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Electrochemical study and dependence of 'transition state' in Co(II) and Ni(II) complexes with some antibiotics and cephalothin

*F. Khan**
Electrochemical Laboratory, Department of Chemistry, Dr. H. S. Gour University, Sagar, India.
** faridkhan58@yahoo.com; farid.fk@rediffmail.com*

Abstract: Electrode kinetics and study of 'transition state' with applied potential in case of [M – antibiotics – cephalothin] system were reported at pH = 7.30 ± 0.01 at suitable supporting electrolyte at 25.0^{0}C. The M = Co or Ni and antibiotics were doxycycline, chlortetracycline, oxytetracycline, tetracycline, minocycline, amoxicillin and chloramphenicol used as primary ligands and cephalothin as secondary ligand. Kinetic parameters viz. transfer coefficient (a), degree of irreversibility (l), diffusion coefficient (D) and rate constant (k) were determined. The values of a and k varied from 0.41 to 0.59 and 2.60 X 10^{-3} cm s^{-1} to 9.67 X 10^{-3} cm s^{-1} in case of [Co – antibiotics – cephalothin] system. In case of [Ni – antibiotics – cephalothin], a and k varied from 0.41 to 0.58 and 2.34 X 10^{-3} cm s^{-1} to 9.19 X 10^{-3} cm s^{-1} respectively confirmed that transition state behaves between oxidant and reductant response to applied potential and it adjusts it self in such a way that the same is located midway between dropping mercury electrode and solution interface. The values of rate constant confirmed the quasireversible nature of electrode processes. The stability constants (logb) of complexes were also determined.

Keywords: electrode kinetics; antibiotics; cephalothin

Introduction

Electrode kinetics between dropping mercury electrode and electro active species in solution interface is important in polarography. Delahay and his coworkers [1] have studied the formation of electrical double layer and its structures in the vicinity of electrodes. Trachtenherg et al [2] studied the adsorption kinetics at electrodes. Koryta [3] studied the kinetics of discharge of Zn at the dropping mercury electrode. Matsuda [4] has studied the kinetics between oxidants and reductants at d.m.e. Gellings [5] has applied Lagrange's theorem in electrochemical kinetics. Khan [6] has reported the kinetic parameters of [Mn - antibiotics – cephaloglycin] system and relates them with transition state and rate constant. On the other hand, Ni and Co are essential elements which play important role in human body. Co as cynocobalamine contributes to the formation of red blood cells and is essential to the normal functioning of all cells, particularly those of bone marrow, nervous and gastro-intestinal systems [7]. Ni is a potent activator of several enzymes and probably plays role as a bioligant in iron absorption, regulation of prolactin and in the structure and function of membranes [8]. But the excess amount of these metals is toxic. Antibiotics and cephalothin are important drugs which are used against many diseases; therefore, the study of Co and Ni complexes with selected antibiotics and cephalothin has great importance. The present paper deals with the kinetic parameters and stability constants of Ni and Co complexes with doxycycline, chlortetracycline, oxytetracycline, tetracycline,

minocycline, amoxicillin and chloramphenicol as primary ligands and cephalothin as a secondary ligands polarographically for which no reference is traced out so far in the literature.

Experimental details

Apparatus and reagents

All the chemicals used were of A. R. grade and their solutions were prepared in doubly distilled water. Cobalt nitrate hexahydrate and Nickel chloride hexahydrate (both Fluka) were used for Co and Ni. The antibiotics were Fluka, Sigma and Aldrich products. The concentration of metal in the analyte was 0.5 mmol L^{-1} while the concentration of antibiotics varied from 0.5 mmol L^{-1} to 30.0 mmol L^{-1} at 0.025 mol L^{-1} and 0.05 mol L^{-1} of cephalothin. The (0.1 mol L^{-1} pyridine + 0.1 mol L^{-1} pyridinium hydrochloride) was used as supporting electrolyte for Co and in case of Ni, 1.00 mol L^{-1} KSCN was used. In both the cases, dilute solutions of NaOH and HNO_3 (BDH) were used to adjust the pH at 7.30 ± 0.01 at 25^{0}C.

Apparatus

Polarograms were recorded on a Polarographic analyzer (Elico, Hyderabad) with capillary of length 5.0 cm and diameter 0.04 mm at $m^{2/3}t^{1/6}$ = 2.40 $mg^{2/3}$ $s^{-1/2}$. A m pH meter (Systronics Model – 361) was used to measure the pH of the analyte at 7.30 ± 0.01. Potassium dihydrogen phosphate – sodium hydroxide buffer was added in the analyte to stabilize the pH of the analyte at 7.30.

Results and Discussion

The chelating ability of antibiotics and their uses in different diseases crate considerable interest in their metal complexes [9,10]. Doxycycline, chlortetracycline, oxytetracycline, tetracycline, minocycline and amoxicillin can make bond with Co and Ni as mentioned in Fig. 1. Co(II) and Ni(II) gave well defined quasireversible [11] waves in (0.1 mol L^{-1} pyridine and 0.1 mol L^{-1} pyridinium hydrochloride) and 1.0 mol L^{-1} KSCN at pH 7.20 to 8.50 at 25^{0}C respectively. The natures of complexes were also quasireversible. The metal and ligands were taken in the ratio of 1:40 in case of binary complexes and 1:40:40 in case of ternary complexes and current – voltage curves were determined at different pH values from 7.10 to 8.80, it has been observed that the maximum shifts of $E_{1/2}$ were obtained at pH range 7.30 to 8.50 but pH 7.30 was selected on account of studying the complexes at human blood pH [12]. De Vries and Kroon method [13] was used to determine the number of electrons involved in the reduction.

