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Voltammetric Study and Thermodynamic Parameters of [Zn–L-Amino Acidate–Vitamin-PP] Complexes vis-à-vis Kinetics of Electrode Reaction

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Abstract

Voltammetric reduction of Zn (II) using L-lysine, L-ornithine, L-threonine, L-serine, L-phenylglycine, L-phenylalanine, L-glutamic acid, L-aspartic acid and vitamin-PP (nicotinamide, niacinamide) at pH = 7.30 ± 0.01, and μ = 1.0 M $NaClO_4$ was reported at 25 and 35 ºC. The nature of current voltage curves was quasireversible and diffusion controlled. 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 L-lysine < L-ornithine < L-threonine < L-serine < L-phenylglycine < L-phenylalanine < L-glutamic acid < L-aspartic acid can be explained on the basis of size, basicity and steric hindrance of ligands. The thermodynamic parameters such as enthalpy (ΔH), free energy (ΔG) and entropy change (ΔS) have also been reported. The kinetic parameters viz. transfer coefficient (α), degree of irreversibility (λ), diffusion coefficient (D) and standard rate constant (k) were calculated. The values of 'α' confirmed the symmetric nature of 'activated complex' between oxidants and reductants response to applied potential between dropping mercury electrode and solution interface.

***Keywords**:* voltammetry, thermodynamic parameters, electrode kinetics, [Zn–L-amino acidate–vitamin-PP] complexes.

Introduction

Complexes of some metal ions with amino acids can be used as models to study the pharmaco-dynamic effects of drugs or for increasing the biocompatibility and minimize the toxic effects of some metal ions [1]. These L-amino acids are used

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in many biological processes in human beings. On the other hand, L-amino acids are also involved in intracellular metabolism and operate specific transport systems of the plasma membrane, they do not affect cardiac function under normal conditions [2]. However, there is a growing body of evidences that certain of them may be vital for myocardial function and survival during ischemia / reperfusion stress. In this respect glutamic acid and aspartic acid seem to be the most important [3]. The invention provides the use of zinc complexes of selected amino acids from D- or L- isomers of proline, lysine, histidine, glycine, arginine and tryptophan and other pharmacologically acceptable salts of zinc. The use of the compound comprises administering an effective amount of said compounds for inhibition of growth: of the malarial parasite, plasmodium falciparum [4]. Vitamin-PP is water-soluble vitamin B-complex**,** a derivative of niacin. This drug is used in the prevention and treatment of diabetes; it also protects the vital pancreatic cells from diabetes inducing factors [5]. The niacin nucleotides NAD^+ (nicotinamide adenine dinucleotide) and $NADP^+$ (nicotinamide adenine dinucleotide phosphate) serve as coenzymes in a large number of reversible oxidation-reduction systems [6, 7]. Therefore, the Zn complexes of these drugs have great importance. The concentrations of zinc in vivo can be reduced by drug therapy, but the specificity of drug and its amount is stability constant dependent [8]. Therefore, the authors have undertaken the present study to determine the stability constants, thermodynamic and kinetic parameters of these ternary complexes with the selected drugs polarographically, for which no reference has so far been traced out in the literature.

Experimental

Instrumentation

Electrochemical experiment, i.e., a simple DC polarography, was carried out using a manual polarograph with a Toshniwal PL-50 polyflex galvanometer. The polarographic cell was of Laitinen and Lingane type in which a 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. A Systronic pH meter 361 was used to measure the pH of the analyte at 7.30±0.01.

Reagents

The following chemicals were used in the experiments: $HClO_4$ (Sigma), NaOH (Sigma), $NaClO_4$ (Fluka), Triton X-100 (Sigma), $ZnCl_2$ (B.D.H.), L-amino acids (Lobachem) and vitamin-PP (Fluka), and their solutions were prepared in double distilled water. The purity of L-amino acids was checked by chromatographic method [9]. Pure nitrogen gas was passed through the analyte for deoxygenation before recording the current–voltage data. The pH of the analyte at 7.30 ± 0.01 was 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.

