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DETERMINATION OF CONSECUTIVE STABILITY CONSTANT OF BINARY COMPLEX OF Mn (II) WITH ANTIBIOTIC TETRACYCLINE HYDROCHLORIDE BY POLAROGRAPHIC METHOD

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ABSTRACT

Polarographic measurements have been used to determine the consecutive stability constants of binary complex of Mn (II) with antibiotic tetracycline hydrochloride (TC) at temperature 25 ± 2°C, in presence of 1.0 M KCl as supporting electrolyte and 0.1% gelatin as a maxima suppressor in an inert nitrogen atmosphere. Polarograms of Mn (II) - TC system at pH 7.3 ± 0.1 in aqueous medium has been used to study the complex stoichiometry. The DeFord-Hume's method was applied for the analysis of polarographic waves arising from ion transfer reactions at DME interface and the successive stability constants of this system have been evaluated. The cathodic shift in $E_{½}$ coupled with decrease in diffusion current with increasing ligand concentration is observed during the experimental work.

Key words: D.C. Polarography, Dropping mercury electrode (DME), Mn (II) complexes, Tetracycline hydrochloride (TC)

INTRODUCTION

Many analytical techniques have been used to study metal ligand complexes, but polarographic studies has not been explored widely. The polarographic study of metal complexes with various ligands has been recognized as a specialized field for the investigation of their stability data. Metal-drug complexes have been a subject of interest as it possesses great importance in biological systems. Among the different drug groups, antibiotics are extensively used to inhibit the growth of microorganism in humans. The tetracyclines are drugs of an antibiotic group, which are effective on both gram-negative, and gram-positive bacteria, which contain a hydronaftacene structure with four rings of six members' fusion[1, 2]. It possesses a great tendency to form complexes with a number of

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chemical species, due to its phenolic β–diketone group, dicarbonyl system and amino-alcohol group, which are the chromophoric groups shown in Fig. 1. It forms complexes most readily with Fe^{+2}, Fe^{+3}, Cu^{+2}, Ni^{+2}, Co^{+2}, Zn^{+2}, Mn^{+2}, Mg^{+2}, Ca^{+2}, Be^{+2} and Al^{+3} among metal ions. Additionally, ternary complexes of a tetracycline+metal+ligand are possible[3, 4]. As tetracycline hydrochloride is extensively used to treat several bacterial infections, study of complex species of this drug with biologically important elements have immense importance. Using simpler polarographic techniques as an electro analytical technique, the electrochemistry of such complex species could be investigated. In the present research work, the consecutive stability constants of Mn (II) complex with tetracycline hydrochloride in KCl media at pH 7.3 ± 0.1 have been determined at Dropping mercury electrode (DME) used in conventional DC polarographic techniques. Deford and Hume method has been used to evaluate consecutive stability constants of this binary system[5].

