

American Journal of Scientific Research and Essays (ISSN:2475-7527)



Analysis of Solvent Effect on Formation Constants and Speciation of Cobalt(II), Copper(II) and Lead(II) Complexes of L-Methionine and Uracil

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ABSTRACT

The analysis of coordination of chelating agents to metal ions in the formation of complexes under different experimental conditions provide information on the effects of the conditions on the extent of the coordination of the ligands to the metal ions for potential applications in bioinorganic and environmental Inorganic Chemistry. The effect of solvent on the coordination of L-methionine (primary ligand) and uracil (secondary ligand) to Co(II), Cu(II) and Pb(II) ions in the formation of binary and ternary complexes have been potentiometrically investigated in water and 40% (v/v) ethanol- water media at 27 °C and ionic strength of 0.02 mol dm⁻³ was maintained by using NaNO₃. The proton-ligand stability constants and formation constants of the binary and ternary systems were established under the experimental conditions. The formation constants of the ternary complexes were numerically compared with the corresponding binary complexes in terms of $\Delta \log K$ and percentage relative stabilization (%RS). Speciation of the metal ions, binary and ternary complexes as a function of pH in the solutions was investigated by using HYSS program. The ligands were observed to form more stable ternary complexes than binary complexes. The proton-ligand stability constants the ligands and the formation constants of the metal complexes were found to be higher in 40% (v/v) ethanol-water than water. The distribution of the species revealed a decrease in the metal ion concentrations with increase in the concentrations of the binary and ternary as pH increased. The chelating agents interacted strongly with the metal ions and showed different selectivity towards the metals ions. These properties can be exploited in combating metal poisoning, separating the metals and expounding the bioinorganic chemistry of the metal ions and the ligands.

Keywords: Formation constants, Methionine, Solvents, Speciation, Uracil

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How to cite this article:

Ishola, K.T., Oladipo, M.A., Ajayeoba, T. A. and Odedokun, O.A. Analysis of Solvent Effect on Formation Constants and Speciation of Cobalt(II), Copper(II) and Lead(II) Complexes of L-Methionine and Uracil. American Journal of Scientific Research and Essays, 2020 5:30.



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Introduction

Coordination compounds have been applied as enzyme inhibitors, anti-bacterial, antiviral and as anti-cancer drugs¹⁻⁵. Transition metal ion chelate complexes have been found to be incorporated in ion exchange resins for identification of metals, detoxification and remediation of heavy metal pollutants. The study of interactions of transition metal ions with different types of chelating agents in different solutions has advanced in the field of inorganic chemistry⁶. This provides information on coordination properties of the ligands and metal complexes under the different experimental conditions which might serve as a tool in environmental inorganic chemistry, bio-inorganic chemistry and analytical chemistry for various applications. The study of coordination chemistry of complexes containing ligands with N, O donor atoms has increased because of the special ability of the ligands to form stable complexes with different metal ions and their potential application as models for biologically important species having N and O as binding sites⁷.

Amino acids are the chemical units of proteins and crucial for several biochemical processes taking place in human system which are responsible for the maintenance of life⁸. Methionine is a sulfur-containing essential amino acid that is not synthesized in the body. It possesses various binding functionalities⁹. Methionine and its metal complexes have been frequently utilized for both biological and chemical applications¹⁰. Uracil is one of important heterocyclic compounds which are an essential constituent of all cells with vital pharmacological activities^{11,12}. Uracil and its complexes have been reported to exhibit remarkable pharmacological efficiency as a result of the presence of pyrimidine ring in it¹³. Methionine and Uracil contain functional groups that are well situated to permit the formation of rings with metal ions hence they are potential chelating agent for the transportation of essential metals, remediation and detoxification of heavy metals.