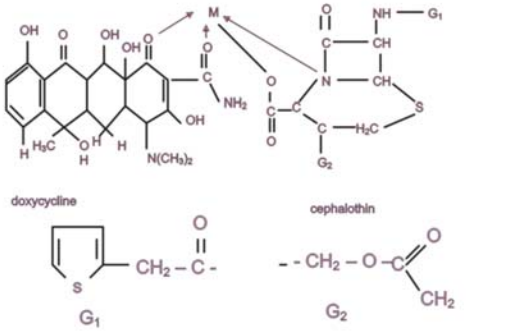


Figure 1. [M – doxycycline – cephradine] system, M = Co or Ni

The concentration of cephalothin varied from 5.0 mmol L^{-1} to 30.0 mmol L^{-1} at 0.5 mmol L^{-1} of metal i.e. Co and Ni in their analytes. The $E_{1/2,}$ values became more negative on increasing the concentration of cephalothin to the metal showed complex formation. Gellings method [14] was used to determine the $E_{1/2}^{reversible}$ from $E_{1/2}^{quasireversible}$ values of complexes by plotting – [E-RT/nF log(I_d-I)/I] vs I{where E, R, T, n, F, I_d and I are the potential on polarograms, solution constant, Kelvin temperature, number of electrons involved in the reduction, Faraday constant, diffusion current and current on the polarogram respectively}then Lingane method [15] confirmed the formation of 1:1 and 1:2 complexes with cephalothin with Co and Ni.

Lingane method is used to determine the composition and stability constants of binary complexes when overall complex formation is taken place. The number of groups (j) attached to the metal ion can be calculated by the following equation

$$d(E_{1/2})c / d \log C_x = -j\ 0.0591 / n \text{ at } 25^0C \quad (1)$$

Then the values of stability constant of complex MX_j is calculated by the equation (2)

$$(E_{1/2})s - (E_{1/2})c = DE_{1/2} = 0.0591/n \log \hat{a}_{MXj} + (0.0591/n)\log C_X \quad (2).$$

where the symbols have the usual meanings [15]. The values of stability constants of Co and Ni complexes were given in Table 1and 2 respectively.

[M – antibiotics] system

The concentration of antibiotics varied from 0.5 mmol L^{-1} to 30.0 mmol L^{-1} in each case at 0.50 mmol L^{-1} of Co or Ni it their respective analytes and polarograms were recorded. After determining the $E_{1/2}^{reversible}$ values of complexes from $E_{1/2}^{quasireversible}$ values by Gellings method [14], Deford and Hume method [16] was used to determine the 1:1, 1:2 and 1:3 complexes of Co and Ni with selected antibiotics. The stability constant values of complexes were given in Table 1 and Table 2 respectively.

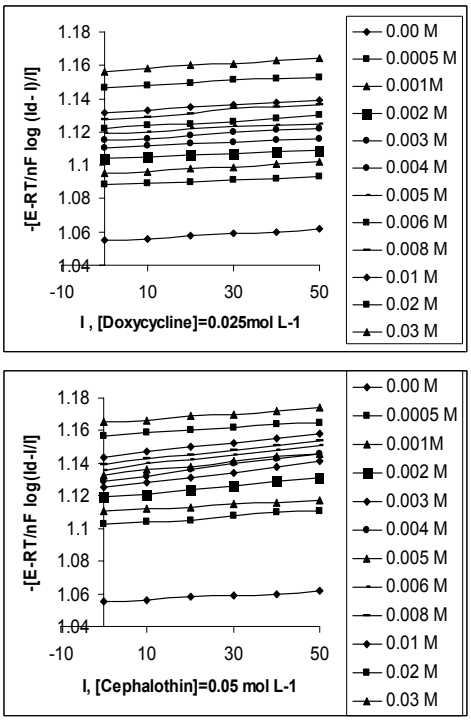


Figure 2. Plots between [E-RT/nF log $(I_d$-I)/I] for [Co - doxycycline – cephalothin] system.

Table 1. Stability constants values for [Co – antibiotics – cephalothin system, [Co (II)] = 0.50 mmol L^{-1}, pH = 7.30 ± 0.01, supporting electrolyte = (0.1 mol L^{-1} pyridine + 0.1 mol L^{-1} pyridinium hydrochloride), T = 25.0 ^{0}C

Ligands	**log β_{01}**	**log β_{02}**	**log β_{10}**	**log β_{20}**	**log β_{30}**	**log β_{11}**	**log β_{12}**	**log β_{21}**
Doxycycline	-	-	3.33	5.00	7.31	4.31	7.38	7.83
Chlortetracycline	-	-	4.46	-	9.63	4.51	7.72	9.69
Oxytetracycline	-	-	4.68	7.93	9.94	4.75	8.13	9.73
Tetracycline	-	-	4.88	8.13	9.98	5.12	8.33	10.02
Minocycline	-	-	4.90	8.20	10.02	5.23	8.46	10.14
Amoxicillin	-	-	4.97	8.31	10.13	5.53	8.57	10.19
Chloramphenicol	-	-	-	8.38	10.21	5.53	-	10.31
Cephaloglycin	1.90	2.81	-	-	-	-	-	-

Table 2. Stability constants of [Ni – antibiotics – cephalothin] system. [Ni(II)] = 0.50 mmol L^{-1}, supporting electrolyte = 1.0 mol L^{-1} KSCN, pH = 7.30 ± 0.01, T = 25.0 ^{0}C values by Gellings method [14], Deford and Hume method [16] was used to determine the 1:1, 1:2 and 1:3 complexes of Co and Ni with selected antibiotics. The stability constant values of complexes were given in Table 1 and Table 2 respectively. [M-antibiotics – cephalothin] system

