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.

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. 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. The DL-Threonine(2-amino-3-hydroxybutanoic acid) (Thr) 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, cytostatin A, fostriecin and
tautomyacin) have impressive antitumor activity in animal models and cell culture. 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. The research studies 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 parameters 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 isoniazid. Joshi 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 Reddy et al. Recently, Polarographic and voltammetric studies of the reduction of the herbicide imazamethabenz acid on mercury electrodes was also determined by Pintadol et al. Cadmium is a toxic element like Arsenic 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 cadmium 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. A recent study and discussion about Glycine amino acid have been carried out on mitigation of COVID-19 associated tissue damage and cytokine Storm. 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), familial spastic paraparesis, multiple sclerosis and spinal spasticity etc.

Sufficient data is not yet available for MLCs of Cd(II) with AA and TFNB. 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 acids 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 KNO$_3$ 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 $30 \pm 2$ °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.

| S. No. | Metal  | Ligands  | $\log \beta_1$ | $\log \beta_2$ | $\log \beta_3$ |
|-------|--------|----------|----------------|----------------|----------------|
| 1     | Cd(II) | TFNB     | 1.7781         | 3.4700         | 5.3800         |
| 2     | Cd(II) | L-Glycine| 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:

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

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

$$D = \beta_{30}$$

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 $\beta_{30}$ 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.
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 \([\text{Cd}(X)_2Y]\) (where \(X = \text{strong ligand} = \text{amino acid}, Y = \text{weaker ligand} = \text{amino acid}\)) 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

| \(\text{Cd(II)}\)-TFNB-L-Glycine | \(\text{Cd(II)}\)-TFNB-DL-Threonine |
|---------------------------------|-----------------------------------|
| \(\log \beta_{11} = 6.6081\)    | \(\log \beta_{11} = 6.3581\)      |
| \(\log \beta_{12} = 8.7800\)    | \(\log \beta_{12} = 8.6400\)      |
| \(\log \beta_{21} = 10.6181\)   | \(\log \beta_{21} = 9.9681\)      |

### Table 5: Data and Results of Cd(II)-L-Glycine-TFNB System at 30 °C, \(\text{TFNB} = 0.0002 \text{ M} \) (fixed)

| \([\text{X}]\) | \(\Delta \varepsilon_{1/2}\) | \(\log(I_m/L)\) | \(F_0\) | \(F_{\text{mix}} \times 10^3\) | \(F_{20} \times 10^{-7}\) | \(F_{30} \times 10^{-9}\) | \(F_{00}\) (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          | 5.474           | 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            |

\(A = 1.0121, B = 2.0793 \times 10^3, C = 5.0120 \times 10^7, D = 6.3096 \times 10^9\)

### Table 6: Data and Results of Cd(II)-L-Glycine-TFNB System at 30 °C, \(\text{TFNB} = 0.0002 \text{ M} \) (fixed)

| \([\text{X}]\) | \(\Delta \varepsilon_{1/2}\) | \(\log(I_m/L)\) | \(F_0\) | \(F_{\text{mix}} \times 10^3\) | \(F_{20} \times 10^{-7}\) | \(F_{30} \times 10^{-9}\) | \(F_{00}\) (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            |

MIXED-LIGANDS COMPLEXES OF CADMIUM(II)

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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 uptight when the coordinated TFBN are completely replaced by L-Glycine and DL-Threonine. 

The complex [Cd(L-Glycine)(TFBN)] accept L-Glycine more easily than accept TFBN 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)-TFBN with AA is the stability constant order observed as follows:

L-Glycine < DL-Threonine.

**Abbreviations:**

TFBN = 4,4,4-trifluoro-1-(2-naphthyl)butane-1,3-dione  
AA = Amino Acid  
MLC = Mixed-ligand complex

