STUDIES OF ELECTRODE KINETICS AND THERMODYNAMICS OF ZINC (II) COMPLEXES WITH SOME SULFONAMIDES AND CEPHAZOLIN ON A DROPPING MERCURY ELECTRODE

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ABSTRACT

Kinetic and thermodynamic parameters of the Zinc (II) complexes with some sulfonamides derivatives and cephazolin have been determined by polarographic technique at pH = 7.30 ± 0.01 in the presence of 1.0 M $NaClO_4$ at 25 ^{0}C. Electrode kinetics was discussed on the basis of kinetic parameters viz. transfer coefficient (α), degree of irreversibility (λ), diffusion coefficient (D) and rate constant (k). The stability constants of complexes and the effect of temperature have been determined by determining thermodynamic parameters such as free energy change (ΔG), enthalpy change (ΔH) and entropy change (ΔS). The formation of the metal complexes has been found to be spontaneous, exothermic and entropically unfavourable at higher temperature. The stoichiometry of these complexes was determined by Schaap and McMaster method and found to be 1:1:1, 1:2:1 and 1:1:2 complexes.

INTRODUCTION

The complexes forming properties of metals have been recognized for centuries and have represented some of the most fundamental breakthroughs in medicinal history The complexes of metal ions and sulfa drugs pointing to the combined antibacterial activity of sulfonamides and the antimicrobial

activity of heavy metals in some cases, and the activity of the metal complexes themselves, constitute an important field of research /1/. On the other hand Electrode kinetics between dropping mercury electrode (DME) and electro active species in solution interface is important in polarography /2/. Khan /3, 4/ has reported the kinetic and thermodynamic parameters of Mn (II) and Zn (II) complexes and relates them with transition state and rate constant. In continuation of these /5/, the author has studied the kinetics of electrochemical reactions and thermodynamic parameters of Zinc (II) complexes with some sulfonamides as primary ligands and cephazolin as a secondary ligand by polarographic technique. The values of transfer coefficient (α) shows that the 'transition state' behaves between reactant and product response to applied potential. The values of rate constants (k) found in order of $\sim 10^{-3}$ cm. sec.$^{-1}$ confirmed the quasireversible nature of the electrode process.

Keywords: polarography, stability constant, sulfonamide, cephazolin, thermodynamics.

EXPERIMENTAL

All the chemicals were of analytical grade quality and their solutions were prepared in doubly distilled water. Zinc chloride (Fluka) was used for the metal solution. Sodium salts of all the selected sulfur drugs (Sigma) and cephazolin (Aldrich) were used without any further purification.

pH measurements of the analytes were made on a Elico pH meter (LI – 10) using glass and calomel electrodes and fixed at 7.30 ± 0.01 which was adjusted with dilute solutions of $HClO_4$ or NaOH (both BDH) as required. It has been observed that the maximum shift of $E_{1/2}$ was obtained at pH range 7.30 - 8.50, but pH = 7.30 ± 0.01 was selected on account of studying the complexes in human blood pH.

The electrochemical behavior of zinc complexes has been investigated in 0.1 M $NaClO_4$ (supporting electrolyte) at 7.30 ± 0.01 using Polarographic Analyzer (Elico, Hyderabad Model CL - 362) with calomel as reference electrode and d.m.e as working electrodes. The polarographic capillary was 5.0 cm. long with diameter 0.06 mm with dropping mercury electrode (DME) characteristics $m^{2/3}t^{1/6} = 2.04$ $mg^{2/3}s^{-1/2}$. All the analytes were deaerated by

pure nitrogen gas before recording the current - voltage data. Potassium dihydrogen phosphate – sodium hydroxide buffer was added with the analyte to stabilize its pH. The entire study was carried out at 25 ^{0}C and 35 ^{0}C.

RESULTS AND DISCUSSION

Zinc and its complexes gave a well-defined two electron quasireversible reduction wave /6/ at pH = 7.20 to 8.50 in the presence of 1.0 M $NaClO_4$ at 25 ^{0}C /7/.

[Zn – sulfonamide – cephazolin] complexes.

