ECLÉTICA Química
www.scielo.br/eq
www.ecletica.iq.unesp.br
Volume 33, número 1, 2008

Stability constants and thermodynamic parameters of cadmium complexes with sulfonamides and cephapirin

M. S. Parihar and F. Khan
Department of Chemistry, Dr. H. S. Gour University, Sagar, M. P. India
** faridkhan58@yahoo.com*

Abstract: Stability constant (log ∈) and thermodynamic parameters of Cd^{2+} complexes with sulfonamide and cephapirin were determined by Polarographic technique at pH = 7.30 ± 0.01 and μ = 1.0 M KNO_3 at 250°C. The sulfonamides were sulfadiazine, sulfisoxazole, sulfamethaxazole, sulfamethazine, sulfathiazole, sulfacetamide and sulfanilamide used as primary ligands and cephapirin as secondary ligand. Cd^{2+} formed 1:1:1, 1:2:1 and 1:1:2 complexes. The nature of electrode processes were reversible and diffusion controlled. The stability constants and thermodynamic parameters (æG, æH and æS) were determined. The formation of the metal complexes has been found to be spontaneous, exothermic in nature, and entropically unfavourable at higher temperature.

Keyword: polarography; stability constant; sulfonamide; cephapirin; thermodynamics.

Introduction

The investigation of metal sulfonamide compounds has received much attention due to the fact that sulfonamides were the first effective chemotherapeutic agents to be employed for the prevention and cure of bacterial infections in humans [1]. The sulphur containing ligands are well known for their anticarcinogenic, antibacterial, tuberculostatic, antifungal, insecticidal, and acaricidal activities [2]. It has been reported that the biological activity of sulphur-containing ligands gets enhanced on undergoing complexation with metal ions [2- 4]. Cephapirin is also a cephalosporin antibiotic which has a broad spectrum of activity against gram-negative bacilli and gram-positive cocci [5]. On the other hand, Cd^{2+} is a non-essential heavy metal that is normally present in very low concentrations in our environment [6]. However, due to industrial uses of Cd^{2+}, some people can be exposed too much higher concentrations [7] as a result of which they suffer from many serious diseases [8,9]. The concentration of Cd^{2+} in blood and urine in human beings can be reduced by ligand therapy [10]. Sulfonamides are used in combination with other drugs as chemotherapeutic agents in bacterial infections and serious diseases in human [11,12]. Therefore sulfonamides alone or in combination with cephapirin could be effective against cadmium toxicity.

Experimental

All the chemicals were of analytical grade quality and their solutions were prepared in bi distilled water. Sodium salts of all the selected sulfur drugs and cephapirin (Fluka, Sigma and Aldrich) were used without any additional 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 HNO_3 or NaOH as required.

Electrochemical Analysis was performed using a Polarographic Analyzer (Elico, Hyderabad Model CL - 362). 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.

Results and discussion

A well defined two electron [13] reversible reduction and diffusion controlled wave Cd^{2+} was observed in 1.0 M KNO_3 at pH = 7.30 to 8.50 [14], but pH = 7.30 was selected to study the complex formation in human blood pH. The value of $E_{1/2}^{reversible}$ for Cd was - 586 mV vs SCE. The nature of current - voltage curve of Cd^{2+} complexes with sulfonamide and cephapirin was also reversible and diffusion controlled.

