the polarographic investigation. As there was no change in the behavior of the polarograms, the authors did not employ buffer solutions in their study. The data shown in the Fig. 3 reveal that the presence of acid (0.3 M sulphuric acid) is essential for the generation of the peak. In view of the results obtained in the further investigation, polarographic determination was carried out in the presence of 0.1M KCl supporting electrolyte in aqueous medium. As shown in Fig. 8, the mercury column height has no effect on the peak current. This fact suggests the catalytic nature of the polarographic waves. The behavior of the peak is highly reproducible for a period of about 2 h as revealed by the studies relating the effect of time.

The results indicate that a complex formed between the hydrolyzed drug and W (VI) is responsible for the catalytic peak current. The unhydrolyzed form of the cephalosporin do not produce catalytic wave. The hydrolysis of cephalosporins produces compounds containing -C-SH group. Such compounds are known to produce catalytic hydrogen waves due to the discharge of loosely bound proton attached to the sulpher atom which enhances in the presence of metal ions (18). In the present work, W (VI) was used to get the enhancement of the peak current. Further in the presence of solvents employed, there was a remarkable decrease in the peak current which suggests that the peak current depends on the changes in dielectric constant of the medium. Following scheme of reactions was therefore proposed to explain the catalytic hydrogen wave in the presence of W (VI).



A comparison to ascertain the novelty and features of proposed method

Al-Momani (5) described a flow injection analysis method for the determination of CTX and CTR. The method is based on the interaction between the hydrolysed cephalosporin and the Fe^{2+} complex of *o*-phenanthroline. Omar et al. (7) reported a kinetic spectrofluorimetric method for the determination of cephalosporins. They spectrofluorimetrically monitored the degradation of these drugs by employing initial rate and fixed time procedures to calculate the reaction rates. Salem and Askal (14) utilised colorimetric and atomic absorption spectrometric procedures for the determination of cephalosporins. The methods consist of reacting the drugs with Reinecke's salt in an acidic medium at a temperature of 25 ± 2 °C. The colorimetric procedure is based on the dissolving the drug-Reinecke's salt precipitate in acetone and measuring the absorbance of the solution. The atomic absorption spectrometric procedure is based on the direct or indirect quantitative determination of the chromium precipitate formed or the residual unreacted chromium in the filtrate. Majdi et al. (17) demonstrated the electrochemical behavior of CTR on a glassy carbon and carbon-nanotube-modified glassy carbon electrodes in phosphate buffer solutions. Nigam et al. (18) described an electrochemical method for the analysis of CTX using carbon paste electrode modified with Schiff base-Zn (II) complex. All methods mentioned involve either an additional complexing agent (5,14), expensive equipment (14), an extraction step (12), temperature sensitive (14) complicated (11) or time sensitive procedures (7,17,18), hence are not useful for the routine analysis in a common laboratory. Dogan et al. (19) described a differential pulse and square wave voltammetric procedures for the determination of CTX in the presence of glassy carbon electrode. The method (3,19) is less sensitive when compared to the one presented in this

article. However there is no simple polarographic method reported especially for analytical determination of CTX and CTR in commercial dosage forms. The results of the present study reveal that the proposed method utilizes a simple, sensitive, selective and economical polarographic procedure for the determination of CTX and CTR in pure form and in their pharmaceutical preparations.

El-Maali et al. (16) utilized square wave voltammetry and cyclic voltammetry to elucidate and confirm the formation of complex between the cephalosporin antibiotics and various metal ions. In their polarographic method for the determination of cephalosporins, Rama Devi et al. (20) reported that hydrolysed cephalexin produces catalytic wave in the presence of metal ion namely Co (II). Swarna Rani et al. (21) reported a polarographic catalytic method for the determination of cephalosporins. They inferred that hydrolysed cephalosporins namely cefachlor, cephalexine and cefuroxime produce catalytic hydrogen wave in the presence of W (VI). Similar observations are reported in this communication.

CONCLUSION

The proposed method is selective, linear (R >0.99), accurate (recovery = 98 to 104%) and precise (RSD <1.62%, calculated as the average of six determinations) in the respective linear concentration ranges. The method is successfully applied for the micro determination of CTX and CTR in the concentration range of 0.47 to 1.41 µg/ml and 1.23 to 3.69 µg/ml respectively in pharmaceutical samples. An additional advantage of the proposed method is that it can also be used for the analytical determination of W (VI).

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