Ligands	log β_{01}	log β_{02}	log β_{10}	log β_{20}	log β_{30}	log β_{11}	log β_{12}	log β_{21}
Doxycycline	-	-	3.42	5.10	7.46	4.41	7.46	7.90
Chlortetracycline	-	-	4.53	5.21	9.73	4.59	7.78	-
Oxytetracycline	-	-	4.73	8.00	10.00	4.81	8.24	9.75
Tetracycline	-	-	4.92	8.23	10.06	5.22	8.43	10.10
Minocycline	-	-	5.00	8.35	10.12	5.36	-	10.21
Amoxicillin	-	-	5.13	-	10.20	5.61	8.62	10.31
Chloramphenicol	-	-	5.23	8.45	10.36	5.67	8.73	10.45
Cephalothin	2.00	2.93	-	-	-	-	-	-

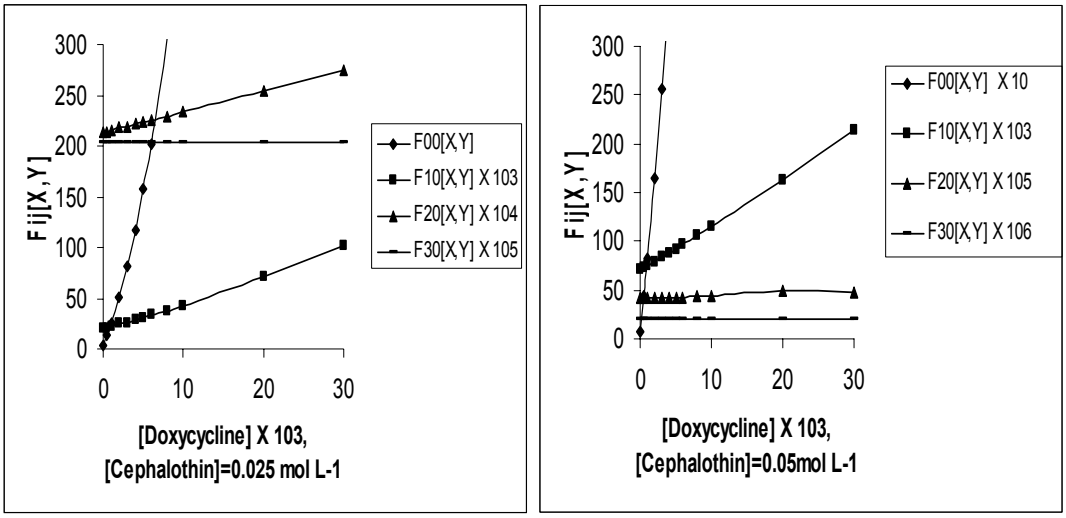


Figure 3. [Co - doxycycline – cephalothin] system.

In this system, the concentration of antibiotics varied from 0.5mmol L^{-1} to 30.0 mmol L^{-1} at 0.50 mmol L^{-1} of metal at 0.025 mol $L^{-1}$and 0.050 mol L^{-1} of cephalothin and current – voltage curves were determined at pH 7.30 ± 0.01 at 25.0 ^{0}C. The $E_{1/2}$ values increased with the addition of [cephalothin] to [M – antibiotics] showed ternary complex formation. After determining the $E_{1/2}^{reversible}$ values from $E_{1/2}^{quasireversible}$ values of complexes by Gellings method, Schaap and McMaster method [17] was used to deter-

Table 3. Polarographic characteristics and Fij [X,Y] values for [Co – doxycycline - cephalothin] system, supporting electrolyte = (0.1 mol L^{-1} pyridine + 0.1mol L^{-1} pyridinium hydrochloride), pH=7.30 ± 0.01 , T = 25.0 ^{0}C [cephalothin] = 0.025 mol L^{-1} [cephalothin] = 0.05 mol L^{-}

[Doxycy.] x 10^3	log Im / Ic	$E_{1/2}{}^r$ -V Vs SCE	F_{00}[X,Y]	F_{10}[X,Y] X 10^3	F_{20}[X,Y] X 10^4	F_{30}[X,Y] X 10^5	log Im /Ic	$E_{1/2}{}^r$ -V Vs SCE	F_{00}[X,Y] X 10	F_{10}[X,Y] X 10^3	F_{20}[X,Y] X 10^5	F_{30}[X,Y] X 10^5
0.00	-	1.0550	-	-	-	-	-	1.0550	-	-	-	-
0.50	0.00694	1.0885	13.73	20.70	214.22	204.10	0.01401	1.1025	43.00	72.85	41.74	20.39
1.00	0.01401	1.0955	25.16	21.78	215.24	204.01	0.02118	1.1105	81.53	74.95	41.84	20.42
2.00	0.02118	1.1105	82.01	26.21	219.32	204.00	0.02840	1.1195	164.93	79.17	42.04	20.41
3.00	0.02118	1.1105	82.01	26.21	219.32	204.00	0.03590	1.1250	256.91	83.44	42.25	20.41
4.00	0.0284	1.1150	117.32	28.48	221.35	203.90	0.03590	1.1290	357.54	87.75	42.45	20.40
5.00	0.0284	1.1190	157.38	30.80	223.41	204.20	0.04340	1.1325	467.08	92.10	42.66	20.42
6.00	0.0359	1.1220	202.33	33.15	225.44	204.00	0.04340	1.1355	585.57	96.48	42.86	20.43
8.00	0.0359	1.1275	307.32	37.99	229.52	204.10	0.05110	1.1395	843.10	105.38	43.27	20.40
10.00	0.0434	1.1315	433.28	42.99	233.59	203.90	0.05890	1.1435	1151.09	114.45	43.68	20.41
20.00	0.0511	1.1465	1411.68	70.41	253.92	204.10	0.05890	1.1570	3250.94	162.21	48.72	20.42
30.00	0.0589	1.1560	3062.45	101.96	274.46	204.20	0.11055	1.1655	6428.35	214.05	47.76	20.41

