

Percentage distribution and structural elucidation of quaternary metal chelates of proline with IMDA and uracil in aqueous medium

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ABSTRACT

A method is described for calculating equilibrium concentrations of all species in multi-metal-multi-ligand mixtures from the pH of the solution; total concentration of each metal, complexing agent, and the relevant equilibrium constants (pK(a) values and stability constants). Ternary and quaternary metal chelates of some biologically important bivalent transition metal ions viz. Co(II), Ni(II), Cu(II) and Zn(II) formed with biologically significant ligands, viz. IMDA/Uracil and Proline have been investigated. The relevant stability constants and complexation equilibria of quaternary metal chelates in solution at 37±1°C and at constant ionic strength (*I*=0.1M NaNO₃) have been studied potentiometrically. Species distribution curves are obtained by plotting percent (%) concentration of the species obtained through SCOGS computer technique against pH. The distribution curves are finally sketched by running the computer program ORIGIN 4.0. The metal ligand formation constant of ML₁, ML₂, ML₁L₂ and M₁M₂L₁L₂ type of complexes follow Irving William order. The order of stability constants of quaternary systems has been observed and probable solution structures of metal complexes with said ligands have been discussed.

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KEYWORDS

IMDA;
Proline;
Uracil;
SCOGS.

INTRODUCTION

The chemistry of metal ions in solution is essentially the chemistry of their complexes. Metal complexes of polydentate ligands continues to activate a great deal of research owing to its relevance in various fields of analytical^[1,2] biological^[3,4] and industrial importance^[5,6]. The polyaminocarboxylic acids have widely been used as antidotes^[7,8] in heavy metal detoxification. The interactions between metals and amino acids have also

become of considerable interest as coordination phenomena as models for metal protein interactions. The use of transition metal complexes of IMDA have been widely adopted in biology, and are gaining use in biotechnology, particularly in the protein purification techniques as immobilized metal ion affinity chromatography (IMAC)^[9]. Proline protects membranes and proteins against the adverse effects of high concentrations of inorganic ions and temperature extremes. Proline may also function as a protein

compatible hydrotrope and as a hydroxyl radical scavenger. Uracil serves as allosteric regulator and coenzyme for reaction in the human body and in plants^[10]. Uracil can be used to determine microbial contamination of tomatoes^[11]. Its derivatives are used in pesticides. It is also used as anti-photosynthetic herbicides and destroys weed^[12].

In the study of bio-fluid, knowledge of formation of ternary and quaternary complexes is important particularly when hyper accumulated metal ions are present of physiological or pathological nature^[13].

In continuation to our recent communication^[14,15] on multi-metal multi-ligand complexes, we report here comparative order of stability of quaternary metal complexes of Cu, Ni, Co and Zn metal ions with IMDA (imino di acetic acid) and Uracil where Proline behaves as secondary and primary ligand respectively using pH-metry in aqueous medium. The species distribution at different pH, formation constant, probable structure and plausible equilibria for the formation of species are reported in this paper.

EXPERIMENTAL

All reagents used were of A.R. grade (sigma) with 99% purity. Solutions were prepared in double distilled CO₂ free water. Metal Nitrate solutions were standardized by EDTA complexometric titration. Carbonate free NaOH solution (0.1M) was used as titrant^[16]. pH measurements were made with century model CP 901-S pH meter using a special glass electrode (accuracy ± 0.01 pH) at 37 ± 1° C. Binary M:L₁/M:L₂ (1:1), ternary M:L₁:L₂(1:1:1) and quaternary M₁:M₂:L₁:L₂(1:1:1:1) metal-ligand mixtures of following composition were prepared for titration, keeping total volume 50ml in each case. Strength of metal and ligand = 0.01M and I = 0.1 M NaNO₃
 Solution A: 5 ml NaNO₃ (1.0 M) + 5ml HNO₃ (0.02M) + water
 Solution B: 5 ml NaNO₃ (1.0 M) + 5ml HNO₃ (0.02M) + 5ml L₁ (0.01M) + water
 Solution C: 5 ml NaNO₃ (1.0 M) + 5ml HNO₃ (0.02M) + 5ml L₁ (0.01M) + 5 ml M₁ (II) (0.01M) + water
 Solution D: 5 ml NaNO₃ (1.0 M) + 5ml HNO₃ (0.02M) + 5ml L₁ (0.01M) + 5 ml M₁ (II) (0.01M) + 5ml L₂ (0.01M) + water