In this system, The concentration of primary ligand i.e. sulfonamides varied from 0.50 mM to 30.0 mM at 0.025 M to 0.050 M constant concentration of cephazolin. The concentration of Zn(II) and $NaClO_4$ were 0.5 mM, 1.0 M respectively. The half wave potential $E_{1/2}$ values became more negative with the addition of cephazolin to the binary complex [Zn – sulfonamide] confirmed the [Zn – sulfonamide – cephazolin] complex formation. The stability constant of ternary complexes were determined by Schaap and McMaster /8/ method which confirmed the formation of 1:1:1, 1:2:1 and 1:1:2 metal ligand complexes. In all the cases, the Gelling method /9/ was used to determine the $E_{1/2}^{reversible}$ values from $E_{1/2}^{quasireversible}$ values. The plots between - [E-RT/nF log $(i_d$-i)/i] vs i for [Zn - sulfadiazine - cephazolin] complex were given in Fig.1. The data and plots between F_{ij}[X, Y] vs [X] for [Zn – sulfadiazine – cephazolin] complex {where X and Y are sulfonamide and cephazolin and i and j are the stoichiometric numbers for primary and secondary ligands respectively} were given in (Table 1) and (Fig. 2) respectively. The values of stability constant of complexes were given in (Table 2).

The value of mixing constant log K_m, which compares the stability of binary and ternary complexes have been calculated by following equation /8/

$$\log K_m = \log\beta_{11} - \tfrac{1}{2}\,[\log\beta_{02} + \log\beta_{20}] \qquad (1)$$

The values of log K_m were -0.285, -0.295, 0.115, -0.355, -0.385, -0.380 and -0.315 for [Zn - sulfadiazine – cephazolin], [Zn – sulfisoxazole –

cephazolin], [Zn – sulfamethoxazole – cephazolin], [Zn – sulfamethazine – cephazolin], [Zn – sulfathiazole – cephazolin], [Zn – sulfacetamide – cephazolin] and [Zn – sulfanilamide – cephazolin] complexes respectively. The negative values of log K_m showed that binary complexes are more stable than their ternary complexes while in case of [Zn – sulfamethoxazole – cephazolin] the positive value indicates that the ternary complex is more stable then their simple binary complexes.

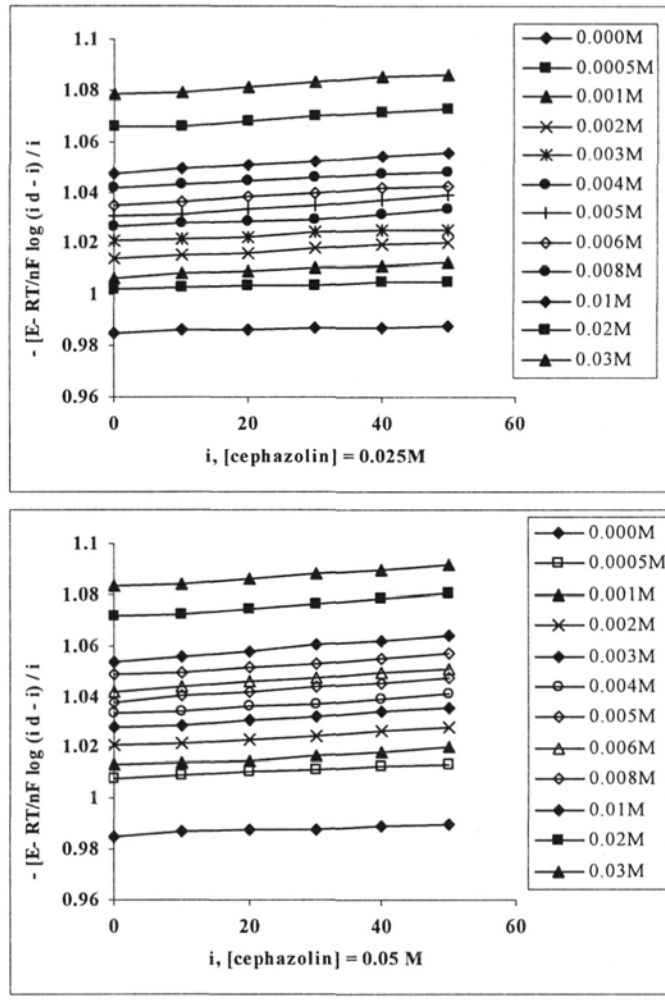


Fig. 1: Plots between - [E-RT/nF log (i_d-i)/i] vs i for [Zn - sulfadiazine - cephazolin] complex.

