A study of Polarographic Characteristics and Kinetic Parameters of Zn(II) Metal Complexes with some Antibiotics and Vitamin-B_5 Systems

Santosh Narayan Chadar*[1], Farid Khan[2]and Manju Singh[1]

[1]Department of Chemistry, UIT-RGPV Bhopal (M.P.) - 462033, India

[2]Department of chemistry, Dr. H. S. Gour UniversitySagar (M.P.) – 470 003, India

E-mail: narayan_santosh@rediffmail.com

Abstract: *Polarographic technique was used for the determination of stability constant (log β) of ternary complexes of Zn(II) with neomycin, chlortetracycline, tetracycline, penicillin-V, penicillin-G, as primary ligands and Vitamin-B_5 as secondary ligand at pH = 7.30 ± 0.01 and ionic strength μ = 1 M $NaClO_4$ at 298 K. The nature of current-voltage curves was quasireversible. Zn(II) formed 1:1:1, 1:1:2 and 1:2:1 complexes with these drugs as confirmed by Schaap and McMaster method. The sequence of stability constant of complexes was neomycin < chlortetracycline < oxytetracyclin < tetracycline < penicillin-V < penicillin-G that can be explained on the basis of nature of ligands and steric hindrance between metal ligands. Kinetic parameters were also determined using Tamamushi and Tanaka method. The value of transfer coefficient (α) confirmed that the 'transition state' behaves between dropping mercury electrode and solution interface. A slight variation of potential affects not only the rate but rate constant greatly.*

Key Words: *Polarographic Characteristics, Kinetic Parameters, Stability Constants, [Zn(II)-Antibiotics-Vitamin-B_5] System.*

1. INTRODUCTION:

Pantothenic acid also known as vitamin B_5 is a water-soluble vitamin that is a precursor in the synthesis of coenzyme A. Coenzyme A is essential to many biochemical reactions that sustain life. Also, the phosphopantetheinyl moiety of coenzyme A is required for the biological activity of several proteins, including the acyl-carrier protein involved in fatty acid synthesis[1].Pantothenic acid is found throughout all branches of life in the form of coenzyme A, a vital coenzyme in numerous chemical reactions[2]. On the other hand, antibiotics are natural compound produced mostly by plant microorganisms[3]. These antibiotics are used against several fungal and bacterial diseases in plants, animal and human beings[4]. The study of antibiotics with vitamin-B_5 has great importance. therefore, In this paper, we report the stability constant (log β) and kinetics parameters[5, 6] of complexes viz. transfer coefficient (α), degree of irreversibility (λ), diffusion coefficient (D) and rate constant (k) of complexes using neomycin, chlortetracycline, oxytetracyclin, tetracycline, penicillin-V and penicillin-G as primary ligands and vitamin-B_5as secondary ligands by polarographic technique for which no reference is available in the literature.

2. MATERIALS AND METHODS:

All the chemicals used were of A.R. grade and their solutions were prepared in conductivity water. Zn(II), the antibiotics and vitamin-B_5 [(+) pantothenic acid sodium salt] were taken in the ratios of 1:40:40 and current voltage curves were obtained in different pH values. It has been observed that the maximum shift of $E_{1/2}$ was obtained within the pH range 7.10 - 8.50, but pH 7.30 was selected for studying the complexes in human blood pH. A Systronic μ pH meter 361 was used to measure the pH of the analyte at

7.30 ± 0.01 adjusted by using dilute solutions of $HClO_4$ or NaOH as required. Potassium dihydrogen phosphate-sodium hydroxide buffer was added to stabilize the pH of the analyte. The current voltage curves were obtained on a manual polarograph using polyflex galvanometer (PL -50). The polarographic cell was of Latinin and Lingane type in which polarographic capillary of 5.0 cm in length with 0.04 mm in diameter was used. The $m^{2/3} t^{1/6}$ value was 2.40 $mg^{2/3} s^{-1/2}$ at 60.02 cm effective height of mercury. As the resistance of the cell was less than 300 Ω, IR correction was not made.

