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# Complex Equilibria and Distribution of Metal (II) lons with Biologically Active Chelating Agents in Aqueous and Aqueous-organic Media

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### Authors' contributions

This work was carried out in collaboration among all the authors. All authors read and approved the final manuscript.

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# ABSTRACT

An understanding of the principles of complex equilibria and species distribution in different solutions is important in expounding and correlating the interaction of different ligands with different metal ions in complex formation. Therefore, acid-base equilibria involved in the formation of binary and ternary complexes of Co (II), Cu (II) and Pb (II) with methionine (Met) and uracil (Urc) have been determined by potentiometric titration technique. The stability constants of the complexes were evaluated at  $35 \pm 0.1^{\circ}$ C and 0.02 M ionic strength (kept constant with NaNO<sub>3</sub>) in aqueous and organic-aqueous media. The species distribution in solutions as a function of pH was determined using the Hyss program. The stability of the ternary complexes relative to the corresponding binary complexes are observed to be more stable than binary complexes in the media except for [CuMetUrc] ternary complex in organic-aqueous mediu. The overall stability of the ternary complexes was found to be

correlated with the covalent index of the metal ions and Jahn Teller distortion. pH-studies of these systems revealed an increase in the concentrations of the ternary complexes with increase in pH. The formation of binary complexes was shown to be favoured in physiological pH range (3-7) while that of the ternary complexes is observed to be favoured in the pH range 5-10.

Keywords: Binary complex; chelating agent; metal ion; stability constant; ternary complex.

# 1. INTRODUCTION

compounds compounds Coordination are containing metal ions and ligands having versatile applications in controlling the chemistry of environmental, industrial and, biological processes. The knowledge of coordination chemistry is crucial in understanding structural and functional features of various biomolecular complexes like metal-loproteins and their medical applications. The study of the complexation reaction of metal ions with different coordinating agents in solution under a series of conditions has come into view as an important area of inorganic chemistry. This provides knowledge on the mechanism and kinetics in analytical prospects reactions and opens new for developing a selective and appropriate method for the determination of concentration and separation of species present in solution [1]. Also, the investigation of interactions of different biologically active ligands with metal ions in different solutions has significantly spread out in the last few years due to the application of the ligands and their metal complexes in catalysis, materials synthesis. photochemistry and biological systems [2,3,4]. The main stimulating subjects for the investigations are to establish the impacts of experimental conditions and the nature of species involved in the interactions of the ligands with metal ions in the formation of complexes for potential industrial and therapeutic applications [5,6].

Metal ions are usually positive charges and act as Lewis acid with the ability to share electron pairs with other molecules known as Lewis base so that a bond or charge-charge interaction can be formed [7]. Metals can be divided into two groups: (i) essential metals (ii) toxic metals. Metals such as cobalt and copper are generally classified as essential metals and an adequate proportion of these metals are needed for normal growth and health of an organism. Lack or excess of these metals can lead to homeostatic disorder or metal toxicity [8]. Metals such as lead, cadmium and arsenic are typical examples of toxic metal. Lead is known as toxic metal that affects the haematopoietic system, the nervous system and the kidneys [9]. Metal toxicity can be addressed by application of chelation therapy whereby metal-distinctive chelating agents are introduced into system as drugs to coordinate and expedite elimination of unwanted excess metal from the organism. A number of properties of the metal ions have been reported to influence their interactions with different ligands in solution. The properties include acceptor character, ionic radius, oxidation state, electronegativity, and metal ion coordination [10,11,7].

Recently, much attention has been paid on the study of the interactions of nitrogen, sulphur and oxvgen donor atoms containing multidentate ligands with transition metal ions in solution as a result of their capability to exert chelate effects on metal complexes [12]. Amino acids with one or more coordinating groups along with the amino group, NH<sub>2</sub>, and carboxyl group, CO<sub>2</sub>H are chelants and potential metal agents in detoxification and remediation of metal pollutants Pyrimidine derivatives containing [13]. heteroatoms are potential ligands capable of forming stable metal complexes. Amino acids such as methionine and pyrimidine derivative such as uracil are chelating agents and considered as typical N, O-donor ligands capable of forming strong complexes with metal ions [14].