Table 1

Polarographic data and $F_{ij}[X, Y]$ values of [Zn - sulfadiazine – cephazolin] complex, Zn(II) = 0.05 mM

[Sulfad.] $X10^3$	[cephazolin]= 0.025 M (Fixed)						[cephazolin] = 0.050 M (Fixed)					
	$E_{1/2}^r$ - v vs SCE	$\log(i_m/i_c)$	$F_{00}[X,Y]$	$F_{10}[X,Y]$ $X10^3$	$F_{20}[X,Y]$ $X10^5$	$F_{30}[X,Y]$ $X10^6$	$E_{1/2}^r$ - v vs SCE	$\log(i_m/i_c)$	$F_{00}[X,Y]$	$F_{10}[X,Y]$ $X10^3$	$F_{20}[X,Y]$ $X10^5$	$F_{30}[X,Y]$ $X10^6$
0.00	0.985	-	-	-	-	-	0.985	-	-	-	-	-
0.50	1.002	0.0071	3.90	2.04	10.65	25.70	1.009	0.0071	6.81	3.02	19.73	25.70
1.00	1.006	0.0142	5.46	2.58	10.78	25.7	1.013	0.0142	9.32	4.02	19.86	25.71
2.00	1.014	0.0215	10.30	3.71	11.04	25.71	1.021	0.0215	17.41	6.06	20.11	25.69
3.00	1.021	0.0290	17.56	4.89	11.29	25.69	1.028	0.0290	29.73	8.15	20.37	25.70
4.00	1.026	0.0365	27.38	6.12	11.55	25.69	1.033	0.0365	46.44	10.30	20.63	25.69
5.00	1.031	0.0442	39.92	7.41	11.81	25.70	1.038	0.0442	67.68	12.50	20.88	25.7
6.00	1.035	0.0520	55.34	8.74	12.06	25.71	1.042	0.0520	93.62	14.70	21.14	25.71
8.00	1.041	0.0681	95.41	11.60	12.58	25.69	1.048	0.0600	160.18	19.40	21.66	25.72
10.00	1.047	0.0681	148.82	14.600	13.09	25.68	1.054	0.0681	247.33	24.20	22.17	25.69
20.00	1.066	0.0681	659.54	32.80	15.66	25.71	1.072	0.0764	1035.50	51.50	24.74	25.69
30.00	1.078	0.0681	1689.45	56.20	18.24	25.72	1.083	0.0764	2524.20	84.96	27.31	25.70

μ =1.0 M $NaClO_4$, pH = 7.30 ± 0.01, Temperature = 25 ^{0}C

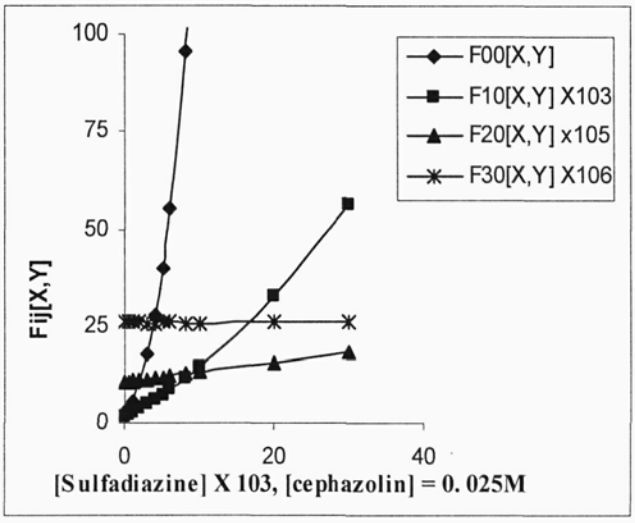
log A = 0.450, log B = 3.177, log C = 6.022, log D = 7.41 log A = 0.724, log B = 3.309, log C = 6.292, log D = 7.41