**REFERENCES**

1. E. J. Underwood, Trace element in human and animal nutrition, Academic Press, London (1991)  
2. B. Weinstein, Chemistry and Biochemistry of Amino Acids, Peptides and Proteins, Marcel Dekker,
New York, 3, 16(1994)
3. J. H. Ottaway and D. K. Apps, Biochemistry, 4th edn. W.B. Saunders Company, London (1984)
4. M. R. Swingle, R. E. Honkanen, and E. M. Ciszak, Journal of Biological Chemistry, 279(32), 33992(2004), DOI: 10.1074/jbc.M402855200
5. R. E. Honkanen and T. Golden, Current Medicinal Chemistry, 9, 2055(2002), DOI: 10.2174/092986702368836
6. M. R. Swingle, L. Amable, B. G. Lawhorn, S. B. Buck, C. P. Burke and P. Ratti, et al., Journal of Pharmacology and Experimental Therapeutics, 331, 45(2009), DOI: 10.1124/jpet.109.155630
7. K. Bonness, I. V. Aragon, B. Rutland, S. Ofori-Acquah, N. M. Dean and R. E. Honkanen, Molecular Cancer Therapeutics, 5, 2727(2006), DOI: 10.1158/1535-7163.MCT-06-0273
8. R. E. Honkanen, FEMS Letters, 330, 283(1993), DOI: 10.1016/0014-5793(93)80889-3
9. D. Chattopadhyay, M. R. Swingle, E. A. Salter, E. Wood, B. D’Arcy, C. Zivanov, et al., Biochemical Pharmacology, 109, 14(2016), DOI: 10.1016/j.bcp.2016.03.011
10. B. G. Lawhorn, S. B. Boga, S. E. Wolkenberg, D. A. Colby, C. M. Gauss and M. R. Swingle et al., Journal of the American Chemical Society, 128, 16720(2006), DOI: 10.1021/ja066477d
11. D. L. Boger, S. Ichikawa and W. Zhong, Journal of American Chemical Society, 123, 4161(2001), DOI: 10.1021/ja010195q
12. M. A. Razak, P. S. Begum, B. Viswanath and S. Rajagopal, Oxidative Medicine and Cellular Longevity, 1(2017), DOI: 10.1155/2017/1716701
13. R. K. Lohiya, P. L. Prathihar, R. V. Singh and Mukherjee, Oriental Journal of Chemistry, 17(3), 391(2001)
14. M. K. Verma and C. P. S. Chandel, Oriental Journal of Chemistry, 19, 49(2003)
15. S. K. Singh and C. P. S. Chandel, Bulletin of Electrochemistry, 19(3), 119(2003)
16. U. Jadwiga, K. Henryk and K. Barbora, Journal of Coordination Chemistry, 25(2), 149(1992), DOI: 10.1080/00958979209409746
17. A. Verma, P. K. S. Chauhan and R. K. Paliwal, Oriental Journal of Chemistry, 20(2), (2004)
18. A. Verma, P. K. S. Chauhan and R. K. Paliwal, Oriental Journal of Chemistry, 20(2), (2004)
19. M. Verma and C. P. S. Chandel, Oriental Journal of Chemistry, 21(1), 9(2005)
20. S. Kalpana, T. Kaur and K. J. Gupta, Journal of the Indian Chemical Society, 82, 61(2005)
21. A. K. Jain and F. Khan, Journal of the Indian Chemical Society, 75(1), 31(1998)
22. R. P. Yadav, Ph.D. thesis, University of Rajasthan, Jaipur, India (2003).
23. F. Khan and P. L. Sahu, Journal of Ultra Scientist of Physical Sciences, 12(1), 106(2000)
24. Z. Khatoon and D. Kabir-ud, Journal of the Indian Chemical Society, 15(3), 217(1990)
25. N. M. Arishy, R. A. Ammar and A. Al-Warthan, Asian Journal of Chemistry, 26(8), 2395(2014), DOI: 10.14233/ajchem.2014.16023
26. P. K. S. Chauhan, A. Verma and R. K. Paliwal, Asian Journal of Chemistry, 17(1), 355(2005)
27. A. Verma, P. K. S. Chauhan and R. K. Paliwal, Asian Journal of Chemistry, 17(2), 1423(2005)
28. P. K. S. Chauhan, A. Verma and R. K. Paliwal, Asian Journal of Chemistry, 17(1), 349(2005)
29. A. Kumar, P. K. S. Chauhan and R. K. Paliwal, International Journal of Chemical Science, 2(3), 379(2004)
30. G. Sharma and C. P. S. Chandel, Asian Journal of Chemistry, 14(1), 23(2002)
31. D. Prakash, M. Shafayat, A. Jamali, A. K. Gupta and D. Prakash, Oriental Journal of Chemistry, 21(3), 555(2005)
32. J. D. Joshi, M. P. Brahm Bhatt, S. Sharma and J. J. Vora, Asian Journal of Chemistry, 15, 373(2003)
33. S. N. Chadar, F. Khan and S. Sharma, Chemifa, 19, (3-4), ( 2008) .
34. K. Angela, A. L. Viorica, C. Nicoleta, R. Ileana and S. Nicolae, Journal of the Serbian Chemical Society, 75(2), 229(2010), DOI: 10.2298/JSC100229K
35. P. Joshi, N. Prasad, R. Khamam, D. Upadhyay, A. Bhandari, R.S. Chauhan and A.K. Goswami, International Journal of Pharmaceutical Sciences and Drug Research, 3(2), 21(2011)
36. G. V. S. Reddy, C. L. Reddy, V. N. Myreddy and S. J. Reddy, Journal of Clinical Medicine Research, 3(3), 35(2011), DOI: 10.5897/JCMR.9000020
37. S. Pintadol, M. R. Montoya and J. M. R. Mellado, International Journal of Electrochemical Science,
6, 2541(2011).
38. A. Mudhoo, S. K. Sharma, V. K. Garg and C. H. Tseng, *Critical Reviews in Environmental Science and Technology*, 41(5), 435(2011), [DOI:10.1080/10643380902945771]
39. Md. R. Rahimzadeh, Ma. R. Rahimzadeh, S. Kazemi and A. A. Moghadamnia, *Caspian journal of internal medicine*, 8(3), 135(2017), [DOI:10.22088/cjim.8.3.135]
40. Y. Wang, X. Wang, H. Yan, C. Jiang, L. Ge and T. Xu, *AIChE Journal*, e17023(2020), [DOI:10.1002/aic.17023]
41. C. Y. Li, *Radiation Research*, 194(3), 199(2020), [DOI:10.1667/RADE-20-00146.1]
42. H. J. Choi, S. J. Cha, J. W. Lee, H. J. Kim and K. Kim, *Brain Sciences*, 10(10), 675(2020), [DOI:10.3390/brainsci10100675]
43. S. Meena and R. Grover, Green Chemistry in Environmental Sustainability and Chemical Education. Springer, Singapore, pp.191-200 (2018), [DOI:10.1007/978-981-10-8390-7_18]
44. L. Hernández, E. D. Carpio, W. Madden, G. Lubes, A. Perez, R. E. Rodríguez-Lugo, V. R. Landaeta, M. L. Araujo, J. D. Martínez and V. Lubes, *Physics and Chemistry of Liquids*, 58, 1, 31(2018), [DOI:10.1080/00319104.2018.1534235] [RJC-6314/2020]