log A = 0.53 , log B = 4.29, log C = 6.32 , log D = 7.31 log A = 0.81 , log B = 4.84 , log C = 6.61 , log D = 7.31

mine the 1:1:1, 1:1:2 and 1:2:1 complexes of Co and Ni with doxycycline, chlortetracycline, oxytetracycline, tetracycline, minocycline, amoxicillin and chloramphenicol with cephalothin. The formation of ternary complexes is given by the following equation

$$M + iX + jY = MXiYj \quad \text{———————(3)}$$

where i and j are the stoichiometric numbers and X and Y are two different ligands species(X is primary ligands i.e. antibiotics and Y is secondary ligand i.e. cephalothin). The Deford and Hume type F_o[X] function [16] may be extended to give a new function F_{oo}[X,Y] expressed in the form

$$F_{oo}[X,Y] = S\, b_{MXiYj}[X]^i[Y]^j \quad \text{———(4)}$$

where activity coefficients have been ignored. As before the F_{oo}[X,Y] function is given by

$$F_{oo}[X,Y] = \text{antilog}\,[0.434nF\,DE_{1/2}/RT] + \log I_s/I_c \quad \text{———(5)}$$

For the simple case where a maximum of the bound ligand of type X and Y occurs, factorization of the F_{oo}[X,Y] function leads to

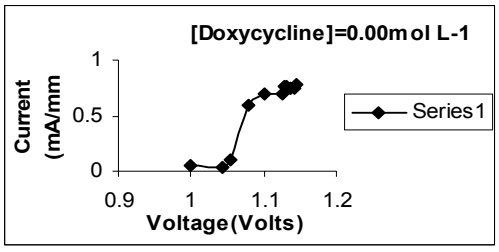
$$F_{oo}[X,Y] = \{b_{oo} + b_{01}[Y] + b_{02}[Y]^2\}[X]^o + \{b_{10} + b_{11}[Y] + b_{12}[Y]^2\}[X] + \{b_{20} + b_{21}[Y]\}[X]^2 + \{b_{30}\}[X]^3 \quad \text{———————(6)}$$

Here [Y] is regarded as maintained constant while [X] is varied. From the equation (6), the values of $b_{11,}$ b_{12} and b_{21} may be calculated. The values of stability constant of Co and Ni complexes were given in Table 1 and Table 2 respectively. The plots between $-[E - RT/nF \log(i_d-i)/i]$ vs i for [Co – doxycycline – cephalothin] system were given in Fig. 2.The data and plots of F_{ij}[X,Y] vs

[X] for (Co – doxycycline – cephalothin) system {where X and Y are doxycycline and cephalothin and i & j are their stoichiometric numbers respectively} were given in Table 3 and Fig. 3 respectively. For the comparison of the values of stability constant of binary complexes to the ternary complexes, the mixing constant (log K_m) values of complexes were calculated by the following equation [17]

$$\log K_m = \log b_{11} - \tfrac{1}{2} [\log b_{20} + \log b_{02}]$$

The values of log K_m were 0.40, -0.62, -0.35, -0.27, -0.03 and –0.06 for [Co-doxycycline – cephalothin], [Co – oxytetracycline – cephalothin], [Co – tetracycline – cephalothin], [Co – minocycline – cephalothin], [Co – amoxicillin – cephalothin] and [Co – chloramphenicol – cephalothin] and 0.395, 0.520, -0.655, -0.360, -0.280, and -0.020 for [Ni-doxycycline-cephalothin], [Ni-chlortetracycline-cephalothin], [Ni-oxytetracycline-cephalothin], [Ni-tetracycline-cephalothin], [Ni-minocycline-cephalothin] and [Ni-chloramphenicol-cephalothin] respectively. The positive values of log K_m showed that ternary complexes are more stable than their binary complexes while the negative values showed that binary complexes are more stable than ternary complexes.



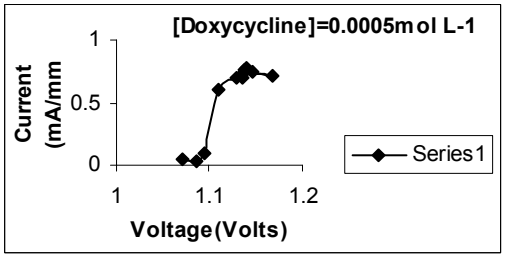
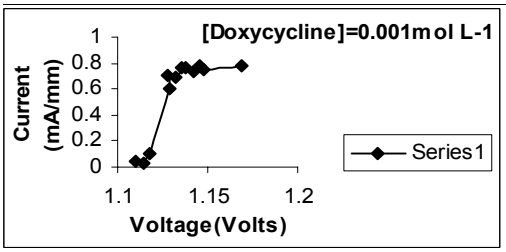
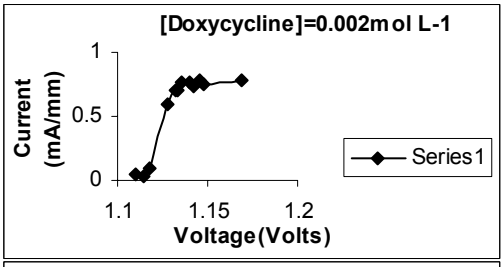
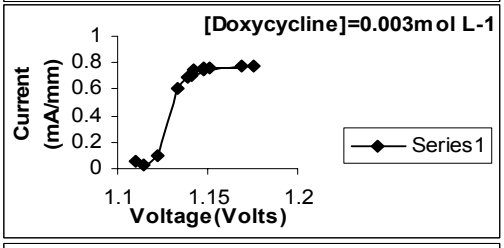


