ELECTRO-ANALYTICAL STUDIES OF FORMATION CONSTANTS OF MIXED-LIGANDS COMPLEXES OF CADMIUM(II) WITH SOME BIO-POTENTIALLY IMPORTANT AMINO ACIDS (L-GLYCINE, DL-THREONINE) AND “4,4,4- TRIFLUORO-1- (2-NAPHTHYL)BUTANE-1,3-DIONE” IN 60% ACETONITRILE MEDIUM

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ABSTRACT

Intensive and compelling electroanalytical study of Cd(II) with “amino acids (L-Glycine, DL-Threonine)” and the ligand “4,4,4-trifluoro-1-(2-naphthyl)butane-1,3-dione” have been carried out in 60% Acetonitrile media under constant ionic strength ($I = 1$), at 30 °C (KNO₃). It was observed that a diffusion-controlled and reversible reduction process involving 2(e⁻) took place for all mixed-ligands-metal-complex systems. While for the simple metal-ligand systems of the subject ligands, stability constants were first determined and subsequently evaluated by the DeFord-Hume & Schaap-McMaster method respectively. The different degrees of reversibility were taken into account in their electro-reduction process. The schematic diagrams were used to explain the stability constants of mixed-ligand-complexes along with statistical data.

Keywords: Metal Complexes, Reductive Electroanalytical Methods, Mixed-ligands Complexes, Chelates, Stability Constants, Amino Acids.

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INTRODUCTION

Metal ions, in solution, form a mixed-ligand complex, consisting of two or more different ligands. Inorganic active substances, mixed chelation usually occurs because millions of biopotential ligands are competing for metallic ions, therefore a crucial role is being played by these MLCs' in routine biological processes.¹ also, their involvement in enzymatic metabolic processes is direct. Significance is shown by amino acids in pharmaceuticals and biological fields and the strong inclination of bio-ligands to form complexes with transition metals is well known. The study of amino acids has great importance in biological process.^{2,3}

The DL-Threonine(2-amino-3-hydroxybutanoic acid) (Thr)⁴ protein phosphatase-5 (PP5) affects several signaling networks which regulate cellular responses to stress and cell growth. However, various organic compounds those target PPP-family phosphatases (i.e., cantharidin, cytosstatin A, fostriecin and tautomycin) have impressive antitumor activity in animal models and cell culture.⁵⁻¹¹

Generally, In our body, the Glycine AA is synthesized from choline, serine, hydroxyproline, and threonine through inter-organ metabolism, in which primarily involved organs are liver and kidneys altogether.¹²

The research studies¹³⁻³² of various MLCs of different metal-ions with different ligands have been carried out in our research laboratory as well as associated laboratories, where the wide scope of pharmaceutical importance was confirmed with similar methods for many drugs.

The thermodynamic parameters³³ like free energy change (ΔG), enthalpy changes (ΔH) and entropy change (ΔS) of interaction are important to interpret the binding mode. The studies have been done of various metal complexes with isoniazid³⁴. Joshi³⁵ *et al* studied the Copper (II) complex with the sodium salt of 3-hydroxy-3-m-tolyl-1-p-sulphonato-phenyltriazene for the activity of antifungal. Reductive electroanalytical studies for non-steroid anti-androgenic and flutamide was carried out at various

concentrations and pH at a DME/hanging Hg drop electrode using different polarographic techniques by Reddy³⁶ *et al.* Recently, Polarographic and voltammetric studies of the reduction of the herbicide imazamethabenz acid on mercury electrodes was also determined by Pintadol³⁷ *et al.*

Cadmium is a toxic element like Arsenic³⁸ for which novel research and discussion is being continued for its treatment and removal from the human body by distinguished scientists across the world. Exposure to cadmium³⁹ in longer-term through water, soil, air and food leads to cancer and toxicity of organ system such as skeletal, urinary, cardiovascular, reproductive, central and peripheral nervous, and respiratory systems. Hence its electroanalytical study is novel research concerning its reactivity and stability of the complexes with important amino acid-like DL-Threonine and L-Glycine, it's further extensive study will help in biomedical research as well.