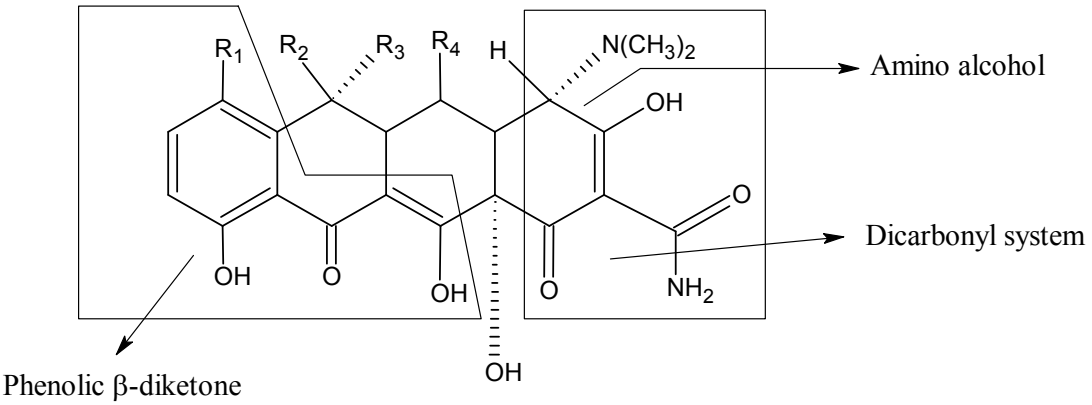

Fig. 1: Metal coordination and chromophoric group of tetracycline

EXPERIMENTAL

Materials

Tetracycline hydrochloride (TC) was supplied by Manish Pharma (Viramgam, India). Other chemicals, $MnSO_4.H_2O$, KCl and gelatin were of analytical reagent grade purchased from Ranbaxy. The concentration of metal ion solution and KCl solution in the test solutions were 0.5 mM and 1.0 M, respectively. Double distilled water was used throughout the experiments. All polarograms were recorded using manual DC polarograph (Elico CL 357) and recorded on paper recorder (Elicord LR 101P). The capillary characteristics were $m^{2/3}t^{1/6}$ = 1.8393 mg.s at 60 cm effective height of mercury column. During the experimental measurements, each set was maintained at pH 7.3 ± 0.1 using pH

meter Elico LI 610 and at temperature 25 ± 2°C. The data for test solutions were recorded after passing pure N_2 gas in order to reduce interferences. Concentration of tetracycline hydrochloride ranges from 0 to 100 mM for experiments. 0.1% Gelatin solution was used as maxima suppressor to remove unwanted humps in polarograms.

Method

Polarographic methods to determine stability constants consist of measurements of change in the half wave potentials, $\Delta E_{1/2,}$ in solutions of various ligand concentration in presence of metal ion solution relative to the half wave potential for the same metal ion solution in the absence of ligand[8]. Pure N_2 gas was passed through the solution to remove dissolved oxygen because it can cause interference during the experiments. Each set contained 10 mL 0.5 mM $MnSO_4$ solution, 5 mL 0.1% gelatin solution, 10 mL 1 M KCl solution and respective concentration of ligand solution. The effective volume of the test solution was maintained 50 mL each time. Tetracycline hydrochloride ligand solution in increasing order of 10 mM ranging from 0 to 100 mM was added, and voltage - current data were recorded. The formation constants of this system were calculated with the help of Deford and Hume method[5]. Based upon $E_{1/2}$ value and current data; $\Delta E_{1/2,}$ I_m, I_c, log I_m/I_c values were found and summarized in Table 1. The data in the last four columns of Table 1 i.e $F_0[X]$, $F_1[X]$, $F_2[X]$ and $F_3[X]$ were calculated graphically using plot of $F_0[X]$ vs. [X], $F_1[X]$ vs. [X], $F_2[X]$ vs. [X] and $F_3[X]$ vs. [X] (Figs. 4a, 4b, 4c and 4d). Further, for different conclusion, plot of E vs. log (i/i_d-i) (Fig. 2), plot of i_d vs. $(h)^{1/2}$ (Fig. 3) and plot of log $F_0[X]$ vs. log [X] (Fig. 5) were plotted.

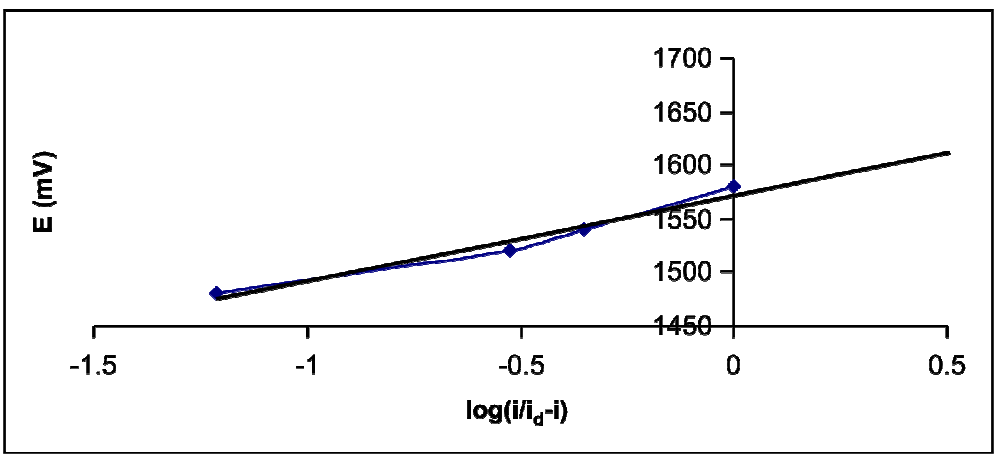

Fig. 2: Plot of E v/s log (i/i_d-i)