Potentiometric studies of binary and ternary complexes of (Fe(III), Pb(II), Co(II), Al(III), La(III), Sr(II), Cr(III), Ti(II) and Zr(II)) with sulphathiazole (as primary ligand) and amino acid glycine (as secondary ligand) at $25^{\circ}\text{C} \pm 0.1^{\circ}\text{C}$ and $I = 0.1 \text{ M NaClO}_4$ in 25% (v/v) pure ethanol-water medium were carried out by¹⁴. Ternary complexes were found to exhibit more stability than the corresponding binary complexes in the study. 4 pH-metrically studied the formation equilibria of copper(II), adenine (A), and amino acids at 25°C in aqueous solution. Ternary complexes were reported to form in a simultaneous mechanism. The amino acid was observed to function as bidentate ligands coordinating through the amino and carboxylate group to the metal ions in the complexes formation. An increase in the stability of the complexes due to the coordination of the imidazole side group of amino acid and thioether group of adenine was observed.

The stability constants of ternary complexes of Ni (II) with bio-molecules (drugs) (L) as primary ligand and amino acids (R) as a secondary ligand were investigated by¹⁵. It was discovered that ternary complexes of amino acids were formed in a stepwise mechanism, whereby (L) binds to Ni (II) and followed by coordination of ligand (R) to the metal ion. The ternary complexes formed was less stable than the corresponding binary 1:1 complexes. The less stability was attributed to the availability of less number of coordination sites for secondary ligands on primary complex ML than on free metal ion. Another study was carried out on the mixed ligand complexes of copper (II) ion with drug dapsone as primary ligand and the amino acids as secondary at 27°C in 80% (v/v) ethanol-water medium by potentiometric method¹⁶. Ternary complexes were observed to be less stable than the binary complexes due to the steric effect exhibited by the primary ligand on the entry of the secondary ligands during the process of coordination.¹⁷ determined stability constants of mixed-ligand complexes of Ni(II) and Cu(II) metal ions with Diethylenetriamine and Ethylenediamine, Glycine, alpha-Alanine,

Phenylalanine, Oxalic acid (ox), Tyrosine at 25°C in aqueous medium at ionic strength of 0.2 M. The binary complexes formed through the coordination of the ligands to the metal ions were reported to exhibit higher stability than the corresponding ternary complexes.

Regarding the viewpoint of coordination chemistry of the coordinating sites present in methionine and uracil, and in order to add to the existing literature on the properties of chelating ligands which could be exploited in chelation therapy or remediation of metals, this study investigated the degree of coordination of the chelating agents with Co(II), Cu(II) and Pb(II) ions. The investigation was carried in different media in the presence of low concentration inert electrolyte with a view to assessing the effect of the solvents on the degree of coordination of each of the two ligands and their mixture to the metals ions.

Experimental

Materials

All chemicals utilized in this investigation were of the analytical grade (AR) and of highest purity. They include Cobalt(II)nitrate hexahydrate, copper(II)nitrate hexahydrate, lead (II) dihydrate, sodium nitrate, nitric acid, sodium hydroxide, double distilled water, ethanol, oxalic acid, methyl orange indicator, EDTA, L-methionine and uracil.

The solution of 0.002M of the metal salts were prepared and the concentrations were determined using complexometric EDTA titrations. Carbonate-free NaOH solution was prepared from a double distilled water and its concentration was standardized by oxalic acid. The ionic strength of each solution was adjusted to 0.02 mol/dm³ by addition of appropriate amount of NaNO₃. 0.01M of nitric acid was prepared and the strength of the solution was determined by titration against standardized sodium hydroxide.

Apparatus

Potentiometric titrations were carried out using Mettler Toledo (FP20 Standard) equipped with combined glass electrode and the electrode was calibrated before each titration using buffer

solutions of 4, 7 and 9. All the titrations were carried out within the slope of 99-105%. The temperature was maintained constant 27°C (± 0.1) throughout the titrations and all the titrations were carried out in multiples. The errors that might occur from the liquid junction, the alkaline and acidic errors of the glass electrode were corrected by using Van Uitert and Hass equation¹⁸.

Procedure

(a). Titration of (40 ml) solution of HNO₃ (0.01) adjusted with 0.02 mol/L NaNO₃.

(b). The proton-ligand stability constants of the ligands were determined potentiometrically by titrating the ligand (40 ml) solution (2.0 × 10⁻³ mol dm⁻³) of constant ionic strength 0.02 mol dm⁻³ adjusted with NaNO₃.