Solution E: 5 ml NaNO₃ (1.0 M) + 5ml HNO₃ (0.02M) + 5ml L₁ (0.01M) + 5 ml M₁ (II) (0.01M) + 5ml L₂ (0.01M) + 5ml M₂(II) (0.01M) + water

Where M₁ (II) and M₂ (II) are Co / Ni / Cu and Zn L₁ = Primary ligand and L₂ = Secondary ligand. Each set of solution was then titrated against alkali (NaOH). The pH meter reading with progressive addition of alkali to the titration mixtures were noted, when the reading of pH meter stabilized. The titration was discontinued at the appearance of turbidity. The pH values were plotted against the volume of NaOH and the titration curves were obtained. From the shift of the pH titration curve the value of $\bar{n}H$, \bar{n} , pL are calculated as:

$$\bar{n}H = \left\{ Y T C L_0 \frac{(N^0 + E^0)(V_2 - V_1)}{(V_0 + V_1)} / T C L_0 \right\} \quad (1)$$

Similarly, \bar{n} values were evaluated by the equation,

$$\bar{n} = \frac{(N^0 + E^0)(V_3 - V_2)}{(V_0 + V_1) \times \bar{n}H \times T C M_0} \quad (2)$$

and pL was calculated by the equation,

$$pL = \log \frac{K_1 [H^+] + K_1 K_2 [H^+]^2 + \dots}{T C L_0 - \bar{n} \times T C M_0} \times \frac{V_0 + V_3}{V_0} \quad (3)$$

The stability constant for the system mentioned above had been calculated using the formula:

$$\log K = \{ \log (T C L_0 \times \bar{n}) - \log (T C M_0) (1 - \bar{n}) + pL \} \quad (4)$$

Where,

- $\bar{n}H$ = Average number of protons attached to the ligand
- Y = Number of dissociable or replaceable protons attached to the ligand
- TCL₀ = Total concentration of the ligand
- N⁰ = Concentration of alkali
- E⁰ = Total concentration of free acid
- V₁ = Volume of alkali needed to reach a specified pH for solution 'A' (i.e. Acid)
- V₀ = The total volume of reaction mixture
- \bar{n} = Average number of ligands attached per metal ion
- V₂ = Volume of alkali required to attain the same pH in the (acid + ligand) curves

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V_3 = Volume of alkali required to attain the same pH in the (acid+ligand+metal) curves

TCM_0 = Total concentration of metal present in solution

K_1^H, K_2^H, K_3^H = Protonation constants of the ligands

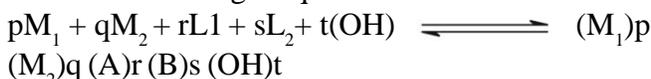
H^+ = Hydrogen ion concentration

$\log(TCL_0 \times n)$ = The amount of complex formed

$\log\{TCM_0 \times (1-n)\}$ = The amount of free metal ion

pL = The concentration of free ligand

For evaluation of stability constants by the SCOGS computer program^[17] in a system of the two different metal ions M_1 and M_2 and two different ligands L_1 and L_2 in aqueous solution, complex formation may be described according to equilibrium.



The overall stability constant (β_{pqrst}) is defined as:

$$\beta_{pqrst} = \frac{[(M_1)_p (M_2)_q (L_1)_r (L_2)_s (OH)_t]}{[M_1]^p [M_2]^q [A]^r [B]^s [OH]^t} \quad (5)$$

may be used to calculate the species distribution curves that provides the clues for the formation equilibria of the complexes.

Values of constants were supplied to the computer as input data to obtain distribution curves of the complexes occurring at different pH. Ionic product of water (K_w) and activity coefficient of hydrogen ion under the experimental conditions were obtained from literature.