Voltammetric procedure

Polarographic studies of the ternary complexes of Zn (II) with some amino acids and vitamin-PP were recorded using depolarizer and ligands (L-amino acids and vitamin-PP) in ratio 1:40:40 and the concentration of amino acids varied from 0.5 mM to 30.0 mM at two fixed concentrations of vitamin-PP, i.e., 0.025 M and 0.050 M. It has been observed that $E_{1/2}$ shifted to more negative side with increase in concentration of L-amino acids. Current–voltage curves were obtained at different pH values. It has been observed that the maximum negative 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 which are compatible to human blood pH [10]. The concentrations of metal, $NaClO_4$ and Triton X-100 (suppressor) in test solutions were 0.5 mM, 1.0 M and 0.001%, respectively.

Results and discussion

Polarographic studies

Zn (II) gave two electron quasireversible reduction waves at pH = 7.30 ± 0.01, μ = 1.0 M $NaClO_4$ at 25 ºC [11]. The nature of current-voltage curves for complexes is also quasireversible. The $E_{1/2}$ values became more negative with addition of vitamin-PP (0.025 M and 0.050 M) to the [Zn – L-amino acids] system which showed ternary complex formation of 1:1:1, 1:1:2 and 1:2:1 complexes. Gelling [12] method was used to determine the values of $E_{1/2}^{reversible}$ from $E_{1/2}^{quasireversible}$ by plotting (E - RT / n F log i_d - i / i) vs. i for all the complexes. To know the values of β_{11} and β_{12}, the study has been carried out at two constant concentrations of vitamin-PP i.e. 0.025 M and 0.050 M. The values of stability constant of complexes, given in Table 1, were obtained by using the Schaap and McMaster [13] method (Fig. 1).

Table 1. Stability constants of binary and ternary complexes, Zn (II) = 0.5 mM, μ = 1.0 M $NaClO_4$, pH = 7.3 ± 0.01, Temperature = 25 ºC.

Ligands	log β_{01}	log β_{02}	log β_{03}	log β_{10}	log β_{20}	log β_{30}	log β_{11}	log β_{12}	log β_{21}
L-lysine	-	-	-	3.80	6.50	9.25	4.37	7.20	9.98
L-ornithine	-	-	-	3.93	6.58	9.42	4.53	7.42	10.20
L-threonine	-	-	-	4.25	7.36	9.55	4.68	-	10.38
L-serine	-	-	-	4.38	7.42	9.68	4.84	7.75	10.60
L-phenylglycine	-	-	-	4.42	7.58	9.78	5.15	8.00	10.72
L-phenylalanine	-	-	-	4.50	7.62	9.97	5.31	8.22	10.94
L-glutamic acid	-	-	-	5.30	8.72	10.00	-	8.96	10.98
L-aspartic acid	-	-	-	5.45	8.95	10.25	5.76	9.18	11.20
vitamin-PP (nicotinamide)	1.91	2.90	3.30						

