Polarographic Determination of Stability Constant of Zn (II) Complexes with Antibiotics – Clindamycin Complexes in Aqueous Medium

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Abstract. Polarographic studies of stability constant of Zn – complexes with neomycin, chlortetracycline, oxytetracycline tetracycline penicillin V and penicillin G primary ligands and clindamycin as the secondary ligand at PH 7.30± 0.01 have been carried out in aqueous medium under varying temperature at 25°C and 35°C and NaClO4 was used as supporting electrolyte. The waves of Zn and its complexes were quasireversible. Zn formed 1:1:1, 1:1:2 and 1:2:1 complexes. Deford and Hume's method has been applied for the determination of composition and stepwise formation constants of complex species.

INTRODUCTION

The study of complexation of metal with various antibiotics polarographically [1] in aqueous media have been carried out from a long time but on clindamycin no work has been done yet, therefore, I have selected clindamycin for our study. Antibiotics are substance which even at low concentrations, inhibit the growth and reproducer of bacteria and fungi. The treatment of infectious diseases would be inconceivable today without antibiotics [2]. Most of the antibiotics were originally derived from microorganisms while the chemotherapeutic agents are from plants [3]. Clindamycin [4] is lincosamide, still used as therapeutic agent in human disease and some animal infections.

A number of analytical methods for the determination of drugs have been reported in literature. However, formation of the metal complex and its characterizations by polarographic method in the field as regards to their extra ordinary detection limit, low cost, rapidly, accuracy, simplicity and non-destructive nature have not been used for the said purpose. The present paper deals with the complexation reaction of Zn(II) and determination of stability constants of various species formed by Zn(II) with neomycin, chlortetracycline, oxytetracycline, tetracycline, penicillin G and penicillin V as primary legands and clindamycin as a secondary ligand in aqueous medium at 25°C and 35°C.

EXPERIMENTAL SECTION

Instrument: The polarographic data (current - voltage curve) were recorded on a manual polarographic using polyflex galvanometer (Toshniwal pl-50). An elico digital pH meter (model LI -120) assembly of glass and calomel electrodes were used to measure the pH of the test solution at 7.30 ± 0.01. Each solution was dereated by passing pure hydrogen gasthroughit for 10 minutes before recording polarograms.

Methods: The concentrations of Zn(II), NaClO4 and triton X-100(as suppressor) in the test solution were 0.50 mM, 1.0M and 0.001% respectively. For ternary system, the concentration of primary ligands i.e neomycin, chlortetracycline, oxytetracycline, tetracycline, penicillin G and penicillin V varied from 0.5 mM to 30mM at 0.025 M and 0.50 M fixed concentration of secondary ligand (i.e. clindamycin). Zn formed 1:1:1, 1:1:2 and 1:2:1 ternary complexes with antibiotics. Zn (II) showed quasireversible reduction wave involving two electrons at pH = 7.30 ± 0.01 and μ=1.0 MNaClO4 at 25°C and 35°C. The nature of current voltage curves for complexes was also quasireversible. The stability constants of ternary system are showed in table 1 and table 2.