(c). The stability constants of the binary complexes were determined by titrating 40 ml of a solution of mixture of each metal ion (2.0 × 10⁻³ mol dm⁻³), each ligand (2.0 × 10⁻³ mol dm⁻³) and 0.02 mol dm⁻³ NaNO₃.

(d). The stability constants of mixed ligand complexes were determined by titrating 40 ml of solution containing each metal ion, uracil and methionine all of concentration (2.0 × 10⁻³ mol dm⁻³) and 0.02 mol dm⁻³ NaNO₃.

All the titration were carried out in water and ethanol-water 40 % (v/v). A certain amount of solution of HNO₃ was added to all the prepared solutions. The obtained values of pH were plotted against volume of alkali added for the above sets of the titrations. From the curves, the equilibrium existing in each solution was examined. The proton-ligand stability constants and the formation constants of binary complexes were determined using Point wise method. These were evaluated by calculating the average number of protons associated with each ligand \bar{n}_A at different pH values (\bar{n}), average number of ligand molecules attached per metal ion (\bar{n}) and free ligand exponent (pL). The formation constants of ternary complexes were determined by using Ramamoorthy and Santapa method¹. The distributions of species were obtained by Hyperquad Simulation and Speciation program.

RESULTS AND DISCUSSION

The proton-ligand stability constants of the ligands were calculated from the titration curves.

For the sake of brevity, only the curves of the ligands, binary complexes and ternary complexes in ethanol-water medium are presented in Figure 1.

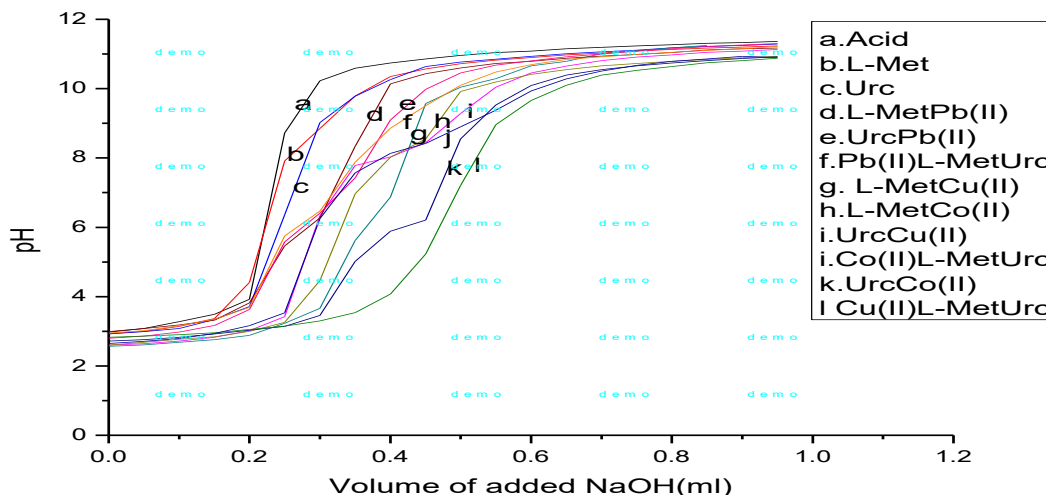


Fig. 1: Potentiometric titration curves of binary (1: 1) and ternary (1 : 1 : 1) complexes ($I = 0.02 \text{ mol dm}^{-3} \text{ NaNO}_3$ at $27.0 \pm 0.1^\circ\text{C}$ in ethanol-water 40:60 (v/v)).

Proton-ligand and Binary complexes stability constants

The titration curves b and c representing ligands curves are observed in Fig. 1 to deviate from curve a (acid curve) to lower pH. The shifts of the ligand curves from acid curve for the same volume of added alkali indicate deprotonation from the ligands¹⁹. Met curve shows two inflection points at pH of 3.7 and 9.0 while only one inflection point at pH of 9.00 is observed in Urc curve. The inflection points are attributed to deprotonation of two and one proton from the ligands respectively^{20,21}.