Stability constant of [Cd – sulfonamide – cephapirin] complexes

In this system, the concentration of Cd^{2+}, KNO_3 and gelatin were 0.50 mM, 1.0 M and 0.001% respectively. Neither cephapirin nor sulfonamide gave their current voltage curves in 1.0 M KNO_3 at pH = 7.30 ± 0.01 at 25 ^{0}C. When [Cd^{2+}] was added with either of the drugs, complex formation was taken place and their current voltage curves were obtained. The concentration of sulfonamide in the analyte varied from 0.50 mM to 30.0 mM at 0.025 M to 0.05 M constant concentration of cephapirin. The half wave potential $E_{1/2}$ values become more negative with the addition of cephapirin to the binary complex [Cd – sulfonamide] confirmed the [Cd – sulfonamide – cephapirin] complex formation. The stability constant of ternary complexes were determined by using Schaap and McMaster [15] method which confirmed the formation of 1:1:1, 1:2:1 and 1:1:2 metal ligand complexes. The values of stability constant of complexes were given in (Table 1). The data and plots between F_{ij} [X, Y] vs [X] for [Cd – sulfadiazine – cephapirin] complex {where X and Y are sulfonamide and cephapirin and i and j are the stoichiometric numbers for primary and secondary ligands respectively} were given in (Table 2) and (Fig. 1) respectively. The polarograms of [Cd - sulfadiazine – cephapirin] at [cephapirin] = 0.025 M were given in (Fig. 2). It is clear from the polarograms that $E_{1/2}$ values of [Cd – sulfadiazine – cephapirin] increased with increased of the concentration of cephapirin confirmed the ternary complex formation. These ligands offered bonding to metal ion through the sulfonamido nitrogen atom and sulfonyl oxygen atom of SO_2 group [16, 17]. In case of cephapirin, N of the €– lactam ring and O of the carboxylic group might take part in bond formation with Cd making 5 membered ring [18].

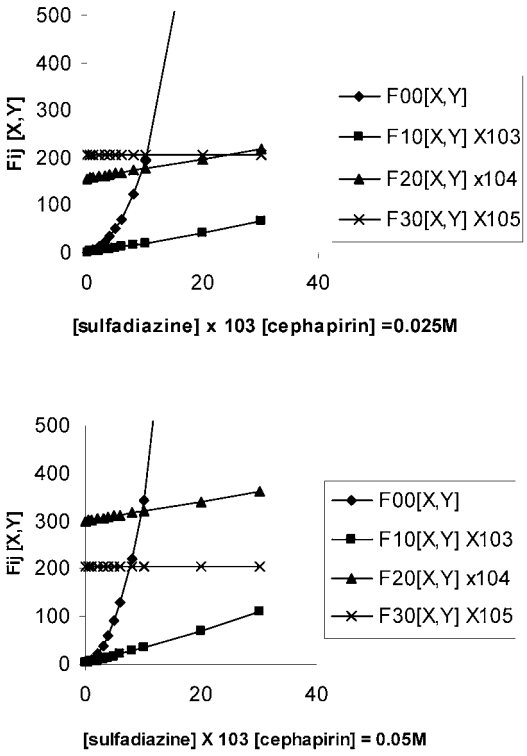

Figure 1. [Cd - sulfadiazine - cephapirin] complex.

Table 1. Stability constant values of [Cd – sulfonamide - cephapirin] complex [Cd^{2+}] = 0.5 mM μ = 1.0 M KNO_3, pH = 7.30 ± 0.01, Temperature = 25 ^{0}C

Primary ligands	$\log\beta_{01}$	$\log\beta_{02}$	$\log\beta_{03}$	$\log\beta_{10}$	$\log\beta_{20}$	$\log\beta_{30}$	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$
Sulfadiazine	-	-	-	3.00	5.10	7.31	3.60	5.31	7.76
Sulfisoxazole	-	-	-	3.30	5.23	7.48	3.70	5.56	7.83
Sulfamethaxyzole	-	-	-	4.23	6.00	8.45	4.45	6.60	8.63
Sulfamethazine	-	-	-	4.30	7.31	8.60	4.56	7.60	8.73
Sulfathiazole	-	-	-	4.46	7.53	8.68	4.63	7.75	8.86
Sulfacetamide	-	-	-	4.60	7.66	8.80	4.91	8.00	9.10
Sulfanilamide	-	-	-	4.70	7.95	9.15	5.00	8.31	9.20
Cephapirin	1.70	2.63	3.45	-	-	-	-	-	-