RESULTS AND DISCUSSION

Proton ionization from uracil in the strongly acid region ($pK < 0.5$) has been reported, based on spectrophotometric data. On the basis of UV measurements^[18,19] in aqueous solution, uracil exists primarily in the diketo form whereas in alkaline solution, it exists as approximately 1:1 mixture of the two possible deprotonated forms.

Two overlapping absorption bands with λ_{max} 260

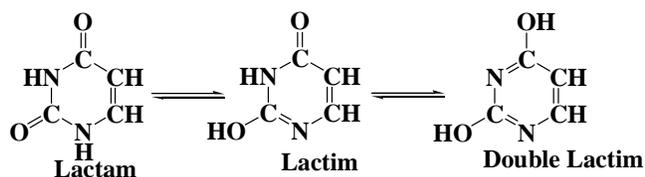


Figure 1 : Keto enol tautomers of Uracil

and 284 nm have been reported for proton ionization from neutral uracil with a conclusion that protons ionize simultaneously from both N_1H and N_3H groups.

Fully protonated form of ligand proline (L^-) is represented by H_2L^+ . It usually functions as bidentate ligand, using one carboxyl and one imino group for coordination. Its protonation can be expressed as:

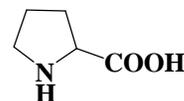
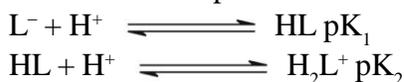


Figure 2 : L pyrrolidine-2-carboxylic acid (Proline)

The complex formation between a transition metal ion, M^{2+} and iminodiacetic acid (IMDA) involve N-imino and O-carboxylato atoms. It behaves as a tridentate ligand, where iminodiacetate diaion (A^{2-}) coordinates as a (\bar{O}, \bar{O}, N) ^[20,21]. With alkaline earth metal ions, it forms only a 1:1 chelate^[22] but with transition metal ions it forms both 1:1 and 1:2 complexes^[23]. Its protonation equilibria are expressed as below:

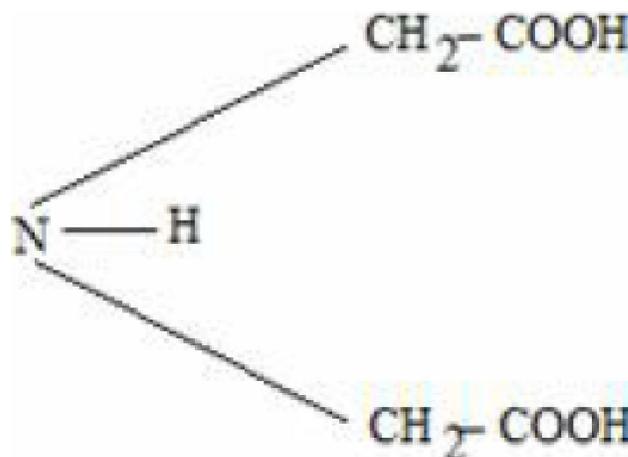
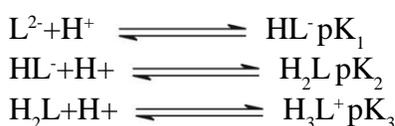


Figure 3 : Iminodiacetic acid (IMDA)

Protonation constants for the ligands have been determined by Irving-Rossotti titration technique^[24] and are presented in TABLE 1. Preliminary estimates of binary and ternary constants obtained by least-square method were further refined by SCOGS. These values are listed in TABLE 2, 3. Which are in good agreement

TABLE 1 : Proton-ligand formation constant (Log β 00rst) of ligands and hydrolytic constants (Log β p000t) of different metal ions under study in aqueous solution at $37 \pm 1^\circ\text{C}$ $I = 0.1\text{M NaNO}_3$

Proton-ligand formation constant (Log β 00rst)			
Ligand	Species	log β	Reference
IMDA	H ₃ L	14.26	13.82
	H ₂ L	12.03	11.98
	HL	08.80	9.12
Proline	H ₂ L	12.79	12.28
	HL	09.37	10.07
Uracil	HL	9.47	9.34

Hydrolytic constants (Log β p000t)