Chelating agents have been widely applied for industrial, domestic and agricultural purposes for the extraction and transportation of metals due to their ability to chelate metal ions. Most of the already applied chelating agents are nonselectivity, non-biodegradable and toxic to biotic system or human health. These intrinsic problems with many of the chelating agents have become a cause for concern. Therefore, to search for chelators that are selective. biodegradable and environmentally harmless, research has now been intensified in the studies of interaction of biomolecular ligands with different metal ions in solution to determine the possibility of using them in chelation therapy and other applications.

Jahangir et al. [15] determined stability constants of mixed ligand complexes of Ni(II) and Cu(II) Diethylenetriamine metal ions with and Ethylenediamine, Glycine, alpha-Alanine, Phenylalanine, Oxalic acid (ox), Tyrosine at 25°C in aqueous medium at ionic strength of 0.2 M. Binary complexes were reported to exhibit higher stability than the corresponding ternarv complexes. Zoltan et al. [16] examined the formation constant, kinetic parameters and relaxivity of Mn (II) complexes from interaction between Mn(II) ion and 12-membered macrocyclic ligands. The decrease in stability of the complexes was observed as a result of decrease in the denticity of the ligands and nature of substituent of the primary.

Atreyapurapu, Dunkana and Pulipaka [17] investigated interaction of succinic acid dihydrazide with Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) in aqueous medium at 303K with ionic strength of the solutions being maintained at 0.1 mol dm-3 . Mononuclear and homo binuclear species in different protonation and deprotonation states in which two metal ions were observed to bind to adjacent coordination pockets of the same ligand with solution phase speciation indicating the formation of a variety of species in which the ligand exists in protonated, unprotonated and deprotonated forms. The Interaction of N-salicylidene-2-aminophenol with the Cu2+ was investigated in the mixture of methanol and 1,4-dioxane Rashmidipta et al., (2014)different temperatures at by spectrophotometric conductometric and methods. Thermodynamic parameters ( $\Delta H$ ,  $\Delta S$ and  $\Delta G$ ) for the formation of the complex were established. The study showed decrease in stability of complex with increase in temperature. The reaction was found to proceed spontaneous manner.

Fatih et al. [18] potentiometrically determined deprotonation constants of 5-hydroxy-5,6-dipyridin-2-yl-4,5-dihydro-2H-[1,2,4] triazine-3thione and the stability constants of its complexes with Hg<sup>2+</sup>, Ni<sup>2+</sup>, Cu<sup>2+</sup>, Pb<sup>2+</sup>, and Zn<sup>2+</sup> ions in 20% ethanol-water at 25  $\pm$  0.1°C and ionic strength of 0.1 M. The different degree of selectivity by the ligand towards the metal ions at

different pH was observed in the study. Chandrathilaka carried et al. [19] out spectrophotometric and pH-metric studies on aqueous binary and mixed ligand complexes of Pb (II), Cd (II), AI (III) and Cu (II) with ascorbic acid and paracetamol at an ionic strength of 0.15 moldm<sup>-3</sup> and temperature of 37.0  $\pm$  0.2°C. The protonation constants of the free ligands and the stability constants of their binary and mixed ligand complexes were determined using pH titration and confirmed by UV data. All the ternary complexes in the study were found to exhibit higher stability than the corresponding binary complexes.

The knowledge of stability constants of complexes formed between chelating agents and different metal ions in solution are essential in order to expound and correlate phenomena in solution, determine the conditions needed for the maximum formation of coordination compounds and establish how concentration of metal ions could be regulated using chelating agents. Therefore, the stability of some complexes in relation to the properties of the metal ions and ligands such as effects of the ionization potential, ionic radius. electronic structure and electronegativity of the metal-ion, and the nature of donor atoms and structural changes in the ligand have been extensively studied. It has been reported that, if interactions between a given set of metal ions and ligands are purely electrostatic, the stability constants for complexes of the metal ions of the same charge are relative to their ionic radii i.e. the higher the radius of a given metal ion, the lesser the stability of the complex formed by the metal ion with a ligand. However, this correlation could be only be justifiable for metal ions of similar electronic configuration but invalid in comparing metal ions of different groups of the periodic system. In order to establish another factor more justifiable than the correlation between ionic radius of a metal ion and stability constant of complex, this study evaluated the ionic combined effects radii and of electronegativity (covalent index) of metal ions on stability constants of complexes. Also, the effects of the nature of ligand, solvent, and pH on the formation of binary and ternary metal complexes are determined.