3. RESULTS AND DISCUSSION:

Zn(II) gave two electron quasireversible reduction wave at pH = 7.30 ± 0.01 and μ = 1.0 M $NaClO_4$ at 298 K[7, 8]. The nature of current-voltage curves for complexes is also quasireversible. The concentration of Zn(II) $NaClO_4$, and triton X-100 (as suppressor) in the test solution were 0.5 mM, 1.0 M and 0.001% respectively. Pure nitrogen gas was passed through the test solution for deareation before recording the current-voltage curves.

In this system, the concentration of antibiotics varied from 0.5 mM to 30.0 mM at two fixed concentration of vitamin-B_5 i.e. 0.025 M and 0.050 M. The $E_{1/2}$ values became more negative with the addition of vitamin-B_5 to the [Zn(II) – antibiotics] system which showed ternary complex formation of 1:1:1, 1:1:2, and 1:2:1 complexes. Gellings[9] method was used to determine the values of $E_{1/2}^{reversible}$ form $E_{1/2}^{quasireversible}$ by plotting (E - RT/nF log i_d-i/i) vs i for all the complexes. The data and plots of F_{ij} [X, Y] against [X] (where F_{ij} is a Schaap and McMaster[10] function to evaluate the stability constant β_{ij}, X = neomycin, Y = vitamin-B_5 and i and j are their stoichiometric numbers respectively) for [Zn (II) – neomycin - vitamin-B_5] system were given in Table 1. and Fig.1 respectively. The Fig.1 is used to determine the values of functions F_{00}[X, Y], F_{10}[X, Y], F_{20}[X, Y], and F_{30}[X, Y],and also to calculate the stability constant.

To know the values of β_{11} and β_{12}, the study has been carried out at two constant concentration of secondary ligand [Y] = [Vitamin-B_5] at 0.025M and 0.050M respectively. The values of stability constant of complexes were given in Table 3.

To compare the stability of binary and ternary complexes. The values of mixing constant logK were calculated by the following equation.

$$\log K_m = \log \beta_{11} - ½ [\log \beta_{02} + \log \beta_{20}]$$

The values of log K_m were -1.09, -0.65, -0.56, and -0.36 for [Zn(II) – neomycin – vitamin-B_5], [Zn(II) – chlortetracycline – vitamin-B_5], [Zn(II) – tetracycline – vitamin-B_5], and [Zn(II) – penicillin -G – vitamin-B_5], respectively. The positive value of log K_m showed that the ternary complex is more stable than their binary complexes while the negative values of log K_m showed that binary complexes are more stable than their ternary complexes. The complexes of compositions 1:1:1 and 1:2 in case of [Zn(II) – oxytetracycline – vitamin-B_5] and [Zn(II) - penicillin-V – vitamin-B_5] were not formed therefore; the values of log K_m were not calculated for these systems. It is clear from the values of stability constants that the trend of stability constants of complexes is neomycin < chlortetracycline < oxytetracycline < tetracycline < penicillin-V < penicillin-G. In the case of neomycin complexes, the fact is that its stability constants are minimum may be due to the presence of many groups in neomycin; therefore, the steric hindrance is maximum between its groups and Zn(II). In case of tetracycline; all the tetracycline have the same structures except in the difference in R_1 and R_2 position. The lesser stability constant of chlortetracycline complex than that of oxytetracycline complex is due to the presence of more electrons withdrawing Cl at R_1 in the former in place of H in the latter. In case of tetracycline, H is present both at R_1 and R_2 hence; there are least electronic disturbances in tetracycline in comparison to other tetracycline complexes[11]. This order of stability supported the order of their pK values of the ligands[12]. In case of both penicillin-V and penicillin-G, it is the ring nitrogen and O of the carboxylic group which take part in complexation with Zn(II). The greater stability of penicillin-G complexes than that of penicillin-V complexes is also supported by the order of the pK values[13-17].

In case of vitamin-B_5, it is the N of amino group and O of carboxylic acid take part in bond formation with Zn(II)[18]. It is clear from the values of stability constant of the complexes that vitamin-B_5 and antibiotics used either singly or simultaneously might be effective to reduce the toxicity[19] of Zn(II) in vivo.