Complex	Cu	reference	Zn	reference	Ni	reference	Co	reference
M(OH) ⁺	-6.29	(-6.4)	-7.89	(-7.9)	-8.10	(-8.5)	-8.23	(-8.7)
M(OH) ₂	-13.10	(-13.3)	-14.92		-16.87	(-16.9)	-17.83	(-18.00)

TABLE 2 : Stability constants of binary ternary and quaternary complexes of IMDA (L₁) and Proline (L₂) with different metal ions in aqueous solution at $37 \pm 1^\circ\text{C}$ $I = 0.1\text{M NaNO}_3$

Metal-Ligand constants (Log β p0r0t/ Log β p00st) Binary System								
Complex	Cu	reference	Zn	reference	Ni	reference	Co	reference
ML ₁	10.07	(10.47)	7.44	(7.24)	8.22	(8.15)	7.42	(6.98)
ML ₂	9.05	(8.95)	5.98	(5.20)	6.54	(6.07)	5.74	(4.82)*

Metal-Ligand constants (Log β p0rst) Ternary System

Complex	Cu	Zn	Ni	Co
ML ₁ L ₂	19.02	13.10	14.70	13.07

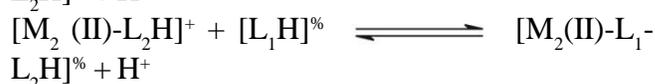
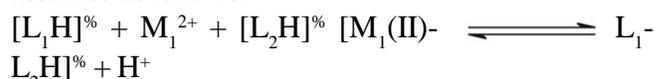
Metal-Ligand constants (Log β pqrst) Quaternary System

Complex	Cu-Ni	Ni-Zn	Cu-Zn
	26.65	23.30	26.42
M ₁ M ₂ L ₁ L ₂	Cu-Co	Ni-Co	Zn-Co
	26.28	22.94	23.24

simultaneous process of complex formation. For quaternary system, the species distribution curve

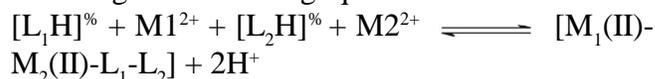
with those reported in the literature^[25].

Larger concentration of mixed ligand complexes relative to binary is reflected in species distribution diagram (Figure 4, 5) which indicates marked stabilization of ternary over binary in each of the system studied. Mixed ligand complexation equilibrium has been assumed as follows:

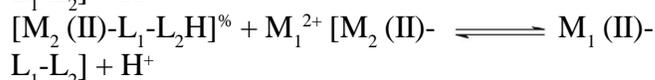
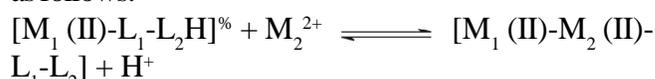


The concentration of quaternary complex is increasing gradually with gradual increase in pH and attains a maximum value \approx (60-95%) in the pH range \sim 3.0-10.5. The complexation starts from the very beginning of the titration \sim 3.1, which shows the

indicates the formation of heterobinuclear complex according to the following equilibria:



The alternative equilibrium may also be indicated as follows:



Formation of hydroxo species viz.-Cu(II)(OH)₂ and Ni(II)(OH)⁺ have been taken into consideration, as the buffer regions corresponding to metal-ligand complex formation equilibria are found to be overlapping with the hydrolytic equilibria of M²⁺(aq.) ions.

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TABLE 3 : Stability constants of binary ternary and quaternary complexes of Proline (L_1) and Uracil (L_2) with different metal ions in aqueous solution at $37 \pm 1^\circ\text{C}$ $I = 1.0 \text{ M NaNO}_3$

Metal-Ligand constants ($\text{Log } \beta_{p0r0t} / \text{Log } \beta_{p00st}$) Binary System								
Complex	Cu	reference	Zn	reference	Ni	reference	Co	reference
ML_1	9.05	(8.95)	5.98	(5.20)	6.54	(6.07)	5.74	(4.82)*
ML_2	8.25		6.61	(6.42)	6.80	(6.82)	6.28	(6.39)