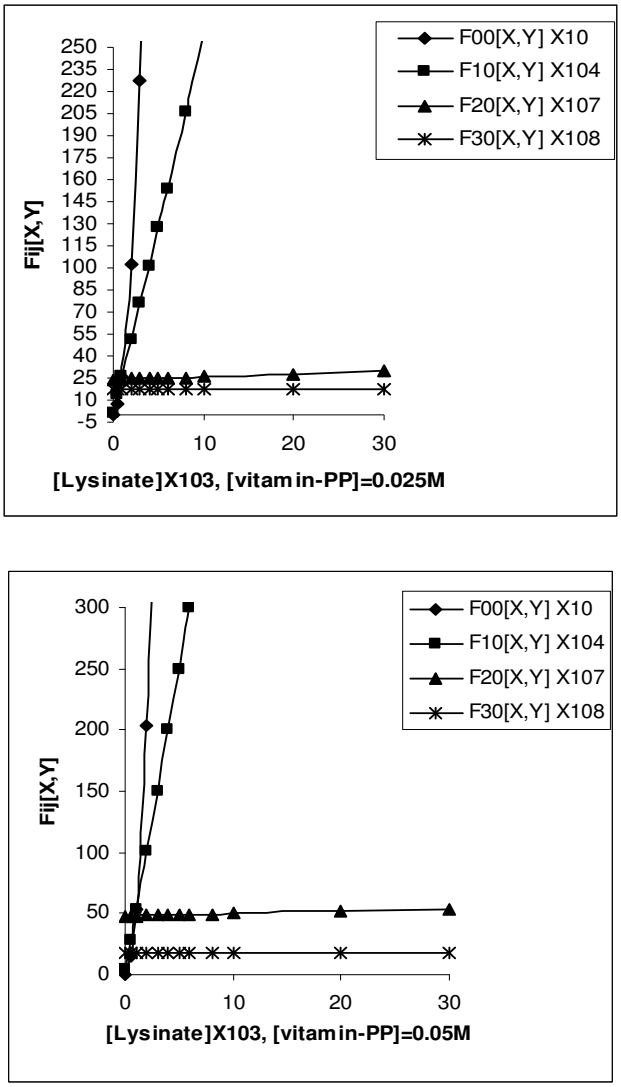


Figure 1. Plot of Fij[X, Y] vs. [X] for [Zn-L-lysinate-vitamin-PP] system.

Comparison of stability of binary and ternary complexes

To compare the stability of binary and ternary complexes, the values of mixing constant log K_m were calculated by the following equation [13]:

$$\log K_m = \log \beta_{11} - 1/2[\log \beta_{02} + \log \beta_{20}] \quad (1)$$

Values of log K_m are -0.33, -0.21, -0.45, -0.32, -0.09, 0.05, -11.62, -0.16, respectively, for [Zn-L-lysinate-vitamin-PP], [Zn-L-ornithinate-vitaminPP], [Zn-L threoninate–vitamin-PP], [Zn–L-serinate–vitamin-PP],[Zn–L-phenylglycinate–vita-min-PP], [Zn-L-phenylalaninate-vitamin-PP], [Zn-L-glutamate-vitamin-PP] and [Zn-L-aspartate-vitamin-PP] complexes. The positive values of log K_m indicate that the ternary complexes are more stable than the binary complexes, while the negative values indicate that the binary complexes are more stable than the ternary ones.

Trend of stability of ternary complexes

The sequence of stability constants of complexes with respect to ligands is L-lys < L-orn < L-thr < L-ser < L-phg < L-phe < L-glu < L-asp. It has been observed that as the size of amino acids increased the stability of its complexes decreased [14]. The stability of L-amino acid complex also depends upon the chelate ring formation and basicities of ligands [15]. In this study, the stability of lysinate complex is minimum owing to the lowest pK value of L-lysine, as expected [16]. In case of L-serine and L-threonine, the stability of the latter is less than the L-serine complex owing to the fact that electron withdrawing OH^- group is nearer to L-threoninate complex than L-serinate complex, causing greater repulsive forces between metal and OH^- group in L-threonine complexes than L-serine complexes. The higher stability of L-aspartate complexes than L-glutamate ones is obvious from the chelate ring formation; in these amino acids, the aspartate forms one five and one six-membered ring with the metal, while L-glutamate forms one six and one seven-membered ring. As the size of the ring in amino acid increases, the stability of complex decreases [17]. The stabilities of L-glutamate and L-aspartate complexes are greater than those of the L-lysinate, L-ornithinate, L-threoninate, L-serinate, L-phenylglycinate, L-phenylalaninate complexes, due to the large difference in their basic strength [18]. The same is evident from pK values of L-amino-acids [19].