The kinetic parameters viz. transfer coefficient (α), degree of irreversibility (λ) and rate constant (k) were determined by Tamamushi and Tanaka methods[20-21] by plotting ($E^r_{1/2}$-E) against log (Z-1) (fig. 2(a) and 2(b).where the terms have the usual significance)[17-18]. The values of kinetic parameters were given in table 2. It is obvious from the value of α that the values varied from [Zn(II) – neomycin – vitamin-B_5] 0.45 to 0.52 (about 0.50), and value of α for other systems were also about 0.50 confirmed that 'transition state' lies midway between dropping mercury electrode and solution interface. The value of rate constant (k) showed that the electrode process were quasireversible. The values of diffusion coefficient as determined by ilkovic equation[22] were as expected.

4. CONCLUSION:

The present study showed that the polarographic reduction of [Zn(II) – antibiotics – vitamin-B_5] was quasireversible. The values of transfer coefficient confirmed that the 'transition state' lies in an exact intermediate between DME and mercury solution interface [23].

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Table 1: Polarographic Characteristics and F_{ij} [X, Y] Values of [Zn- Neomycin – Vitamin-B_5] System
Zn(II) = 0.5 mM; μ = 1.0 M $NaClO_4$; pH = 7.30 ± 0.01; Temp. = 25°C

[Vitamin – B_5]= 0.025 M (Fixed)								[Vitamin – B_5]= 0.050 M (Fixed)						
[Neo.] $X10^3$ M	$(E_{1/2})^r$ -V vs SCE	$\Delta E_{1/2}$ V	$\log I_m/I_c$	F_{00}[X,Y] X 10^1	F_{10}[X,Y] X 10^4	F_{20}[X,Y] X 10^6	F_{30}[X,Y] X 10^8	$(E_{1/2})^r$ -V vs SCE	$\Delta E_{1/2}$ V	$\log I_m/I_c$	F_{00}[X,Y] X10^1	F_{10}[X,Y] X 10^4	F_{20}[X,Y] X 10^6	F_{30}[X,Y] X 10^8
0.00	0.985	-	-	-	-	-	-	0.985	-	-	-	-	-	-
0.50	1.110	0.0415	0.0074	2.58	3.91	59.83	1.258	1.110	0.0513	0.0074	5.52	8.25	115.80	12.58
1.00	1.114	0.0551	0.0149	7.59	6.96	60.46	12.59	1.115	0.0643	0.0149	15.50	14.10	116.43	12.59
2.00	1.118	0.0713	0.0226	27.15	13.26	61.72	12.59	1.118	0.0802	0.0149	53.40	26.00	117.69	12.60
3.00	1.122	0.0814	0.0226	60.07	19.81	62.98	12.60	1.121	0.0899	0.0226	115.84	38.14	118.95	12.60
4.00	1.128	0.0889	0.0226	107.10	26.62	64.24	12.60	1.127	0.0971	0.0226	203.59	50.54	120.21	12.61
5.00	1.131	0.0947	0.0226	169.00	33.67	65.60	12.61	1.131	0.1028	0.0226	317.41	63.20	121.47	12.61
6.00	1.137	0.0993	0.0304	246.53	10.98	66.76	12.61	1.137	0.1075	0.0226	458.03	76.10	122.73	12.61
8.00	1.141	0.1069	0.0384	451.47	56.53	69.29	12.61	1.142	0.1148	0.0304	822.77	102.67	125.25	12.62
10.00	1.148	0.113	0.0384	727.98	72.73	71.81	12.61	1.147	0.1207	0.0304	10303.5	130.25	127.79	12.62
20.00	1.151	0.1325	0.0465	3396.03	169.77	84.42	12.61	1.152	0.1391	0.0465	5667.14	283.28	140.41	12.62
30.00	1.157	0.1447	0.0465	8761.35	292.02	97.03	12.61	1.157	0.1508	0.0384	13848.1	461.55	153.03	12.62
log A = 0.75, log B = 3.95, log C = 7.70, log D = 9.10								log A = 1.15, log B = 4.40, log C = 8.05, log D = 9.10						

Table 2: Kinetic Parameters of [Zn- Neomycin – Vitamin-B_5] System
Zn(II) = 0.5 mM, μ = 1.0 M $NaClO_4$, pH = 7.30 ± 0.01, Temp. = 25°C