Table 2. Polarographic data and $F_{ij}[X, Y]$ values of [Cd - sulfadiazine – cephapirin] complex, [Cd^{2+}] = 0.50 mM, μ =1.0 M KNO_3, pH = 7.30 ± 0.01, Temperature = 25 ^{0}C

[Sulfa.] $X10^3$	[Cephapirin]= 0.025 M (Fixed)						[Cephapirin] = 0.050 M (Fixed)					
	$E_{1/2}$ r - V vs SCE	$\log(i_m/i_c)$	$F_{00}[X,Y]$	$F_{10}[X,Y]$ $X10^3$	$F_{20}[X,Y]$ $X10^4$	$F_{30}[X,Y]$ $X10^5$	$E_{1/2}$ r - V vs SCE	$\log(i_m/i_c)$	$F_{00}[X,Y]$	$F_{10}[X,Y]$ $X10^3$	$F_{20}[X,Y]$ $X10^4$	$F_{30}[X,Y]$ $X10^5$
0.00	0.586	-	-	-	-	-	0.586	-	-	-	-	-
0.50	0.602	0.0072	3.57	2.01	157.41	204.17	0.610	0.0072	6.53	3.22	301.20	204.17
1.00	0.607	0.0145	5.38	2.81	158.43	204.18	0.615	0.0145	9.66	4.74	302.22	204.18
2.00	0.617	0.0219	11.44	4.44	160.47	204.17	0.624	0.0219	20.52	7.80	304.26	204.19
3.00	0.624	0.0295	20.88	6.10	162.51	204.16	0.632	0.0295	37.63	10.90	306.30	204.18
4.00	0.630	0.0371	33.81	7.81	164.55	204.18	0.638	0.0371	61.12	14.05	308.34	204.17
5.00	0.635	0.0450	50.36	9.56	166.59	204.17	0.643	0.0450	91.10	17.23	310.38	204.18
6.00	0.639	0.0529	70.66	11.35	168.63	204.16	0.647	0.0529	127.70	20.46	312.43	204.19
8.00	0.646	0.0611	122.96	15.05	172.71	204.17	0.653	0.0611	221.25	27.04	316.51	204.16
10.00	0.652	0.0611	191.70	18.91	176.80	204.18	0.659	0.0693	342.74	33.78	320.59	204.17
20.00	0.670	0.0693	816.24	40.68	197.21	204.17	0.677	0.0693	1403.66	69.94	340.99	204.18
30.00	0.681	0.0693	1998.66	66.54	217.61	204.16	0.688	0.0693	3310.17	110.17	361.41	204.17
log A = 0.409, log B = 3.089, log C = 6.194, log D = 7.31							log A = 0.692, log B = 3.233, log C = 6.448, log D = 7.31					

Thermodynamic parameters of [Cd - sulfonamide - cephapirin] complexes:

The thermodynamic parameters, free energy change (æG), enthalpy change (æH) and entropy change (æS) were calculated by following relationships [19].

$$æH = \frac{2.303\ R\ T_1T_2\ (\log€_2 - \log€_1)}{T_1T_2}$$

$$- æG = RT \log æ$$

and

$$æG = æH - TæS$$

The thermodynamic parameters of the [Cd - sulfonamide - cephapirin] complexes were given in (Table 3). It is clear from the thermodynamic parameters of complexes that:

a) The stability constants ($\log€_1$) and ($\log€_2$) decreased with increased of temperature, confirming that complexes are not stable at higher temperature [19, 20].

b) Sufficiently large negative value of æG showed that spontaneous formation of the complexes. Spontaneity increased with temperature, except in the Cd^{2+} complex [21].