In the case of vitamin-PP, N- atom of pyridine group and O- atom of amide group may take part in bond formation with Zn (II), forming a six-membered ring [20].

It is clear from the values of stability constants of the complexes that vitamin-PP and amino acids used either singly or simultaneously might be effective to reduce the toxicity of metal in vivo.

Thermodynamic parameters

The kind of complex species that reduces on a mercury electrode depends on thermodynamic aspects [21]. Thermodynamic parameters such as enthalpy change (ΔH), free energy change (ΔG) and entropy change (ΔS) of the complexes have been calculated by the following equation [22]:

$$\Delta H = 2.303\ R\ T_1\ T_2\ (\log\beta_2 - \log\beta_1) / T_2 - T_1 \qquad (2)$$

$$\Delta G = -2.303\ RT \log K \qquad (3)$$

$$\Delta G = \Delta H - T\Delta S \qquad (4)$$

It is clear from the values of ΔS, ΔG and ΔH in Table 2 that the stability constants ($\log \beta_1$) and ($\log \beta_2$) decreased with increase of temperature, confirming that complexes are not stable at higher temperature [23]. The values of ΔS are more negative at higher temperature and ΔG are less negative at higher temperature, confirming that complexes are not stable at higher temperature [24]. The negative values of ΔH show that these reactions are exothermic in nature [25].

Table 2. Thermodynamic parameters of ternary complexes of [Zn-aminoacidate-vitamin-PP] system.

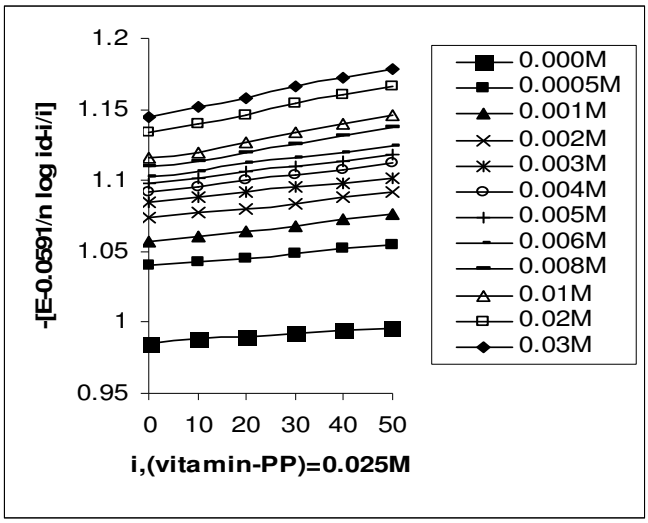
System	Stability constants			- ΔH kcal./mole			- ΔG kcal./mole			- ΔS cal./degree/mole		
	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$
	25ºC/35ºC	25ºC/35ºC	25ºC/35ºC	(35ºC-25ºC) for difference of 10ºC			25ºC/35ºC	25ºC/35ºC	25ºC/35ºC	25ºC/35ºC	25ºC/35ºC	25ºC/35ºC
[Zn⁻ L- lysinate	4.37	7.20	9.98	11.340	10.080	21.840	5.9591	9.8183	13.6093	18.0573	0.8788	27.6214
⁻vitamin-PP]	4.10	6.96	9.46				5.7785	9.8094	13.3329	18.0575	0.8792	27.6220
[Zn⁻L-ornithinate⁻	4.53	7.42	10.20	14.238	13.532	16.892	6.1773	10.1213	13.9123	27.0501	11.4475	10.0015
vitamin- PP]	4.19	7.10	9.80				5.9067	10.0067	13.8121	27.0504	11.4479	10.0022
[Zn⁻ L-threoni nate	4.68	-	10.38	20.160	-	15.960	6.3819	-	14.1547	46.2367	-	6.0590
⁻vitamin- PP]	4.20	-	10.00				5.9194	-	14.0940	46.2370	-	6.0596
[Zn⁻ L -serinate ⁻	4.84	7.75	10.60	18.480	11.340	16.472	6.6001	10.5683	14.4577	39.8668	2.5902	6.7617
vitamin-PP]	4.40	7.48	10.21				6.2013	10.5423	14.3899	39.8671	2.5907	6.7623
[Zn⁻L-	5.15	8.00	10.72				7.0228	10.9092	14.6184	4.6219	5.6745	3.0937
phenylglycinate	4.95	7.70	10.35	8.400	12.600	15.540	6.9765	10.8523	14.5872	4.6223	5.6750	3.0944
⁻vitamin-PP]												
[Zn⁻L-phenylalannate	5.31	8.22	10.94	13.86	12.26	16.89	7.2410	11.2120	14.9214	22.2124	3.5311	6.6153
⁻vitamin-PP]	4.98	7.93	10.54				7.0188	11.1765	14.8550	22.2127	3.5316	6.6159
[Zn⁻ L-glutamate	-	8.96	10.98	-	15.120	16.800	-	12.2183	14.9729	-	9.7381	6.1322
⁻vitamin-PP]	-	8.60	10.58				-	12.1208	14.9114	-	9.7387	6.1329
[Zn⁻ L-aspartate⁻	5.76	9.18	11.20	15.960	16.052	16.892	7.8546	12.5213	15.2759	27.2003	11.8502	5.4255
vitamin-PP]	5.38	8.80	10.80				7.5825	12.4027	15.2215	27.2006	11.8508	5.4262