Table 1 : Fij [X,Y] Values for [Zn(II)- Neomycin- Clindamycin] Ternary System

Zn (II)= 0.5mM, μ= 1.0 M NaClO4, pH= 7.30±0.01, Temperature = 25°C

[Neo] X 10^{-3} M	[Clindamycin] = 0.025 M (Fixed)						
	$E_{1/2r}$ - V Vs SCE	$\Delta E_{1/2}$ – V	Log (lm/lc)	F_{00}[X,Y] x10^{-1}	F_{10}[X,Y] x10^{-4}	F_{20}[X,Y] x10^{-7}	F_{30}[X,Y] x10^{-8}
0.00	0.985			2.95	1.144	1.122	12.58
0.50	1.036	0.047	0.0068	41.44	7.09	1.12	12.58
1.00	1.051	0.062	0.0068	13.40	12.80	1.13	12.51
2.00	1.068	0.079	0.0137	49.42	24.41	1.14	12.44
3.00	1.078	0.089	0.0137	109.44	36.28	1.16	12.50
4.00	1.086	0.097	0.0280	194.23	48.40	1.17	12.62
5.00	1.091	0.102	0.0208	304.48	60.77	1.18	12.60
6.00	1.096	0.107	0.0280	440.92	73.38	1.19	12.57
8.00	1.104	0.115	0.0280	795.09	99.31	1.22	12.47
10.00	1.110	0.121	0.0353	1263.38	126.27	1.24	12.47
20.00	1.129	0.140	0.0427	5523.16	276.12	1.37	12.49
30.00	1.140	0.151	0.0503	13534.1	451.11	1.49	12.51
[Neo] X 10^{-3} M	[Clindamycin] = 0.050 M (Fixed)						
	$E_{1/2r}$- V Vs SCE	$\Delta E_{1/2}$ - V	Log (lm/lc)	F_{00}[x,Y] x10^{-1}	F_{10}[x,Y] x10^{-4}	F_{20}[x,Y] x10^{-8}	F_{30}[x,Y] x10^{-8}
0.00	0.985			5.75	4.46	2.18	12.58
0.50	1.045	0.056	0.0068	8.37	15.59	2.22	12.58
1.00	1.061	0.070	0.0137	27.33	26.75	2.22	12.52
2.00	1.077	0.088	0.0137	99.13	49.27	2.23	12.43
3.00	1.087	0.098	0.0208	216.74	72.05	2.25	12.51
4.00	1.094	0.105	0.0208	380.96	95.09	2.26	12.61
5.00	1.100	0.111	0.0280	591.72	118.22	2.27	12.00
6.00	1.105	0.116	0.0280	851.99	141.90	2.29	12.57
8.00	1.109	0.120	0.0353	1517.73	189.64	2.31	12.46
10.00	1.118	0.129	0.0427	2385.02	238.14	2.33	12.47
20.00	1.136	0.147	0.0503	9949.87	497.46	2.46	12.50
30.00	1.147	0.158	0.0579	23444.20	781.45	2.58	12.500

Table 2: Stability constant of Ternary complexes of Zn at 25°C

Primary ligand	Secondary ligand	Stability constant		
		Log β_{11}	Log β_{12}	Log β_{21}
Neomycin	Clindamycin	4.363	7.201	9.640
Chlortetracycline	Clindamycin	4.460	7.315	10.211
Oxytetracycline	Clindamycin	4.661	7.501	10.465
Tetracycline	Clindamycin	-	7.952	10.890
Penicillin - V	Clindamycin	5.112	8.102	10.903
Penicillin - G	Clindamycin	5.322	8.309	-