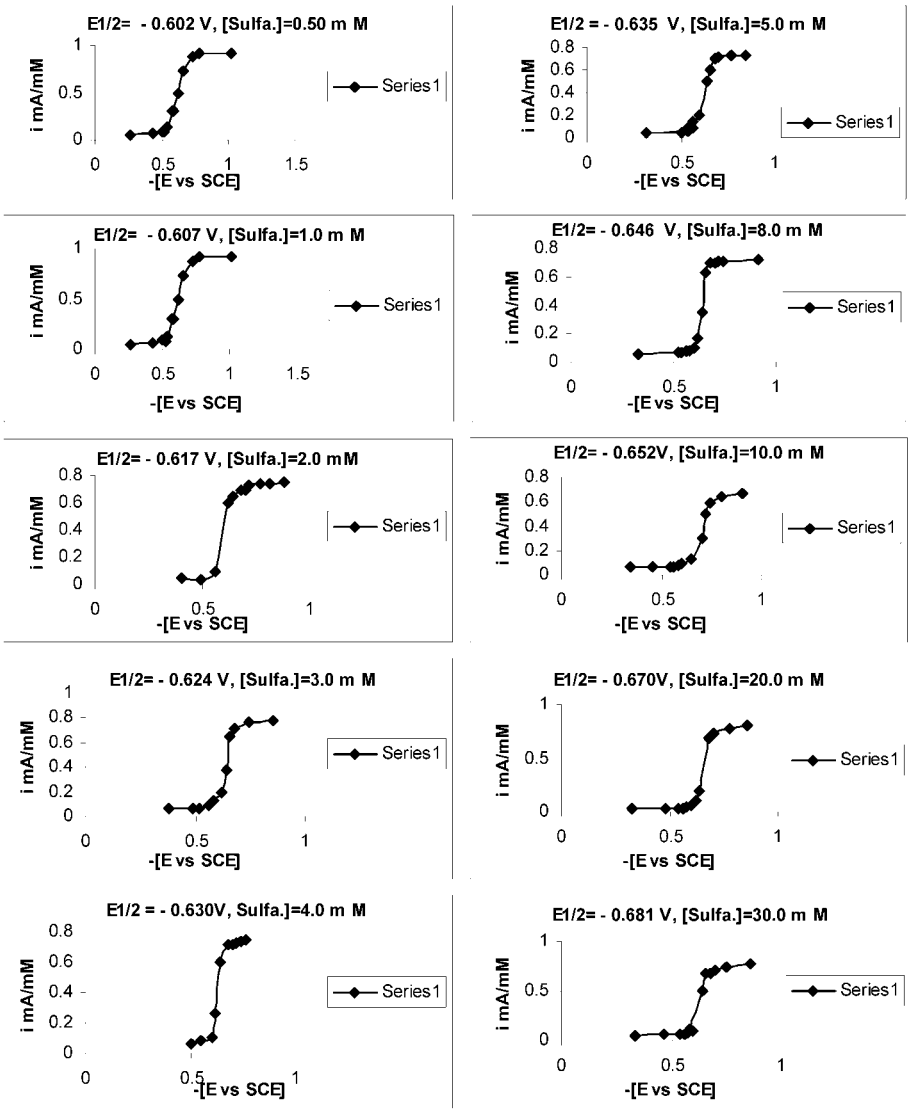

Figure 2. Polarograms of [Cd – Sulfadiazine – Cephapirin] System, [Cephapirin] = 0.025M

c) Negative values of æH indicated the exothermic nature of the metal-ligand interaction [21].

d) The æS values for the ligand complexes are negative, confirming that the complex formation is entropically unfavourable [22].

Comparison of stability of the binary and ternary complexes:

The value of mixing constant log K_m, which compares the stability of binary and ternary complexes have been calculated by following equation [15].

$$\log K_m = \log \epsilon_{11} - 1/2 [\log \epsilon_{02} + \log \epsilon_{20}]$$

The values of log K_m were -0.265, -0.230, 0.135, -0.410, -0.450, -0.235 and -0.290 for [Cd - sulfadiazine – cephapirin], [Cd – sulfisoxazole – cephapirin], [Cd – sulfamethaxazole – cephapirin], [Cd – sulfamethazine – cephapirin], [Cd – sulfathiazole – cephapirin], [Cd – sulfac-

Table 3. Stability constants and the thermodynamic parameters of [Cd - sulfonamide - cephapirin] complexes at 25 ^{0}C and 35 ^{0}C.