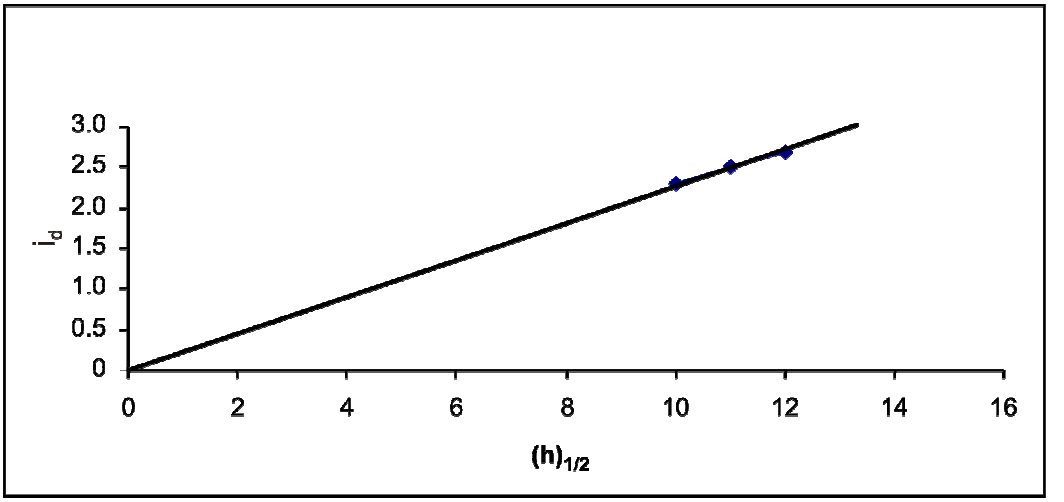

Fig. 3: Plot of i_d v/s $(h)^{1/2}$

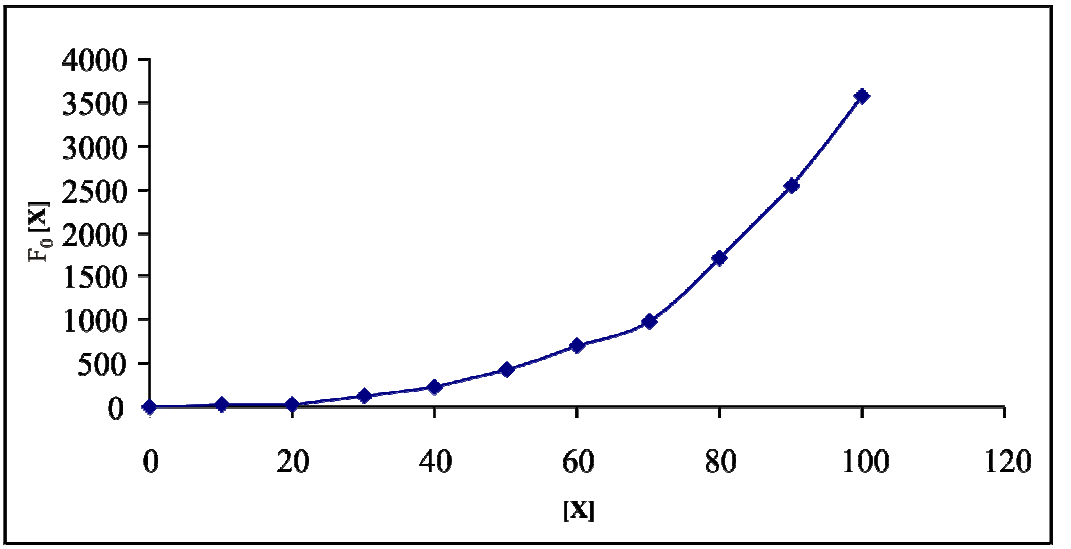

Fig. 4(a): $F_0[X]$ v/s [X] where $\beta_0 = 1.0$