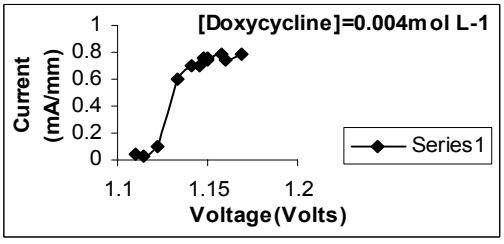
Table 4. Kinetic parameters of [Co - doxycycline – cephalothin] system, Co(II) = 0.5 mmol L^{-1}, pH = 7.30 ± 0.01, supporting electrolyte.= (0.1 mol L^{-1} pyridine + 0.1 mol L^{-1}pyridinium hydrochloride), T = 25.0 ^{0}C[cephalothin] = 0.025 mol L^- [cephalothin] = 0.05 mol L^{-1}

|Doxycy. \] x 10^3	$E_{1/2}^{qr.}$ V vs SCE	–Slope mV	α	λ sec$^{-1/2}$	D 10^3 cm^2s^{-1}	x k 10^3 $cm\,s^{-1}$	x $E_{1/2}^{qr.}$ vs SCE	–V Slope	α	λ Sec$^{-1/2}$	D 10^3 cm^2s^{-1}	x K x 10^3 $cm\,s^{-1}$
0.00	1.0700	35	0.44	2.14	4.15	8.90	1.0700	35	0.44	2.14	8.90	5.08
0.50	1.1000	36	0.54	1.51	4.08	6.20	1.1200	37	0.54	1.51	4.08	6.20
1.00	1.1150	37	0.42	2.40	4.01	9.66	1.1250	36	0.43	1.70	3.95	6.73
2.00	1.1200	36	0.40	2.40	3.95	9.48	1.1350	36	0.42	1.51	3.88	5.90
3.00	1.1250	36	0.43	1.70	3.39	6.73	1.1400	36	0.51	1.07	3.82	4.10
4.00	1.1300	38	0.42	1.51	3.88	5.90	1.1450	36	0.46	1.35	3.82	5.17
5.00	1.1350	38	0.47	1.70	3.88	6.62	1.1500	37	0.48	1.35	3.75	5.08
6.00	1.1350	37	0.44	1.70	3.82	6.50	1.1550	37	0.57	1.07	3.75	4.03
8.00	1.1400	37	0.48	1.51	3.82	5.80	1.1700	37	0.52	1.07	3.69	3.96
10.00	1.1500	37	0.43	1.07	3.75	4.03	1.1750	37	0.43	1.20	3.62	4.36
20.00	1.1600	36	0.43	1.51	3.69	5.60	1.1750	36	0.42	1.20	3.62	4.37
30.00	1.1650	37	0.42	1.20	3.63	4.36	1.1800	36	0.55	0.87	3.55	3.10









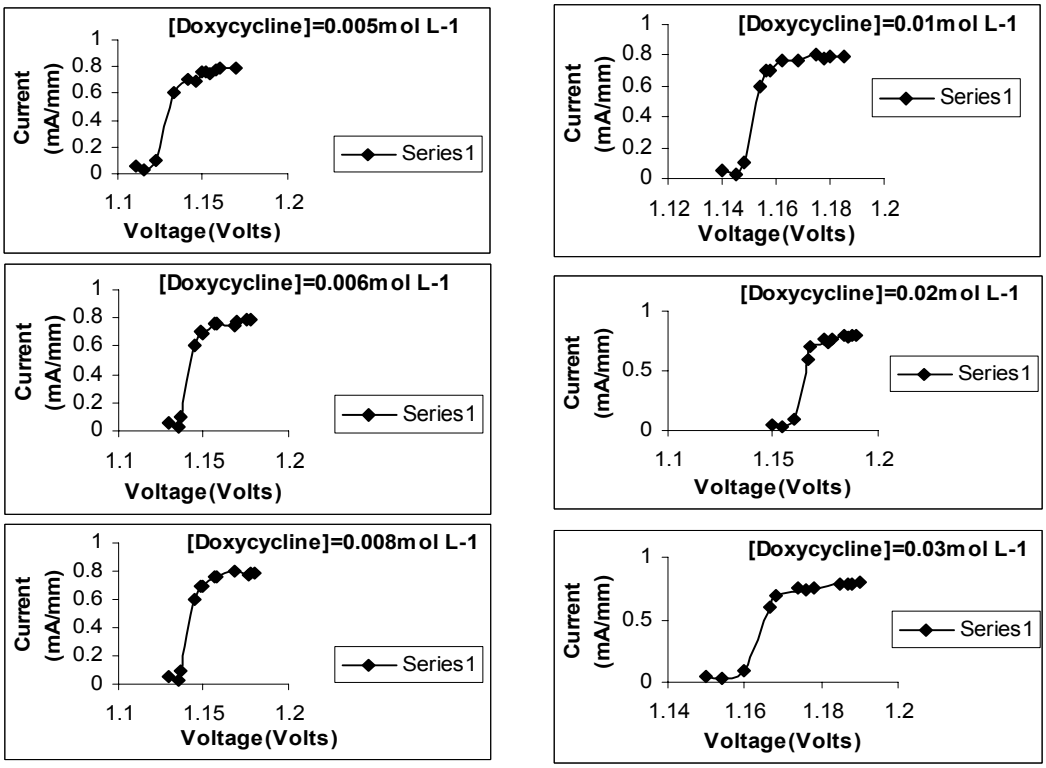
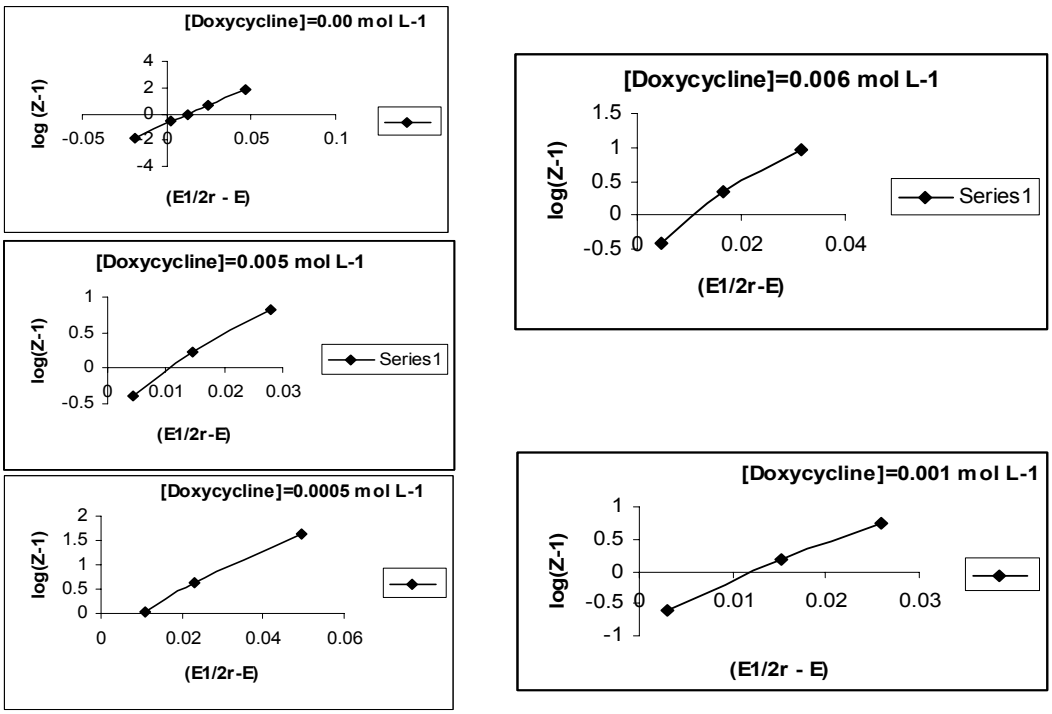