Also, upon the addition of the metal ions to the solutions of the ligands, the curves are observed shift to the right and the shifting suggests the formation of the binary complexes through the displacement of proton(s) on the ligands²². The inflection points at pH of 5.50, 7.00, 5.50 and 5.00, 6.30 and 5.60 are observed in MetCo(II), MetCu(II), MetPb(II) and UrcCo(II), UrcCu(II) and UrcPb(II) curves respectively. From the inflection points, \bar{nA} and \bar{nB} were evaluated and from the evaluated values, the proton-ligand stability constants and metal-ligand formation constants were calculated and presented in Table 1.

Table 1: Proton-ligand and Binary complexes stability constants in water and ethanol-water with $I = 0.02 \text{ M (NaNO}_3)$ at 27°C

Lig- and	Water					Ethanol-water 40:60% (v/v)				
	LogK_1^{H}	LogK_2^{H}	$\text{LogK}_{\text{CoL}}^{\text{Co}}$	$\text{LogK}_{\text{CuL}}^{\text{Cu}}$	$\text{LogK}_{\text{PbL}}^{\text{Pb}}$	LogK_1^{H}	LogK_2^{H}	$\text{LogK}_{\text{CoL}}^{\text{Co}}$	$\text{LogK}_{\text{CuL}}^{\text{Cu}}$	$\text{LogK}_{\text{PbL}}^{\text{Pb}}$
Met	2.7509	11.139	6.2508	8.0877	6.8370	3.3532	11.456	6.6134	8.1111	7.5361
Urc	3.0331	11.343	4.6520	6.5731	7.1852	-	11.665	6.6052	8.4881	7.2001

The average number of ligand bound per metal (\bar{n}) was estimated to be in the range of 0.1–0.5. The inflection points in the curves and the range confirmed the formation of 1:1 binary complexes^{23,24}.

The mean $\text{Log}K_2^H$ value of 11.1329 at 27°C and $\text{Log}K_1^H$ value of 2.7509 obtained for Met as shown in Table 1, are attributed to the deprotonation at amino group NH_2 and COOH group of the ligand respectively while $\text{Log}K_1^H$ and $\text{Log}K_2^H$ values of 3.0331 and 11.3430 at 27°C of Urc are ascribed to deprotonation of protons at N_7H and N_3H groups respectively in water^{22,24,25}.

The $\text{Log}K_2^H$ value of 11.4536 and $\text{Log}K_1^H$ value of 3.3532 obtained in ethanol-water as shown in Table 1, are attributed to the deprotonation at amino group NH_2 and COOH groups of the ligand respectively. While $\text{Log}K_2^H$ value of 11.6625 of Urc ligand is attributed to deprotonation at N_3H group of the ligand. The proton-ligand stability constants are higher in ethanol-water than water medium and this is attributed to difference in dielectric constant of the media²⁵.

Met coordinated to Co(II) , Cu(II) and Pb(II) ions in both media to form binary complexes with the stability constants in the order of $\text{Log}K_{\text{CuMet}}^{\text{Cu}} > \text{Log}K_{\text{PbMet}}^{\text{Pb}} > \text{Log}K_{\text{CoMet}}^{\text{Co}}$. The order could be attributed to effects of covalent index of the metal ions on the stability. The extent of coordination of Urc to the metal ions was observed in the order of $\text{Log}K_{\text{PbUrc}}^{\text{Pb}} > \text{Log}K_{\text{CuUrc}}^{\text{Cu}} > \text{Log}K_{\text{CoUrc}}^{\text{Co}}$ in water while in ethanol-water medium, the order of $\text{Log}K_{\text{CuUrc}}^{\text{Cu}} > \text{Log}K_{\text{PbUrc}}^{\text{Pb}} > \text{Log}K_{\text{CoUrc}}^{\text{Co}}$ was observed. The order could be attributed to effects of covalent index and polarizability of the metal ions on stability^{26,27}. The extra stability exhibited by Cu(II) -Met complex could be ascribed to the unique electronic configuration of Cu^{2+} and the Jahn-Teller effect^{28,29}. The extra stability of Cu(II) ion in both media could also be attributed to the presence of a single electron outside the filled d electrons that participate in metallic bonding which influences Cu(II)

ion to form complexes with more covalent nature thus greater stability³⁰.