Metal-Ligand constants ($\text{Log } \beta_{p0rst}$) Ternary System				
Complex	Cu	Zn	Ni	Co
ML_1L_2	16.51	11.40	11.66	11.54

Metal-Ligand constants ($\text{Log } \beta_{pqrst}$) Quaternary System			
Complex	Cu-Ni	Ni-Zn	Cu-Zn
	23.35	19.68	23.15
$M_1M_2L_1L_2$	Cu-Co	Ni-Co	Zn-Co
	22.84	19.61	19.15

*hydroxy proline

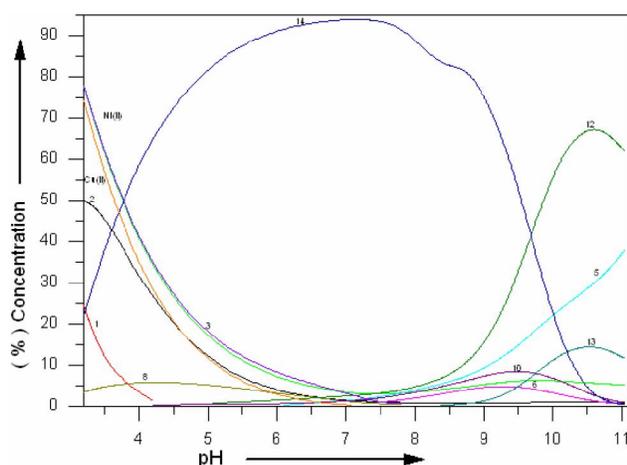
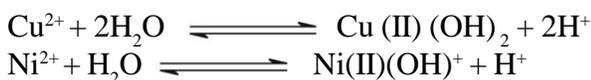


Figure 4 : Distribution Curves of 1:1:1:1 Cu (II)-Ni (II)-Proline-Uracil system; (1) L_1H_2 (2) L_1H (3) L_2H (4) $\text{Cu}(\text{OH})^+$ (5) $\text{Cu}(\text{OH})_2$ (6) $\text{Ni}(\text{OH})^+$ (7) $\text{Ni}(\text{OH})_2$ (8) CuL_1 (9) CuL_2 (10) NiL_1 (11) NiL_2 (12) CuL_1L_2 (13) NiL_1L_2 (14) CuNiL_1L_2



CONCLUSION

We have confined our discussion to transition metal centers, copper (II), nickel (II) cobalt (II) and zinc (II).

In aqueous solutions Cu^{2+} (d^9) is tetragonally

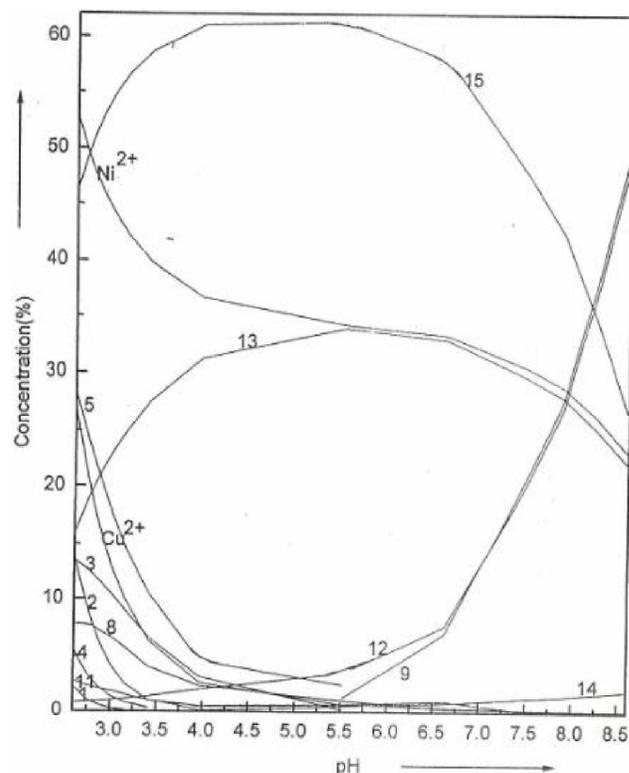


Figure 5 : Speciation curves of quaternary Cu(II)-Ni(II)-IMDA-Proline system: (1) H_3A (2) H_2A (3) HA (4) H_2B (5) HB (6) $\text{Cu}(\text{OH})^+$ (7) $\text{Ni}(\text{OH})^+$ (8) CuA (9) $\text{CuA}(\text{OH})$ (10) NiL_1 (11) CuL_2 (12) NiL_2 (13) CuL_1L_2 (14) NiL_1L_2 (15) Cu-NiL_1L_2