Complexes	Stability constants			- ΔH K cal./mole			- ΔG K cal./mole			- ΔS 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^{0}C/ 35^{0}C	25^{0}C/ 35^{0}C	25^{0}C/ 35^{0}C	(35^{0}C-25^{0}C) for difference of 10 ^{0}C			25^{0}C/ 35^{0}C	25^{0}C/ 35^{0}C	25^{0}C/ 35^{0}C	25^{0}C/ 35^{0}C	25^{0}C/ 35^{0}C	25^{0}C/ 35^{0}C
[Cd - sulfadiazine – cephapirin]	3.36	5.31	7.76	10.5002	13.0203	19.3204	4.909	7.241	10.582	18.76180	19.39328	29.32330
	3.35	5.00	7.30				4.722	7.047	10.289	18.76182	19.39329	29.32332
[Cd –sulfisoxazole - cephapirin]	3.70	5.56	7.83	12.1803	17.2204	20.1604	5.046	7.582	10.678	23.94190	32.34353	31.82183
	3.41	5.15	7.35				4.806	7.259	10.359	23.94192	32.34355	31.82185
[Cd - sulfamethoxyzole – cephapirin]	4.45	6.6	8.63	12.3903	16.7584	20.1604	6.068	9.002	11.769	21.21456	26.03404	28.16097
	4.16	6.20	8.15				5.856	8.740	11.487	21.21458	26.03406	28.16099
[Cd – sulfamethazine – cephapirin]	4.56	7.60	8.73	13.0203	18.9004	23.1005	6.218	10.364	11.905	22.82533	28.64604	37.56935
	4.25	7.15	8.18				5.990	10.077	11.529	22.82535	28.64607	37.56938
[Cd - sulfathiazole – cephapirin]	4.63	7.75	8.86	15.9604	20.8745	24.3605	6.314	10.568	12.082	32.371	34.58394	41.20274
	4.25	7.25	8.28				5.990	10.223	11.670	32.37101	34.58396	41.20277
[Cd – sulfacetamide – cephapirin]	4.91	8.00	9.10	15.1203	21.5885	24.3185	6.696	10.909	12.409	28.27084	35.83595	39.96354
	4.55	7.49	8.52				6.413	10.551	12.010	28.27086	35.83597	39.96357
[Cd -sulfanilamide – cephapirin]	5.0	8.31	9.20	15.9604	23.5205	25.9986	6.818	11.332	12.546	30.67785	40.90073	45.14364
	4.62	7.75	8.58				6.512	10.924	12.094	30.67786	40.90075	45.14367

etamide – cephapirin] and [Cd – sulfanilamide – cephapirin] complexes respectively. The negative values of log K_m showed that binary complexes are more stable than their ternary complexes while in case of [Cd – sulfamethaxazole – cephapirin] the positive value indicates that the ternary complex is more stable then their simple binary complexes.

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 [23]. 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 [24] in sulfisoxazole complexes than sulfamethoxazole complexes. Similar is the case with sulfamethazine and sulfathiazole complexes. In case of sulfactamide and sulfanilamide, the former is the N^1 – acetyl-substituted derivatives of sulfanilamide formed complexes with Cd having lesser stability constants than sulfanilamide complexes might be the fact that it has CH_3CO group [24]. 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 [23]. The values of stability constants varied from 1.70 to 9.20 confirmed that either sulfonamides itself or cephapirin or in combination or their metal complexes could be effective against Cd toxicity [25].