Vitamin – B_5 = 0.025 M (Fixed)							Vitamin – B_5 = 0.050 M (Fixed)				
[Neo.] $X10^3$ M	$(E_{1/2})^{qr}$ -V vs SCE	Slope mV	α	Λ $sec^{-1/2}$	$D^{1/2}X10^{-3}$ $cm^2 sec^{-1}$	k x 10^{-3} cm sec^{-1}	$(E_{1/2})^{qr}$ -V vs SCE	Slope mV	α	λ $sec^{-1/2}$	$D^{1/2}X10^{-3}$ cm^2sec^{-1}	k x 10^{-3} cm sec^{-1}
0.00	1.000	36.00	0.45	1.18	4.87	5.74	1.000	36.00	0.48	1.18	4.82	5.74
0.50	1.113	42.00	0.42	1.42	4.52	4.78	1.113	44.00	0.42	1.47	4.86	4.52
1.00	1.116	40.00	0.35	1.58	4.37	4.15	1.117	42.00	0.35	1.56	4.15	4.78
2.00	1.121	44.00	0.40	1.63	4.56	4.34	1.122	35.50	0.40	1.14	4.73	4.15
3.00	1.126	35.50	0.48	1.14	4.89	3.56	1.128	37.50	0.44	1.23	3.25	3.25
4.00	1.131	37.00	0.45	1.78	3.14	3.48	1.131	40.00	0.48	1.89	3.64	4.64
5.00	1.135	45.00	0.52	1.98	3.25	3.14	1.135	42.00	0.52	1.94	3.14	4.15
6.00	1.141	42.00	0.40	1.25	3.47	5.71	1.139	35.00	0.42	1.14	3.48	3.56
8.00	1.147	44.00	0.44	1.14	4.85	4.25	1.144	45.00	0.35	1.25	4.89	3.78
10.00	1.151	35.00	0.42	1.56	4.12	3.14	1.148	40.00	0.40	1.56	4.73	3.12
20.00	1.155	35.50	0.40	1.78	3.14	3.67	1.153	35.50	0.52	1.34	4.79	4.64
30.00	1.160	45.00	0.35	1.34	4.56	4.86	1.160	44.00	0.48	1.94	3.25	4.83

Table 3: Stability Constant of [Zn- Antibiotics- Vitamin- B_5] System
Zn (II) = 0.5 mM, μ = 1.0 M $NaClO_4$, pH = 7.30 ± 0.01, Temp. = 25°C

Ligand		Stability Constants							
Primary	Secondary	$\log \beta_{01}$	$\log \beta_{02}$	$\log \beta_{10}$	$\log \beta_{20}$	$\log \beta_{30}$	$\log \beta_{11}$	$\log \beta_{12}$	$\log \beta_{21}$
Neomycin	Vitamin-B_5	2.20	3.31	3.60	6.51	9.10	3.82	6.91	9.35
Chlortetracycline	Vitamin-B_5			4.40	7.61	9.50	4.81	7.71	9.83
Oxytetracycline	Vitamin-B_5			4.50	7.81	9.86	-	8.00	10.10
Tetracycline	Vitamin-B_5			4,80	8.01	9.91	5.10	8.36	10.25
Penicillin-V	Vitamin-B_5			4.91	-	10.00	5.18	8.43	-
Penicillin-G	Vitamin-B_5			4.96	8.12	10.10	5.35	8.53	10.45