Kinetic parameters

The kinetic parameters, viz., transfer coefficient (α), degree of irreversibility (λ), and standard rate constant (k), determined by Tamamushi and Tanaka method [46, 47] by plotting (E – RT/nF log i_d – i / i) against i and log (Z-1) against ($E^r_{1/2}$ – E) for [Zn – L-lysinate–vitamin-PP] system, are given in Fig. 2 and 3(a, b), respectively. Parameter Z is calculated by the following equation [26, 27]:

$$Z = \text{anti log } \{n F / 2.303RT (E^r_{1/2} - E)\} + \log i_d - i / I \qquad (5)$$

Values of kinetic parmeters are given in Table 3. It is obvious that α values varied from [Zn – L-lysinate – vitamin-PP] 0.357 to 0.555 (about 0.50), and values of α for other systems were also about 0.50, confirming that the 'transition state' lies midway between the dropping mercury electrode and the solution interface. The values of rate constant (k) varying from 3.28 to 9.60 $cm.sec^{-1}$, confirm that the electrode processes are quasireversible. The values of diffusion coefficient (D), as determined by Ilkovic equation, [28], are as expected.



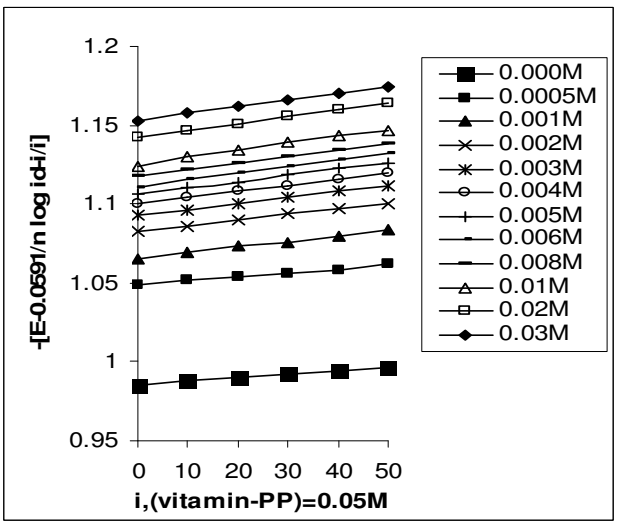


Figure 2. Plots between – [E-RT/nF log (id-i)/i] for Zn-L-lysinate-vitamin-PP system.