Conclusion

It is clear from the study that the shift of $E_{1/2}$ became more negative on increasing the concentration of sulfonamide and cephapirin to $[Cd^{2+}]$ which confirmed the complex formation. The slope varied from 30 ± 2 mV confirmed that the nature of current voltage curves of metal and their complex formation is reversible. The plots between i_d vs $h^{1/2}$ are straight lines passing through origin confirmed that the polarograms were diffusion controlled. Cd^{2+} formed 1:1:1, 1:2:1 and 1:1:2 complexes. The values of stability constants varied from 1.70 to 9.20 confirmed that either sulfonamide or cephapirin alone or in combination could be effective against Cd toxicity [25]. The study was also carried out at 35 ^{0}C to determine the stability constant and thermodynamic parameters. The values of thermodynamic parameters confirmed that the complexes are not stable at higher temperature [19, 20].

Acknowledgements

The authors are thankful to Head, Department of Chemistry, Dr. H. S. Gour University, Sagar, for providing the laboratory facilities and M.P. Council of Science and Technology, Bhopal for enabling the Junior Research Fellowship to M. S. Parihar.

Received 17 November 2007
Accepted 10 February 2008

References

[1] S. Bellu, E. Hure, M. Trape, M. Rizzotto, Quim. Nova 26 (2003) 188.
[2] M. Jain, R. V. Singh, Bioinorg. Chem. Appl. 13743 (2006) 1.
[3] K. K. Chaturvedi, R. V. Singh, J. P. Tandon, J. Pract. Chem. 327(1) (1985) 144.
[4] K. Singh, Indian J. Chem. 30A (1991) 283.
[5] H. G. Robson, M. I. Bowmer, Antimicrob. Ag. Chemother. 6 (1974) 274.
[6] B. Cicik, K. Engin, Turk. J. Vet. Anim. Sci. 29 (2005) 113.
[7] G. S. Shukla, R. L. Singhal, Can. J. Physiol. Pharmacol. 62 (1984) 1015.
[8] Principles and Methods of Toxicology, A. Wallace Hayes. Taylor and Francis Publishing Inc.; Philadelphia, 4th ed., 2001.
[9] I. H. Bukhari, M. N. Hassan, A. Haleem, M. Bhatti, Res. J. Agric. & Biol. Sci. 2 (2005) 190.
[10] F. Khan, J. Chin. Chem. Soc. 52 (2005) 569.
[11] J. G. Hardman, L. E. Limbird, Goodman & Gilmans, The Pharmacological Basis of Therapeutics, The McGraw-Hill Companies, New York, 10th ed., 2001, p.1173.
[12] C. R. Craig, R. E. Stitzel, Modern pharmacology with clinical Application, Lippincott Williams and Wilkins. 6th ed., 2003.
[13] T. Devries, J. L. Kroon, J. Am. Chem. Soc. 75 (1953) 2484.
[14] L. Meites, Polarographic Technique, Interscience Pub., New York, 2nd ed., 1965, p. 62.
[15] W. B. Schaap, D. L. McMaster, J. Am. Chem. Soc. 83 (1961) 4699.
[16] S. Pritchett, P. Gantzel, P. J. Walsh, Organometallics 18 (1999) 823.
[17] G. N. Mukherjee, P. Dhar, J. Indian Chem. Soc. 64 (1987) 142.
[18] F. Khan, J. Chin. Chem. Soc. 54 (2007) 673.
[19] F. Khan, L. Tantuvay, J. Pharm. Biomed. Anal. 27 (2002) 933.
[20] A. A. Al-sarawy, Chem. Pap. 58(2) (2004) 109.
[21] T. Atalay, E. G. Akgemci, Turk. J. Chem. 24 (2000) 89.
[22] E. G. Akgemci, T. Atalay, Turk. J. Chem. 22 (1998) 123.
[23] R. C. Kapoor, B. S. Aggarwal, Principles of Polarography, Wiley Easter Ltd., Delhi (1991).
[24] M. Calvin, A. E. Martell, Chemistry of Metal Chelate Compounds, Prentice Hall Inc., New York, 2nd ed., 1953, p.134.
[25] M. D. Walker, D. R. Williams, J. Chem. Soc. (Dalton) (1974) 1186.