coordinated by six water molecules. Two axial water molecules lie at longer distances from the copper and are more labile than the four other water molecules.

The hydrated nickel ion presents regular octahedral configuration. Six equivalent sites of coordination are available unless a stronger ligand field provokes a tetragonal distortion and ultimately a square planar configuration. Hexacoordinated nickel is expected to form a greater number of isomeric complex species than copper, whose coordination geometry is usually dominated by the four "equatorial bonds".

The configuration of zinc can easily move from tetrahedral geometry to octahedral geometry depending upon the nature of bound ligands^[26]. Consequently the

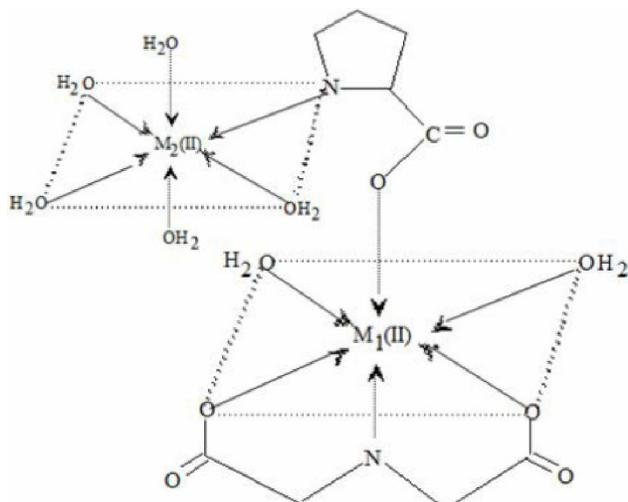


Figure 6 : Probable structure of quaternary $M_1(\text{II})$ - $M_2(\text{II})$ -IMDA-Proline system ($M_1(\text{II})$ and $M_2(\text{II})=6$ coordinated)

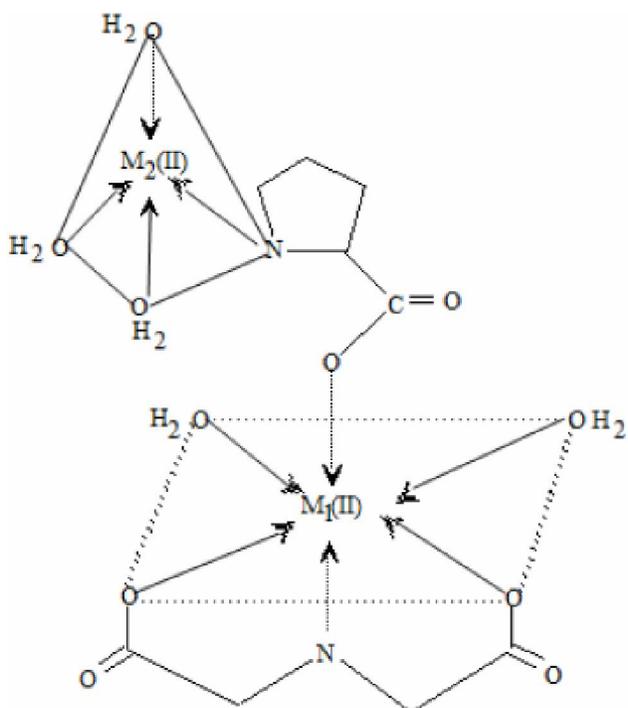


Figure 7 : Probable structure of quaternary $M_1(\text{II})$ - $M_2(\text{II})$ -IMDA-Proline system ($M_1(\text{II})=6$ coordinated, $M_2(\text{II})=4$ coordinated)

possible mixed species are in greater number than with copper.