### 2. METHODOLOGY

#### 2.1 Preparation of Solutions

Solution of carbonate-free 0.13M NaOH was prepared and standardized by oxalic acid. Solutions of metal ions (0.002M) were prepared from Co (NO<sub>3</sub>)<sub>2</sub>.6H<sub>2</sub>O, Cu(NO<sub>3</sub>)<sub>2</sub>.6H<sub>2</sub>O and Pb(NO<sub>3</sub>)<sub>2</sub>.6H<sub>2</sub>O and their concentrations were standardized with ethylenediaminetetraacetic acid. Solution of 0.002 M of each ligand was also prepared in double distilled water. Nitric acid 0.01M was prepared and standardized by NaOH solution.

### 2.2 Instrumentation and Procedure for Titration

The direct reading digital pH-meter (Mettler Toledo) equipped with a combined electrode was used. Each time, the pH indicator scale was calibrated with standard buffer solutions of pH 4.00, 7.00 and 9.20. The readings were taken only when the instrument registered a stable value for at least one minutes. Titrations of each set were carried out in multiple to check the reproducibility of the data. The electrode slope was calculated for each titration which fell within 100-107% and all the titrations were carried out within this range. The potential errors that could affect the readings were corrected by Van Uitert and Hass equation:

 $-\log[H] = Z + \log f + U_H$ 

Six sets of titration mixture were prepared. The total volume in each set was kept at 40.00 ml in 100 ml glass beaker and allowed to attain the equilibrium at the temperature. The ionic strength of the solutions was maintained at 0.02 M by addition of estimated amount of NaNO3 salt and the solutions were magnetically stirred in the beaker in a water bath maintained at temperature of 35 ±0.1°C. Irving and Rossotti titration method was used where different sets of solutions were titrated against standard alkali solution and the change in the pH of the solution was measured after each addition of 0.05 ml of 0.13 M NaOH. The titrations were carried out in water and ethanol-water (40:60) media. The sets of the titration mixtures include:

1. Nitric acid

- 2. Nitric acid + ligand, L1
- 3. Nitric acid + ligand, L1+ metal ions
- 4. Nitric acid + ligand, L<sub>2</sub>

Ishola et al.; CSIJ, 30(8): 25-38, 2021; Article no.CSIJ.69187

- 5. Nitric acid + ligand, L<sub>2</sub> + metal ions
- 6. Nitric acid + ligand, L<sub>1</sub> + ligand, L<sub>2</sub> + metal ions

## 2.3 Determination of Proton-ligand and Metal-ligand Stability Constants

The values of pH obtained during the titrations were plotted against volume of alkali added to obtained titration curves for the sets of solution using Origin 8 software. The Proton-ligand and metal-ligand stability constants were calculated using Point wise method of calculation.

The proton-ligand stability constants  $K_1$  and  $K_2$  for the ligands were obtained by comparing the ligand and mineral acid curves using:

$$\overline{nA} = y - \frac{(V_2 - V_1)(N^o + E^o)}{(V^o + V_1)T_{cl^o}}$$

 $Logk_2$ 

$$= pH + \frac{\overline{nA}}{(1-\overline{nA})} \tag{0.2:0.8}$$

$$Logk_1 = log \frac{\bar{n} - 1}{(2 - \bar{n})} + pL$$
 (1.2:1.8)

 $(\overline{nA})$  is the average number of protons associated with the ligand at different pH values.

Metal-ligand stability constants were calculated by utilizing the mineral acid, ligand and the mixture metal and ligand curves using:

$$\bar{n} = \frac{(V_3 - V_2)(N^o + E^o)}{(V^o + V_2)\bar{n}\bar{A}T_{cm^o}}$$

$$pL = \log\left\{\frac{1 + K_1^H[H^+] + K_1^H K_2^H[H^+]^2 + \cdots}{T_{cl^o} - \bar{n}\bar{T}_{cm^o}} \times \frac{V^o + V_2}{V^o}\right\}$$

$$Logk_1 = log \frac{n}{(1-\bar{n})} + pL$$
(0.2:0.8)

$$Logk_2 = log \frac{\bar{n} - 1}{(2 - \bar{n})} + pL$$
 (1.2:1.8)

 $(\bar{n})$  is average number of ligand molecules attached per metal ion, (pL) is free ligand exponent, y is number of dissociable protons from the ligands,  $V_1$ ,  $V_2$  and  $V_3$  are volumes of alkali employed in bringing the solutions of mineral acid, ligand, and metal with lignad to same pH value,  $T_{cl^o}$  is total concentration of the ligand and  $T_{cm^o}$  is total concentration of metal ion.