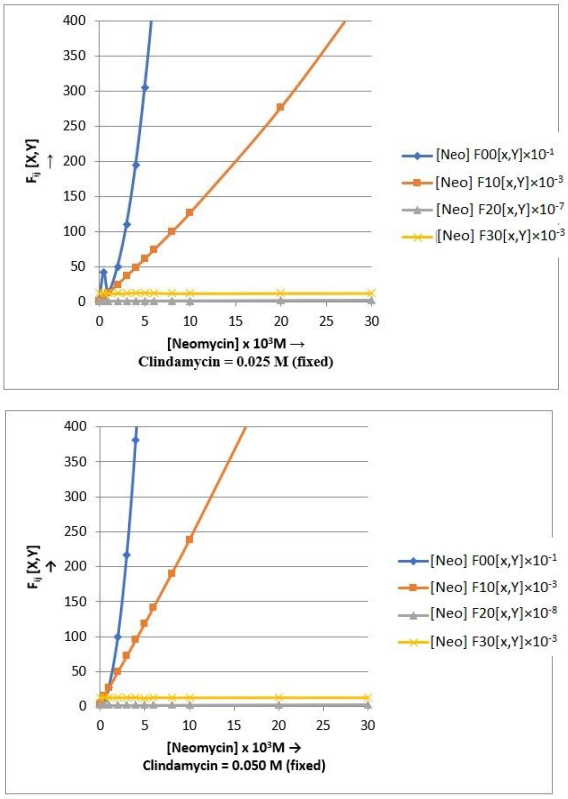


Fig. 1: [Zn- Neomycin- Clindamycin] System

RESULTS AND DISCUSSION

The reduction of Zn(II) complex with ligand give well define wave and reduction was found to be quasireversible and defussioncontrol in aqueous medium at different temperature (25°C and 35°C). The reduction process involves two electrons transfer.In each test solution, $NaClO_4$ was used as a supporting electrolyte to maintain the constant ionic strength (μ=1.0M). Triton X-100 was used in all solution to suppress the observed maxima. The temperature was kept constant (25°C and 35°C) using Thermostat. The D.M.G used had the following characteristics $m^{2/3+1/6} = 2.40mg^{2/3}\ 5^{1/2}$ 60.0cm effective height of mercury.

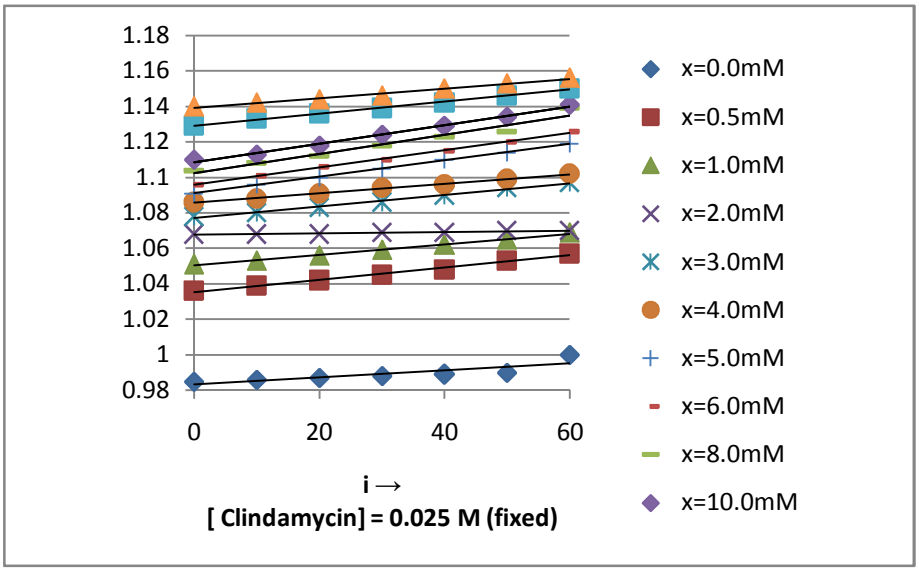
The polarographic [5, 6, 7] data and plots of Fij[X,Y] against [X] where βij is a Schaap and Mc master function [8] to evaluate the stability constant βij, X= primary ligand, Y = secondary ligand and i and j are their stoichiometric number respectively for [Zn -antibiotics – clindamycin] systems are shown in table 2 and figure 1 respectively. The polarographic data are used to determine the values of function F_{00}, F_{10}, F_{20} and F_{30}. The values of $E_{1/2}{}^{r}$ from $E_{1/2}{}^{qr}$ were determined by Gellings methods by plotting the graph between [E-RT/nFlog(id-i)/i] Vsi for all the complexes were given in figure 2respectively.

Gelling method [14,15] was applied to evaluate the reversible half wave potential ($E_{1/2}{}^{r}$) because the slope of log plots indicated the quasireversible nature of reduction.