Table 2

. Stability constant values of [Zn – sulfonamide - cephazolin] complexes, Zn(II) = 0.50 mM, μ = 1.0 M $NaClO_4$, pH = 7.30 ± 0.01, Temperature = 25 ^{0}C

primary ligands	$\log\beta_{01}$	$\log\beta_{02}$	$\log\beta_{10}$	$\log\beta_{20}$	$\log\beta_{30}$	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$
sulfadiazine	-	-	3.10	5.16	7.41	3.61	5.36	7.56
sulfisoxazole	-	-	3.40	5.36	7.61	3.70	5.53	7.70
sulfamethaxyzole	-	-	4.40	6.16	8.65	4.51	6.43	8.63
sulfamethazine	-	-	4.56	7.40	8.73	4.66	7.51	8.88
sulfathiazole	-	-	4.63	7.60	8.83	4.73	7.75	9.00
sulfacetamide	-	-	4.75	7.83	9.00	4.85	8.00	9.20
sulfanilamide	-	-	4.93	8.00	9.20	5.00	8.10	9.31
cephazolin	1.81	2.63	-	-	-	-	-	

The order of the stability constants of the formed complexes follows the sequence sulfadiazine < sulfisoxazole < sulfamethaxyzole < sulfamethazine < sulfathiazole < sulfacetamide < sulfanilamide. The influence of substituents on the stability of the complexes was examined on the basis of electron repelling property of the substituent. It is clear from the values of stability constants of complexes that sulfadiazine formed the complexes of minimum stability as its complexes showed the lowest values of $E_{1/2}$ in comparison to the other sulfonamide complexes /10/. The stability constants of sulfisoxazole complexes are lesser than sulfamethoxazole complexes is due to the presence of two electron withdrawing —CH_3 groups in former than in the latter caused greater steric hindrance /11/ in sulfisoxazole complexes than sulfamethoxazole complexes. Similar is the case with sulfamethazine and sulfathiazole complexes. In case of sulfacetamide and sulfanilamide, the former is the N^1 – acetyl-substituted derivatives of sulfanilamide formed complexes with Zinc having lesser stability constants than sulfanilamide complexes might be the fact that it has —CH_3CO group /11/. The highest values of stability constants of sulfanilamide complexes amongst all other sulfonamide are due to having the largest shift of $E_{1/2}$ in its complexes /10]. These ligands offered bonding to metal ion through the sulfonamido nitrogen atom and sulfonyl oxygen atom of —SO_2 group /12, 13/. In the case of cephazolin, N of the β – lactam ring and O of the carboxylic group might take part in bond formation with Zinc making five membered ring /3/.



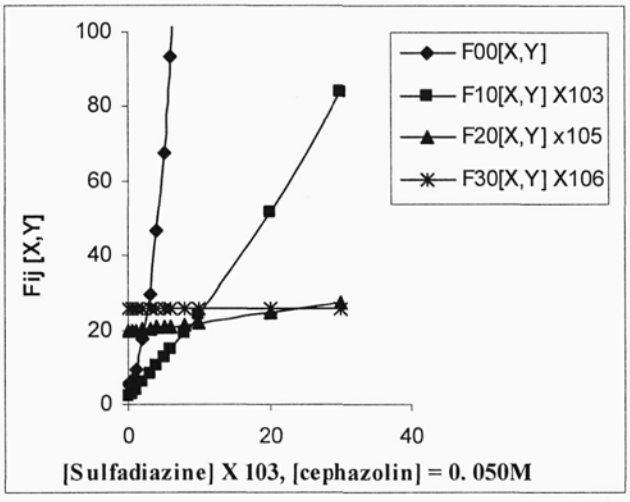


Fig. 2: Plots between $F_{ij}[X, Y]$ vs [X] for [Zn - sulfadiazine - cephazolin] complex.

Kinetic parameters of [Zn - sulfonamide - cephazolin] complexes.