All the ligands formed more stable binary complexes in ethanol-water medium than water medium. The ligands showed different degree of coordination towards the metals in the media; in aqueous medium, both Met and Urc are selective towards Cu(II) and Pb(II) ions respectively while in ethanol-aqueous medium, Urc is more selective towards Cu(II) ion than Met as shown Table 1.

Stability constants of ternary complexes

The formation of the ternary complexes were confirmed by the deviations of the ternary complexes curves from binary curves³¹ as shown in Fig. 1 and non superimposable nature of the ternary complexes curves with either of the simple binary curves suggests simultaneous complexation of the two ligands to the metal ions in the ternary complexes³². The curves of ternary complexes of CoMetUrc , CoMetUrc and PbMetUrc show inflection points at pH of 8.30, 8.00 and 8.20 respectively. The inflection points are attributed to the coordination of both ligands to the metal ions in the formation of 1:1:1 ternary complexes²². The calculated stability constants of the ternary complexes are given in tables 2 and 3.

$\Delta \log K$ in the media was found to be positive in all the complexes except CuMetUrc ternary complex which has negative value in aqueous-organic medium. The positive value indicates more stability of the ternary complexes than the corresponding binary complexes and the stability could be attributed to intramolecular hydrophobic stacking³¹. The negative $\Delta \log K$ value is ascribed to less stability of the ternary complexes in comparison with the corresponding binary complex of the primary ligand^{33,34}. The stability constants showed the order of $\text{Cu(II)} > \text{Pb(II)} > \text{Co(II)}$ for all the complexes, and the extra stability exhibited by Cu(II) complexes could be attributed to the unique electronic configuration of Cu(II) ion and distorted geometry of the metal ion by Jahn Teller distortion³⁵. The

percentage Relative Stabilization (%RS) confirmed the more stability of ternary complexes than the corresponding binary complexes except the ternary complex of CuMetUrc which is less

stable in comparison with binary complex of secondary ligand in aqueous medium. The ligands formed more stable ternary complexes with the metal ions in ethanol-water medium than water.

Table 2: Stability constants of ternary complexes in water at 27°C ($I = 0.02$ M NaNO_3 , $M = \text{Co(II)}$, Cu(II) & Pb(II) $A = \text{Met}$ & $B = \text{Urc}$)

Complex	$\text{Log}K_{MAB}^M$	$\text{Log}K_{MA}^M$	$\text{Log}K_{MAB}^{MA}$	$\text{Log}K_{MB}^M$	$\Delta\text{log}K$	RS%
CoMetUrc	14.9305	6.2508	8.6797	4.6520	+4.0277	38.9
CuMetUrc	15.9364	8.0877	7.8487	6.5131	+1.3356	-2.96
PbMetUrc	15.3744	6.8370	8.5374	7.1852	+1.3520	1.70

Table 3: Stability constants of ternary complexes in ethanol-water at 27°C ($I = 0.02$ M NaNO_3 , $M = \text{Co(II)}$, Cu(II) & Pb(II) $A = \text{Met}$ & $B = \text{Urc}$)

Complex	$\text{Log}K_{MAB}^M$	$\text{Log}K_{MA}^M$	$\text{Log}K_{MAB}^{MA}$	$\text{Log}K_{MB}^M$	$\Delta\text{log}K$	RS%
CoMetUrc	15.0476	6.6134	8.4246	6.6052	+1.8194	27.0
CuMetUrc	16.2169	8.1111	8.1292	8.4881	-0.3589	0.22
PbMetUrc	15.7119	7.5361	8.1758	7.2001	+0.9757	8.50

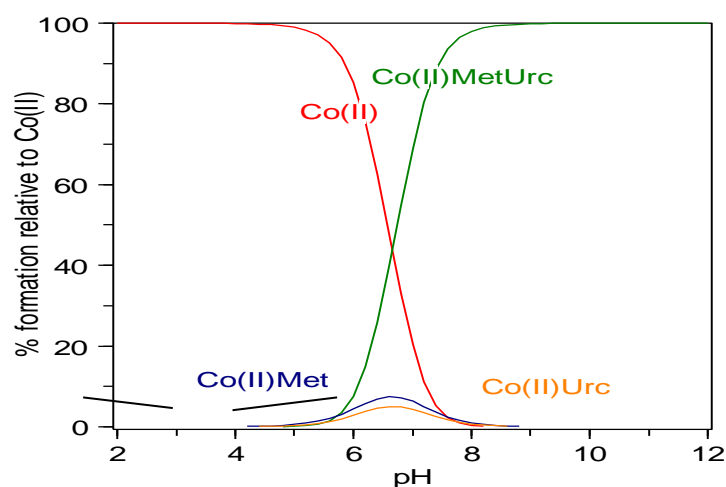


Fig. 2: Distribution diagram of the species in the (1 : 1 : 1)Co(II):Met:Urc ternary system at 27°C in water