### 2.4 Characterization of the Formation Tendency and Speciation of the Mixed Ligand Complexes

The formation constants of ternary complexes formed by the ligands with the metal ions were determined using Ramamoorthy and Santapa method [20]. The distributions of species as a function of pH were obtained by Hyperquard Simulation and Speciation program.

The change in the stability of the ternary complexes with respect to their binary complexes of secondary ligand (i.e. is the the coordination tendency of a secondary ligand to binary complex of primary) ligand was characterized by  $\Delta \log K$  and Relative Stabilisation (% R.S.) [21-23].

$$\Delta \text{LogK}_{\text{exp}} = \text{LogK}_{\text{ML}_{\text{p}}\text{L}_{\text{s}}}^{\text{ML}_{\text{p}}} - \text{LogK}_{\text{ML}_{\text{s}}}^{\text{M}}$$

$$\% \text{R. S.} = \left(\frac{\text{LogK}_{ML_{p}L_{s}}^{ML_{p}} - \text{LogK}_{ML_{s}}^{M}}{\text{LogK}_{ML_{s}}^{M}}\right) \times 100$$

The formation constants of ternary complexes were statistically evaluated by using:

$$\Delta \text{LogK}_{\text{stat}} = \text{LogK}_{\text{MLpL}_{s}}^{\text{MLp}} - \text{LogK}_{\text{ML}_{s}}^{\text{M}}$$
$$\text{LogK}_{\text{MLpL}_{s}}^{\text{MLp}} = 2\sqrt{\text{LogK}_{\text{ML}_{s}}^{\text{M}}}\sqrt{\text{LogK}_{\text{MLp}}^{\text{M}}}$$
$$\text{LogK}_{\text{ML}_{s}}^{\text{M}} = \text{Log2} + \frac{1}{2}\text{LogK}_{\text{ML}_{s}}^{\text{M}} + \frac{1}{2}\text{LogK}_{\text{MLp}}^{\text{M}}$$

The possibility of ligand–ligand interaction during the complexation reaction in the formation of ternary complexes was examined by finding difference between experimental and statistical values.

# 2.5 Determination of Covalent indices of the Metal Ions

The covalent indices for the metal ions were calculated by using equation formulated by Nieboer and Richardson [10] as:

Covalent Index= X<sup>2</sup>m r

In the equation, Xm is the metal-ion electronegativity, and r is its ionic radius. The electronegativity values calculated by Keyan and Dongfeng [24] and the crystal ionic radii (in angstrom units) compiled by Shannon [25] for the hexahydrated metal ions were employed. The equation has correlated with, or taken into account, solvent effects [26,27].

The polarizability and dipole moment of the ligands, which can affect their interactions with the metal ions are obtained from literature [28, 29].

### 3. RESULTS AND DISCUSSION

### **3.1 Potentiometric Titration Curves**

In this study dilute solutions (0.002M) were used to avoid any possibility of the formation of polynuclear complexes. The potentiometric curves obtained for the sets of reacting mixtures in the media are presented in Figs. 1 and 2.

The curves b and c (ligands curves) are observed to deviate from acid curve(a) to lower pH region as shown in Figs. 1 and 2,. The divergences indicate the release of proton from the ligands [30]. Inflection points at pH of 8.70 and 9.10 respectively are observed in Met and Urc curves in Fig. 2 while inflection points at pH of 9.00 are observed in the ligands curves. The observed inflection points are ascribed to deprotonation processes occurring at the pH values [31,32]. The ligands curves are observed in both Figures to shift to lower pH regions upon the addition of Metal (II) ions; the shifts are attributed to the interactions of the ligands with the metal ions through displacement of proton(s) from the ligands in the formation of complex [33]. In water medium, the binary complexes of MetCo(II), Met Cu(II) and MetPb(II) show inflection points at pH of 7.20, 4.90 and 6.15 respectively. UrcCo(II), UrcCu(II), and UrcPb(II) curves show inflection points at pH of 8.20, 6.00 and 5.90, respectively, as shown in Fig. 1. The binary complexes curves of MetCu(II). MetCo(II). and MetPb(II) in water-ethanol, as observed in Fig. 2 give inflection points at pH of 6.00,7.70 respectively, while the curves of and 6.90. UrcCo(II), UrcCu(II) and UrcPb(II) binary complexes display inflection points at pH of 7.25, 5.20 and 6.00 respectively.