Glycine is being used for treating schizophrenia as well as its derivatives for Bipolar membrane electrodialysis.⁴⁰ A recent study and discussion about Glycine amino acid have been carried out on mitigation of COVID-19 associated tissue damage and cytokine Storm.⁴¹

While the Threonine amino acid works as building blocks to make proteins for the body. Various nervous system disorders were treated by Threonine Amino Acid including amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease)⁴², familial spastic paraparesis, multiple sclerosis and spinal spasticity etc.

Sufficient data is not yet available for MLCs of Cd(II) with AA and TFNB⁴³. In this paper, the study of MLCs of Cd(II) with amino acids and TFNB has been carried out for the assessment of the overall stability constants. Whereas the weak ligand TFNB is used in this experiment is a biochemical reagent which is an ion probe and chelator for fluorescent indicator and spectroscopy. Recent research of stability constants determination of ternary Cu(II) complexes formed with amino acids⁴⁴ exhibits the novelty of the research related to metal complexes with biopotential ligands based on stability constants.

EXPERIMENTAL

All AR-grade chemicals were used for the experimental analysis. TFNB, L-Glycine and DL-Threonine were used as complexing agents. Solutions were prepared in - 60% acetonitrile medium. A supporting electrolyte is used as KNO₃ to maintain constant ionic strength. Polarograms were recorded on ELICO DC instrument. Reference electrode used SCE (saturated calomel electrode) with the counter electrode as Pt-electrode.

Capillary characteristics:

$m = 1.96$ mg per second

$t = 4.05$ s/drop

$h = 40$ cm.

All polarographic measurements were carried out at constant temperature 30 ± 2 °C. The value of $E_{1/2}$ was calculated simultaneously with the steady voltage increment application to get the graph current vs voltage (polarogram) for recording the current.

RESULTS AND DISCUSSION

The stability constants of the complex formation of Cadmium-II metal ion with L-Glycine, DL-Threonine and TFNB were determined by the method developed by Deford & Hume. The simple ligand constants of Cd(II) metal with simple ligand complexes are summarized in Table-1.

Table 1: Simple Cd(II) Complexes at 30 °C

S. No.	Metal	Ligands	Formation Constant		
			$\log \beta_1$	$\log \beta_2$	$\log \beta_3$
1	Cd(II)	TFNB	1.7781	3.4700	5.3800
2	Cd(II)	L-Gylcine	4.3000	7.7000	9.8000
3	Cd(II)	DL-Threonine	4.0600	7.0600	9.0200

The MLCs

The transition metal Cadmium-II has a coordination number of six which is the highest possible. The concentration of the TFNB is kept constant - 0.0002M and 0.002 M.

Stronger ligands (L-Glycine/DL-Threonine) concentration range 0.001–0.010 M.

The cathodic shift in $E_{1/2}$ is witnessed as a function of L-Glycine and DL-Threonine concentrations. Data are observed and tabulated in Tables-5, 6, 7 and 8.

Ligand displacement technique has been utilized in the case of mixed-ligand systems wherein more intricate/complex species are added to the combination of weak complexing species with the metal ion.

In Table-2 and 3 calculated of log values of A, B, C and D are presented.

Following equations used to derive values of B, C and D:

$$B = \beta_{10} + \beta_{11}[Y] + \beta_{12}[Y]^2$$

$$C = \beta_{20} + \beta_{21}[Y]$$

$$D = \beta_{30}$$

Table 2: Cd(II)-TFNB and L-Glycine system at 30 °C

TFNB is fixed (M)	log(A)	log(B)	log(C)	log(D)
0.0002 C _x	0.0052	4.3179	7.7000	9.8000
0.002 C _x	0.0545	4.4918	7.7014	9.8000

Table 3: Cd(II)-TFNB and DL-Threonine system at 30 °C

TFNB is fixed (M)	log(A)	log(B)	log(C)	log(D)
0.0002 C _x	0.0052	4.0776	7.0600	9.0200
0.002 C _x	0.0545	4.2502	7.0614	9.0200

Here weaker ligand is TFNB and stronger ligands are - L-Glycine, DL-Threonine.

Scheme denotation as follows:

Tfnb = 4,4,4-trifluoro-1(2-naphthyl)butane-1,3-dione

Gly= L-Glycine

Thr= DL-Threonine

The log β_{30} well agrees to the mean value of log(D) when all TFNB ligands are substituted by L-Glycine or DL-Threonine.