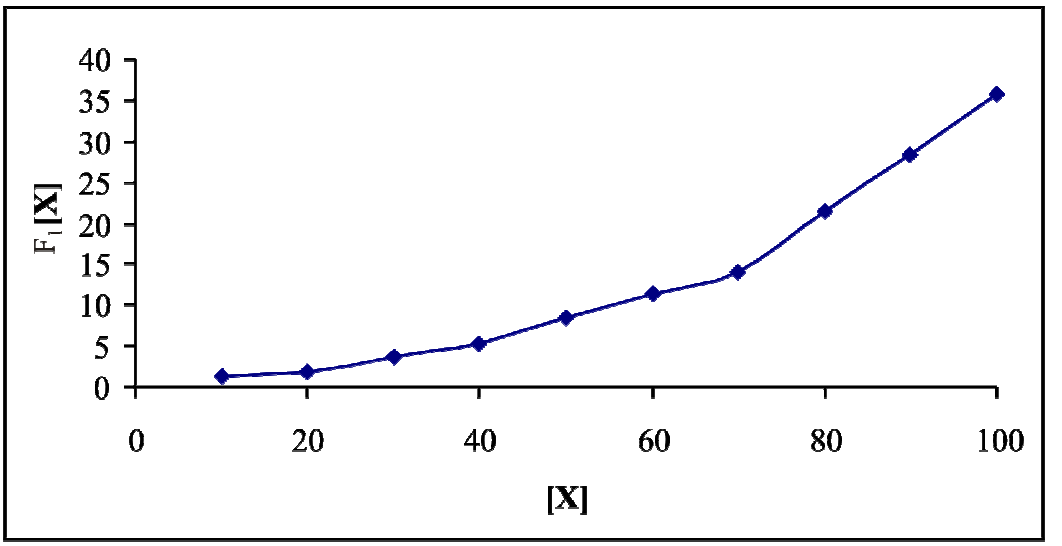

Fig. 4(b): $F_1[X]$ v/s [X] where $\beta_1 = 2.1267$

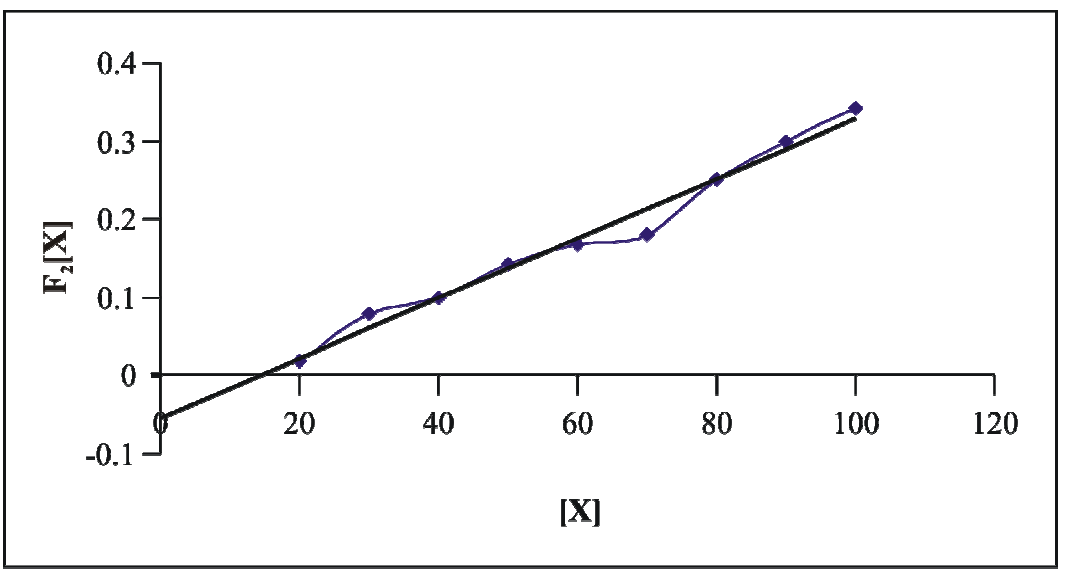

Fig. 4(c): $F_2[X]$ v/s [X] where $\beta_2 = 0.035$