Fig. 1. Potentiometric titration curves for binary (1 : 1) and ternary (1 : 1 : 1) complexes (*I* = 0.02 molL−1 NaNO<sub>3</sub> at 35.0 ± 0.1°C in water)



Fig. 2. Potentiometric titration curves for binary (1 : 1) and ternary (1 : 1 : 1) complexes (I = 0.02M NaNO<sub>3</sub> at 35.0 ± 0.1°C in ethanol-water 40:60 (v/v)

Also, the ternary complexes curves are displayed in the Figures to lie below the ligands and binary complexes curves. The lying of the curves below the binary complexes suggest the formation of the ternary complexes, and the non superimposable nature of the ternary complexes curve with either of the simple binary curves suggests simultaneous coordination of the two ligands to the metal ions in the ternary complexes [34], Sangita et al. [35]; Ishola et al. [32].

The calculated values of covalent indices of the metal ions, polarizability and dipole moment of the ligands, proton-ligands stability constants, stability constants of the binary and ternary complexes are presented in Tables 1, 2, 3, 4 respectively.

	lonic radius(A°)	Electronegativity	Covalent Index (A°)	Polarizability	Dipole moment
Co (II)	0.745(Hs)	1.321	1.300		
	0.650(Ls)	1.377	1.232		
Cu (II)	0.730	1.372	1.374		
Pb (II)	1.190	1.225	1.786		
Methionine				105.060	3.100
Uracil				70.000	1.430

Table 1. Covalent index of the metal ions and the Properties of the selected Ligands

Ls=Low spin; Hs=High spin

# Table 2. Proton-ligand stability constants and formation constants of binary complexes (I = 0.02 M, L=Met, Urc)

Ligand	Water				Water: ethanol (40:60)					
	$LogK_2^H$	$LogK_1^H$	$LogK_{CoL}^{Co}$	$LogK_{CuL}^{Cu}$	$LogK_{PbL}^{Pb}$	LogK	$\frac{H}{2} Log K_1^H$	$LogK_{CoL}^{Co}$	$LogK_{CuL}^{Cu}$	$LogK_{PbL}^{Pb}$
Met	-	10.5877	5.2950	7.2526	6.1038	-	11.2013	5.6904	8.0408	6.5264
Urc	-	10.0849	3.9504	5.4954	5.6162	-	11.5805	6.5194	7.8798	7.0891

#### Table 3. Stability constants of Ternary complexes of Methionine and Uracil in water (I = 0.02 M, M= Cu(II), Co(II) and Pb(II), A=Primary ligand, L=Secondary ligand)

Complex	$L$ og $K_{MAL}^{M}$	$L$ og $K_{MA}^{M}$		$L$ og $K_{ML}^{M}$	$\Delta Log K_{exp}$	$\Delta LogK_{stat}$	RS%
[MetCoUrc]	12.4819	5.2950	7.1869	3.9504	+3.2365	-0.0929	81.9284
[MetCuUrc]	15.7108	7.2526	8.4582	5.4954	+2.9628	-0.1534	53.9141
[MetPbUrc]	13.9500	6.1038	7.8462	5.6162	+2.2300	-0.1139	39.7100

Table 4. Stability constants of Ternary complexes of Methionine and Uracil in ethanol-water 40/60 v/v (I = 0.02 M, M= Cu(II), Co(II) and Pb(II), A=Primary ligand, L=Secondary ligand)

Complex	$L$ og $K_{MAL}^{M}$	$LogK_{MA}^{M}$	LogK <sup>MA</sup>	$L$ og $K_{ML}^{M}$	$\Delta LogK_{exp}$	$\Delta LogK_{stat}$	RS%
[MetCoUrc]	13.3254	6.5194	6.8060	5.6904	+1.1156	-0.0984	4.3961
[MetCuUrc]	15.8442	8.0408	7.8034	7.8798	-0.0764	-0.1678	-0.9696
[MetPbUrc]	14.8282	7.0891	7.7391	6.5204	+1.2187	-0.1253	9.1690

The measure of capacity of each of the metal ions to exhibit covalent interactions with the ligands and polarizability and dipole moment of the ligands are shown in Table 1. The probable order of covalent interaction of each metal ion with the ligands to form stable complexes is given as Pb(II)>Cu(II)>Co(II).