Figure 4. Polarograms of [Co - doxycycline - cephalothin] system, [cephalothin] = 0.025M



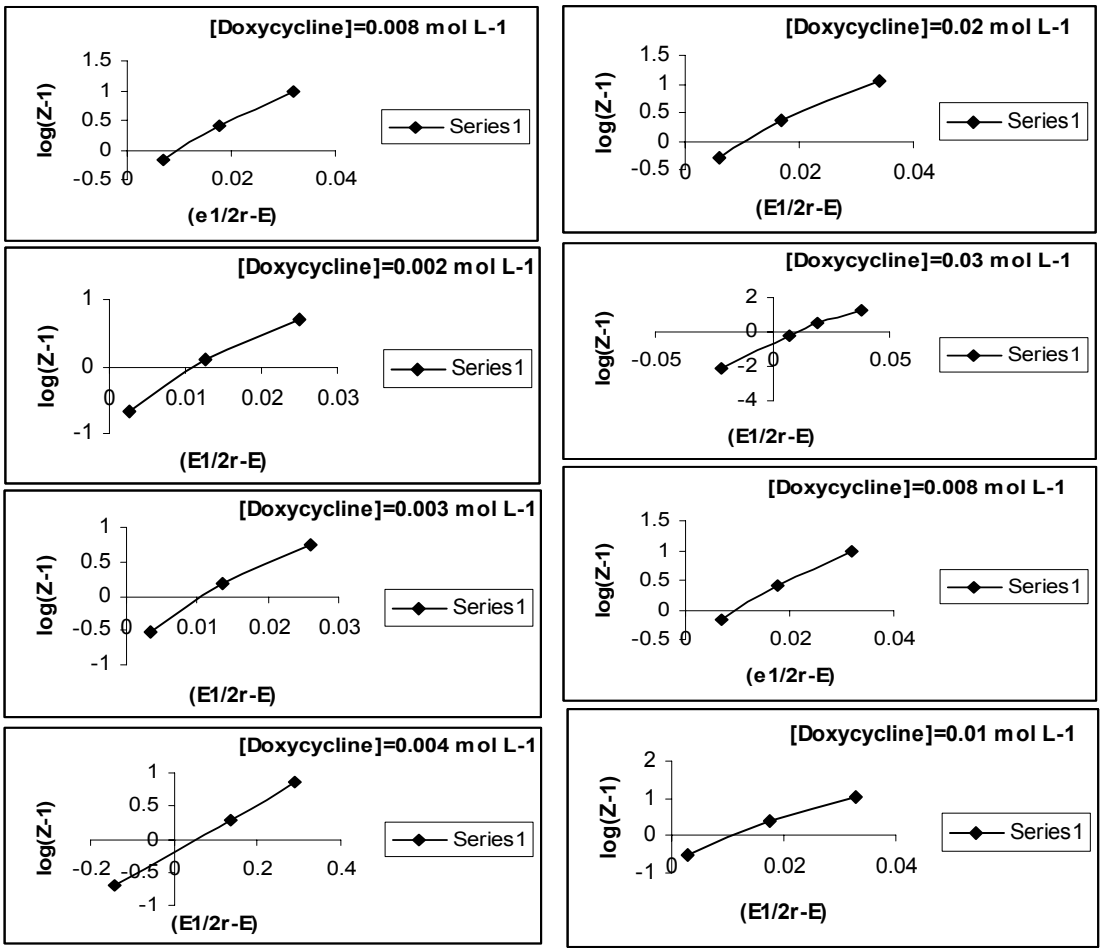
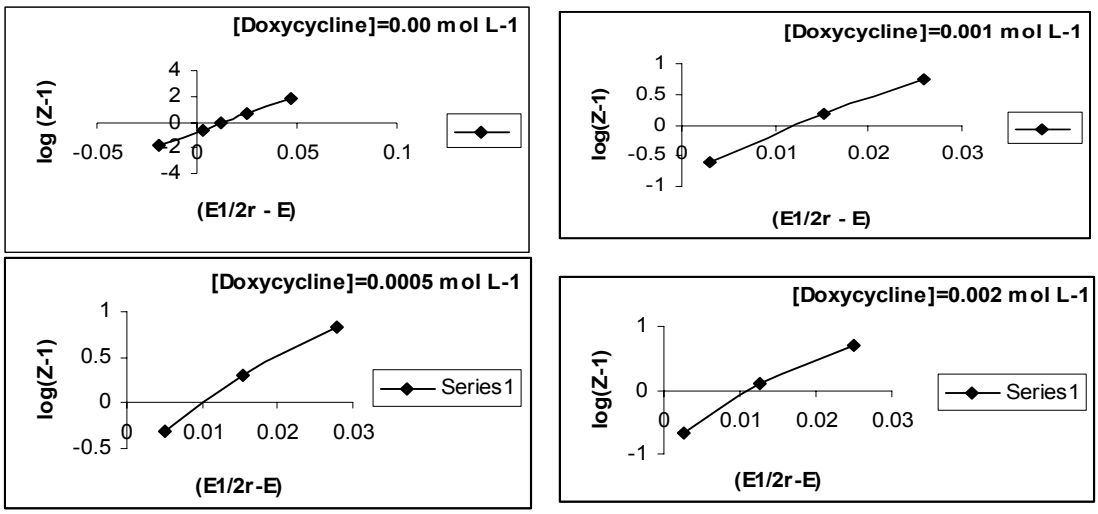