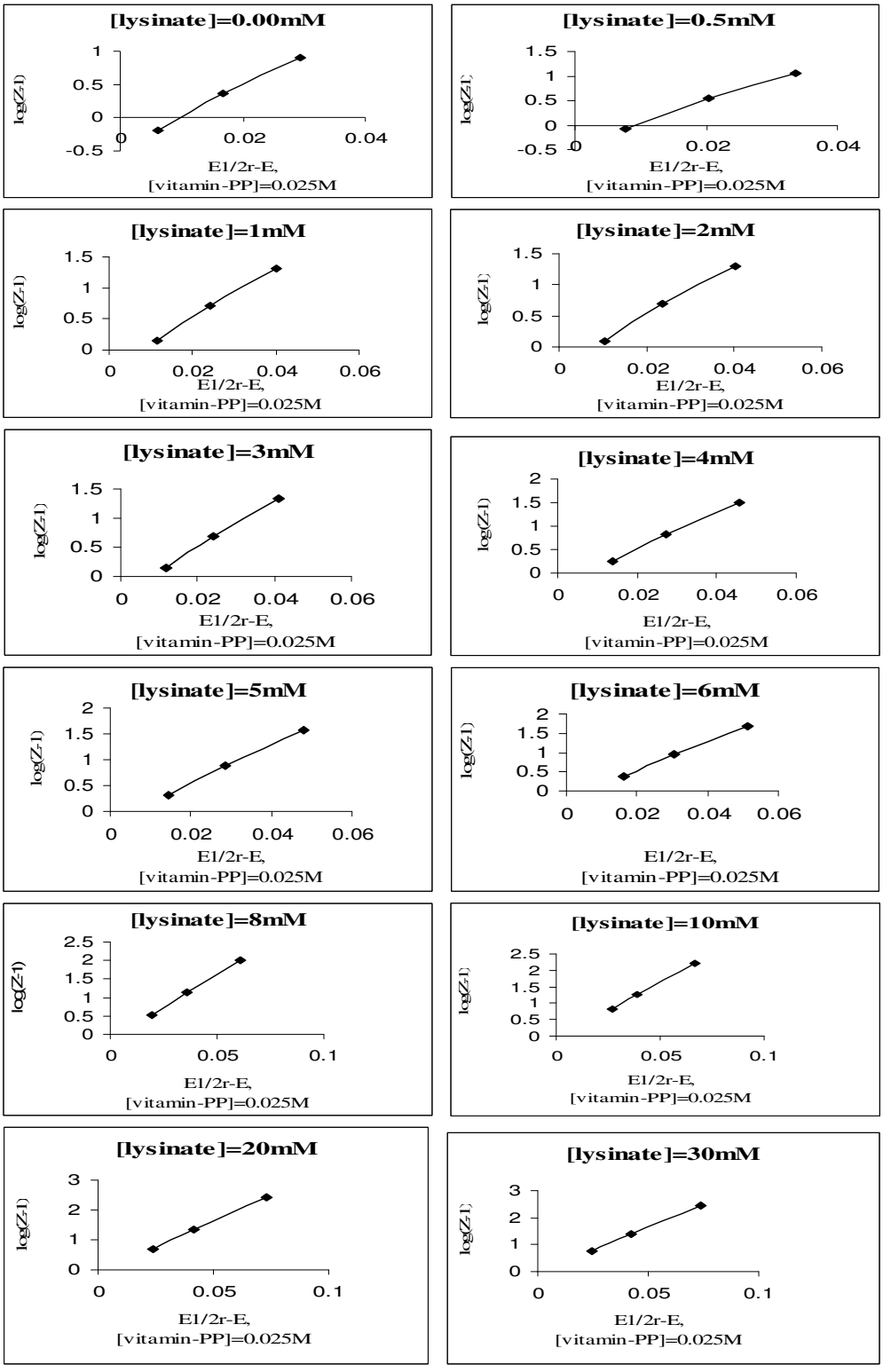


Figure 3a. Zn-L-lysinate-vitamin-PP system, plot of ($E^r_{1/2}$ - E) versus lg (Z-1). Y-axis = lg(Z-1), X-axis = ($E^r_{1/2}$ - E), vitamin-PP = 0.025 M (fixed).