The values of  $\overline{nA}$  from 0.6 to 0.9 were obtained for Met and Urc in the media. The values indicate deprotonation of a proton from each ligand [35].  $LogK_1^H$  value of 10.0849 of Urc in water is attributed to the proton-ligand formation constant at N<sub>3</sub>H while  $LogK_1^H$  of 10.5449 obtained for Met is assigned to proton-ligand formation constant at amino group NH<sub>2</sub> as shown in Table 2 [31]. In ethanol-water medium, 0.70-0.95 is obtained for the calculated values of  $\overline{nA}$  for the ligands suggesting deprotonation of only one proton from the ligand.  $LogK_1^H$  values of 11.2013 and 11.5805 obtained for Met and Urc in Table 2 are attributed to deprotonations at amino NH<sub>2</sub> group and N<sub>3</sub>H of the ligands respectively (Nath et al., 2005; Naciye and Aksoy [36]). The proton-ligand stability constants observed to be higher in ethanol-water medium than water medium may be attributed to decrease in the dielectric constant of the media [37]. This could be as a result of the ability of a solvent with relatively low dielectric constant to enhance the electrostatic forces between the proton and the ligand anion and therefore increase in  $LogK_1^H$  [38].

The  $\bar{n}$  range of 0.0 to 0.5 is obtained for the complexes in the media. The values within the range confirmed the formation of 1:1 binary complexes by the ligands with the metal ions in media [39-40]. The formation constants of the binary complexes are exhibited in Fig. 2. The ligands formed binary complexes with metal ions in water with the formation constants in the order of  $LogK_{CoMet}^{Co} > LogK_{CoUrc}^{Co}$ ,  $LogK_{CuMet}^{Cu} > LogK_{CuUrc}^{Cu}$  and  $LogK_{PbMet}^{Pb} > LogK_{PbUrc}^{Pb}$  as shown if Table 2. The order does not agree with the basicity effect of the ligands and, therefore, could be attributed to the polarizability and dipole moment of the ligands (Kannapan et al., 2009; Ammar et al. [31]).

In ethanol-water medium, the order of  $LogK_{CuUrc}^{Cu} > LogK_{CuMet}^{Cu}$  which could be attributed to the polarizability and dipole moment of the ligands and/or participation of sulfur donor atom of Met in the complex formation processes by the ligand is observed Ammar et al. [31]). However, the order of formation constants observed for  $LogK_{CoUrc}^{Co} > LogK_{CoMet}^{Co}$  and  $LogK_{PbUrc}^{Pb} > LogK_{PbMet}^{Pb}$ is not in conformity with the effects of the polarizability and dipole moment of the ligands. This order could be ascribed to the basicity of the lugand and  $M{\rightarrow}$  L  $\pi$  - formation in the Urc complex in addition to L  $\rightarrow$  M  $\sigma$  - bond by the back donation of electrons from the metal  $d\pi$ orbitals to the vacant  $p\pi$  orbitals of the Urc [41,42].

Urc interacts with the metal ions in water medium with the formation constants in the order of  $Log K^{Pb}_{PbUrc} \text{>} Log K^{Cu}_{CuUrc} \text{ > } Log K^{Co}_{CoUrc} \text{ which could}$ be attributed to the covalent index of the metal ions (Nieboer & Richardson [10]; Oladipo et al. [43]). Met in water medium and the ligands in ethanol-water medium formed binary complexes with the metal ions in the order of  $Log K_{CuMet}^{Cu} >$  $Log K_{PbMet}^{Pb} > Log K_{CoMet}^{Co}$ and LogK<sup>Cu</sup><sub>CuUrc</sub> >  $Log K_{PbUrc}^{Pb} > Log K_{CoUrc}^{Co}$ . The deviation of the order from the covalent index effect of the metal ion could be as a result of tendency of Cu(II) ion to undergo Jahn Taller distortion. The distortion exerts extra stability on the complex of Cu (II) ion than Pb(II) [44-45]. The formation of more stable binary complexes by ligands with the metal ions in ethanol-water medium than in water medium is attributed to the difference in dielectric constants

of the media and existence of the complexes in ionic form.