The cobalt (II) chelate of the dipeptide glycylglycine was also found to absorb oxygen reversibly^[27]. This field has been recently reviewed by Wilkins^[28]. These examples tend to show that oxygen absorption is a specific property of cobalt complexes.

Metals having higher $\log\beta$ value of metal-L complex will be the first to attach with ligand (L_1) which further

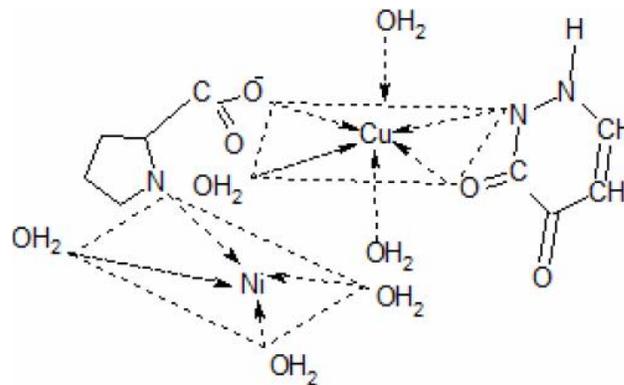


Figure 8 : Probable structure of Quaternary $M_1(\text{II})$ - $M_2(\text{II})$ -Proline-Uracil ($M_1(\text{II})$ and $M_2(\text{II})=6$ coordinated)

attaches to another ligand (L_2) to satisfy its coordination number. Coordination sites of ligands still left free will then be occupied by another metal ion. In all the binary, mixed ligand and mixed-metal mixed-ligand systems of present study following possibilities for the binding of ligands with various metal ions taken under study may be deduced:

In the cases where $M_1(\text{II})$ and $M_2(\text{II})$ both have octahedral geometry. M_{12+} ion is coordinated to IMDA by the two carboxylate O-atoms on the equatorial plane. The imino N-atom however coordinates axially, thus IMDA coordinates with M_{12+} ion in a tridentate manner^[29,30]. Coordinately unsaturated M_1 -IMDA complex binds with O-atom of proline and takes up two molecules of solvent H_2O as additional ligands, thereby satisfying coordination number. M_{12+} does not coordinate with the imino-N of proline because of stereo chemical considerations. This coordination site is left for M_{22+} , which takes up required molecules of H_2O to complete the coordination number. However in case of tetrahedral metal ions, metal having higher stability binds with three coordination positions of IMDA in a tridentate manner and with one carboxylate oxygen of proline. Thus, no additional water is taken up by it. Another metal ion gets bound to the imino nitrogen or proline and three water molecule.

In the formation of mixed-ligand complexes, the secondary ligand (Uracil) coordinates through N and carboxyl atoms with the tetra coordinated or hexa coordinated metal ions which are already coordinated with the primary ligand Proline. Valences are satisfied utilizing water molecules, while one imino 'N' atom still remains free. This may further lead to the formation of quaternary complex while adding secondary metal ion

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in the above mixed ligand complex.

The probable structure of the chelates in solution are shown in figures 6-8

The overall stability constants of mixed-metal mixed-ligand

[IMDA (L₁)-M₁ (II)-Proline (L₂)-M₂ (II)] quaternary systems have been found to follow the following order: Cu-Ni > Cu-Zn > Cu-Co > Ni-Zn > Zn-Co > Ni-Co and for

[Proline(L₁)-M1(II)-Uracil(L₂)-M2(II)] quaternary systems have been found to follow the following order: Cu - Ni > Cu - Zn > Cu - Co > Ni - Zn > Ni - Co > Co - Zn