The electrochemical reactions between complex species and a dropping mercury electrode can be understood in the following manner:

$$O(S) + ne\ (DME) \xrightarrow{k_{red}} R$$

where O in the electroactive species may be Zn(II) or Zn - complex system and R is the reduced species.

The values of rate constant k_{red} for a redox system is given by the following equation /14/

$$k_{red} = Z\,e\left[\frac{\{-\Delta G_{red\ no\ voltage}}{RT}\frac{\{-\alpha FV\}}{RT}\right] \quad (2)$$

where the terms have the usual meanings /14/.

The values of transfer coefficient (α), degree of irreversibility (λ) and rate constant (k) were determined by the Tamamushi and Tanaka method /14,15/ by plotting ($E_{1/2}^{r}$-E) against log (Z-1) using the following equations:

$$\log (Z-1) = \log \frac{1.13}{\lambda t^{1/2}} + \frac{(1-\alpha)\, nF\,(E_{1/2}^{reversible} - E)}{RT} \quad (3)$$

The values of Z can be calculated by the following equation /14]

$$Z = \text{antilog}\ \frac{[N\ F]}{RT\left(E_{1/2}^{r} - E\right)} + \log\frac{[i_d - i]}{i} \quad (4)$$

where the terms have the usual meanings /14,15/. The values of kinetic parameters for the [Zn- sulfadiazine - cephazolin] complex are given in (Table 3). The value of transfer coefficient (α) for the [Zn - sulfonamide - cephazolin] complexes varied from 0.42 to 0.56 showed that "transition state" is a function of applied potential and its value of 0.50 means that the 'transition state' behaves between oxidant and reductant response to applied potential and it always lies in an exact mid of between dropping mercury electrode and solution interface /14/. The values of diffusion coefficient D that is a measure of the thickness of the diffusion layer also have the expected values /16/. The rate constant (k) depend only on applied voltage and its

values for the [Zn - sulfonamide - cephazolin] complexes varied from 4.21 x 10^{-3} cm.sec.$^{-1}$ to 9.67 x10^{-3} cm.sec.$^{-1}$ confirmed the quasireversible nature of electrode processes /17/. A small variation in potential not only affects the rate but rate constant greatly.

Thermodynamic parameters of [Zn - sulfonamide - cephalothin] complexes.

The thermodynamic parameters viz. free energy change (ΔG), enthalpy change (ΔH) and entropy change (ΔS) were calculated by the following well known relationships /18/

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$$\Delta H = \frac{2.303\, R\, T_1 T_2 \left(\log \beta_2 - \log \beta_1\right)}{T_2 - T_1} \qquad (5)$$

$$-\Delta G = RT \log \beta \qquad (6)$$

and

$$\Delta G = \Delta H - T\Delta S \qquad (7)$$

where $\log \beta_1$ = stability constants at 25 ^{0}C and $\log \beta_2$ = stability constants at 25 ^{0}C.

All thermodynamic parameters of the [Zn - sulfonamide - cephazolin] complexes were recorded in Table 4. From these results the following conclusions can be made:

i) All the stability constants ($\log \beta_1$) and ($\log \beta_2$) decrease with increasing temperature, confirming that complexes are not favorable at higher temperature /18,19].

ii) The negative value of ΔG for the complexation process suggests a spontaneous nature of such process /20].

iii) The ΔH values are negative, meaning that the exothermic nature of metal-ligand interaction and favourable at lower temperature /20].

iv) The ΔS values for the ligand complexes are negative, confirming that the complex formation is entropically unfavourable /21/.

Table 3

. Kinetic Parameters of [Zn - sulfadiazine – cephazolin] complex, Zn(II) = 0.50 mM, μ =1.0 M $NaClO_4$, pH = 7.30 ± 0.01, Temperature = 25 ^{0}C