The evaluated stability constants for the mixedligand system of Met and Urc in the formation of the ternary complexes in both media are shown in Tables 3 and 4. Met serves as primary ligand in all the ternary complexes in aqueous medium while Urc serves as secondary ligand; Urc acts as primary ligand in the formation of ternary complexes of Co(II) and Pb(II) in aqueousorganic system and met acts as secondary ligand. The  $\Delta log K_{exp}$  and R.S. % values are evaluated to be positive for the all the ternary complexes in aqueous medium. The positive values suggest more stability of the ternary complexes than the corresponding binary complexes of the secondary ligand; the stability could be attributed to interactions outside the coordination sphere such as intramolecular hydrophobic stacking [46], Usama et al. [47]; Thanavelan et al. [48]; Bindu and Rao [49]. However, in aqueous-organic medium,  $\Delta \log K_{exp}$ and R.S. % are obtained to be positive for the ternary complexes except for MetCuUrc complex where negative values are obtained for  $\Delta \log K_{exp}$  and R.S. %. The negative value implies the less stability of the ternary complex in comparison with the corresponding binary complex of the secondary ligand [23].

According to statistical contention, for a given polyvalent hydrated metal ion, more coordination positions are expected to be available for the primary ligand than for the secondary one i.e. the tendency of the metal ion to get bound with the ligands decrease with increase in the number of bound ligands, therefore,  $\Delta \log K$  is expected to be negative but several exceptions have been reported to cause deviation from the statistical postulate [50,51,23]. Contrary to the statistical considerations, the positive experimental values of  $\Delta \log K$  obtained in this study for the ternary complexes in both aqueous and aqueous-organic system to exceed the statistical value as shown in Tables 3 & 4 suggest the existence of ligandligand interactions during the formation of the ternary complexes and coordination of secondary ligand to the metal ions through O-O donor atoms. The negative value obtained for the ternary complex of [MetCuUrc] in aqueousorganic system as shown in Table 3, suggests lack of ligand-ligand interactions and coordination of secondary ligand to the metal ion through O-N donor atoms [52,50,53].

The stability in order of Cu(II) > Pb(II) > Co(II) is observed for all the complexes in the media. The order could be ascribed to covalent index of the metal ions and Jahn Taller distortion. Cu (II) has a tendency of undergoing Jahn Taller distortion, thereby forming more stable complexes than Pb (II) [54,44,45]. The mixed ligand is observed to form more stable complexes in aqueous-organic system than the aqueous system.

# 3.2 Distribution Diagrams

Distribution diagrams of the all the binary and ternary systems were drawn using HYSS computer program as shown in Figs. 3-8. The changes in the distributions of binary and ternary complexes as a function of the pH in the media were examined by using the stability constants of the binary and ternary complexes given in Tables 2 and 3.

The distributions of binary and ternary complexes in an aqueous solution are shown in Figs. 3-5. The formation of Co(II)Met binary complex is observed in Fig. 3 to begin at pH of 5.7 and reaches maximum level (3%) at pH of 7.3. The compex begins to disintegrate and disappears completely at a pH of 10.0 while Co(II)Met is not detectable. The Co (II)Met:Urc ternary complex begins to form at a pH of 5.7 and reaches its maximum level (96%) at pH of 9.4. The ternary complex is observed to remain stable as a dominant complex between pH of 5.7 to 11.3. The formation of binary and ternary complexes of Cu(II)Met and Cu(II)Met Urc respectively begin at the same pH of 3.7, as shown in Fig. 4. The binary complex reaches maximum level (7%) at pH of 5.53 and disappears completely at pH of 7.8while Cu (II)Met is not discoverable. The Cu (II)Met:Urc ternary complex begins to form at pH of 5.7 and reaches its maximum level (96%) at pH of 9.4. Likewise, the ternary complex is observed to continue as a dominant complex between pH of 3.7 to 8.8. Pb(II):Met:Urc ternary complex formation displays different trends from the other complexes, as shown in Fig. 5. The binary complexes of Pb(II)Met and Pb(II)Urc begin at the same pH of 4.9, and they reach their maximum level (4%) at pH of 6.5. The two binary complexes begin to dissociate gradually at pH of 6.5 and completely vanish at pH of 9.3. The formation of ternary complex Pb(II)Met Urc is

observed from the graph to come to an existence at pH of 4.9 and reaches its maximum level (97) at pH of 8.8. The complex also exists as a single dominant complex species at pH of 5.3 to 10.