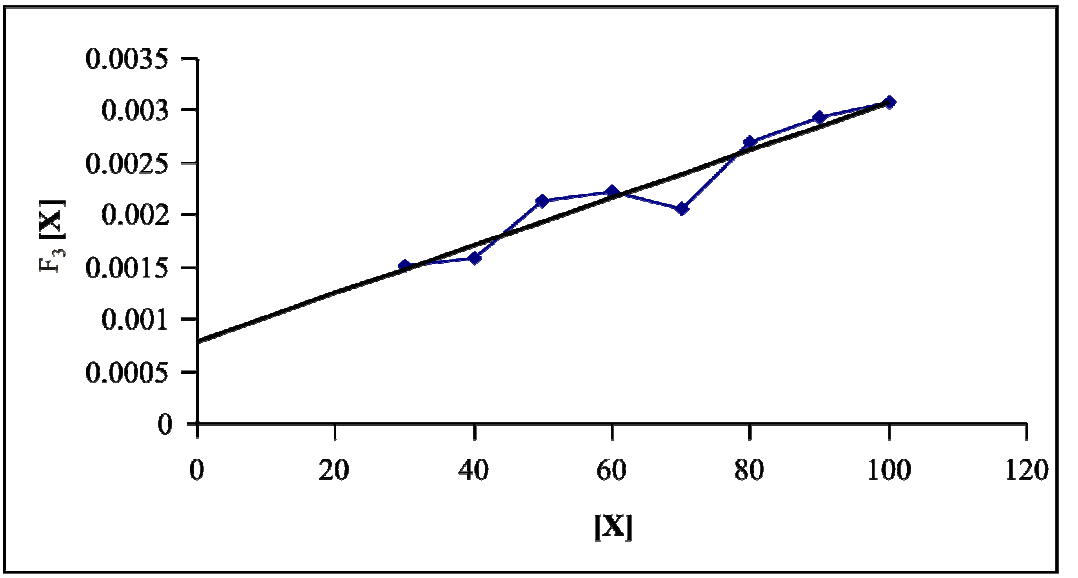

Fig. 4(d): $F_3[X]$ v/s [X] where $\beta_3 = 0.0024$

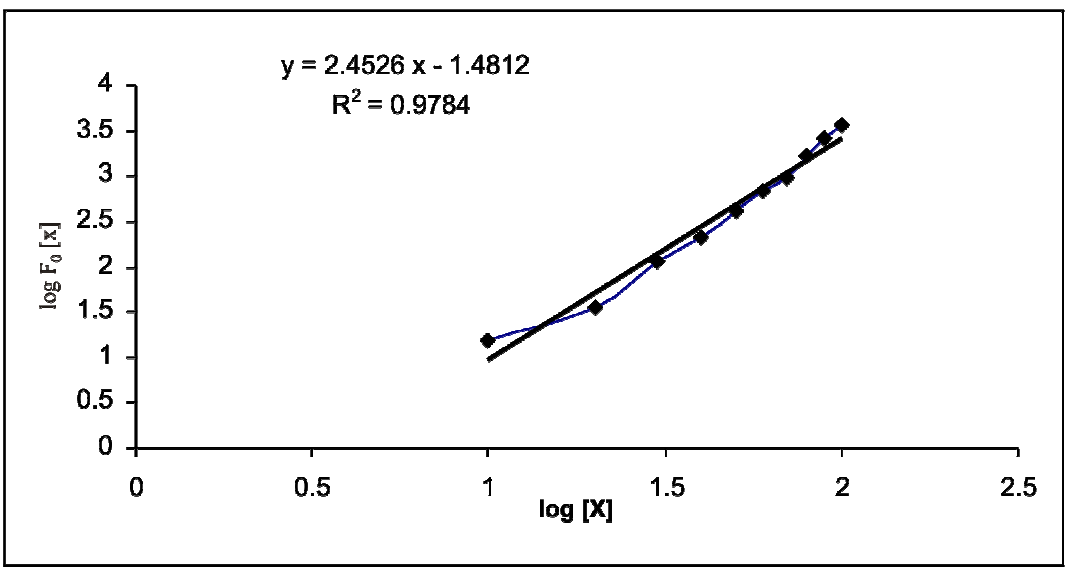

Fig. 5: Plot of log $F_0[X]$ v/s log [X]