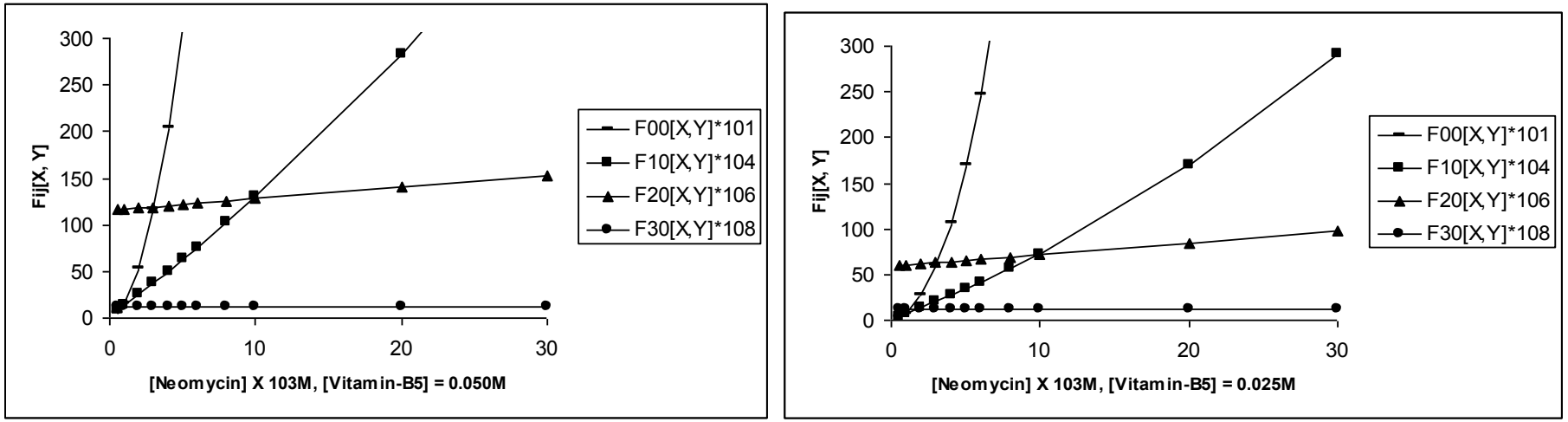

Fig.1: [Zn-Neomycin-Vitamin-B_5] System

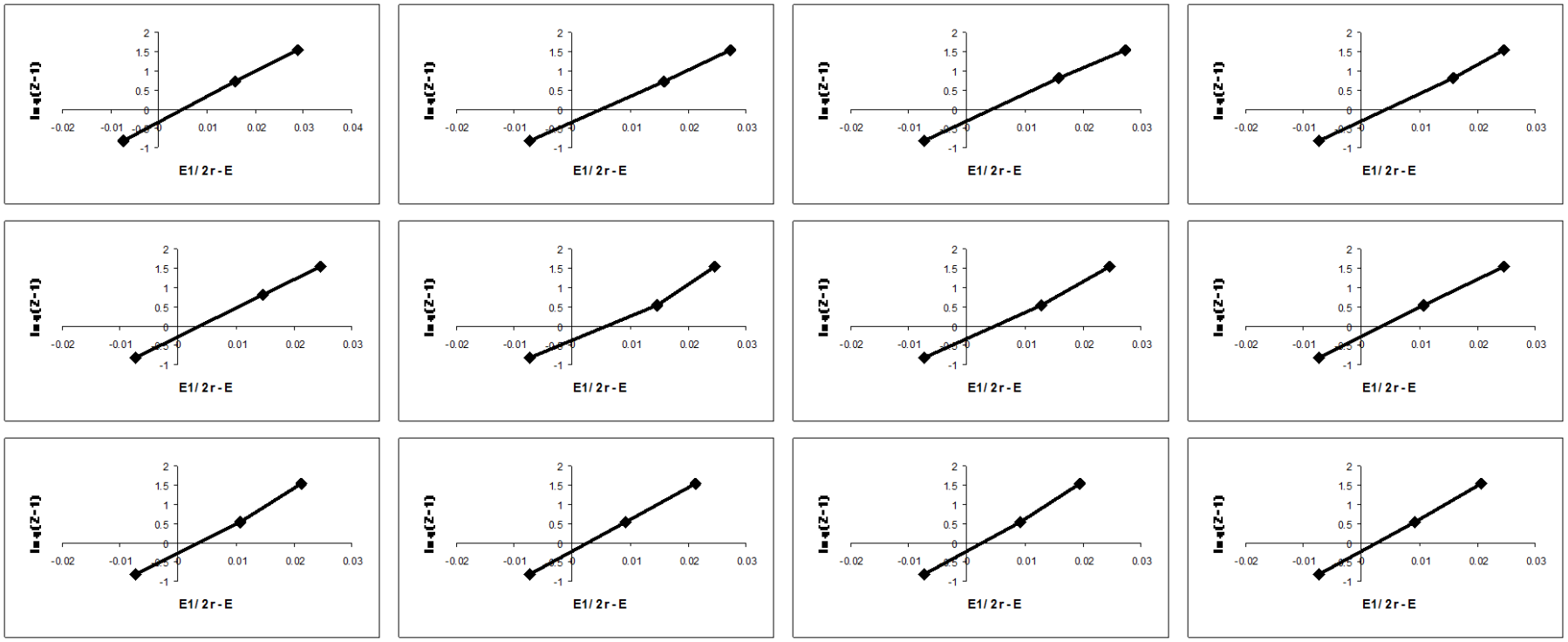

Fig. 2 (a) : [Zn-Neomycin-Vitamin-B_5] System, [Vitamin-B_5] = 0.025mM
Plot of ($E_{1/2}^{r}$-E) Vs log(Z-1), Y-axis = log(Z-1), X-axis = ($E_{1/2}^{r}$-E)

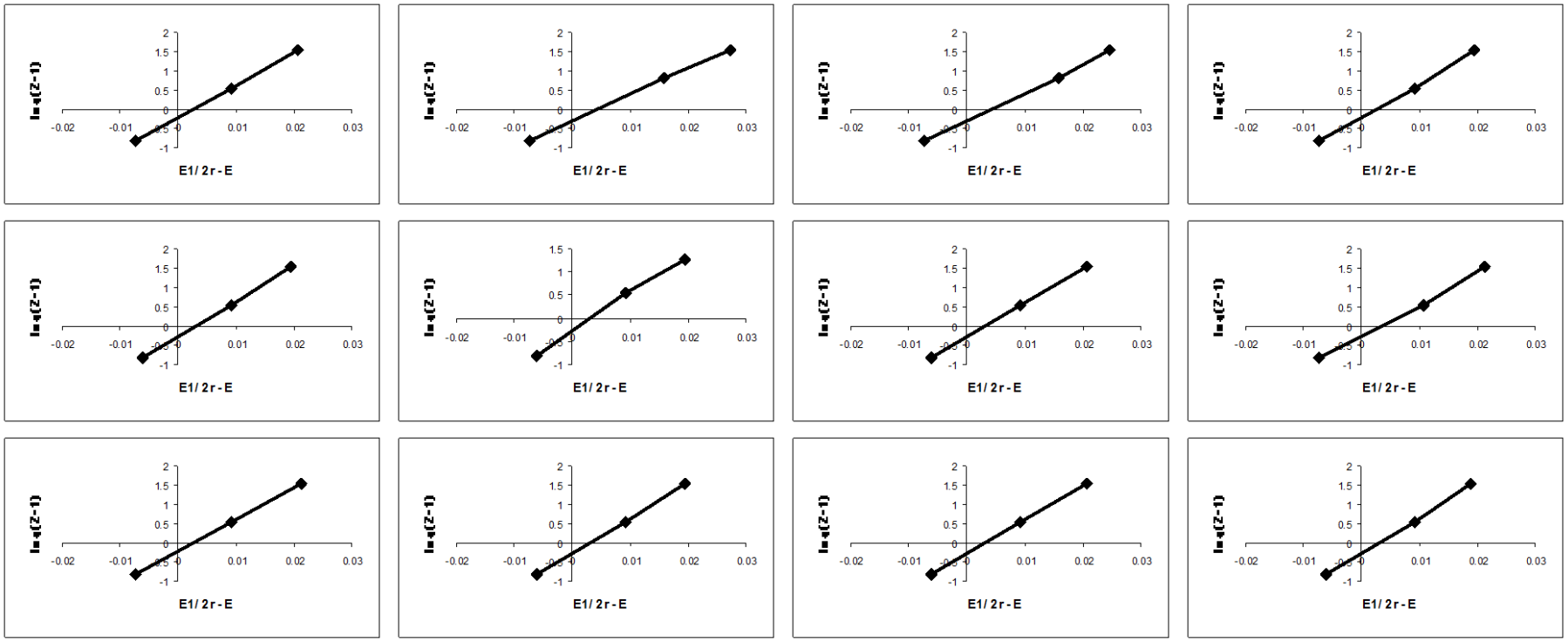

Fig. 2(b) : [Zn-Neomycin-Vitamin-B_5] System, [Vitamin-B_5] = 0.050mM
Plot of ($E_{1/2}^{r}$-E) Vs log(Z-1), Y-axis = log(Z-1), X-axis = ($E_{1/2}^{r}$-E)