The trends of the stability constants of the complexes was found neomycin< chlortetracycline< oxytetracycline< tetracycline<penicillin V< penicillin G. In this study, the stability of the neomycin complex is minimum, owing to the fact that the neomycin formed the complexes of lowest stability because of having the steric hindrance the metal and various group present in neomycin. The higher stability of penicillin complexes than that of other antibiotics is a result of lesser steric hindrance in penicillin complexes than that of other antibiotics.

The values of stability constant (log β) varied from 4.363 to 10.903 at25°C and 3.861 to 10.524 at 35°C. The values of stability constants were given in Table 2 and Table 3.Therefore, Zn– antibiotics - clindamycin complexes are more stable at low temperature as compared to high temperature. The fact that stability constant has been found

to be appreciably greater than zero is perhaps one of the most convincing pieces of evidence for the existence of the complex in the solution.



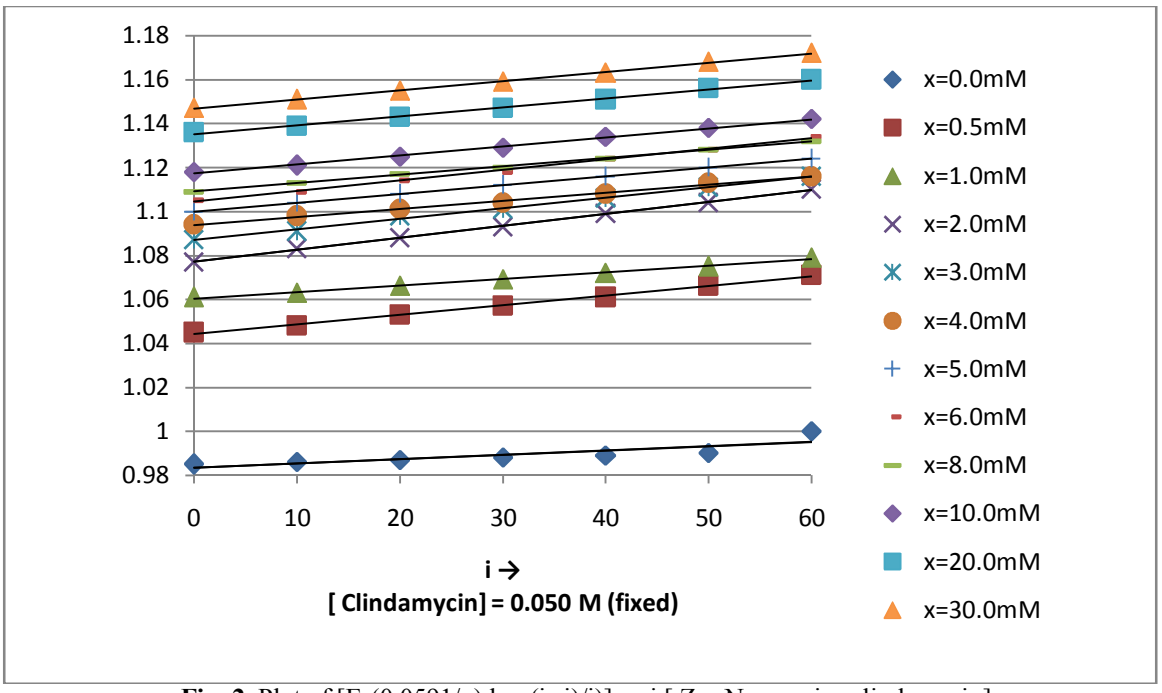


Fig. 2. Plot of [E-(0.0591/n) log (i_d-i)/i)] vs i [Zn- Neomycin- clindamycin]

CONCLUSIONS

The aim of the present study is the complex formation of Zn with selected antibiotic as primary ligands and clindamycin as a secondary ligand and also to determine the stability constants of complexes. On the basis of stability constants value of complexes, we can get an idea about the possibilities whether these drugs of their

complexes could be used against metal toxicity or not. The values of stability constant (log β) showed that these drug and their metal complexes could be used against Zinc metal toxicity. The drugs should not be toxic can be excreted easily from the body.

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