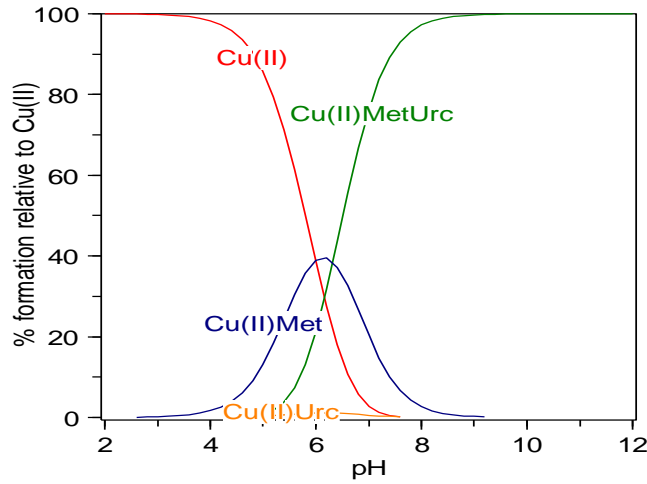


Figure 3: Distribution diagram of the species in the (1 : 1 : 1)Cu(II):Met(A):Urc(B) ternary system at 27°C in water

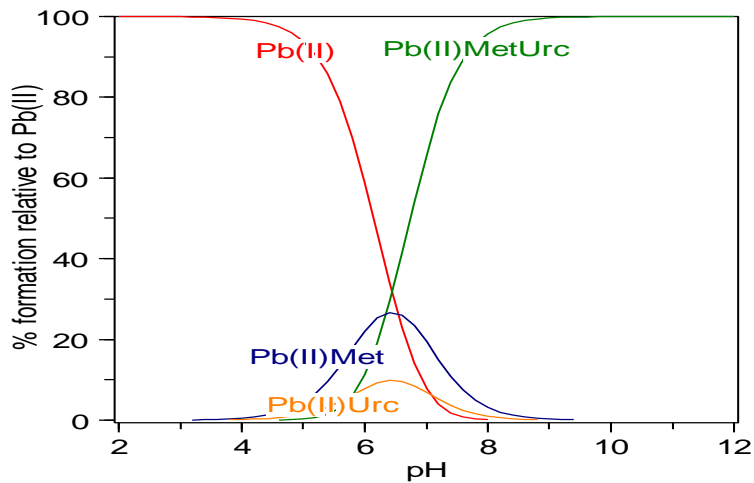


Figure 4: Distribution diagram of the species in the (1 : 1 : 1)Pb(II):Met:Urc ternary system at 27°C in water

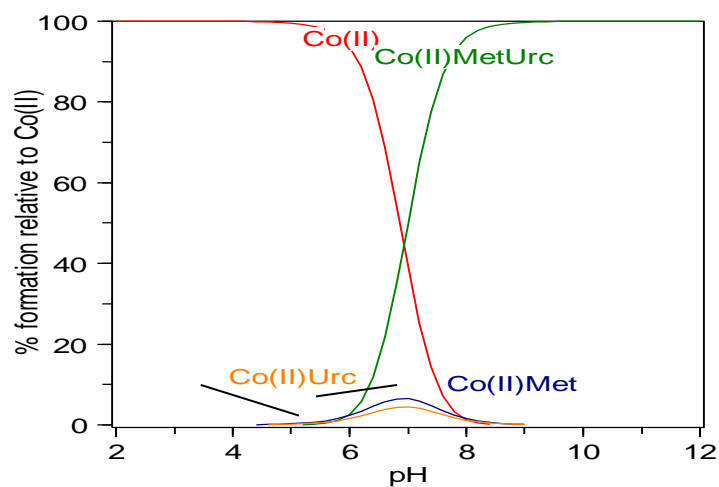


Figure 5: Distribution diagram of the species in the (1 : 1 : 1)Co(II):Met:Urc ternary system at 27°C in ethanol-water 40-60%(v/v)