REFERENCES

- [1] X.Y.Yang, C.Pin; *Analyst*, **3**, 453 (2000).
- [2] J.Y.Jin, F.Xu, T.Miwa; *Electroanalysis*, **12**, 610 (2000).
- [3] A.Sigel, H.Sigel; *Metal ions in biological system*, Marcel Dekker, New York, **1-38**, (1971-2000).
- [4] J.M.Mortal, M.J.Martinez, Ferrer, H.R.Jimenez, A.Donaire, J.Castells, J.J.Salgado; *Inorg. Biochem.*, **45**, 231 (1992).
- [5] J.Y.Jin, F.Xu, T.Miwa; *Electroanalysis*, **12**, 610 (2000).
- [6] S.Srivastava, R.C.Srivastava; *Industrial Health*, **31**, 29 (1993).
- [7] Bohne.Plansas, M.Lehmann; *Toxicol. Appl. Pharmacol*, **67**, 408 (1983).
- [8] M.A.Basinger, M.M.Jones; *J.Toxicol. Environ. Health*, **23**, 77 (1988).
- [9] F.H.Arnold; *BioTechnology*, **9**, 151 (1991).
- [10] Yu-Hung Chiu, J.W.Canary; *Inorg.Chem.*, **9**, 5107 (2003).
- [11] A.Hidalgo; *J Agric Food Chem.*, **53(2)**, 349-55 (2005).
- [12] S.Bandyopadhyay, G.N.Mukherjee; *Proc.Indian Acad.Sci.(Chem.Sci)*, **4**, 115, 249 (2003).
- [13] F.J.Welcher; *The Analytical uses of ethylene diaminetetraacetic acid*, Van Nostrand, New York, (1957).
- [14] S.Sinha, V.P.Shukla, P.P.Singh, V.Krishna; *Chemical science Transcation*, **3(2)**, (2014).
- [15] D.Bartaria, P.Chandra, M.Singh, V.Krishna; *Int. J. Res. Chem. Environ.*, **2(4)**, 45-51 (2012).
- [16] Chandra Pallavi, Singh Monika, Bartaria Divya, V.Krishna; *J.Indian Chem. Soc.*, **87**, 955 (2010).
- [17] I.G.Sayce; *Talanta*, **15**, 1397 (1968).
- [18] D.Shugar, J.Fox; *J.Biochim. Biophys. Acta*, **9**, 199 (1952).
- [19] J.Lang, J.Strum, R.Zana; (a) *J. Phys. Chem.*, **77**, 2329 (1973); (b) *J. Phys. Chem.*, **78**, 80 (1974); (c) *Biopolymers*, **10**, 2639 (1971).
- [20] Roman-Alpsite, M.J.Martin-Ramos, A.Castineiras; J.D.Campos, E.Bugella-Altamirano, A.G.S.Illia Zafar, Gonzalez, J.M.Perez, Niclos, Z.J.Gutierrez; *Polyhedron*, **18**, 3341 (1999).
- [21] I.S.Cuvea-Torregrosa, J.M.Gonzalez-Perez, Sicilia, G.Zafar, E.Bugella-Altamirano, J.Niclos-Gutierrez; *Castinerias Campos A, J.Coord.chem.*, **51**, 235 (2000).
- [22] F.J.Welcher; *The Analytical uses of Ethylene diamine tetraacetic acid*, D.Van Nostrand company, New York, (1957).
- [23] S.Chaberek, A.E.Martell; *J.Am.Chem.Soc*, **71**, 5052 (1952).
- [24] F.J.C.Rossotti Rossotti; *The Determination of Stability Constants*, McGraw Hill Book Company, Inc, New York, **84**, (1961).
- [25] D.D.Perrin; *Stability Constants of Metal Ion Complexes*, Pergamon, New York, (1979).
- [26] H.C.Freeman; *Advan. Protein Chem.*, **22**, 257 (1967).
- [27] J.B.Gilbert, M.C.Ofey, J.E.Price; *J. Biol. Chem.*, **71**, 173, (1948).
- [28] R.G.Wilkins, H.Sigel; *Metal ions in biological systems*, **35**, 61, 252, 101, 102, 267 (1988).
- [29] S.Bandyopadhyay, G.N.Mukherjee; *Proc.Indian Acad.Sci.(Chem Sc.)*, **4**, 115, 249 (2003).
- [30] Patel; R.P.Shrivastava, N.A.Singh, S.Kumar, K.B.Pandeyay, *Indian J.Chem.*, **40A**, 361 (2001).