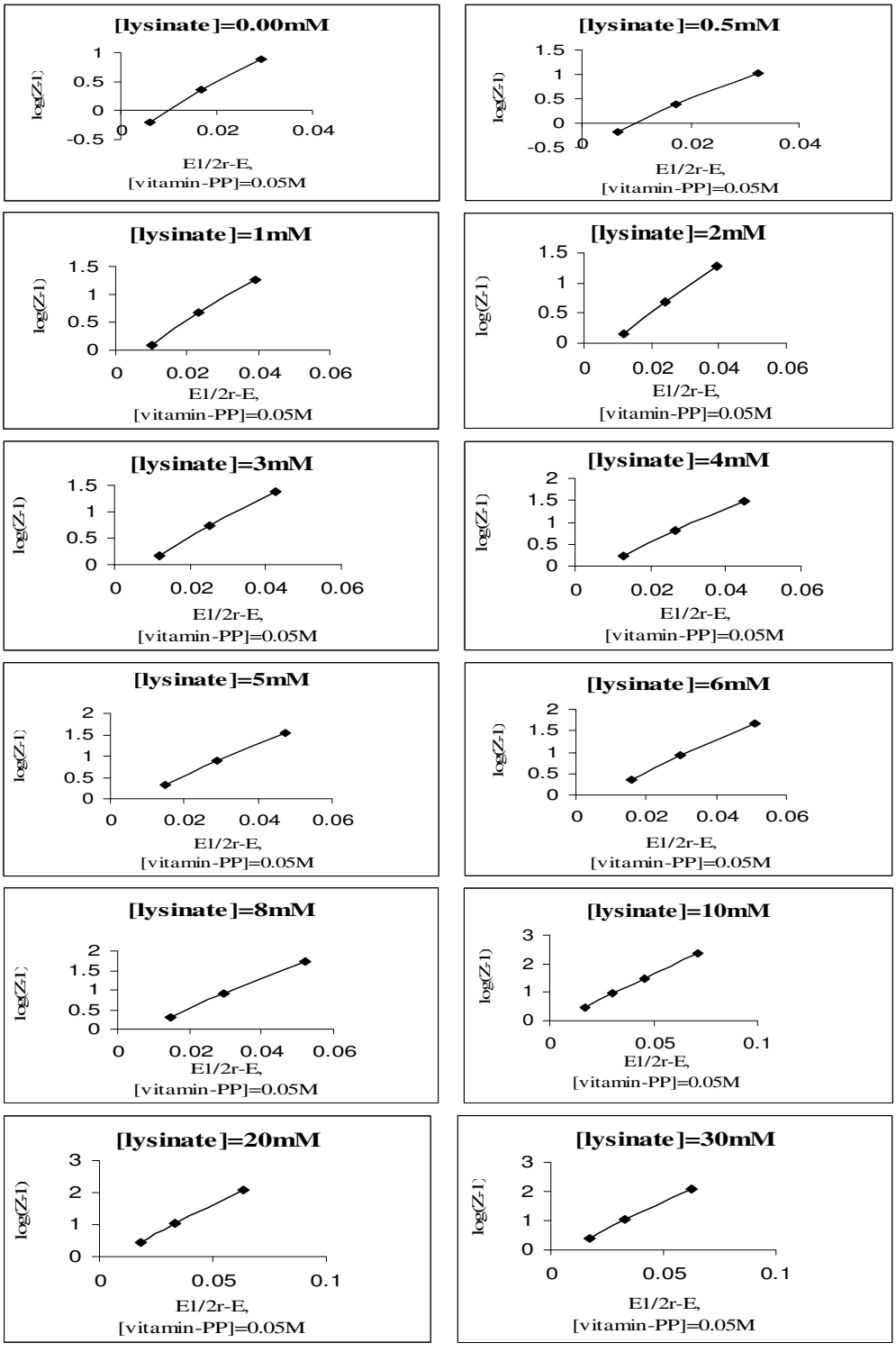


Figure 3b. Zn-L-lysinate-vitamin-PP system, plot of ($E^r_{1/2}$ - E) versus lg (Z-1). Y-axis = log(Z-1), X-axis = ($E^r_{1/2}$ - E), vitamin-PP = 0.05 M.

Table 3. Kinetic parameters of [Zn-L-lysinate-vitamin-PP] system. Zn (II) = 0.5 mM, μ =1.0 M $NaClO_4$, pH =7.30 ± 0.01, Temperature = 25 ºC.

[L-lys.] X 10^{-3}	**[vitamin-PP] = 0.025 M (fixed)**						**[vitamin-PP] = 0.05 M (fixed)**					
	$(E_{½})^{qr}$-V vs. SCE	Slope (mV)	α	λ $s^{-½}$	$D^{½}$ x 10^3 cm^2s^{-1}	k x10^3 cm s^{-1}	$(E_{½})^{qr}$-V vs. SCE	Slope (mV)	α	λ $s^{-½}$	$D^{½}$ x 10^3 $cm^2s^{-½}$	k x10^3 cm s^{-1}
0.00	1.000	36	0.357	1.702	4.085	6.955	1.000	36	0.403	1.517	4.085	6.198
0.50	1.043	37	0.486	1.517	4.019	6.098	1.054	36	0.357	1.910	4.019	7.677
1.00	1.060	36	0.532	1.074	3.953	4.246	1.070	37	0.505	0.952	3.953	3.785
2.00	1.077	38	0.464	1.205	3.888	4.685	1.087	37	0.406	1.702	3.887	6.618
3.00	1.088	37	0.508	1.205	3.828	4.606	1.097	37	0.518	1.205	3.822	4.606
4.00	1.095	38	0.508	1.074	3.756	4.034	1.105	37	0.532	1.074	3.756	4.034
5.00	1.101	38	0.518	1.074	3.690	3.963	1.111	36	0.449	1.205	3.690	4.447
6.00	1.106	37	0.555	0.957	3.624	3.469	1.115	36	0.403	1.517	3.624	5.498
8.00	1.113	36	0.508	2.698	3.558	9.600	1.123	36	0.505	1.074	3.558	3.822
10.00	1.119	36	0.535	1.074	3.492	3.751	1.128	37	0.546	0.853	3.492	2.979
20.00	1.138	37	0.555	0.957	3.426	3.280	1.147	36	0.505	1.074	3.426	3.680
30.00	1.149	38	0.518	0.957	3.426	3.280	1.157	36	0.571	0.853	3.426	2.923

Conclusion

In the present paper, interaction of Zn between L- amino acids and vitamin-PP in pH 7.30 ± 0.01 was investigated using simple DC polarography. The results indicated that current voltage curves are quasireversible and diffusion controlled in 1.0 M $NaClO_4$ at pH = 7.30 ± 0.01 and at 25 and 35 ºC. It is clear from the stability constant values of the complexes that vitamin-PP and amino acids used either singly or simultaneously might be effective to reduce the toxicity of metal in vivo. The negative values of ΔH indicated the exothermic nature of the metal-ligands interaction. The complexes were not stable at higher temperature which was confirmed by the values of ΔG and ΔS. Values of transfer coefficient (α) varied from 0.357 to 0.555 (0.50), showing that the 'transition state' behaves between oxidant and reductant response to applied potential and it lies in the midway between dropping mercury electrode and solution interface. The values of rate constant (k) varied from 3.28 to 9.60 $cm.sec^{-1}$ confirming the quasireversible nature of electrode processes.

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