The results suggest that the size and charge neutralizing capacities of both ligands vary significantly in MLCs. The MLC [Cd(L-Glycine)(TFNB)] able to accept DL-Threonine quite easily as compared to the addition of TFNB exhibits DL-Threonine contribution to more charge neutralizing because of its strong ligand nature.

Scheme-1: Cd(II)-TFNB L-Glycine system at 30 °C

Experimental proof of chelation confirmed for each of the ligands for Cadmium-II with exhibiting the highest stoichiometric ratio is 1:3. Similar results were obtained for the strong ligand – DL-Threonine. For both complexes $[Cd(X)_2Y]$ (where X = strong ligand = amino acid, Y = weaker ligand = amino acid) has achieved the highest overall stability constant exhibits the highest stability of the complex.

Scheme-2: Cd(II)-TFNB-L-DL-Threonine System at 30 °C

Table 4: Overall Stability Constants

Cd(II)-TFNB-L-Glycine	Cd(II)-TFNB-DL-Threonine
$\log \beta_{11} = 6.6081$	$\log \beta_{11} = 6.3581$
$\log \beta_{12} = 8.8700$	$\log \beta_{12} = 8.6400$
$\log \beta_{21} = 10.6181$	$\log \beta_{21} = 9.9681$

Table-5: Data and Results of Cd(II)- L-Glycine - TFNB System at 30 °C, [TFNB] = 0.0002 M (fixed)

TFNB = 0.0002 M, $\mu = 1.0$ (KNO₃), [X] = Conc. of Strong Ligand in M

[X]	$\Delta E_{1/2}$	$\log(I_m/I_c)$	F_{00}	$F_{10} \times 10^{-3}$	$F_{20} \times 10^{-7}$	$F_{30} \times 10^{-9}$	$F_{00}(\text{Cal})$	$\Delta F_{00} \%$
0.0001	0.014	0.09040	3.599	25.869	5.075	6.310	3.599	-0.01
0.0002	0.023	0.09380	7.226	31.070	5.138	6.310	7.227	0.01
0.0003	0.029	0.11190	11.931	36.397	5.201	6.310	11.930	-0.01
0.0004	0.034	0.11818	17.753	41.851	5.264	6.310	17.752	0.00
0.0005	0.038	0.12906	24.728	47.431	5.328	6.310	24.729	0.01
0.0006	0.041	0.15319	32.894	53.137	5.391	6.310	32.896	0.00
0.0007	0.044	0.16249	42.291	58.969	5.454	6.310	42.290	0.00
0.0008	0.046	0.19362	52.954	64.928	5.517	6.310	52.954	0.00
0.0009	0.048	0.21559	64.923	71.013	5.580	6.310	64.924	0.00
0.0010	0.050	0.23005	78.236	77.223	5.643	6.310	78.235	0.00

A = 1.0121, B = 2.0793 $\times 10^4$, C = 5.0120 $\times 10^7$, D = 6.3096 $\times 10^9$

Table-6: Data and Results of Cd(II)-L-Glycine-TFNB System at 30 °C, TFNB = 0.002 M (fixed)

[X]	$\Delta E_{1/2}$	$\log(I_m/I_c)$	F_{00}	$F_{10} \times 10^{-3}$	$F_{20} \times 10^{-7}$	$F_{30} \times 10^{-9}$	$F_{00}(\text{Cal})$	$\Delta F_{00} \%$
0.0001	0.018	0.07751	4.746	36.121	5.092	6.310	4.746	0.00
0.0002	0.026	0.10826	9.402	41.339	5.155	6.310	9.402	0.00
0.0003	0.032	0.11554	15.139	46.683	5.218	6.310	15.139	0.00
0.0004	0.036	0.14474	21.995	52.153	5.281	6.310	21.996	0.01

0.0005	0.040	0.14656	30.009	57.750	5.344	6.310	30.008	0.00
0.0006	0.043	0.16299	39.217	63.472	5.407	6.310	39.217	0.00
0.0007	0.046	0.16571	49.658	69.321	5.470	6.310	49.658	0.00
0.0008	0.048	0.19114	61.370	75.296	5.533	6.310	61.370	0.00
0.0009	0.050	0.20817	74.391	81.397	5.596	6.310	74.391	0.00
0.0010	0.052	0.21832	88.758	87.624	5.659	6.310	88.757	0.00