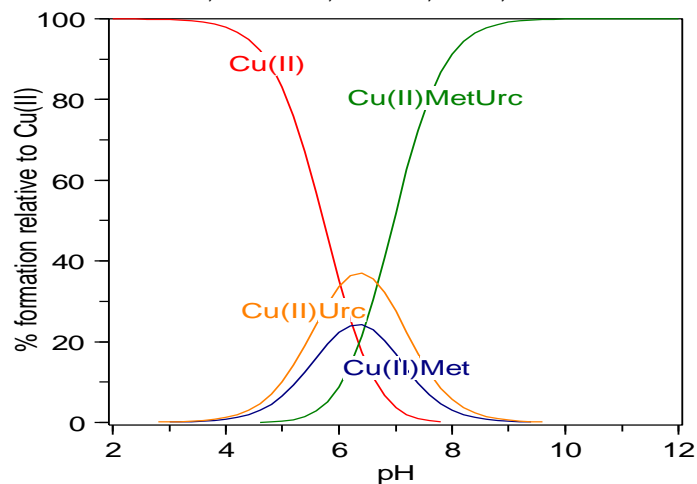


Figure 6: Distribution diagram of the species in the (1 : 1 : 1)Cu(II):L-Met(A):Urc(B) ternary system at 27°C in ethanol-water 40-60%(v/v)

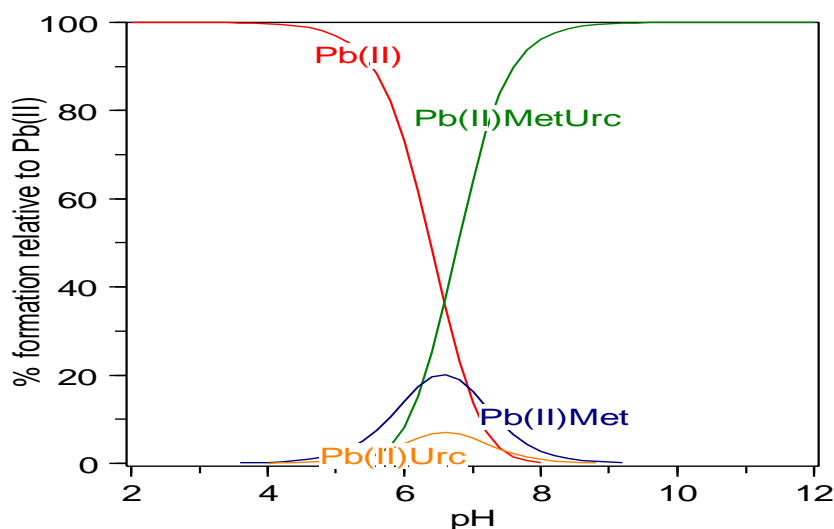


Figure 7: Distribution diagram of the species in the (1 : 1 : 1)Pb(II):Met:Urc ternary system at 27°C in ethanol-water 40-60%(v/v).

Speciation Diagrams

The distribution of species of the metal ions, binary and ternary complexes in the solutions as a function of pH are presented in Figures 2,3,4,5,6 and 7.

The percentage concentrations of Co(II), Cu(II) and Pb(II) ions are observed in all the distribution diagrams above to decrease with increase in the concentrations of their binary and ternary complexes to a certain level as pH increases. The decrease and increase in the concentrations suggest the involvement of the metal ions in the formation of the complexes ^{36,37}.