[sulfad.]	[cephazolin] = 0.025 M					[cephazolin] = 0.025 M				
X 10^3	$(E_{1/2})^{qr}$ -V vs SCE	α	λ $s^{-1/2}$	$D^{1/2}$ X 10^3 cm^2s^{-1}	k X 10^3 cms^{-1}	$(E_{1/2})^{qr}$ -V vs SCE	α	λ $s^{-1/2}$	$D^{1/2}$ X 10^3 cm^2s^{-1}	k X 10^3 cms^{-1}
0.00	1.000	0.47	1.20	4.08	5.08	1.000	0.47	1.20	4.08	5.08
0.50	1.003	0.50	1.70	4.02	6.84	1.010	0.43	2.40	4.02	9.67
1.00	1.007	0.42	2.40	3.95	9.51	1.014	0.45	1.91	3.95	7.55
2.00	1.015	0.44	1.70	3.89	6.62	1.022	0.44	2.40	3.89	9.35
3.00	1.022	0.44	2.40	3.82	9.19	1.030	0.45	2.14	3.82	8.19
4.00	1.028	0.43	1.91	3.76	7.17	1.033	0.50	1.70	3.76	6.39
5.00	1.033	0.44	1.91	3.69	7.05	1.040	0.44	1.52	3.69	5.60
6.00	1.036	0.49	1.52	3.62	5.50	1.043	0.45	1.70	3.62	6.17
8.00	1.041	0.42	1.70	3.49	5.95	1.050	0.50	1.52	3.56	5.40
10.00	1.050	0.50	1.21	3.49	4.21	1.055	0.44	1.70	3.49	5.95
20.00	1.067	0.42	1.70	3.49	5.95	1.073	0.49	1.52	3.43	5.20
30.00	1.080	0.44	1.52	3.49	5.30	1.085	0.49	1.52	3.43	5.20

Table 4

. Stability constants and the thermodynamic parameters of [Zn - sulfonamide - cephazolin] complexes at 25 ^{0}C and 35 ^{0}C

complexes	stability constants			- Δ H K cal./mole			- Δ G K cal./mole			- Δ S K cal./mole		
	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$
	25°C/ 35°C	25°C/ 35°C	25°C/ 35°C	(35°C-25°C) for difference of 10°C			25°C/ 35°C	25°C/ 35°C	25°C/ 35°C	25°C/ 35°C	25°C/ 35°C	25°C/ 35°C
[Zn - sulfadiazine–	3.61	5.36	7.56				4.9228	7.3093	10.3093	18.7160	12.1173	41.5139
cephazolin]	3.36	5.10	7.02	10.5002	10.9202	22.6805	4.7357	7.1881	9.8942	18.7161	12.1174	41.5140
[Zn - sulfisoxazole	3.70	5.53	7.70				5.0456	7.5411	10.5003	15.4853	19.7959	12.6847
- cephazolin]	3.47	5.21	7.36	9.66021	13.4403	14.2803	4.8907	7.34313	10.3734	15.4854	19.7960	12.6848
[Zn-sulfamethaxyzole	4.51	6.43	8.63				6.1502	8.7684	11.7685	20.2352	17.0869	8.4289
– cephazolin]	4.22	6.10	8.29	12.1803	13.8603	14.2803	5.9478	8.59752	11.6842	20.2353	17.0870	8.4290
[Zn - sulfamethazine	4.66	7.51	8.88				6.3547	10.2412	12.1094	28.0054	10.7353	31.2452
- cephazolin]	4.31	7.19	8.37	14.7003	13.4403	21.4205	6.0746	10.1338	11.7969	28.0055	10.7354	31.2453
[Zn - sulfathiazole	4.73	7.75	9.00				6.4502	10.5684	12.2730	29.0945	22.3219	22.2395
- cephazolin]	4.37	7.34	8.55	15.1203	17.2204	18.9004	6.1592	10.3452	12.0506	29.0946	22.3220	22.2396
[Zn - sulfacetamide -	4.85	8.00	9.20				6.6138	10.9094	12.5458	14.4511	16.9496	11.4583
cephazolin]				10.9202	15.9603	15.9603						
	4.59	7.62	8.82				6.4693	10.7399	12.4312	14.4512	16.9497	11.4584
[Zn -	5.00	8.10	9.31				6.8184	11.0457	12.6958	40.5438	37.6334	25.0492
sulfanilamide -	4.55	7.57	8.83	18.9004	22.2605	20.1604	6.4129	10.6694	12.4453	40.5439	37.6335	25.0493
cephazolin]												

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