Figure 5(a). [Co -doxycycline – cephalothin] system, [cephalothin] = 0.025 M



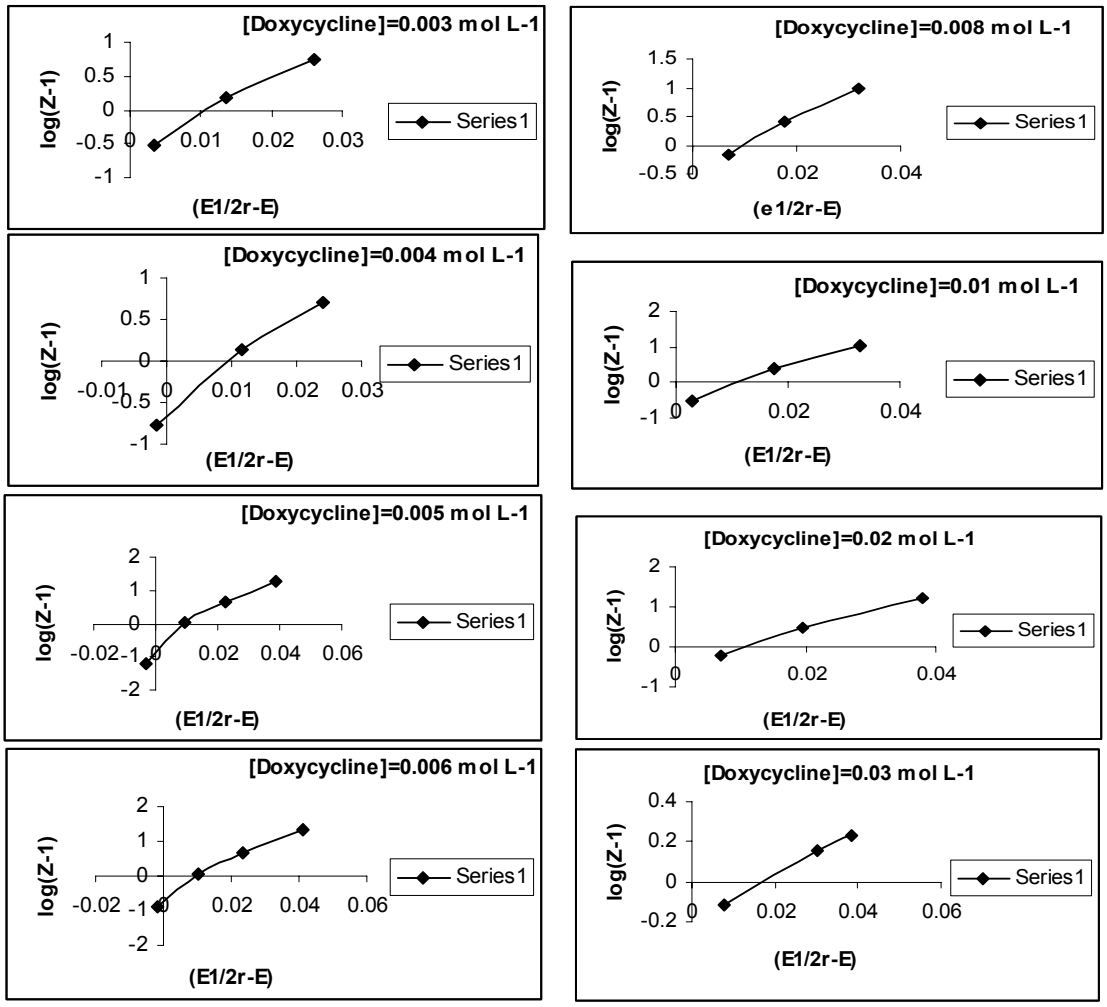


Figure 5(b). [Co -doxycycline – cephalothin] system, [cephalothin] = 0.05 M
1:1:1 complex in [Co - chlortetracycline – cephalothin] and 1:2 complex in [Ni-amoxicillin – cephalothin] systems were not formed; therefore, the log K_m values were not calculated for these systems.