A = 1.1337, B = 3.1029 x 10⁴, C = 5.0284 x 10⁷, D = 6.3095 x 10⁹

Table-7: Data and Results of Cd(II)-DL-Threonine acid-TFNB System at 30 °C, [TFNB] = 0.0002 M (fixed)

[X]	$\Delta E_{1/2}$	$\log(I_m/I_c)$	F ₀₀	F ₁₀ x 10 ⁻³	F ₂₀ x 10 ⁻⁷	F ₃₀ x 10 ⁻⁹	F ₀₀ (Cal)	ΔF_{00} %
0.0001	0.010	0.03347	2.324	13.114	1.159	1.047	2.323	0.00
0.0002	0.016	0.05553	3.871	14.293	1.169	1.047	3.871	0.00
0.0003	0.020	0.08750	5.660	15.494	1.180	1.047	5.660	0.00
0.0004	0.024	0.08800	7.698	16.715	1.190	1.047	7.699	0.00
0.0005	0.027	0.10139	9.991	17.958	1.201	1.047	9.991	0.00
0.0006	0.029	0.13372	12.545	19.221	1.211	1.047	12.545	0.00
0.0007	0.031	0.15530	15.366	20.506	1.221	1.047	15.367	0.00
0.0008	0.033	0.16844	18.461	21.811	1.232	1.047	18.461	0.00
0.0009	0.035	0.17481	21.835	23.137	1.242	1.047	21.835	0.00
0.0010	0.037	0.17560	25.496	24.484	1.253	1.047	25.496	0.00

A = 1.0121, B = 1.1955 x 10⁴, C = 1.1481 x 10⁷, D = 1.0471 x 10⁹

Table-8: Data and Results of Cd(II)- DL-Threonine acid - TFNB system at 30 °C, [TFNB] = 0.002 M (fixed)

[X]	$\Delta E_{1/2}$	$\log(I_m/I_c)$	F ₀₀	F ₁₀ x 10 ⁻³	F ₂₀ x 10 ⁻⁷	F ₃₀ x 10 ⁻⁹	F ₀₀ (Cal)	ΔF_{00} %
0.0001	0.013	0.04881	3.029	18.952	1.162	1.047	3.029	0.00
0.0002	0.019	0.08063	5.161	20.135	1.173	1.047	5.161	0.00
0.0003	0.023	0.11197	7.535	21.339	1.183	1.047	7.535	0.00
0.0004	0.026	0.14193	10.159	22.564	1.194	1.047	10.159	0.00
0.0005	0.029	0.15050	13.039	23.810	1.204	1.047	13.039	0.00
0.0006	0.031	0.17769	16.180	25.078	1.215	1.047	16.180	0.00
0.0007	0.033	0.19420	19.590	26.366	1.225	1.047	19.589	0.00
0.0008	0.035	0.20249	23.273	27.674	1.236	1.047	23.272	-0.01
0.0009	0.037	0.20431	27.238	29.004	1.246	1.047	27.239	0.00
0.0010	0.038	0.23401	31.489	30.355	1.257	1.047	31.489	0.00

A = 1.1337, B = 1.7789 x 10⁴, C = 1.1518 x 10⁷, D = 1.0471 x 10⁹

CONCLUSION

- The values of MLCs and stability constants give evidence to support higher stability of the ternary complexes than the binary complexes.
- Value of $\log(D)$ is equivalent to the value of $\log \beta_{30}$ which upholds the theoretical principle upright when the coordinated TFNB are completely replaced by L-Glycine and DL-Threonine.
- The complex [Cd(L-Glycine)(TFNB)] accept L-Glycine more easily than accept TFNB indicates the stronger ligand is L-Glycine and is more charge neutralizing.
- In Schemes-1 and 2, the illustration and explanation of MLC formation along with equilibrium amongst them of all of the mixed-ligand - complexes of the system are as represented above. For the MLCs of Cd (II)-TFNB with AA is the stability constant order observed as follows:

L-Glycine < DL-Threonine.

Abbreviations:

TFNB = 4,4,4-trifluoro-1-(2-naphthyl)butane-1,3-dione

AA = Amino Acid

MLC = Mixed-ligand complex

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