The distribution of binary and ternary complexes of Co(II) with Met and Urc in aqueous medium is shown in Fig. 1. There are appearances of Co(II)Met and Co(II)Urc curves at p of 4.2 and 4.5 respectively. The curves reach the maximum levels at pH of 6.7 with 8% and 6% respectively. The complexes begin to dissociate with an increase in pH and vanish totally at pH of 8.7 and 8.4 respectively. The formation of Co(II)MetUrc ternary species comes into existence at pH of 4.8 and reaches a maximum level of 99% at pH of 8. The curves of Cu(II)Met and Cu(II)Urc begin at pH of 2.8 and 4.5 as shown in Fig. 2. The concentrations of the binary complexes reach maximum levels at pH of 6.0 with 39% and

6% respectively. The concentrations of the complexes begin to decrease with an increase in pH and disappear totally at pH of 9.0 and 7.5 respectively. The formation of Cu(II)MetUrc ternary species comes into existence at pH of 5.0 and reaches the maximum level of 95% at pH of 8.0.

The formation curves of the binary complexes of Pb(II)Met and Pb(II)Urc start at pH of 3.3 and 3.8 respectively in Fig.3. The concentrations of the complexes increase and reach maximum level at pH of 7.0 with 28% and 10% respectively. The binary complexes begin to dissociate and disappear utterly at pH of 9.2 and 8.8 respectively. The complexation curve of Pb(II)MetUrc ternary species begins at pH of 4.8 and reaches a peak (99%) at pH of 8.0. In the formation of binary and ternary complexes of Co(II) as depicted in Fig.4, the two ligands begin to coordinate to the metal ion at pH of 4.5 and 4.6 to form Co(II)Met and Co(II)Urc binary complexes respectively. The concentrations of the binary complexes reach the peaks at pH of 6.0 and 7.0 with 4% and 4% respectively. The complexes begin to dissociate with a rise in pH and vanish away at pH of 8.4 and 9.0 respectively. The ligands begin to form Co(II)MetUrc ternary complex at pH of 4.6 and gets to the peak(97%) at pH of 8.5.

The two ligands begin to coordinate to Cu(II) ion to form Cu(II)Met and Cu(II)Urc at pH of 3.2 and 3.0 respectively as shown in Fig. 4. The curves get to the peaks at pH of 6.0 with 23% and 37% respectively. The complexes begin to disintegrate with a rise in pH and disappear at pH of 9.0 and 9.5 respectively. The formation of ternary complex of Cu(II)MetUrc starts at pH of 4.6 and gets to the peak (98%) at pH of 8.5. It is observed in Fig. 7 that the formation curves of Pb(II)Met and Pb(II)Urc start at pH of 3.5 and 4.0 respectively. The concentrations of the complexes increase and reach maximum levels at pH of 6.6 with 20% and 7% respectively. The binary complexes begin to dissociate and disappear utterly at pH of 9.2 and 8.78 respectively. The curve of Pb(II) MetUrc ternary species

begins at pH of 4.0 and gets to the peak (97%) at pH of 8.6.

Conclusion

All the ternary complexes exhibited positive $\Delta\log K$ except Cu(II)MetUrc in aqueous which showed negative value. The positive $\Delta\log K$ and %RS obtained for the complexes revealed more stability of the ternary complexes than the corresponding binary complexes due to the occurrence of ligand-ligand interaction in the ternary complexes. The $\Delta\log K$ negative indicate less stability of the ternary complex than the binary complex of the primary ligand. The stability of the ternary complexes was found in the order of Cu(II) > Pb(II) > Co(II) and the order is attributed to difference in the covalent index and polarizability of the metal ions, and Jahn Teller distortion. The ligands showed different degrees of coordination to the metal ion in the solvents. The ligands strongly coordinated to the metal ions in aqueous-organic than aqueous medium due to variation in dielectric constant of media. The two ligands formed stable binary complexes with the metal ions within pH of 2.5-7.0 and they could be for extraction/transportation of the metal ions within the pH range and this range, the ligands could be recovered for reuse. The mixed-ligand formed stable ternary complexes with the metal ions within pH of 4.0-8.2. The ligands demonstrated strong binding ability and different selectivity towards the metal ions in both aqueous and aqueous-organic media. Therefore, they can be applied in chelation therapy for remediation and detoxification of the metal ions. The mixture of the ligands could be applied where high quantity of metal is needed to be removed from or transported to vulnerable sites. The mixed-ligand can be immobilized onto solid support for purification purposes in extracting the metal ions.

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