The trend of stability constant of complexes was doxycycline < chlortetracycline < oxytetracycline < tetracycline < minocycline < amoxicillin < chloramphenicol. All the tetracycline including doxycycline and minocycline are having the same structures except in the difference in R_1 and R_2 positions [18]. They all made bond with oxygen of 1, C and oxygen of amide ($CONH_2$) group at 2, C atom with Co and Ni. The doxycycline formed the complexes of minimum stability with metal ions. The lesser stability of chlortetracycline complexes than that of oxytetracycline complexes is due to the presence of more electrons withdrawing Cl at R_1 in the former in place of H in the latter [19]. In case of tetracycline, H is present both at R_1 and R_2 therefore; there is the least electronic disturbance in tetracycline in comparison to other tetracycline complexes. This order supported the order of their pK values also [20]. The stability of minocycline complexes is lesser than that of amoxicillin complexes is owing to the presence of 6 membered ring with two double bonds in former while the later made 5 membered

saturated ring together with b - lactam ring with metal ions. The complex with saturated 5 membered ring is more stable than complex with unsaturated 6 membered ring [21]. The chloramphenicol made complexes of the maximum stability is due to the fact that this complex system has maximum shift of $E_{1/2}$ that might be the result of the formation of one 4 and one 5 membered ring with Co and Ni [22]. The polarograms of [Co – doxycycline – cephalothin] system at [cephalothin] = 0.025 M were given in Fig. 4. In the case of cephalothin, O of the COOH and N of the b-lactam ring may take part in bond formation with Co or Ni.

Electrode Kinetics

Consider the electrochemical reaction at d.m.e

$$O(s) + e(d.m.e.) = R(s) \quad \underset{k_{ox}}{\overset{k_{red}}{\rightleftharpoons}} \quad \text{(i)}$$

Where O(s) is the metal complex species. The current flowing is given by the following equations

$$i_a = - FAk_{ox.} [R]_o \qquad \text{(2)}$$

and

$$I_c = - FAk_{red.} [O]o \qquad \text{(3)}$$

where the terms have the usual meanings[22]. To establish how the rate constant $k_{Red.}$ and k_{Ox} are affected by applied potential, transition state theory is used in which we consider that the reaction is precede via an energy barrier. In electrochemical reactions, free energy is a function of the applied potential which derive electro active species from solution interface to the transition state and form reductants after gaining electrons from d.m.e. Using these concepts, the corresponding rate constants are given by the following equations

$$k_{Red.} = Ze^{[(-DG_{Red}./RT)(-aFV)/RT]} \quad (4).$$

and

$$k_{Ox.} = Ze^{[(-DG_{Ox}./RT)(1-a)FV/RT]} \quad (5).$$

But at anode, the electrode reactions are almost negligible because the concentration of depolarizer is lesser than 1.0 mM [23- 24]. The parameter a is called the transfer coefficient which has a value of 0.50. Physically, it provides an inside into the way the 'transition state' is influenced by the applied potential. A value of 0.5 means that the 'transition state' is a function of applied potential. It also defines the symmetric behaviour of energy barrier. A small variation in potential not only affects the rate of the electrochemical reaction but also rate constant greatly. The values of kinetic parameters were determined by Tamamushi and Tanaka methods [23, 24] by plotting $(E_{1/2}^{r}-E)$ vs log (Z-1) for metals complexes by equation (7).

$$\ln (I_d - I / I) = x + \log e Z \qquad (6)$$

$$\ln (Z - 1) = \log_e 1.13 / l t^{1/2} - (1 - a) x \qquad (7)$$

Where $x = nF / RT (E- E_{1/2}^{r})$. The values of Z can be calculated by the following equation [23]

$$Z = \text{antilog } [nF / RT (E_{1/2}^{r} - E)] + \log (I_d - I) / I \quad (8)$$

then the value of rate constant k can be calculated by

$$k = l D^{1/2} \qquad (9)$$

The plots between $(E_{1/2}^{r} – E)$ vs log (Z-1) for [Co– doxycycline – cephalothin] were given in Fig. 5(a) and 5(b) respectively while the values of kinetic parameters were given in Table 4. The values of a and k were varied from 0.41 to 0.59 and 2.60 X 10^{-3} cm s^{-1} to 9.67 X 10^{-3} cm s^{-1} in case of [Co – antibiotics – cephalothin] system while in case of [Ni – antibiotics – cephalothin], a and k were varied from 0.41 to 0.58 and 2.34 X 10^{-3} cm s^{-1} to 9.19 X 10^{-3} cm s^{-1} confirmed that transition state behaves between oxidant and reductant response to applied potential and energy barrier adjusts it self in such a way that it locates always midway between dropping mercury electrode and solution interface. The values of rate constant were of the order of 10^{-3} cms^{-1} confirmed the quasireversible nature of electrode processes. A small variation in rate constant (k) not only affects the rate of the electrochemical reaction but also the rate constant greatly.

Conclusions

The aim of the present study is to study the complex formation of Co and Ni with selected antibiotics and cephalothin and also to determine the stability constants and kinetic parameters of complexes. On the basis of these parameters, one can confirm the exact nature of electrode processes between DME and solution interface. On the basis of stability constants values of complexes, we can get an idea about the possibilities whether these drugs or their complexes could be used against metal toxicity or not [25]. The values of transfer coefficient (a) showed that transition state behaves between oxidant and reductant response to applied potential and energy barrier locates always midway between d.m.e. and solution interface. The values of rate constant (k) confirmed the quasireversible nature of electrode processes. The values of stability constant (logb) of complexes varied from 1.90 to 10.31 in case of Co and 2.00 to 10.45 in case of Ni showed that these drugs or their metal complexes could be used against these metals toxicity [25]. The aim of drug therapy is to excrete a toxic metal complex but we have also to consider the complex formation (if any) of other metals present in human body with our drugs. The drug should not be toxic can be excreted easily from body.

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