Table 1. Experimental data

S.No.	[X] = C_x(mM)	$E_{1/2}$ (mV)	id (μA)	$\Delta E_{1/2}$ (V)	log (Im/Ic)	F_0[X]	F_1[X]	F_2[X]	F_3[X]
1	0	1575	5.2	0.000	0.0000	1	-	-	-
2	10	1572	4.3	0.003	1.0825	15.2757	1.4275	-	-
3	20	1570	4.2	0.005	1.3937	36.5426	1.7773	0.0175	-
4	30	1562	3.7	0.013	1.6246	115.9845	3.8324	0.0802	0.0015
5	40	1560	3.1	0.015	1.8271	216.0230	5.3756	0.0987	0.0016
6	50	1555	2.9	0.020	1.9531	426.1868	8.5045	0.1415	0.0021
7	60	1552	2.7	0.023	2.0622	692.1492	11.5190	0.1682	0.0022
8	70	1550	2.6	0.025	2.1460	981.0700	14.0000	0.1796	0.0021
9	80	1545	2.5	0.030	2.2210	1721.0758	21.5010	0.2509	0.0027
10	90	1542	2.4	0.033	2.2900	2548.5901	28.3050	0.2987	0.0029
11	100	1540	1.2	0.035	2.3684	3566.9745	35.6630	0.3423	0.0031

RESULTS AND DISCUSSION

Upon increasing the concentration of antibiotic drug as a ligand, $E_{1/2}$ of the system shifted to a more negative side due to the complex formation. Mn (II) gave well-defined two-electron wave in 1M KCl at 25°C. All the waves obtained were reversible as revealed from the straight line plot of E vs. log (i/i_d-i) (Fig. 2). The straight-line plot of i_d vs. $h^{1/2}$ passing through origin shows that the process is involving the diffusion controlled reaction mechanism (Fig. 3) (where, E = voltage of the wave in mV, i = average diffusion current in μA, h = height of mercury column in cm). The experimental data are given in Table 1.

The formation constants of different consecutive complexes Mn-TC were found to be $\beta_0 = 1.0$, $\beta_1 = 2.126$, $\beta_2 = 0.035$ and $\beta_3 = 0.0024$ as revealed by Deford and Hume's method, which are represented in Figures 4a, 4b, 4c, and 4d and are also presented in Table 1. From the plot of $\log F_0[X]$ vs. log [X], the slope at any point on this curve gave the value of $\bar{n}$ which was found to be 2.4526 which is equivalent to 3.0. Substitution of n into the relation $\bar{n} = C_X - [X]_{free} / C_M$ provide a value of free ligand concentration near the true value. It is apparent that, on increasing Cx, the composition of the system approaches that of highest mole ratio (1 : 3) of metal and ligand complex formation. Under this limiting condition $I_M = I_C$ and $[X]_{free} = C_X$, which can be seen from the Table 2.

Table 2. Calculation of [X]

C_x	C_m	$\bar{n}$	$[X]_{free}$	C_x	C_m	$\bar{n}$	$[X]_{free}$
10	1	2.4526	7.5474	60	1	2.4526	57.5474
20	1	2.4526	17.5474	70	1	2.4526	67.5474
30	1	2.4526	27.5474	80	1	2.4526	77.5474
40	1	2.4526	37.5474	90	1	2.4526	87.5474
50	1	2.4526	47.5474	100	1	2.4526	97.5474

CONCLUSIONS

The value of stability constants calculated from Deford and Hume's method decreases consecutively, which supports the hypothesis that stability decreases for higher complex formation for Mn (II) – TC system. The experimental data supports the theoretical calculations. These results show that in the present work, the ligand number, $\bar{n}$ is found to be equivalent to 3.0 so the highest complex formed must be MX_3. From the Table 1, it is

noticeable that the value of higher functions becomes unreliable at low ligand concentration. Thus, the polarographic technique, involving direct measurement of half-wave potentials of aqua and complexed metal ions, may be used to determine the consecutive stability constants of metal-ligand systems of varied types. The limitation of this is that the method used here is applicable to the both; simple and complexed species involving reversible complex formation reaction.

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