The binary and ternary complexes display different degree of distribution in aqueousorganic medium as shown in Figs. 6-8. The binary complexes of Co(II)Met and Co(II)Urc begin at pH of 4.3 and 5.8, respectively. Co(II)Met reaches its maximum level (4%) at pH of 7.8 while Co(II)Urc reaches its maximum level (29%) at pH of 8.2 as depicted in Fig. 6. The two binary complexes begin to dissociate gradually and completely vanish at pH of 12.0. The formation of ternary complex Co(II)Met Urc is observed from the graph to come to existence at pH of 6.4 and reaches its maximum level (97) at pH of 10. The complex also exists as a single dominant complex species at pH of 6.4 to 10.0. The formation of binary and ternary complexes of Cu(II)Met and Cu(II)Met Urc respectively begin at the same pH of 3.6 and 4.0, respectively (Fig. 7). The binary complexes reach their maximum levels (34 and 20 %) at pH of 6.4 and 6.8, correspondingly. They begin to disintegrate at the pH values and disappear completely at pH of 9.0 and 9.9, respectively. The Cu(II)Met:Urc ternary complex begins to form at pH of 5.0 and reaches its maximum level (98%) at pH of 9.5. Likewise, the ternary complex is observed to continue as a dominant complex between pH of 5.0 to 9.5.

The binary complexes of Pb(II)Met and Pb(II)Urc begin at pH of 5.0 and 5.1 respectively and reach their maximum levels (13% and 19%) at pH of 7.4 and 7.3, individually. The complexes begin to dissociate at the pH values and completely vanish at pH of 11.0 and 10.2, individually. The formation of ternary complex Pb(II)Met Urc is observed to start at pH of 5.9 and reaches its maximum level (97) at pH of 10.0, and exists as a single dominant complex species at pH of 5.9 to 10.0.

It can be observed from Figs. 3, 4, 5, and 7 that Met acts as the primary ligand forming more stable binary complex than Urc and in Figs. 6 and 8, Urc acts as primary ligand capable of forming more stable comple than Met.

Ishola et al.; CSIJ, 30(8): 25-38, 2021; Article no.CSIJ.69187



Fig. 3. Distribution diagram of the species in the (1 : 1 : 1)Co(II):Met:Urc ternary system in aqueous solution (1) Co(II) (2) Co(II)Met (3) Co(II)MetUrc



Fig. 4. Distribution diagram of the species in the (1 : 1 : 1)Cu(II):Met:Urc ternary system in aqueous solution



Fig. 5. Distribution diagram of the species in the (1 : 1 : 1)Pb(II):Met:Urc ternary system in aqueous solution
 (1) Pb(II) (2) Pb(II)Met (3) Pb(II)Urc (4) Pb(II)MetUrc

Ishola et al.; CSIJ, 30(8): 25-38, 2021; Article no.CSIJ.69187



Fig. 6. Distribution diagram of the species in the (1 : 1 : 1)Co(II):Met:Urc ternary system in aqueous-organic solution



Fig. 7. Distribution diagram of the species in the (1 : 1 : 1)Cu(II):Met:Urc ternary system in aqueous-organic solution (1) Cu(II) (2) Cu(II)Met (3) Cu(II)Urc (4) Cu(II)MetUrc



Fig. 8. Distribution diagram of the species in the (1 : 1 : 1)Pb(II):Met:Urc ternary system in aqueous-organic solution (1) Pb(II) (2) Pb(II)Met (3) Pb(II)Urc (4) Pb(II)MetUrc

Ishola et al.; CSIJ, 30(8): 25-38, 2021; Article no.CSIJ.69187

## 4. CONCLUSION

The present study provides information on the formation constants of Co(II), Cu(II) and Pb(II) binary and ternary complexes in different solutions using low concentration of inert electrolyte. The proton-ligand stability constants exhibited by all the ligands were observed to be high. The interactions of the ligands with the metal ions under investigation resulted in to the formation of 1:1 binary and 1:1:1 ternary complexes with high stability constants. The extent of interaction of the ligands in forming binary complexes was affected by polarizability of ligands, solvent and covalent index of the metal ions, and Jahn Taller distortion. The ternary complexes were found to show more stability than the corresponding binary complexes of secondary ligand in both media as a result of the presence of interligand interaction outside the coordination sphere.

The proton-ligand, binary, and ternary stability constants are higher in aqueous-organic system than aqueous system. The ligands demonstrated high metal binding capability with the investigated metal ions. They are recommended for transportation of the metals to or from vulnerable target site. Their binary metal complexes can be exploited for the transport of organic chemotherapeutic drugs capable of binding with their 1:1 binary complexes to or from target organs. The information on the role of pH for effective interaction of the ligands with the metal ions in forming stable complexes for potential applications in agriculture, medicine and industry has been provided.

# **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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